
بسم الله الرحمن الرحيم

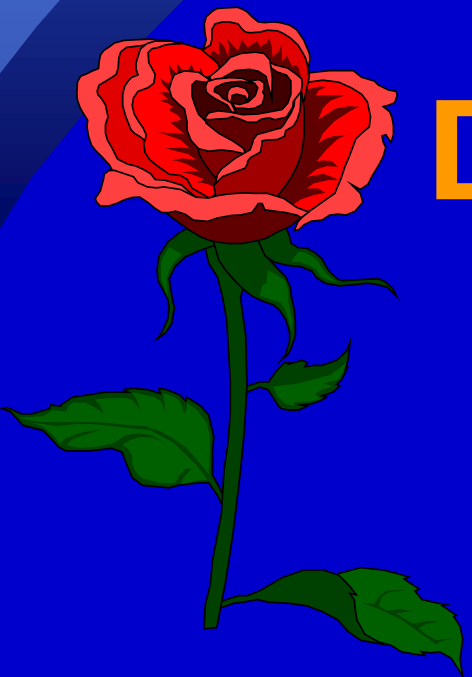
قالوا سبحانك

لا علم لنا إلا ما علمتنا

إنك أنت العليم الحكيم

سورة البقرة - الآية ٣٢

Optimization of Prognosis of Ovarian Cancers



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Introduction

- Ovarian cancer is the 3rd common gynecologic cancer that accounts for 32% of all gynecologic malignancies.
- It causes 55% of all gynecologic cancer deaths.
  It is the 4th leading cause of cancer deaths in females

Prognosis

- ***Prognosis*** *refers to the probable course and/or outcome of a disease or condition.*
- ***Cancer prognosis*** *is most often expressed as the percentage of patients who are expected to survive over five or ten years..*

Factors affecting ovarian cancer prognosis

- 1)Factors related to the patient.
- 2) 1)Factors related to the tumor :
  - a) Stage.
  - b) Pathological type.

PROGNOSIS	ECT	GCT	SCST
Best	Mucinous T	Dysgerminoma	LOW GRADE MALIGNACY
Worst	Serous T	EST	

Factors affecting ovarian cancer prognosis

- *C) Degree of differentiation.*
- *d) Residual tumor mass.*
  - *>2cm… bad prognosis.*
  - *<2cm… good prognosis.*
- *e) DNA content*
  - *Diploid… good prognosis.*
  - *Aneuploid… bad prognosis.*

- *3) Factors related to the treatment offered.*

The five-year survival rates after treatment for each stage of ovarian cancer are as follows:

- **Stage 1:** 90%
- **Stage II:** 70%
- **Stage III:** Patients diagnosed at this stage had an average 5-year survival of 15 to 20% in the past, but newer drugs and more aggressive treatments have extended the survival for many women.
- **Stage IV:** 1% to 5%

Ovarian cancer has the worst prognosis of gynecologic malignancies

- *WHY?*

  *a) LATE Diagnosis as e*arly symptoms are vague *so o*ver 75% of Ovarian Cancer cases are diagnosed at an advanced stage.

  b) Early dissemination as it lies inside the peritoneal cavity.

- *c) Para-aortic LN is the 1st relay (?).not usually resectable.*

- *d) Bilateral oophorectomy is the only prophylactic method.*

How to Optimize Ovarian cancer Prognosis?

- ***Early diagnosis through:***
  - ***Identifying women at risk.***
  - ***Prompt investigation of suspicious symptoms.***
  - ***Development of screening tests.***
- ***Prevention:***
  - ***Prophylactic oophorectomy.***
- ***Improvement of use of existing therapeutics.***
- ***Further development of experimental therapies***

Early diagnosis

- 1. Identify woman at risk.
- 2. Symptomatology.
- 3. Screening tests.
  - 1. Pelvic examination.
  - 2. Cytology.
  - 3. Imaging.
  - 4. Tumor markers

Identify women at risk

- Age: no age is immune but it is common in
  - Peri, postmenopausal, median age 60.
- Geography:
  - 5 times more in developed countries.
  - Highest in Sweden, Israel, least in Japan..
  - Residence is more important than race.
- Race; White more susceptible

Identify women at risk

- *Reproductive history:*
  - *Late age of 1st pregnancy.*
  - *Nulligravida or low parity.*
  - *No use COC. protection of OCP proportional with duration of use.*
  - *INCESSANT OVULATION HYPOTHESIS, index of ovarian cancer =time from menarche to cessation of ovulation – time of anovulation due to pregnancy and lactation.*

Identify women at risk

- *Hyperestrogenic conditions.*
- *Dysgenetic gonads.*

Identify women at risk

- *Past history:*
  - *Primary BREAST, COLON, ENDOMETRIUM.*
  - *Rubella at age 12-18, mumps antibody titer, has higher risk.*
  - *Sanitary pads with talc.*
- *Family history:*
  - *If mother or sister have ov cancer, BRCA1,2*

Investigations of suspicious symptoms.

- ***Vague symptoms*= Late diagnosis = *poor prognosis***

Screening Tests:

- *DEF: early detection of disease in asymptomatic individual.*
- *CRITERIA OF IDEAL SCREENING TEST.*
- *VALUE OF SCREENING TEST.*

Screening Tests:

- **Pelvic Examination.**
- ***Cytology.***
- ***Imaging.***
- ***Tumor Markers.***
- ***Recent screening.***

Annual bimanual Pelvic Examination.

- ***Palpable ovaries** in postmenopausal women is abnormal. (?Palpable ovary syndrome)*

Cytology

- ***Pap smear, paracetesis, Pouch of Douglas peritoneal cytology ,U/S GUIDED needle aspiration,*** **questionable and unreliable.**

Imaging

- **Us**: little value…… increased ovarian volume twice the mean volume is suspicious. Presence of cystic ov are suspicious.
- **Doppler us**: detect neovascularization.
- **3D U/S**.
- **Cat**? Impractical
- **MRI**? Impractical
- **Radioimmuno localization**.

Tumor Markers

- Oncodevelopmental (CEA).
- Carcinoplacental. AFP, HCG.
- Metabolic.LDH
- Tumor specific or tumor associated (CA 125).
  - Could help in monitoring the prognosis.
  - Poor sensitivity

Recent screening

- *Multimodal screening=use CA125 AS 1st line test, if abnormal TVU/S will be done. (cost, TVU/S, sensitivity, specificity)*
- *Use transcriptional profiling of ovarian cancer cell line(prostasin& aserine protease are higher in ovarian cancer cells)*

Recent screening

- *Proteomic pattern identification in serum using (SELDI-TOF-MS).100%sesetivity,95%speceficity.*

- *Genetic testing for ..BRCA1,BRCA2 mutation carriers.*

Prevention

Prophylactic oophorectomy:

- **Def:** surgical removal of healthy ovaries to protect against future malignancies?
- **Indication:**
- **Advantages:** prevent cancer,ovaries,tube.and breast.
- **Disadvantage:** menopausal symptoms,1ry peritoneal cancer, surgical complication.

Improve Existing Treatment.

- **Surgery** (cornerstone of treatment).
  - Staging.
  - Surgical procedure.
- **Postoperative treatment**.
  - Chemotherapy.
  - Radiotherapy
- **Adjuvant therapy**.
- **Monitoring treatment**.

Surgery

- ***Staging laparotomy*: *1ry method for, diagnosis, staging, treatment and follow up.***
  - *Vertical incision.*
  - *Aspirate, or saline washing.*
  - *Careful assessment., Liver, rt subphrenic space (because lymph of peritoneal cavity drain to inferior surface of diaphragm before getting mediastinal LN. Diaphragmatic metastases 10% stage I, 20% stage II.), All other organs as omentum, intestine,….*
  - *Para-aortic LN sampling.*
  - *Proper staging, for prognosis, selection of adjuvant therapy…..*

Staging: *FIGO staging for ovarian cancer is as follows:*

- *Stage I - Growth limited to the ovaries*
  - *Stage Ia - Growth limited to 1 ovary, no ascites, no tumor on external surface, capsule intact*
  - *Stage Ib - Growth limited to both ovaries, no ascites, no tumor on external surface, capsule intact*
  - *Stage Ic - Tumor either stage Ia or Ib but with tumor on surface, ruptured capsule, ascites with malignant cells or positive peritoneal washings*

- *Stage II - pelvic extension*
  - *Stage IIa - Extension and/or metastases to the uterus or tubes*
  - *Stage IIb - Extension to other pelvic tissues*
  - *Stage IIc - Stage IIa or IIb but with tumor on surface of one or both ovaries, ruptured capsule, ascites with malignant cells or positive peritoneal washings*

- *Stage III – Abdominal extension*
  - *Stage IIIa - Microscopic disease on abdominal peritoneal surfaces.*
  - *Stage IIIb - implant dose not exceed 2 cm in diameter and lymph nodes are negative*
  - *Stage IIIc - Abdominal implants larger than 2 cm in diameter and/or positive lymph nodes*

- *Stage IV - Distant metastases; pleural effusion must have a positive cytology to be classified as stage IV; parenchymal liver metastases equals stage IV*

Surgical Procedure.

- *1)Conservative surgery (unilateral salpingio-oophorectomy) Indicated in:*
  - *a) Young patient want to keep fertility.*
  - *b) Stage Ia tumor .*
  - *c)Reliable follow up.*
    - *ALLTOGETHER MUST TO BE PRESENT SO IT IS RARELY DONE.*

Surgical Procedure

- *2)Radical surgery= TAH+ BSO+ Omentectomy +/-Appendectomy.*
  - *Indications: stage Ia ,Ib ,IIa with negative peritoneal wash (rarely done).*

Surgical Procedure

- *3)Debulking=Cytoreductive surgery.*
  - *Aim: remove a tumor bulk, will allow chemotherapy to act.*
  - *Structures to be removed= TAH+ BSO+ Omentectomy +Appendectomy+ Remove any removable infiltrated organ.*

Surgical Procedure

- *Types of debulking:*
  - *1)Primary Debulking: commonly done (Advanced cases).*
  - *2) Interval Debulking.*
    - *Following suboptimal 1ry debulking.*
    - *Chemotherapy– debulking– Chemotherapy.*
    - *1ry Chemotherapy--- Interval debulking*
  - *3)Secondary Debulking.*
    - *Recurrent cancer.*
    - *Aggressive disease from the start will require 2ndry debulking.*

Surgical Procedure

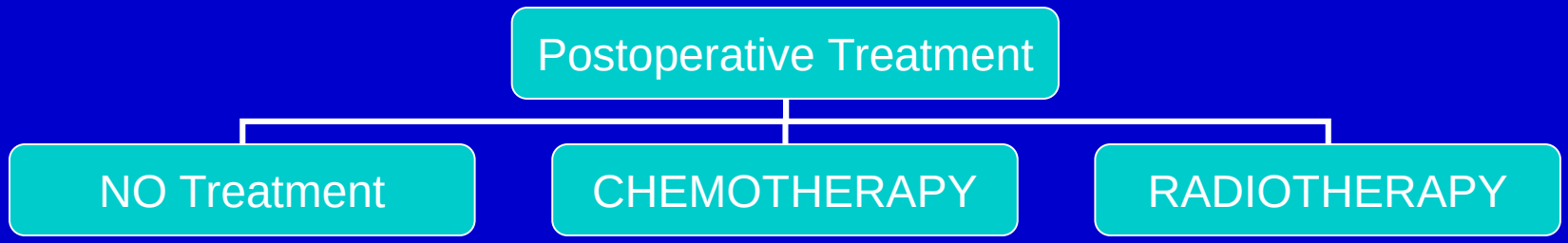
- ***Optimum Cytoreductive surgery*** ***=reduce residual tumor to minimum, but now=complete absence of disease at end of surgery.***

- ***Prognosis high if residue <1.6cm(<0.5cm).***

Postoperative Treatment depends on:

- **Prognostic indicators:**
  - **Residual mass.**
  - **Tumor grade. Then..**
  - **Stage , age, histology.**

Postoperative Treatment



No Postoperative Treatment

- *1) well differentiated border line tumors.*

- *2)stage Ia well differentiated tumors.*

Postoperative
CHEMOTHERAPY

- *Single regimen. (well differentiated tumor)*
- *Combination regimen. (poorly differentiated tumor)*

Postoperative
RADIOTHERAPY

- *Must be pelvi-abdominal.*
- *Only in endometroid tumor.*

Chemotherapy.

- *Rules of chemotherapy: (combination, courses, sequential, high dose, under strict monitoring)*
- *Chemotherapy used:*
- *Advancement:*
  - *1)Intraperitoneal administration.*
  - *2)In vitro sensitivity tests (stem cell assay)*
  - *3)**Reversal of drug resistance.***

Chemotherapy.

- *4)Development of new lines:*
  - *a) Paclitaxel.*
  - *b) Topotecan.*
- *ROLE OF CHEMOTHERAPY INIMPROVING PROGNOSIS: studies concluded that surgery had small effect survival of women with advanced ovarian cancer ,and the type of chemothe3rpy used was more important in improving median survival time.*

RADIOTHERAPY

- *1)Intraperitoneal radiotherapy.*
- *2)Whole external Abdomino-pelvic radiotherapy.*
- *Recent reports proved that radiotherapy can provide an effective adjuvant that may improve prognosis.*

Monitoring treatment

- *Aim:*
  - *Early detection of persistence or recurrence.*
  - ***To confirm complete response, to stop chemo.***
  - ***To avoid premature discontinuation of TT.***

Monitoring treatment

- *Noninvasive:*
  - *Clinical; S&S of recurrence*
  - *Investigations;*
    - *T. markers.*
    - *Imaging.*
- *If +ve..2nd line chemotherapy.*
- *If-ve 2nd look lap. after 6-12m.*

- *Invasive:*
- *2nd look laparotomy.*
- *2nd look laparoscopy good +ve but not a good –ve.?*

Development of experimental therapies.

- 1)New cytotoxic agents, platinum analogues.
- 2)Hormonal therapy; Anti-estrogen
- 3)Stem cell assay,
- 4)NEW DRUGS;
  - Angiogenesis inhibitors.
  - Matrix metalloproteinase inhibitors.

- ***5)Gene therapy.***
  - ***Def:*** ***introduction of genetic materials into host cell for a therapeutic purpose.***
  - ***TARGETS:***
    - ***1)Repairing defects in tumor genes.***
    - ***2)specefic anti-tumor cell immunity.***
    - ***3)Tumor cell cytotoxicity.***
  - ***Vector:*** ***ADENOVIRUS (highly infectious+ wide prevalence of receptors).***
  - ***Results:*** ***used in recurrent cases with hope to improve prognosis.***

- ***6)Viral therapy:***
  - ***DEF:*** ***Viruses have evolved to infect, replicate in, and kill human cells.***
  - ***Types;***
    - ***1)selectively engineered: Adenovirus.***
    - ***2)Nonselectively engineered: New castle disease virus.***
  - ***Advantages:*** ***no cross resistance with standard therapies.***
  - ***Results:*** ***great promise to improve prognosis in patient with advanced and recurrent ovarian cancer.***

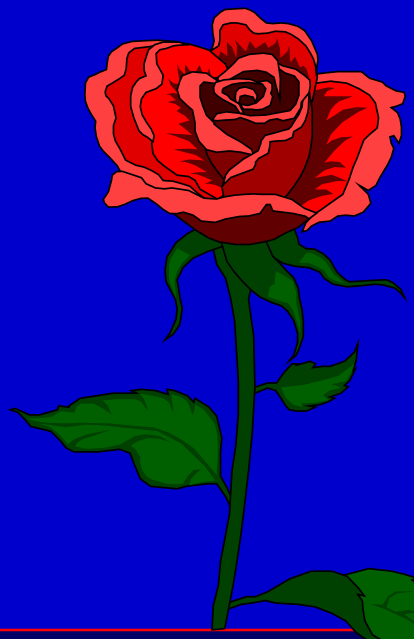
Development of experimental therapies.

- **7)Immunotherapy:**
  - **a) Nonspecific;** attempts to stimulate cell mediated immunity, Corynebacterium Parvum.
  - **b) Specific;**
    - Tumor specific MCA.
    - Lymphokine activated killer cells.
    - Tumor infiltrating lymphocytes.
    - HER2/NEU passive or active immunization.(HER2/NEU = Oncogenic protein its overexepression in ovarian cancer is related to bad prognosis)
- **8)Mullarian inhibitory factor (under trial)**

Development of experimental therapies

- *Recently there are trial of cryopreservation of oocytes, embryos, and ovarian tissues to preserve ovarian function in such patients.*
- *Inspite of the mentioned efforts ovarian cancer still has the worst prognosis among all gynecologic cancers.*

Thank you



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