

Ovarian Cancer

About the Guideline

- The National Comprehensive Cancer Network (NCCN) Guideline Panel consisted of 29 medical doctors and 3 nonphysician members.
- All recommendations are considered appropriate.
- Most of the recommendations are considered NCCN Category 2A (based on lower-level evidence with uniform NCCN consensus.)
- These guidelines discuss epithelial ovarian cancer and less common ovarian histopathologies, as well as fallopian tube cancer and primary peritoneal cancer.

Overview

- Epithelial ovarian cancer is the leading cause of gynecological related death and ranks as the 5th most common cause of female mortality.
- Risk of ovarian cancer increases with age and is most prevalent in the sixth and seventh decades of life. Other risk factors include nulliparity or older age at first pregnancy and birth.
- There is a decreased risk for ovarian cancer in patients with younger age at first pregnancy and birth, use of oral contraceptives and/or breastfeeding.
- Family history (including linkage with BRCA1/2) is associated with early-onset disease, but only accounts for 15% of all women with ovarian cancer.
- Greater than 70% of patients present with advanced disease.
- It is now widely accepted that the Fallopian tube is the origin of most serous ovarian and primary peritoneal cancers.

Key Clinical Considerations

Clinical Presentation and Screening

- Diagnosing ovarian cancer at an earlier, more curable state can be challenging because of the location of the ovaries and the biology of the cancer.
- Patients may present with an abdominal or pelvic mass, ascites and/or abdominal distention.
- Symptoms suggestive of ovarian cancer can include bloating, pelvic or abdominal pain, feeling full quickly, difficulty eating, and urinary frequency or urgency. These symptoms are especially concerning if they are new and frequent, occurring more than 12 days per month.
- Routine screening in the general population is not currently recommended by any professional society.

Diagnosis without Prior Malignancy

- For women presenting with an undiagnosed pelvic mass, the primary workup should include:
 - Abdominal/pelvic exam
 - Complete blood count (CBC), chemistry profile, and liver function studies (LFTs)
 - Evaluation of nutritional condition
 - Family history
 - Referral to a gynecologic oncologist for clinically suspicious lesions

- The following studies should be completed, as clinically indicated:
 - Abdominal/pelvic ultrasound and/or computerized tomography (CT) or magnetic resonance imaging (MRI) of the abdomen/pelvis
 - Chest CT or chest X-ray
 - Cancer Antigen 125 (CA-125) or other tumor markers
 - May be useful for determining malignancy
 - NCCN panel does not recommend use of biomarkers for determining status of undiagnosed pelvic mass
 - Gastrointestinal (GI) evaluation
- A surgical biopsy will confirm the diagnosis.
- Fine-needle aspiration should be avoided for diagnosis of ovarian cancer to prevent breakage of the cyst.
- All other non-ovarian cancers and conditions, as well as benign ovarian cysts must be ruled out.
- Epithelial ovarian cancer accounts for 90% of ovarian cancer diagnoses.

Staging

- Staging is determined using the American Joint Committee on Cancer (AJCC) Tumor-Node-Metastasis (TNM) staging system and the International Federation of Gynecology and Obstetrics (FIGO) staging system for a surgical specimen.
- New AJCC/FIGO guidelines (effective January 2018) combine staging for Fallopian tube carcinoma and ovarian cancer.
- The NCCN guidelines reflect the importance of stage and grade of disease on prognosis and treatment recommendations.
- All patients (except stage 1, grade 1 tumors) should be encouraged to enter clinical trials for both primary and recurrence therapy.

Primary Treatment Options

- Ovarian cancer, fallopian tube cancer, and peritoneal cancer are all treated in the same manner.
- Patients of child-bearing age should be referred to an appropriate fertility specialist.
- Primary treatment consists of surgical staging and surgical debulking followed by chemotherapy for most patients.
- The treatment regimen will be determined by the surgeon's report that includes:
 - The extent of the initial disease
 - Residual disease
 - Whether a complete or incomplete resection was performed
- For most patients (stage II, III, and IV), surgical intervention involves a total abdominal hysterectomy with a bilateral salpingo-oophorectomy.
- Surgical debulking is recommended for stages II, III, and IV.
- Lymph node dissection is recommended for patients with tumors outside of the pelvis sized 2 cm or less.
- Chemotherapy

- Neoadjuvant chemotherapy may be offered to patients with bulky stage III or IV, or to those who are poor surgical candidates, and not appropriate for patients with disease confined to ovary.
- Taxane/carboplatin and liposomal doxorubicin/carboplatin regimens are used for neoadjuvant treatment.
- Intraperitoneal (IP) chemotherapy is recommended for stage III cancers.
 - Stage II cancer patients may receive IP chemotherapy; however, no studies have been published as to whether this is more effective than the standard of care.
 - IP chemotherapy is not recommended for stage I or stage IV.
 - Agents used in IP chemotherapy include paclitaxel and cisplatin.
- Observation is recommended for patients with stage IA or IB.
- Three to six cycles of intravenous platinum-based chemotherapy are recommended for stage IC.
- Six cycles of platinum-based chemotherapy are recommended for patients staged II through IV.
- Anti-angiogenesis agents
 - Bevacizumab along with carboplatin/paclitaxel may be beneficial in patients who have ascites.
- Post-remission therapy
 - Paclitaxel and pazopanib are a post-remission therapy option for patients with stages II through IV of ovarian cancer, fallopian tube cancer, and peritoneal cancer who achieved complete remission and experience recurrence.
- Radiation therapy (RT)
 - Abdominal radiation is rarely used for any of the three cancers and not included in the treatment recommendations.
 - Palliative localized RT may be used to control symptoms in patients with advanced stages.

