

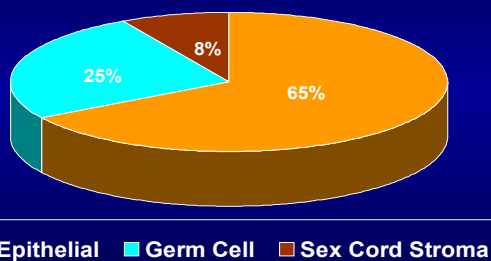
LAPAROSCOPY AND OVARIAN CANCER

Laparoscopy and Ovarian Cancer

Konstantin Zakasnas, M.D.
January 28, 2005

Epidemiology

- 2004: 25,580 new cases; 16,090 deaths
- Lifetime probability of developing ovarian cancer is 1.4% (1 in 70)
- It is the most lethal gynecologic malignancy
- Most women are diagnosed with advanced stage disease (FIGO II/IV), and stage inversely correlates with survival



FIGO Stage

Stage	Description	Incidence	Survival
I	Confined to Ovaries	20%	93%
II	Confined to Pelvis	5%	65%
III	Spread IP or Nodes	58%	21%
IV	Distant metastases	17%	<5%

Early Disease

Stage	Description
I	Tumor limited to ovaries
A	One ovary, surface intact, no ascites
B	Two ovary, surface intact, no ascites
C	Surface involved, ascites or washings +
II	Ovaries with pelvic spread
A	Extension to uterus and/or tubes
B	Extension to other pelvic tissue
C	IIA or IIB with surface involvement, ascites or washings +

Advanced Disease

Stage	Description
III	IP or nodal spread
A	Microscopic only outside pelvis
B	Nodules <2cm outside pelvis
C	Nodules >2cm outside pelvis; + nodes
IV	Distant spread, liver parenchyma

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Standard of Care: 2004

Early disease

- Staging – critical for management and decision making
- Chemotherapy following surgery with the presence of the risk factors
 - Paclitaxel 175 mg/m²/3h
 - Carboplatin AUC 5-7.5
 - Every 3 wks for 6 cycles

Surgical Staging: Early Disease

- TAH/BSO
 - preservation of reproductive function in some cases
- Pelvic peritoneal biopsies
 - lateral pelvic sidewalls, cul-de-sac, uterovesicle fold, rectal and bladder serosa
- Abdominal biopsies
 - infracolic omentum, both abdominal gutters, both diaphragms, any adhesions
- Lymph node sampling
 - bilateral pelvic and paraaortic
- Peritoneal washings

Standard of Care: 2004

Advanced disease

- Maximum attempt at surgical cytoreduction
- Chemotherapy following surgery
 - Paclitaxel 175 mg/m²/3h
 - Carboplatin AUC 5-7.5
 - Every 3 wks for 6 cycles

Surgical Management: Advanced Disease

- Primary goal: cytoreduction
 - TAH/BSO
 - omentectomy
 - appendectomy
 - selective lymph node sampling
 - bowel, bladder, spleen resection, if necessary
 - inspection of infradiaphragmatic surface
- Secondary goal: optimal debulking
- Neoadjuvant chemotherapy

•Recurrent Disease Therapy

- A majority will not achieve long-term control of disease.
 - Large-volume advanced disease: 80-85%
 - Small-volume advanced disease: 60-70%
 - High-risk limited disease: 20%
 - Low-risk limited disease: 10%
- An overall 62% will have either recurrent or persistent disease and be candidates for further therapy.

Secondary Cytoreduction

- Controversial
- Inconsistent definitions
- Benefit appears confined to patients likely to respond to additional chemo:
 - >12 month PFI
 - Isolated site of recurrence
 - Disease completely resectable

LAPAROSCOPY AND OVARIAN CANCER

Evolution of Laparoscopy in Gynecology

- Diagnostic laparoscopy
- Tubal sterilization & minor procedures
- Infertility surgery
- Extirpative operations (ie. LAVH /TLH BSO)
- Reconstructive Surgery
- **Oncology Surgery**

Advantages of Operative Laparoscopy

- Smaller Incision
- Shorter Hospital Stay and Recovery
- Less Pain and Pain Medication
- Better Visualization
- Fewer Adhesions
- Fewer Potential Complications

Laparoscopic Management of Gynecologic Malignancies Concerns

- Accuracy of Diagnosis
- Adequacy of Surgical Margin and Radicality
- Complications
- Risk of Dissemination & Abdominal wall implantation
- Quality of life
- Cost
- **Survival**

Laparoscopic Staging for Early Ovarian Cancer Concerns

- Miss extra-ovarian disease (small bowel mesentery)
- Spread of cancer cells
- Limited data on effect of laparoscopic approach on survival
- No randomized data with adequate follow-up

Laparoscopy and Ovarian Cancer Indications

Early Stage:

- Evaluation and management of adnexal mass
- Staging for early borderline/invasive cancer
- Restaging for unstaged presumably early ovarian and fallopian tube cancer

Advanced Stage:

- Laparoscopic triage for operability
- Second look assessment
- Limited debulking/ hand assisted

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Laparoscopic Management of Adnexal Masses

Adverse consequences of laparoscopic management of ovarian neoplasms subsequently found to be malignant:

- Possible consequences of delay of definitive surgery
- Possible consequences of cyst rupture/puncture

Maiman, Seltzer and Boyce; Ob Gyn 77:563,1991

Incidence of Malignancies in Laparoscopies for Pelvic Mass

Nezhat et al., 1992	4 / 1,011	0.4%
Mecke et al., 1992	2 / 773	0.26%
Hulka, 1992	55 / 13,739	0.4%
Canis et al., 1994	15 / 757	2.5%
Blanc et al., 1994	78 / 5,307	1.4%
Marana et al., 1995	2 / 949	0.21%
Wenzl et al., 1996	108 / 16,601	0.65%
Hiddebaugh et al., 1997	8 / 405	2.0%
Guglielmika et al., 1997	34 / 803	4.2%
Malik et al., 1998	11 / 292	3.4%
Mettler, 2001	12 / 493	1.6%
TOTAL	329 / 41,130	1.5%

Unexpected Malignancy at Operative Laparoscopy for Adnexal Masses in Postmenopausal Patients

Author, Year	No. Malignancies/Total pts	Rate
Parker et al 1990	0/25	0%
Mann et al 1992	0/44	0%
Canis et al 1994*	7/92	7.6%
Parker et al 1994	0/61	0%
Shalev et al 1994	0/55	0%
Hesseling et al 1996	7/184	3.8%
Total	14/461	3.0%

* Patients > 50 years

Laparoscopic Management of Suspicious Adnexal Masses

Author	Menopausal Status	Age	% of Malignancy
Childers et al 1996	Pre & Post	52 (9-91)	14% (19-138)
Canis et al 1997	Pre & Post	50±15.6	15% (37/247)
Dottino et al 1999	Pre & Post	52.2±13.1	13% (21/160)
Biran et al 2002	Pre & Post	N/A	18.9% (18/95)

Laparoscopic Management of Ovarian Pathology

Surgical Technique

- Careful peritoneal evaluation
- Biopsy of suspicious areas
- pelvic & peritoneal Washings
- Intact removal vs. aspiration (Endo bag)
- Frozen section
- **Surgical Staging** (laparoscopy/laparotomy)

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- Evaluation and management of adnexal mass
- **Staging for Early Borderline/Invasive Cancer**
- **Restaging for Unstaged Presumably Early Ovarian and Fallopian Tube Cancer**

Advanced Stage:

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Laparoscopic Staging for Borderline Ovarian Tumors

Author	Pts	complications	Conversions	Mean F/U (mth)	Recurrence	Survival
Darai '98	25†	none	8	41	3‡	100%
Seracchioli '01	19	none	0	42±19	1¶	100%
Querleu '03	30*	Injury to inferior epigastric A, abdominal wall hematoma, subphrenic abscess	0	29	1	97%
Total	74	3	8	37	5	72

