Epithelial Ovarian Cancer

CLINICAL PRESENTATIONS AND WORK-UP

Clinical Suspicion of Ovarian Cancer

- Symptoms of bloating, dyspepsia, nausea, constipation, distension, abdominal or pelvic pain, urinary frequency or urgency
- Palpable pelvic or abdominal mass
- Ascites/pleural effusion

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WORK UP

- Personal and family history
- Thorough clinical examination
- Haematological and biochemical investigations
- Serum tumor markers: CA-125, CEA, CA 19.9
- Ultrasound/CT scan/MRI of abdomen and pelvis
- Upper and Lower GI endoscopy if clinically indicated
- Ascitic fluid/ pleural fluid cytology (if present)
- FNAC/ Biopsy of the mass if primary surgery not indicated

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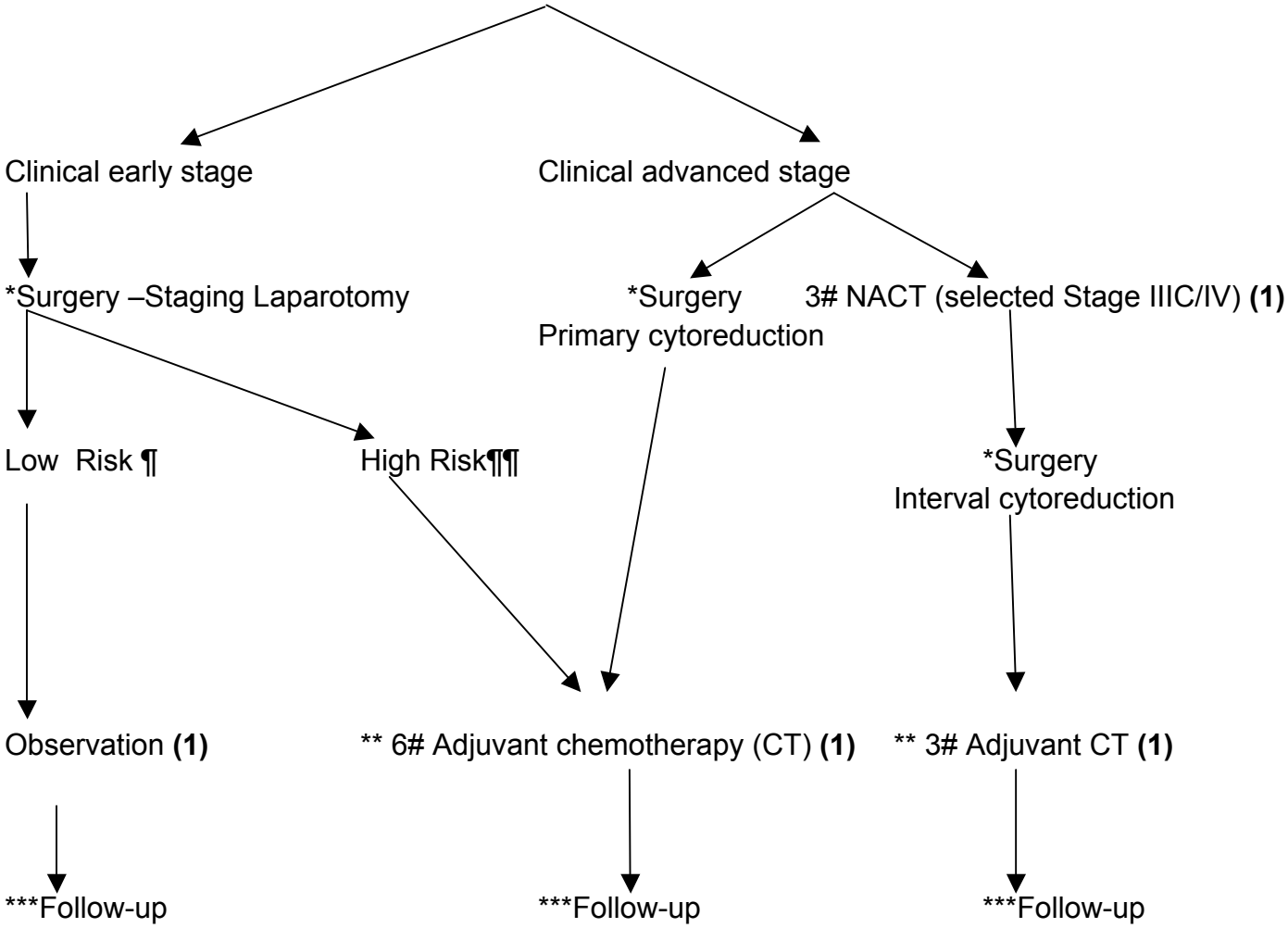
PRIMARY TREATMENT