Recommendations after Primary Treatment

- Observation with follow up is recommended for patients whose cancer shows no progression after initial treatment.
- In patients whose cancer has remained stable or progressed after initial treatment, second-line treatment is recommended.
- Patients are recommended to undergo genetic-risk evaluation for a diagnosis of any of the three cancers, however primary treatment should not be delayed for genetic testing.

Follow-up

- Follow-up visits after primary treatment should be scheduled every 2 to 4 months for 2 years, then 3 to 6 months for 3 years, and then annually after 5 years.
- Chest/abdominal/pelvic CT, MRI, PET scans and chest x-ray ordered as clinically indicated.
- Recurrence can be identified using imaging, an elevated CA-125 level, or symptoms such as pelvic pain and weight loss. If the CA-125 was initially elevated, then a repeat level or other tumor markers is recommended.

- Prognosis is poor for patients who progress after 2 consecutive chemotherapy regimens or whose disease recurs in less than 6 months.
 - Retreatment with a platinum compound or paclitaxel is not recommended due to the disease resistance to primary regimen.
 - Assessment for palliative care should be considered.
 - NCCN panel does not have a recommendation of a single therapeutic agent as the treatment of choice; regimens and agents are preferred based on expert opinion, decreased toxicity and/or increased effectiveness.
 - Platinum-based combination chemotherapy is recommended for total of 6 cycles.

Considerations for Less Common Ovarian Histopathologies (LCOH)

- LCOH include:
 - Carcinosarcoma
 - Clear cell carcinoma of the ovary
 - Mucinous carcinoma of the ovary
 - Low-grade serous/grade 1 endometrioid epithelial carcinoma
 - Ovarian borderline epithelial tumors
 - Malignant sex cord-stromal tumors
 - Malignant germ cell tumors.
- Tumor markers can be completed, including CA-125, inhibin, alpha-fetoprotein, and beta-human chorionic gonadotropin, if clinically indicated, to assess for pregnancy, and less common ovarian histopathologies (LCOH).
- A surgical biopsy will confirm the diagnosis.
- Minimally invasive procedures may be useful to determine if cytoreduction can be achieved.
- The treatment regimen will be determined by the surgeon's report that includes:
 - The extent of the initial disease
 - Residual disease
 - Whether a complete or incomplete resection was performed
- Staging is determined using the TNM staging system and the FIGO staging system.
- LCOH post-surgical and chemotherapy recommendations:
 - Carcinosarcoma
 - For stage I to IV, chemotherapy is recommended as per epithelial ovarian cancer.
 - Clear cell carcinoma of the ovary
 - For stage IA to IC, IV platinum-based chemotherapy for 3 to 6 cycles is recommended.
 - For stage II to IV, chemotherapy is recommended as per epithelial ovarian cancer.
 - Mucinous carcinoma of the ovary
 - For stage IA to IB, observation is recommended.
 - For stage IC to IV, platinum-based chemotherapy for 3 to 6 cycles is recommended.

- For stage II to IV, chemotherapy as per epithelial ovarian cancer is recommended.
- Low-grade serous/grade 1 endometrioid epithelial carcinoma
 - For stage IA to IB, observation is recommended.
 - For stage IC to IV, platinum-based chemotherapy for 3 to 6 cycles is recommended.
 - For stage II to IV, chemotherapy as per epithelial ovarian cancer is recommended.
- Ovarian borderline epithelial tumors
 - Observation is recommended.
- Malignant sex cord-stromal tumors
 - For stage I low-risk, observation is recommended.
 - For stage I high-risk, platinum-based chemotherapy is recommended.
 - For stage II to IV, platinum-based chemotherapy for 3 to 6 cycles is recommended, or radiation therapy in the case of limited disease.
 - Follow-up includes a physical exam and tumor markers, as clinically indicated based on stage.
 - Follow-up imaging is only completed on patients with symptoms, elevated tumor markers or findings on a physical exam.
- Malignant germ cell tumors
 - The patient's desire for fertility must be determined before surgery takes place.
 - Post-surgery tumor markers and imaging will determine the next course of action, either observation or chemotherapy.
 - Follow-up includes a physical exam and tumor markers every 2 to 4 months for 2 years, and then annually.
 - Follow-up imaging may be completed, as clinically indicated.

Reference:

National Comprehensive Cancer Network. (2019). Ovarian cancer including fallopian tube cancer and primary peritoneal cancer, version 1.2019.

Link to Practice Guideline:

https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf