Assessment of Adult Women with Ovarian Masses and Treatment of Epithelial Ovarian Cancer: ASCO Resource Stratified Guideline

Vanderpuye and Clemenceau et al.
Overview

1. Background & Methodology
   - Introduction
   - Framework of Resource Stratification
   - ASCO Guideline Development Methodology
   - Adapted Guidelines
   - Clinical Questions
   - Target Population and Audience

2. Summary of Recommendations

3. Discussion
   - Special Commentary: Pathology
   - Limitations of the Research & Future Directions
   - Additional Resources
   - Expert Panel Members
1. Background & Methodology
Introduction

• The purpose of this guideline is to provide expert guidance on the diagnosis and treatment of adult women 18 years of age or older with epithelial ovarian cancer (including fallopian tube and primary peritoneal cancer) to clinicians, public health leaders, patients, and policymakers in resource-constrained settings.

• Different regions of the world have variable access to diagnosis and treatment of epithelial ovarian cancer. Due to these disparities, the ASCO Resource-Stratified Guidelines Advisory Group chose epithelial cancer of the ovary as a priority topic for guideline development.

• ASCO has established a process for development of resource-stratified guidelines,¹ which includes mixed methods of evidence-based guideline development, adaptation of the clinical practice guidelines of other organizations, and formal expert consensus.

• ASCO has adopted its framework of resource stratification from the four-tier resource setting approach (basic, limited, enhanced, maximal) developed by Breast Health Global Initiative and modifications to that framework based on the Disease Control Priorities 3.²,³

• This guideline is not intended for patients in maximal setting.
Framework of Resource Stratification

<table>
<thead>
<tr>
<th>Setting</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic</td>
<td>Core resources or fundamental services that are absolutely necessary for any public health/primary health care system to function; basic-level services typically are applied in a single clinical interaction. Vaccination is feasible for highest need populations.</td>
</tr>
<tr>
<td>Limited</td>
<td>Second-tier resources or services that are intended to produce major improvements in outcome such as incidence and cost-effectiveness and are attainable with limited financial means and modest infrastructure; limited-level services may involve single or multiple interactions. Universal public health interventions feasible for greater percentage of population than primary target group.</td>
</tr>
<tr>
<td>Enhanced</td>
<td>Third-tier resources or services that are optional but important; enhanced-level resources should produce further improvements in outcome and increase the number and quality of options and individual choice. (Perhaps ability to track patients and links to registries).</td>
</tr>
<tr>
<td>Maximal</td>
<td>May use high-resource settings’ guidelines. High-level/state-of-the art resources or services that may be used/available in some high-resource countries and/or may be recommended by high-resource setting guidelines that do not adapt to resource constraints but that nonetheless should be considered a lower priority than those resources or services listed in the other categories on the basis of extreme cost and/or impracticality for broad use in a resource-limited environment.</td>
</tr>
</tbody>
</table>

NOTE. Data adapted. To be useful, maximal-level resources typically depend on the existence and functionality of all lower level resources. Maximal level recommendations are not included in this guideline.
ASCO Guideline Development Methodology

• The ASCO Clinical Practice Guidelines Committee guideline process includes:
  ▪ a systematic literature review by ASCO guidelines staff
  ▪ an expert panel provides critical review and evidence interpretation to inform guideline recommendations
  ▪ final guideline approval by ASCO CPGC

• The full ASCO Guideline methodology manual can be found at: www.asco.org/guideline-methodology

• More information on the ASCO Resource-Stratified Guidelines methodology can be found in the 2018 JCO Global Oncology article by Al-Sukhun et al¹: https://ascopubs.org/doi/full/10.1200/JGO.18.00113
Adapted Guidelines

