

Surgery in Gynecologic Cancers

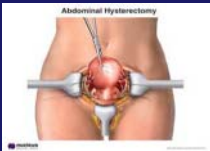
Stefanie M. Ueda, M.D.
Associate Clinical Professor
UCSF Division of Gynecologic Oncology

Lee-may Chen, M.D.
Clinical Professor
UCSF Division of Gynecologic Oncology

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

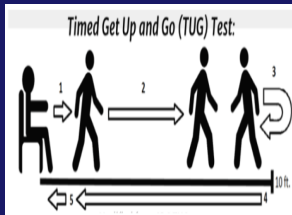
ASA Classification

- 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

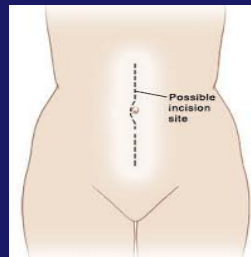


Preoperative Preparation



- 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

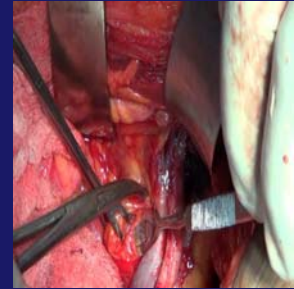
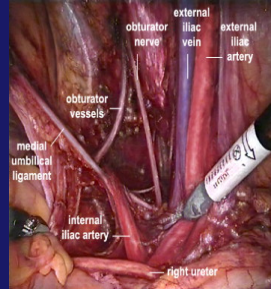


Source: B. Y. Karlan, R. S. Britton, A. J. Li. Gynecologic Oncology: Clinical Practice and Surgical Atlas. www.obgyn.mhmedical.com. Copyright © McGraw-Hill Education. All rights reserved.

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

Lymphatic spread in 5-20%
-20% upstaged

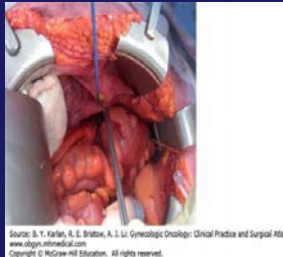
Pelvic Node Dissection



Additional Biopsies



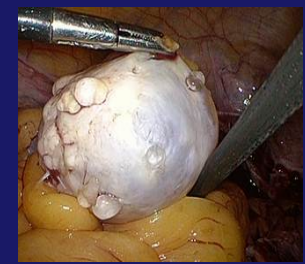
Appendectomy



Peritoneal biopsies

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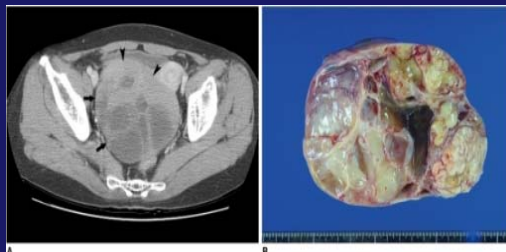
Serous Borderline Tumors



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



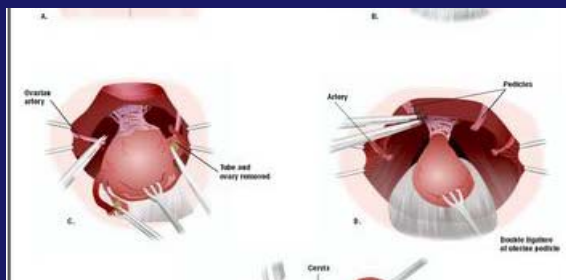
Mucinous Borderline Tumor

Frozen Section of Tumor

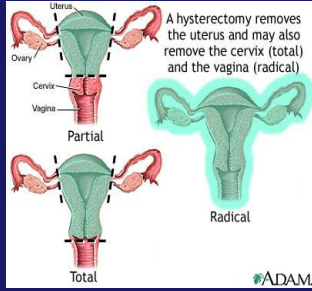
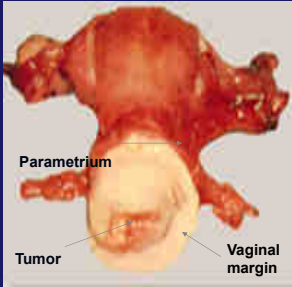


Frozen section of borderline tumors changes on final pathology 11-30%

Simple Hysterectomy

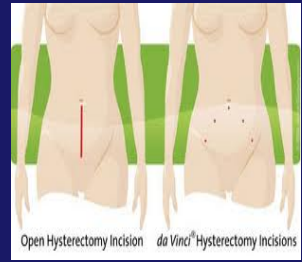


Radical Hysterectomy

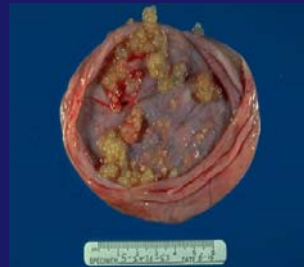


Implications of Hysterectomy

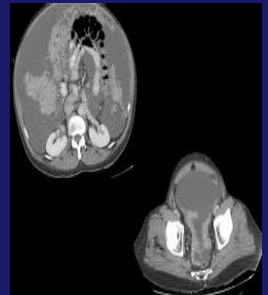
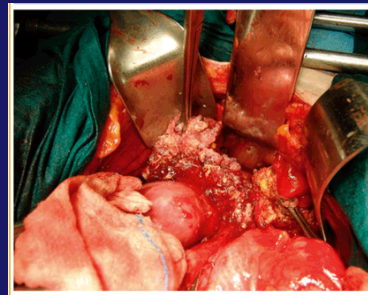
- Generally, frequency of sexual activity increases and problems with sexual functioning decrease
- Alters ovarian function over the long-term, even if the ovaries are conserved
- Associated with a risk of subsequent surgery for pelvic organ prolapse and urinary stress incontinence



Ovarian Cancer



Advanced Ovarian Cancer



First Line Therapy?



Surgery with maximum cytoreduction effort

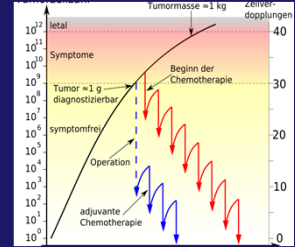


Platinum + Taxane Chemotherapy

2004 Consensus Statements on the Management of Ovarian Cancer:
Final Document of the 3rd International GCI/Ovarian Cancer Consensus Conference (GCI/OCCC 2004).
Annals Of Oncology 16 (Supplement 8) VIII7-VIII12, 2005

Cytoreductive Surgery in Ovarian Cancer

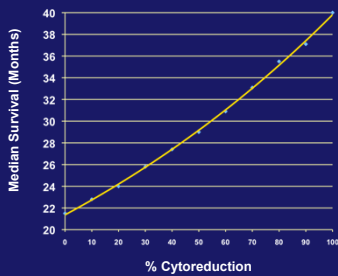
- Reduction in tumor mass
- Shorter chemotherapy exposure with less development of drug resistance
- Improved tumor perfusion
- Fewer non-active (G_0) cells
- Enhanced immunological competence (smaller tumors may be more amenable to control by host defenses)



Each chemotherapy course produces 90% cell kill

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



Bristow et al, J Clin Oncol 2002

Maximal Primary Cytoreduction

Author	Year	Residual Disease	Patients	Median survival	5-Yr OS (%)
Hoskins	1994	No gross	41		60
		≤1 cm	62		35
		1-2 cm	12		35
		≥2 cm	65		<20
Chi	2006	No gross	67	106	
		≤0.5 cm	70	66	
		0.6-1 cm	99	48	
		1-2 cm	53	33	
Du Bois	2010	No gross	1,046	99.1	
			975	36.2	
			1,105	29.6	

Shih et al, J Gynecol Oncol 2010

Intraperitoneal Chemotherapy

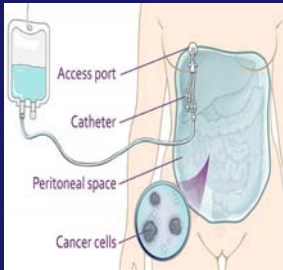


Figure 1: Intraperitoneal (IP, left) and intravenous (IV, right) ports for delivery of chemotherapy. (See text for a detailed comparison of features.)

Evidence of Advanced Disease



Omental Caking

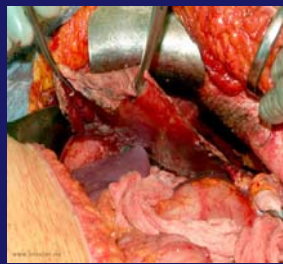


Ascites

Upper Abdominal Disease

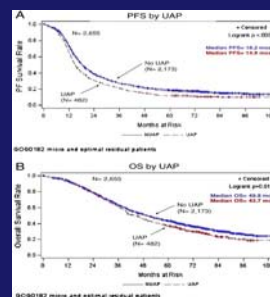


Liver Metastases



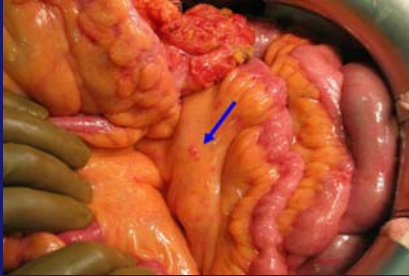
Diaphragm Peritonectomy

Upper Abdominal Procedures in Advanced Ovarian Cancer



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

Rodriguez et al, Gynecol Oncol 2013

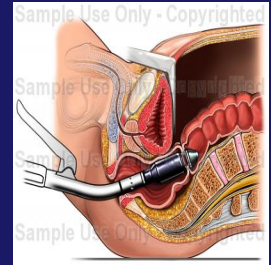


Bowel mesentery with several small implants

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

¹Barakat et al, *Principles and Practice of Gyn Onc* 2013

Postoperative Complications



Figure 1. Upper midline wound on postoperative day 10 showing purulent drainage.
Figure 2. Lower midline wound on postoperative day 12 showing erythema in the middle of the wound and exudate mostly along the caudal wound edges.

