



OVARIAN CANCER SURGERY GUIDELINES



These guidelines are focused on the role, objectives, and standards of the surgical management of diagnosed epithelial ovarian, fallopian tube, and peritoneal cancer. The management of non-epithelial tumours and borderline tumours is not included. Screening of ovarian cancer and prophylaxis are not addressed. Diagnosis and management of adnexal masses will be addressed only regarding the minimal necessary preoperative workup. Medical management is not addressed, as the standards of medical management (referred to as “chemotherapy”) will be defined at the time of a forthcoming consensus conference in collaboration with the European Society of Medical Oncology (ESMO).

A five-step development process was followed:



The objectives of the guidelines are to improve and homogenise the management of patients with ovarian cancer. The guideline covers diagnosis and preoperative workup, specialised multidisciplinary decision-making, and surgical management for patients over the age of 18 years with epithelial ovarian cancer and provides information for discussion with patients and carers.

It excludes the management of borderline tumours and does not include any economic analysis of the strategies. Any clinician seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment.

To ensure that the statements made in this document are evidence-based, the current literature was reviewed and critically appraised. A comprehensive literature review of the studies published between January 2005 and May 2016 was carried out.

The guidelines were retained if they were supported by sufficient high-level scientific evidence and/or when a large consensus among experts was obtained. By default, a guideline is the standard clinical approach. If an approach is judged to be acceptable but is not unanimously recognized as a criterion-standard clinical approach, indication is given that it is still subject to discussion and/or evaluation.

These guidelines have five different “strength of guideline” ratings (SIGN grading system¹):

- A** At least one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population; or
A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating an overall consistency of results.

- B** A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 1++ or 1+.

- C** A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or
Extrapolated evidence from studies rated as 2++.

- D** Evidence level 3 or 4; or
Extrapolated evidence from studies rated as 2+.

- ✓** Recommended best practice based on the clinical experience of the guideline development group.

1++ high quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias; 1+ well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias; 2++ high quality systematic reviews of case control or cohort studies/high quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal; 2+ well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal; 3 non-analytic studies, e.g., case reports, case series; 4 expert opinions.

¹ <http://www.sign.ac.uk/guidelines/fulltext/50/annexoldb.html>

DIAGNOSIS AND PREOPERATIVE WORKUP

✓	Clinical examination, including abdominal, vaginal, and rectal examinations; assessment of the breast, groins, axilla, and supraclavicular areas; and auscultation of the lungs should be performed.
B	Routine pelvic (transvaginal and transabdominal) ultrasound should be used as a primary workup tool in any adnexal mass.
B	Specialised pelvic, abdominal, and thoracic complementary imaging should be performed in case of suspected carcinoma of the ovary, or indeterminate or suspicious masses at routine ultrasound examination.
✓	A tumour marker assessment should be performed for at least CA 125 levels. HE4 has also been proposed. Additional markers, including AFP, hCG, LDH, CEA, CA 19-9, inhibin B or AMH, estradiol, testosterone, would be useful in specific circumstances such as young age, or imaging suggesting a mucinous, or non-epithelial, or tumour of extra-adnexal origin.

SPECIALISED MULTIDISCIPLINARY DECISION-MAKING

C	Women with non-emergency clinical presentation and suspected adnexal/peritoneal malignancy should be referred to a specialist in gynaecological oncology ² .
✓	Surgery in low-volume and low-quality centres is discouraged. The existence of an intermediate care facility and access to an intensive care unit management are required. Participation in clinical trials is a quality indicator.
C	Treatment should be preoperatively planned at a multidisciplinary team meeting, after a workup aimed at ruling out (1) unresectable metastases and (2) secondary ovarian and peritoneal metastasis from other primary malignancies when family history, symptoms, radiological features, or Ca125/CEA ratio is suggestive. Informed consent of the patient must be obtained.
✓	All patients should be reviewed postoperatively at a gynaecological oncology multidisciplinary meeting.

² Certified gynaecological oncologist or, in countries where certification is not organized, by a trained surgeon dedicated to the management of gynaecologic cancer (accounting for over 50% of his or her practice) or having completed an ESGO-accredited fellowship.

SURGICAL MANAGEMENT FOR STAGE I-II OVARIAN CANCER (ALGORITHMS 1-2)

B	Midline laparotomy is recommended to surgically manage early ovarian cancers. Apparent stage I could potentially be managed laparoscopically by a gynaecological oncologist with the appropriate expertise able to perform an adequate surgical staging laparoscopically. Rupture of an intact primary tumour with spillage of tumour cells at the time of dissection and extraction of the specimen should be avoided.
B	Intraoperative rupture of a yet-unruptured adnexal mass should be avoided.
B	The availability of frozen section may allow the necessary surgical assessment to be completed at the time of initial surgery. It is understood that frozen section may not be conclusive and that definitive pathology is the gold standard of diagnosis.
✓	In the absence of frozen section or in the case of an inconclusive frozen section, a two-step procedure should be preferred.
✓	Total hysterectomy and bilateral salpingo-oophorectomy are standard.
C	Fertility-preserving surgery (unilateral salpingo-oophorectomy) should be offered to selected premenopausal patients desiring fertility ³ .
B	Laparoscopic restaging is an acceptable approach if performed by a gynaecologic oncologist with adequate expertise to perform a comprehensive assessment.
✓	Visual assessment of the entire peritoneal cavity is recommended.
C	Peritoneal washings or cytology, taken prior to manipulation of the tumour, are recommended.
C	When no suspicious implants are found in the pelvis, paracolic areas, and subdiaphragmatic areas, blind peritoneal biopsies are recommended.
C	At least infracolic-omentectomy is recommended.
B	Bilateral pelvic and para-aortic lymph node dissection up to the level of the left renal vein (with the exception of stage I expansile type mucinous adenocarcinomas) are recommended.
✓	When early carcinoma is incidentally found at surgery for a suspected 'benign' condition, second surgical procedure will be required when the patient has not been comprehensively staged.
✓	Reassessment for the only purpose of performing appendectomy is not mandatory even in case of mucinous histology if the appendix has been examined and found normal.

³ Discussion on fertility must be mentioned in the patient record; final decision is made after comprehensive staging surgery based on final stage and grade: fertility preservation is accepted in case of stage IA or IC1, low-grade serous or endometrioid carcinoma, or expansile type mucinous tumours; other stage I substages or pathologic subtypes, subject to individualised decision; uterine preservation with bilateral salpingo-oophorectomy can be considered in selected young patients with apparent stage IB low-risk invasive carcinoma and normal endometrial biopsy finding, but this is not standard management, and there are few data to support this policy.

SURGICAL MANAGEMENT FOR STAGE III-IV OVARIAN CANCER (ALGORITHMS 2-3)

✓	Midline laparotomy is required to manage stage III-IV ovarian cancers.
A	Complete resection of all visible disease is the goal of surgical management. Voluntary use of incomplete surgery (upfront or interval) is discouraged.
✓	Criteria against abdominal debulking are: <ul style="list-style-type: none"> • Diffuse deep infiltration of the root of small bowel mesentery; • Diffuse carcinomatosis of the small bowel involving such large parts that resection would lead to short bowel syndrome (remaining bowel < 1.5 m), • Diffuse involvement/deep infiltration of <ul style="list-style-type: none"> – Stomach/duodenum (limited excision is possible), and – Head or middle part of pancreas (tail of the pancreas can be resected); • Involvement of truncus coeliacus, hepatic arteries, left gastric artery (coeliac nodes can be resected).
✓	Metastatic (stage IVB) disease may be resectable. Central or multisegmental parenchymal liver metastases, multiple parenchymal lung metastases (preferably histologically proven), nonresectable lymph node metastases, and multiple brain metastases are not resectable.
A	Primary surgery is recommended in patients who can be debulked upfront to no residual tumour with a reasonable complication rate.
✓	Risk-benefit ratio is in favour of primary surgery when: <ul style="list-style-type: none"> • There is no unresectable tumour extent • Complete debulking to no residual tumour seems feasible with reasonable morbidity, taking into account the patient's status. Decisions are individualised and based on multiple parameters⁴. • Patient accepts potential supportive measures as blood transfusions or stoma.
A	Interval debulking surgery should be proposed to patients fit for surgery with response or stable disease compatible with complete resection.
✓	If a patient did not have the opportunity of surgery after 3 cycles, then a delayed debulking after more than 3 cycles of neoadjuvant chemotherapy may be considered on an individual basis.
✓	A patient with inoperable tumour who progresses during neoadjuvant chemotherapy should not be operated unless for palliative reasons that cannot be managed conservatively. Careful review of pathology in serous adenocarcinoma (possible lowgrade) and additional workup in mucinous adenocarcinoma (possible GI tract secondary) is recommended when applicable in this circumstance.