• Based on content and methodology reviews, the Expert Panel chose six non-ASCO guidelines and three ASCO guidelines for adaptation
  - Scottish Intercollegiate Guidelines Network (SIGN), Management of epithelial ovarian cancer (SIGN CPG 135)⁵
  - Belgian Health Care Knowledge Center (KCE), Ovarian cancer: diagnosis, treatment and follow-up⁶
  - ASCO/Society of Gynecologic Oncology (SGO), Neoadjuvant chemotherapy for newly diagnosed, advanced ovarian cancer⁷,⁸
  - Ontario Health - Cancer Care Ontario (OH-CCO), Systemic Therapy for Recurrent Ovarian Cancer⁹
  - Japan Society of Gynecologic Oncology (JSGO), Guidelines 2015 for the treatment of ovarian cancer including primary peritoneal cancer and fallopian tube cancer.¹⁰
  - British Gynaecological Cancer Society (BGCS), Epithelial Ovarian Cancer/Fallopian Tube/Primary Peritoneal Cancer Guidelines¹¹
  - Irish National Clinical Effectiveness Committee (NCEC), Diagnosis and staging of patients with ovarian cancer¹²
  - 2020 ASCO guidelines, Germline and Somatic Tumor Testing in Epithelial Ovarian Cancer¹³, PARP Inhibitors in the Management of Ovarian Cancer¹⁴
Adapted Guidelines

- The Expert Panel used these guidelines, literature suggested by the Expert Panel, and clinical experience as guides.
- The Expert Panel formally vetted the included guidelines’ content and development methodology.
- This ASCO guideline reinforces selected recommendations offered in the SIGN, Belgian KCE, ASCO/SGO, ASCO, OH-CCO, JSGO, BGCS, Irish NCEC guidelines and acknowledges the effort put forth by the authors and aforementioned societies to produce evidence-based and/or consensus-based guidelines informing practitioners and institutions who provide care to patients with ovarian masses and/or ovarian cancer.
Clinical Questions

This clinical practice guideline addresses four overarching clinical questions for each of the three resource-constrained settings levels:

A. What are the optimal diagnosis/staging strategies for adult women with ovarian masses and/or epithelial ovarian cancer (including fallopian tube and primary peritoneal cancer)?

B. What is the optimal surgery for women with stages I-IV epithelial ovarian cancer (including fallopian tube and primary peritoneal cancer)?

C. What is the optimal adjuvant/systemic therapy for stages I-IV epithelial ovarian cancer (including fallopian tube and primary peritoneal cancer)?

D. What is the optimal therapy for women with recurrent epithelial ovarian cancer (including fallopian tube and primary peritoneal cancer)?
Target Population and Audience

Target Population

- Adult women (18 years of age or older) in three resource-constrained settings levels with ovarian masses and/or diagnosed with epithelial ovarian cancer (including fallopian tube and primary peritoneal cancer

Target Audience

- This guideline globally targets health care providers (including gynecologic oncologists, medical oncologists, radiation oncologists, obstetricians and gynecologists, surgeons, nurses, and palliative care clinicians), and non-medical community members, including patients, caregivers, and member(s) of advocacy groups.
Summary of Recommendations
Summary of Recommendations:
Staging & Surgery

<table>
<thead>
<tr>
<th>Staging for Suspected Stage I/II</th>
<th>Fertility-Sparing and Laparoscopic Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic</strong></td>
<td></td>
</tr>
<tr>
<td>Elective surgical staging for ovarian cancer is not recommended on a routine basis.</td>
<td>Patients with apparent stage I ovarian cancer should be referred to a higher-level care center with trained experts to perform appropriate surgical staging</td>
</tr>
<tr>
<td><strong>Limited</strong></td>
<td></td>
</tr>
<tr>
<td>Metastatic workup and referral for staging surgery</td>
<td>If sufficient expertise exists, may perform staging surgery</td>
</tr>
<tr>
<td><strong>Enhanced</strong></td>
<td></td>
</tr>
<tr>
<td>Metastatic workup and staging surgery</td>
<td>Fertility sparing surgery or referral to higher-level cancer center</td>
</tr>
</tbody>
</table>

Elective laparoscopic surgical staging for apparent stage I ovarian cancer is not recommended.

No role for fertility-sparing surgery in early-stage disease.

Effective minimally invasive laparoscopic surgery may be performed for select patients with apparent stage I ovarian cancer.
# Summary of Recommendations: Staging & Surgery (cont.)

<table>
<thead>
<tr>
<th>Staging and Surgery</th>
<th>Surgery for Stage III/IV</th>
<th>Surgery after NACT for Stage III/IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Basic</strong></td>
<td>Evaluated for surgical management taking into account tumor burden, PSA, comorbidity</td>
<td>Counsel patients on treatment options and refer them to a cancer treatment center with specialized surgical services</td>
</tr>
<tr>
<td></td>
<td>Basic setting recommendations</td>
<td>If unable to travel to a distant health center, refer to palliative care recommendations</td>
</tr>
<tr>
<td><strong>Limited</strong></td>
<td>Complete tumor cytoreduction to no gross residual disease/remove all macroscopic visible disease OR refer to higher-level cancer center</td>
<td>NACT and interval debulking in FIGO stage IIIC or IV, in expectantly high morbidity surgery and patients with poor PS or unresectable disease OR refer to higher-level cancer center</td>
</tr>
<tr>
<td></td>
<td>Basic setting recommendation</td>
<td></td>
</tr>
<tr>
<td><strong>Enhanced</strong></td>
<td>Complete tumor cytoreduction to no gross residual disease/remove all macroscopic visible disease</td>
<td>If performed with curative intent, maximal effort cytoreductive surgery with the aim to remove all intra-abdominal macroscopic tumor</td>
</tr>
<tr>
<td></td>
<td>Basic setting recommendation</td>
<td></td>
</tr>
</tbody>
</table>

*Not feasible*
Summary of Recommendations: Adjuvant/Systemic Therapy
Summary of Recommendations: Adjuvant/Systemic Therapy (cont.)

Adjuvant/Systemic Therapy for Stage II/III Who Have Received Surgery & No Chemotherapy

- **Basic**
  - No role for adjuvant chemotherapy
  - No role for intraperitoneal chemotherapy
  - No role for targeted therapy

- **Limited**
  - Combination platinum adjuvant therapy* for patients with stages II or III and PS 0-2 unless patients have contraindications
  - Single-agent carboplatin for PS >2 and/or contraindications to combination therapy
  - Basic setting recommendation
  - Targeted therapy is not recommended in limited settings on a routine basis for patients with stage III

- **Enhanced**
  - Limited setting recommendations
  - Patients referred to be assessed for appropriate evidence-based intraperitoneal chemotherapy, following optimal debulking, where there are resources & expertise to manage toxicities
  - Assess patients with stage III for appropriate evidence-based targeted therapy, all patients with high risk features, and PS 0-2
Summary of Recommendations: Adjuvant/Systemic Therapy (cont.)

Adjuvant/Systemic Therapy for Stage IV Who Have Received Surgery & No Chemotherapy

Basic
- Refer to higher-level cancer center for systemic chemotherapy, symptomatic therapy, and pain control
- Combination platinum adjuvant therapy* for patients with stages II or III and PS 0-2 unless patients have contraindications
- Single-agent carboplatin for PS ≥2 and/or contraindications to combination therapy
- Basic setting recommendations
- Targeted therapies are not cost effective in most resource-constrained regions unless patients are being treated at enhanced or maximal level
- No role for targeted therapy

Limited
- Carboplatin + paclitaxel for six cycles OR refer to higher-level cancer center
- Limited setting recommendations
- Cost-effectiveness data are emerging: awaiting outcomes for primary therapy maintenance settings for PARPi
- Limited setting recommendation
- Targeted therapy is not recommended in limited settings on a routine basis for patients with stage IV

Enhanced
- Carboplatin + paclitaxel for six cycles
- Cost-effectiveness data are emerging: awaiting outcomes for primary therapy maintenance settings for PARPi
- Limited setting recommendation
- Assess patients with stage IV for appropriate evidence-based targeted therapy; all patients with high risk features, and PS 0-2
Summary of Recommendations:
Maintenance Systemic Therapy

- **Basic**: No role for maintenance systemic therapy.
- **Limited**: Maintenance systemic therapies (anti-angiogenic, targeted therapies) are not recommended for patients who have received surgery and prior chemotherapy.
- **Enhanced**: May discuss maintenance systemic therapies (e.g., anti-angiogenic, targeted therapies) for patient who have received surgery and prior chemotherapy. For guidance regarding the use of PARPi, refer to the ASCO guideline.
Summary of Recommendations:
Recurrent Ovarian Cancer

Surgery for Recurrent Epithelial Ovarian Cancer

- **Basic**
  - Not feasible

- **Limited**
  - For select patients with a small volume platinum-sensitive recurrent disease, may refer to higher level cancer center for surgical consideration

- **Enhanced**
  - For select patients with a small volume platinum-sensitive recurrent disease, may perform complete secondary cytoreductive debulking surgery

Systemic/Palliative Treatment for Recurrent Ovarian Cancer

- clinicians may recommend treatment with second-line chemotherapy to patients with platinum-sensitive and platinum resistant/refractory ovarian cancer or refer to higher-level cancer center