† 15 conservative tx/10 radical sx; ‡ had cystectomy

¶ 1 died of intercurrent disease; 1 lost to fu; *Restaine cases

Laparoscopic Staging for Early Ovarian Cancer

Author	Pts	OR time (min)	EBL (ML)	LOS (DAYS)	Complications	Restaging	Delay in staging	Upstaged
Querleu '94	9	227	<300	2.8	Post-op ecchymosis	9	N/A	N/A
Childers '95	14	196	N/A	1.6	Vena cava injury, abdominal wall ecchymosis	5	N/A	40%
Pomel '95	8	313	N/A	4.8	PE, post-op bleeding requiring laparotomy	8	5-12 wks	12%
Amara '96	5	215	N/A	2.5		3	4-16 wks	33%
Tozzi* '04	24	166	N/A	N/A	Post-op chylos ascites	11	4-21 days	0
Total	60	223	-	2.9	6	36		

No Trocar site metastases

* DFS 91.6% & Overall Survival 100% after mean f/u of 46 months

Laparoscopic Staging in Patients with Incompletely Staged Cancer of the Ovary, Primary Fallopian Tube Carcinoma and Primary Peritoneal Carcinoma GOG 9302

Objectives:

- To determine the feasibility of laparoscopically staging patients with incompletely staged cancer of the ovary, primary fallopian tube carcinoma and primary peritoneal carcinoma
- To evaluate the adverse effects related to laparoscopic staging

Closed:06/2004

Laparoscopy and Ovarian Cancer Indications

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Advanced Stage:

- Laparoscopic Triage for Operability**
- Second Look Assessment
- Limited debulking/ hand assisted

Triage for Operability

Vergote '00

Belgium

Ansquer '01

France

Kuhn '01

Germany

Triage for Operability

- 1993-1997
- Open laparoscopic triage for primary debulking or neoadjuvant chemotherapy.
- 114 patients
- Operative time 25 min, LOS 2 days, EBL 10 cc.
- Primary and interval debulking in 36% & 63% respectively
- 76% of primary debulking cytoreduced to <0.5cm
- 10 trocar site metastases (7 alive; 3 died-had no trocar mets after definitive Sx /chemothx)

Vergote et al; Semin. Surg. Oncol., 2000

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Advanced Stage:

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- **Second Look Assessment**
- Limited debulking/ hand assisted

Steps of 2nd Look

- Detailed inspection of abdomen and pelvis
- Peritoneal Washings
- Multiple peritoneal biopsies
- Possible Omentectomy
- Possible pelvic and para-aortic lymph node sampling

False Negative 2nd Look Laparoscopy for Ovarian Cancer

Series	Year	# of Laparoscopies	False Negative	%
Mangioni	1979	18	6	33
Ozols	1981	22	12	55
Cohn	1983	54	24	44
Smith	1997	11	5	45

2nd Look Laparoscopy for Ovarian Cancer

Series	Procedure	#pts	Positive Findings %	Complications %	Recurrence %	Conversion*
Abu-Rustum '96	Lsc	31	54.8	0	14.8	8
	Lap	70	61.4	27	14.3	
Casey '96	Lsc	57	52.6	8.6	12.2	11
	Lap	69	53.6	41	10.1	

*Due to adhesions

Laparoscopy vs Laparotomy Survival after Second Look

Series	Procedure	# pts	Disease free survival
Gadducci '98	Lsc	34	Decreased survival in Lsc P= 0.006
	Lap	158	
Nezhat '99	Lsc	25	similar
	Lap	27	

Second Look Surgery

Should Laparotomy be replaced by Laparoscopy?

BENEFITS

- Less Invasive
- Less blood loss
- Shorter OR time
- Shorter hospitalization

DISADVANTAGES

- Higher failure rate of complete intraperitoneal inspection (41% vs 95%)
-mostly due to adhesions

Casey et al 1996; Abu-Rustum et al 1996; Clough et al 1999; Husain et al 2001

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- Second Look Assessment
- **Limited Debulking/ Hand Assisted**

Laparoscopic Cytoreduction

- 4 pts, 7 debulking procedures (including secondary/tertiary)
- Time interval after Initial Dx: 0-20 mths
- Operative Time: 100- 370 min.
- EBL: 10-800 ml
- Complications:

Enterotomy	1
SBO	1
Transfusion	1
- No Port site metastases

Amara & Nezhat et al, Surg Lap Endosc; 1996

Hand Assisted Laparoscopic Staging of Ovarian Cancer (HALS)

- 22/25 (88%) surgeries completed by HALS
- Optimally cytoreduced to < 1cm.
- Procedures – Hysterectomy(11), radical hysterectomy(1), BSO(13), pelvic ¶-aortic lymphadenectomy(19), appendectomy(17), omentectomy(22), small bowel resection(3), colectomy(2) and anterior resection(2).
- OR time 200 min, EBL 265 cc, LOS 1.8 days.
- No port-site metastases in 17 months f/u.

Krivak et al; Abstract, 33rd SGO, 2002

Laparoscopic Management of Ovarian Cancer Summary

- **Benign Adnexal Mass:** **Definite Role.** Prospective Randomized Data
- **Suspicious Adnexal Mass:** Retrospective Large Case Series suggest laparoscopic approach with frozen section reasonable.
- **Staging Presumably Early Ovarian/ Borderline Cancer:** Retrospective short term outcome data promising. Survival and Prospective Randomized data lacking.
- **Debulking:** Limited Retrospective data. Still laparotomy is the preferred approach
- **Triage for Operability:** Limited retrospective data. Primary cytoreductive traditional surgery still standard of care
- **2nd Look:** Retrospective data suggest laparoscopy as the initial approach.

Port Site Metastases

- Incidence for laparoscopy, laparotomy and paracentesis 1%
- Reported for both gynecologic and nongynecologic cancers
- Average time from procedure 81 (8-180) days for gynecologic malignancies

Port Site Metastases Causes

Combination of:

- Tumor cell entrapment
- Exfoliation & spread of tumor cells
- Direct contamination
- Chimney effect
- Preferential growth of malignant cells at port sites

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Trocar Implantations

Primary Ovarian Carcinoma	83
Recurrent	21
Trocar Implantation	9/104 (9%)
Closed Lps.	7/12 (58%)
Open Lps.	2/92 (2%)
P=	.001

Related to presence of Ascites and delay in surgery/chemotherapy

Van Dam, Am J OB/GYN, 1999

MSSM Experience

- Overall incidences for all gynecologic cancers
 - per procedure 2.3% (2/87)
 - per port 2.4% (8/330)
- For cancer of the ovary, peritoneum, and fallopian tube 6.25% (2/32)

Results Cont.

- No port site metastases in primary ovarian/fallopian tube cancers
- 20 procedures performed for recurrence of ovarian or peritoneal cancer (ascites in 4)
- No port-site metastases (0/16) occurred in the absence of ascites
- 50% (2/4) of patients with ascites developed port-site metastases ($p < .035$)

Trocar Site Metastases

- 1991-2003
- 1,335 laparoscopies for 1,288 Gyn malignancies
- 13 (0.97%) trocar site metastases.
- All with carcinomatosis/ synchronous metastases to other sites
- All in cases with advanced/recurrent abdominopelvic disease

Abu Rustum et al, Obstet Gynecol 2004

Incidence: 219 Patients

Laparoscopy	7/43 (16%)
Paracentesis	3/30 (10%)
TOTAL	10/73 (13%)

Kruitwagen et al., 1996

Results

-
- Corrected, Survival
 - Worse, Although Not Statistically Significant

Kruitwagen et al., Gyn Onco, 1996

LAPAROSCOPY AND OVARIAN CANCER

Port Site Metastases Prevention

- Avoid direct contamination
- Irrigation of port site
- Port closure
- Early onset of postoperative chemotherapy
- Port site radiation

Laparoscopy in Gynecologic Oncology

Future Goals

- Defining guidelines
- Prospective comparative randomized trials addressing:
 - ✓ Adequacy and safety
 - ✓ Survival benefits