Wound Infection

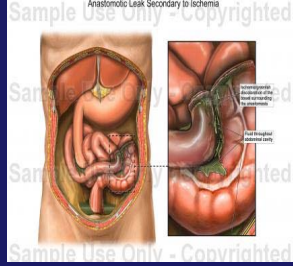


Deep Vein Thrombosis

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

¹Barakat et al, Principles and Practice of Gyn Onc 2013

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

Ovarian, tubal or peritoneal cancer
FIGO stage IIIc-IV (n = 718)

Randomization

Primary Debulking Surgery

3 x Platinum based CT

Interval debulking
(not obligatory)

≥ 3 x Platinum based CT

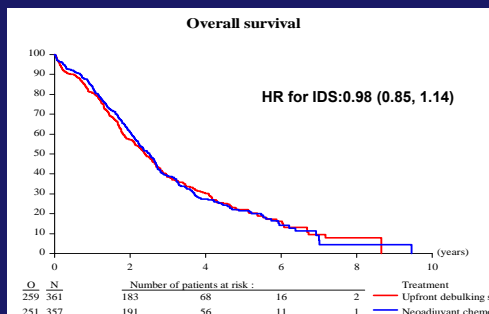
Neoadjuvant chemotherapy

3 x Platinum based CT

Interval debulking if no PD

≥ 3 x Platinum based CT

EORTC 2010



Preoperative Predictors of Cytoreductive Outcome

- Prospective multicenter trial of 350 patients who underwent primary cytoreduction
- Criteria significantly associated with suboptimal debulking
 - Age \geq 60 years
 - CA-125 \geq 500
 - ASA 3-4
 - Suprarenal retroperitoneal nodes $>$ 1cm
 - Diffuse small bowel adhesions/thickening
 - Lesions $>$ 1cm in the small bowel mesentery, root of the superior mesenteric artery, perisplenic area, and lesser sac

Predictive Score	Suboptimal Rate
0	5%
1-2	10%
3-4	17%
5-6	34%
7-8	52%
\geq 9	74%

Suidan et al, Gynecol Oncol 2014

Secondary Tumor Debulking (SCRS)

- Cochrane review of 1194 women in 9 non-randomized studies¹
 - Cytoreduction to no visible disease in women with platinum sensitive recurrent ovarian cancer associated with significant improvement in OS
- CALYPSO Trial²
 - 975 patient with platinum sensitive recurrent disease
 - Randomized
 - 19% SCRS, 80% chemotherapy alone
 - OS better in those with SCRS (49.9 vs 29.7 mos, p=0.004)
 - 3 year OS 72% in those with no measurable disease

¹Al Rawahi et al, Cochrane Database Syst Rev 2013

²Lee et al, Gynecol Oncol 2015

Identifying Ideal Candidates for SCRS

- Pooled analysis of 1100 patients found that those with:¹
 - Longer progression free interval
 - No ascites
 - Localized disease
- Risk models have suggested prognosticators include:²
 - Ascites
 - Number and size of implants
 - Performance status
 - Progression free interval
 - Preoperative CA-125? ($<$ 250)



Figure 1. Computed tomography shows recurrence at the right internal iliac lymph node.

¹Zang et al, Br J Cancer 2011

²Tian 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

Minimally Invasive Surgery

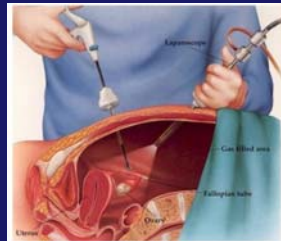
- Vaginal surgery
- Laparoscopy
- Robotic assisted laparoscopy
- Natural orifice transluminal endoscopic surgery (NOTES)
- Single incision laparoscopic surgery (SILS)

Vaginal Hysterectomy

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



Laparoscopy

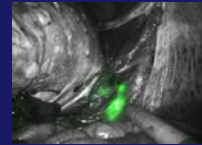
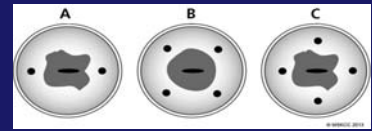


LAP2

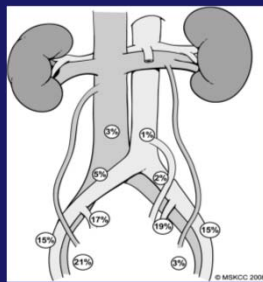
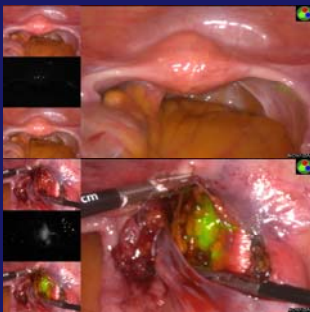
1996-2005: Randomized study of Stage I-IIA endometrial cancer patients --1696 laparoscopy, 920 laparotomy
 26% conversion to open (15% visualization)
 Laparoscopy with shorter LOS, fewer post-op complications
 Less LND performed but no difference in Stages
 Median follow-up of 59 mo. HR for recurrence,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



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

Surgery Video