- Combination chemotherapy with carboplatin preferably for patients with platinum-sensitive recurrent ovarian cancer or refer to higher-level cancer center

- Single-agent non-platinum chemotherapy or best supportive care for patients with platinum-resistant/refractory recurrent ovarian cancer or refer to higher-level cancer center

- No systemic treatment is recommended for tumor marker-positive (CA-125) only recurrent ovarian cancer in the absence of symptoms

Limited setting recommendation
Summary of Recommendations:
Palliative Care

- Basic
  - Clinicians should offer palliative care, including cancer pain and symptom management, to all patients diagnosed with ovarian cancer.
  - Early referral to palliative care where available.

- Limited
  - Basic setting recommendations

- Enhanced
  - Basic setting recommendations
Discussion
Special Commentary: Pathology

• Pathology is an important part of diagnosing the type of epithelial ovarian cancer and guiding management of women with this disease. There is variable availability and financing for pathology services around the world. In some regions, clinicians may even have to make diagnoses without pathology.

• As resource-constrained regions develop pathology services, the Expert Panel would like to make some suggestions specific to ovarian cancer.
  ▪ The clinical presentation and imaging findings of both benign and other malignancies may mimic those of ovarian cancer. Consequently, a histopathologic diagnosis should be undertaken prior to definitive treatment.
  ▪ Pathologic diagnosis may be rendered on a peritoneal or omental biopsy, particularly in patients for whom there is the potential for neoadjuvant intervention, or on resection specimens following laparotomy or laparoscopy. Usually, routine histologic processing of formalin-fixed tissue is sufficient for pathologic diagnosis. Immunohistochemical studies may provide additional confirmatory evidence.
  ▪ Alternatively, a cytopathologic diagnosis may be enough if this specialized service is available. In some limited and enhanced settings, ascitic fluid can be sent to pathology for cell block in major cities. Where labs are of variable quality, cytology alone can be problematic. In some cases, immunohistochemical tests can be sent to a central lab to confirm diagnosis, especially if a sample is mucinous.
Limitations of the Research & Future Directions

• There were limitations on the evidence, due to many factors, such as prioritization of patient care and limited funding and infrastructure for research.

• Limitations include:
  ▪ Insufficient research conducted in resource-constrained settings
  ▪ Lack of conclusive research on primary/prevention screening
  ▪ Lack of published data on ovarian cancer genetic risk evaluation and management adapted to resource-constrained settings.

• A shortage of trained gynecologic oncologists has led to task-shifting with variation in skills set among general practitioners, obstetrics/gynecologists, general surgeons, and oncologists

• There is a significant need to further ovarian cancer research in resource-constrained settings, considering issues of surgery and chemotherapy access, treatment effectiveness, genetic research, and cost effectiveness.

• The use of targeted therapy in adjuvant, maintenance, and recurrent ovarian cancer is actively under investigation and further guidelines will include updates.
Additional Resources

• More information, including a supplement and clinical tools and resources, is available at www.asco.org/resource-stratified-guidelines

• Patient information is available at www.cancer.net
## Guideline Panel Members

<table>
<thead>
<tr>
<th>Name</th>
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<th>Role/Area of Expertise</th>
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</thead>
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</tbody>
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Abbreviations

- ASCO, American Society of Clinical Oncology
- BCGS, British Gynaecological Cancer Society
- CA-125, cancer antigen 125
- CEA, carcinoembryonic antigen
- CT, computed tomography
- FIGO, International Federation of Gynecology and Obstetrics
- FSA, functional status assessment
- JSGO, Japan Society of Gynecologic Oncology
- KCE, Belgian Health Care Knowledge Center
- LMP, low malignant potential
- MRI, magnetic resonance imaging
- NACT, neoadjuvant chemotherapy
- NCEC, Irish National Clinical Effectiveness Committee
- OH-CCO, Ontario Health – Cancer Care Ontario
- PARPi, poly (ADP-ribose) polymerase inhibitor
- PS, performance status
- SIGN, Scottish Intercollegiate Guidelines Network
- SGO, Society of Gynecologic Oncology
References

5. SIGN - Scottish Intercollegiate Guidelines Network: Management of epithelial ovarian cancer (SIGN CPG 135), 2013
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