PRIMARY TREATMENT (Levels of evidence in parentheses)



¶ Low Risk- Stage IA/IB , Grade 1, Non-Clear cell Histology

¶¶ High Risk – Stage IA/IB, Grade 2/3, Clear cell histology, Stage IC, Stage II

NOTES

I. FIGO (International Federation of Gynaecology & Obstetrics) Staging for Ovarian Cancer 2013 [2]

Ovarian malignancies are staged surgico-pathologically. Patients with stage I and II are considered early stage disease, whereas stage III and IV fall into the category of advanced stage disease. Stage IIIc is the most common stage of presentation

Stage I: Tumor confined to ovaries or fallopian tube(s) **T1-N0-M0**

IA: Tumor limited to 1 ovary (capsule intact) or fallopian tube; no tumor on ovarian or fallopian tube surface; no malignant cells In the ascites or peritoneal washings T1a-N0-M0

IB: Tumor limited to both ovaries (capsules intact) or fallopian tubes; no tumor on ovarian or fallopian tube surface; no malignant cells in the ascites or peritoneal washings T1b-N0-M0

IC: Tumor limited to 1 or both ovaries or fallopian tubes,with any of the following:

IC1: Surgical spill T1c1-N0-M0

IC2: Capsule ruptured before surgery or tumor on ovarian or fallopian tube surface T1c2-N0-M0

IC3: Malignant cells in the ascites or peritoneal washings T1c3-N0-M

Stage II: Tumor involves 1 or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or primary peritoneal cancer **T2-N0-M0**

IIA: Extension and/or implants on uterus and/or fallopian tubes and/or ovaries T2a-N0-M0

IIB: Extension to other pelvic intraperitoneal tissues T2b-N0-M0

Stage III: Tumor involves 1 or both ovaries or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes **T1/T2-N1-M0**

IIIA1: Positive retroperitoneal lymph nodes only (cytologically or histologically proven):

IIIA1(i) Metastasis up to 10mm in greatest dimension

IIIA1(ii) Metastasis more than 10mm in greatest dimension

IIIA2: Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes T3a2-N0/N1-M0

IIIB: Macroscopic peritoneal metastasis beyond the pelvis up to 2cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes

T3b-N0/N1-M0

IIIC: Macroscopic peritoneal metastasis beyond the pelvis more than 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes

T3c-N0/N1-M0

Stage IV: Distant metastasis excluding peritoneal metastases

Stage IVA: Pleural effusion with positive cytology

Stage IVB: Parenchymal metastases and metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of the abdominal cavity)

Any T, any N,M1

Extension of tumor from omentum to spleen or liver (stage IIIC) should be differentiated from isolated parenchymal metastases (stage IVB).

II. * SURGERY

Early Stage Disease

- Primary surgery for diagnosis, staging and treatment is the mainstay.
- The surgery should entail peritoneal fluid cytology, systematic exploration of the abdomen and pelvis, multiple peritoneal biopsies,total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymphadenectomy. Conservative surgery i.e. unilateral salpingo-oophorectomy with preservation of the normal contralateral ovary and uterus may be considered in young patients desirous of child bearing with stage IA, low grade disease or borderline tumours. Close observation is essential in these cases.

Advanced Stage Disease

- Cytoreductive surgery includes systematic exploration of the abdomen and pelvis, total abdominal hysterectomy with bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymphadenectomy and removal of all metastatic disease.
- The optimal goal of cytoreductive surgery is to leave behind no visible or palpable residual disease but the minimum goal is to leave behind less than 1cm (preferably less than 0.5 cm) residual disease at any given site.

III. ** **CHEMOTHERAPY**

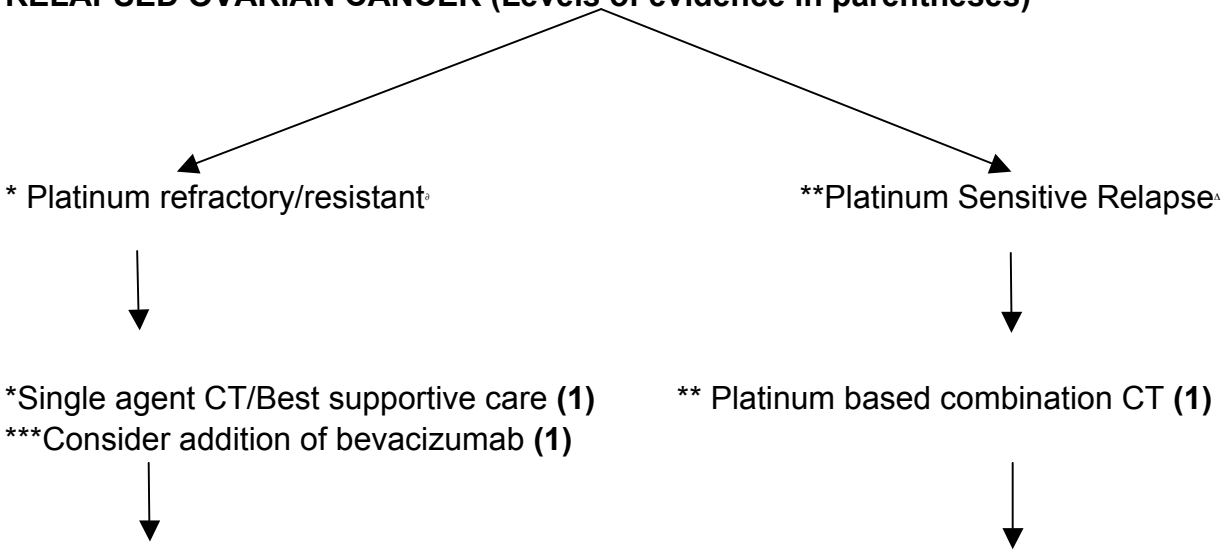
- Six cycles of paclitaxel and carboplatin every 3 weekly is the standard adjuvant chemotherapy. [1, 3]
- Dose dense weekly paclitaxel and carboplatin is also a valid option.[4]
- Single agent carboplatin or cisplatin and cisplatin/doxorubicin/cyclophosphamide (CAP) are alternative regimens. [5,6]
- Three cycles of neoadjuvant chemotherapy followed by interval debulking surgery and 3 cycles of adjuvant platinum based chemotherapy is an appropriate option for patients with bulky stage IIIC or IV ovarian carcinoma.[7]
- Intraperitoneal chemotherapy may be considered in patients with optimal cytoreduction in centres with experience.[8]

IV. ***FOLLOW UP

- History and clinical examination every 3 monthly for 2 years, 6 monthly for 5 years and then yearly life long
- Ca-125 at every visit if initially elevated
- Imaging as clinically indicated(ultrasound / CT / Chest X ray)
- Hematological and biochemical investigations as clinically indicated

(Note: LEVELS OF EVIDENCE IN PARENTHESES)

RELAPSED OVARIAN CANCER (Levels of evidence in parentheses)



Treat until best response or unacceptable toxicity. Duration of chemotherapy unclear. Patients can receive subsequent lines of chemotherapy or best supportive care depending on their performance status. **(4)** No response or progression on previous platinum therapy or progression within 6 months of itscompletion. Progression more than 6 months after completion of previous platinum chemotherapy

NOTES

I. * The standard management of platinum refractory or resistant relapse is single agent chemotherapy or best supportive care. This is based on six randomized trials showing lack of benefit from combination therapy in this setting. Appropriate single agents include pegylated liposomal doxorubicin (PLD), oral etoposide, gemcitabine, weekly paclitaxel and topotecan. [9]

II. **The standard management of platinum sensitive relapse comprises combination chemotherapy. This is based on randomized trials showing survival benefit over single agents in this setting. [10,11] Appropriate combination regimens include PLD plus carboplatin, paclitaxel or docetaxel plus carboplatin, gemcitabine plus carboplatin. [9]

III. *** The addition of bevacizumab to combination chemotherapy can be considered in patients with platinum sensitive relapse. However, physicians should be cognizant of the possibility of severe adverse effects including intestinal perforation. [12]

IV. **** Patients with isolated serological relapse (CA 125 rise), can be observed until symptomatic or radiologic progression **(1)**.[13]However, this decision needs to be individualized.

V. **** Surgical resection of relapsed disease may be considered in patients with a long disease-free interval and localized relapse **(3).**

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