



Primary and secondary cyto reduction in EOC

“The middle path”

TYPES OF SURGERY in Ovarian Cancer

- Primary surgery
- Interval cytoreduction
- Second look
- Secondary cytoreduction
- Palliative surgery

WHAT IS OPTIMAL SURGERY

➤ OPTIMAL PROCEDURE

Staging and

T.A.H.+ BSO + Omentectomy + relevant biopsies

USO in selected cases

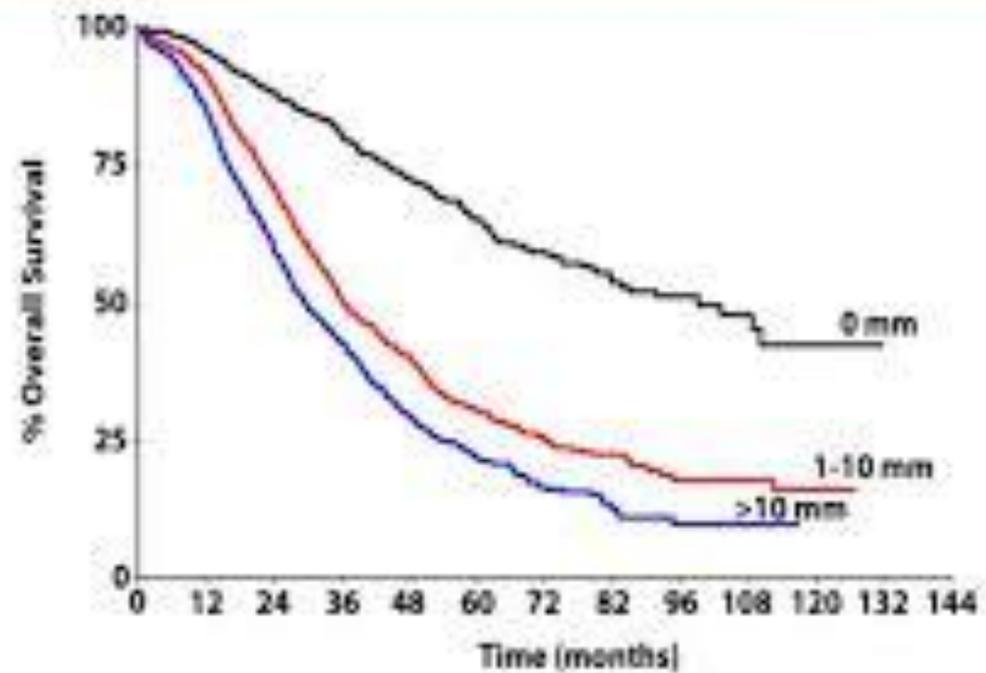
➤ OPTIMAL RESIDUAL DISEASE

Removal of all macroscopic disease

Current understanding

- Complete resection of visible tumor is the most important determinant of prognosis in EOC
- Complete resection or optimal cytoreduction to tumor size of $<2.5\text{mm}$ should be the goal of cytoreductive surgery

Cytoreductive Surgery to NO visible disease has the greatest impact on Overall Survival



Dubois et al, Cancer, 2009



Primary disease: Options for surgery

Goal : Complete/optimal cytoreduction

Modalities:

Initial or primary cytoreductive surgery

Interval cytoreduction



Primary cytoreduction

Destroy or be destroyed-there is
no middle way! Let us then be
the destroyers!

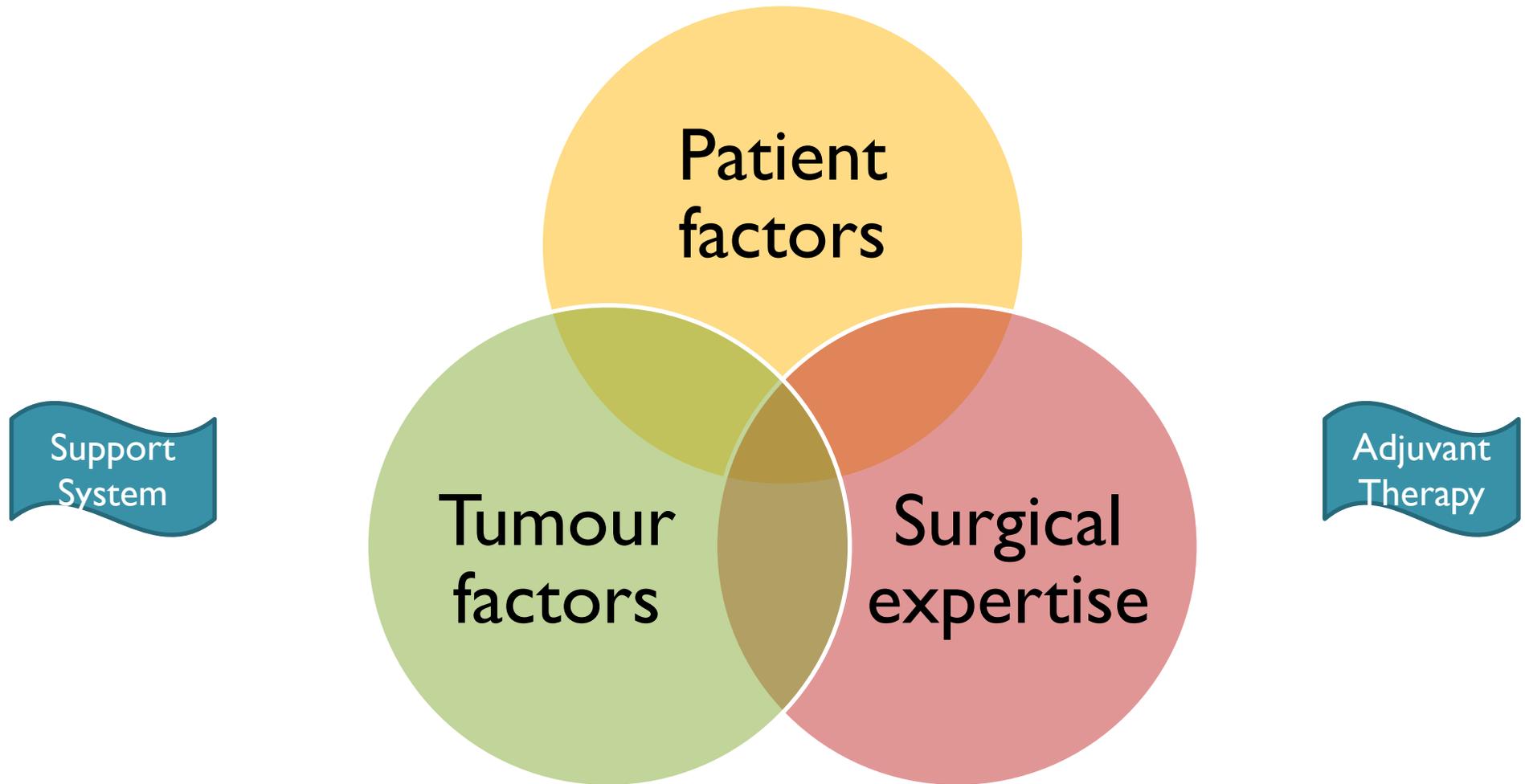
Mikhail Bakunin

Primary Debulking

- Aggressive surgical procedures*
 - Multiple or extensive bowel resection
 - Rectosigmoid resection
 - Resection of ureteral/bladder segment
 - Diaphragm stripping, peritonectomy
 - Resection of liver, spleen, kidney, diaphragm

**Justified only if optimal residual status can be achieved SAFELY*

Factors influencing success of cytoreductive surgery



Tumour factors

- Extent
- Location
- Biology

Patient factors

- Performance status
- Co morbidities,
- Social issues

Surgical expertise

- Radical gynecologic surgery
- Upper abdomen surgery
- GI
- Urology
- Vascular

Support system

- Infrastructure and Equipment
- Post-op monitoring and expert care

Adjuvant therapy

- Systemic
 - Chemotherapy
 - Targeted therapy
- IP
- HIPEC

PROBLEMS OF CASES WITH UNRESECTABLE DISEASE

- No survival benefit of procedure
- Increased post-op morbidity
- Delay in initiation of chemotherapy
- Poor quality of life



HOW TO IDENTIFY CASES WHO ARE LIKELY TO
HAVE UNRESECTABLE DISEASE ?

- 
- Clinical exam
 - Imaging
 - *Tumor markers*
 - Laparoscopy

Use of laparoscopy to judge operability

Definitions for inoperability:

- Extensive visceral peritoneal disease
- Extensive small bowel involvement
- Gross involvement of upper abdomen (diaphragm, liver, porta)
- Heavily bleeding tumors

Laparoscopy : Adverse features /scoring

LAPAROSCOPIC SCORING		Points
Peritoneal carcinomatosis	<u>0</u>	<u>0</u> (2)
Diaphragm disease	<u>0</u>	<u>0</u> (2)
Mesenteric disease	<u>0</u>	<u>0</u> (2)
Omental disease	<u>0</u>	<u>0</u> (2)
Bowel infiltration	<u>0</u>	<u>0</u> (2)
Stomach infiltration	<u>0</u>	<u>0</u> (2)
Liver metastases	<u>0</u>	<u>0</u> (2)
Total score		<u>0</u>

Limitations of laparoscopic assessment

Lesions in the retrohepatic area, suprahepatic veins, retroperitoneal space and/or infiltration of the liver pedicle may be underestimated while the presence of these findings is a major determining factor for suboptimal cytoreduction

NEOADJUVANT CT INDICATIONS

- Poor performance status
- Significant pleural effusion
- Rapidly accumulating ascites
- Gross upper abdominal disease
- Widespread intraperitoneal implants or retroperitoneal disease
- Extensive pelvic soft tissue infiltration
- Hepatic or extra peritoneal metastasis

RCTs NACT vs PDS

- EORTC 2010 & CHORUS 2015 Pooled analysis
Median OR 27.6 (NACT) vs 26.9 (PDS)
Stage IV NACT better, Stage IIIC <5cms mets PDS better
- SCORPION
PFS 14 vs 15 mo;
Significantly higher mortality and morbidity in PDS arm



Optimal debulking surgery is the strongest independent prognostic factor for overall survival. Hence, optimal debulking (to no residual tumor) should remain the goal of every surgical effort. The timing of this procedure (PDS or IDS) does not seem to play a role

IS THERE A CONSENSUS ?



Criticism of EORTC & CHORUS trials

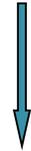
- Suboptimal attempt at PDS
- Median operating time 165 & 120 min
- Optimal debulking (<1 cms) rates ~40%
- Limited upper abdomen surgery
- PFS and OFS after PDS lower than other studies

Trial of radical upfront surgical therapy in advanced ovarian cancer (TRUST)

- International open, randomized, controlled multicenter trial investigating overall survival after PDS vs NACT and subsequent IDS in pts with FIGO stage IIIB-IVB ovarian, tubal, and peritoneal carcinoma.
- Secondary objectives are safety of complete tumor resection, progression-free survival and quality of life (QoL) as well as surgical morbidity.
- Specific quality assurance criteria for participating centers for eligibility > 50 % optimal resection rate and >36 surgeries per year

ADVANCED STAGE DISEASE

Clinical assessment & imaging indicate feasibility of
cytoreductive surgery

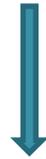


Cytoreductive surgery and adjuvant chemotherapy

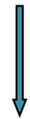
ADVANCED STAGE DISEASE

Cytoreductive surgery not feasible

Neoadjuvant chemotherapy



Interval cytoreduction



Adjuvant chemotherapy

PROGNOSTIC FACTORS

- Tumour stage
- Volume of residual disease
- Histological grade & subtype

- Others : Ca 125, genetic, DNA ploidy



SECONDARY CYTOREDUCTION

SECONDARY CYTOREDUCTIVE SURGERY

Has been evaluated in

1. Progression during first line chemotherapy
2. Residual disease identified at the time of second look laparotomy.
3. Recurrent cancer after a disease free interval ✓

PROGNOSTIC FACTORS AT RELAPSE

- Disease free interval
- Performance status
- Number of sites of disease
- Ca 125 levels

SURGERY IN RECURRENT OVARIAN CANCER

Important considerations



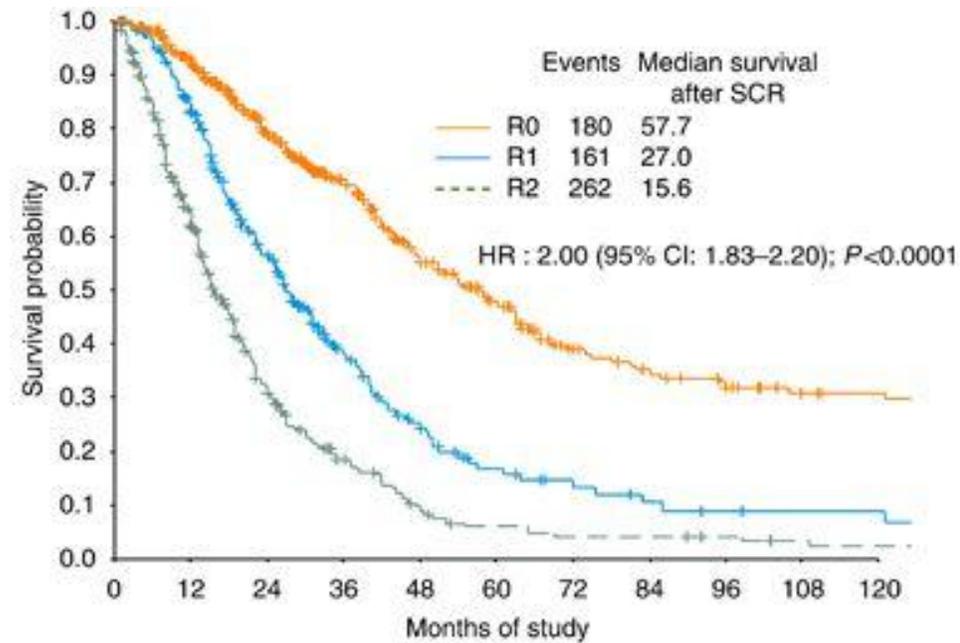
Probability of a successful resection

Influence on survival

Impact upon quality of life

Survival after SCR in patients with recurrent ovarian cancer

British Journal of Cancer volume 105, pages 890–896 (Sep 2011)



Numbers at risk

434	411	332	229	166	112	78	53	45	36	28
247	238	181	97	50	28	15	11	7	5	4
323	312	181	77	39	18	10	7	6	5	3

DESKTOP I

- Trial was undertaken to form a hypothesis for a panel of criteria for selecting patients who might benefit from surgery in relapsed ovarian cancer
- A combination of PS, early FIGO stage initially or no residual tumor after first surgery, and absence of ascites could predict complete resection in 79% of patients
- Only complete resection was associated with prolonged survival in recurrent ovarian cancer.

DESKTOP II

- To validate the resectability criteria prospectively
- Resectability criteria (1) complete resection at first surgery, (2) good performance status, and (3) absence of ascites.
- Rate of complete resection was 76%.
- Positive prediction of complete resectability in 2 or more of 3 patients
- Perioperative mortality 0.8%

DESKTOP III

- 1st relapse after 6+ mos platin-free interval (TFIp)
- Positive AGO-score (PS ECOG 0, ascites \leq 500 ml, and complete resection at initial surgery)
- Randomized to 2nd-line chemotherapy alone vs cytoreductive surgery followed by chemotherapy
- 407pts were randomized 2010-2014. The TFIp exceeded 12 mos in 75% and 76% pts in both arms.
- Complete resection was achieved in 67% of pts
- Median PFS was 14 mos without and 19.6 mos with surgery
- PFS-2 between 1st and 2nd relapse equalled or even exceeded PFS-1 before 1st relapse in 26% after surgery and only 16% without-surgery

SECONDARY CYTOREDUCTIVE SURGERY

Optimal candidates

- Relapse > 12 mo after chemotherapy
- Limited sites of disease & absence of significant ascites
- Tumors responsive to primary CT
- High performance status
- Potential for complete resection



In politics the middle way is
none at all.

~ John Adams

My take

- Surgery in any setting is justified only if optimal cytoreduction can be done with acceptable morbidity, hence appropriate case selection is vital.
- Surgical expertise and tumor biology have a complex inter relation that ultimately determines survival.

THANK YOU