⁴ Examples of potentially resectable extra-abdominal disease:

- Inguinal or axillary lymph nodes,
- Retrocrural or paracardiac nodes,
- Focal parietal pleural involvement,
- Isolated parenchymal lung metastases.

Examples of resectable intra-abdominal parenchymal metastases:

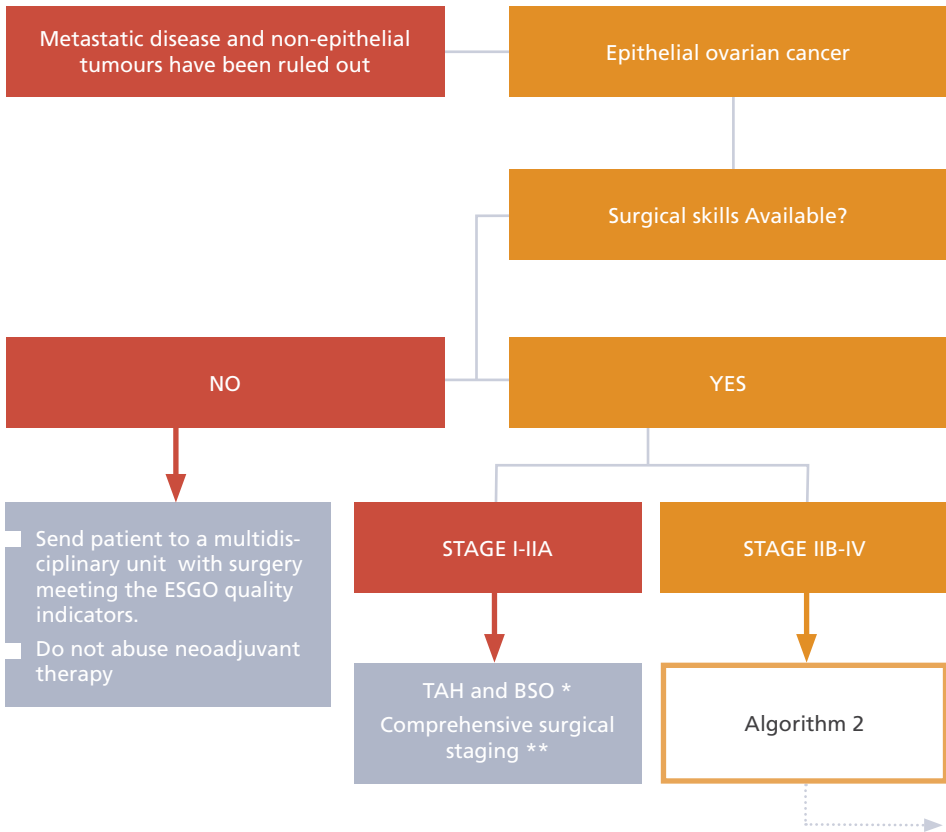
- Splenic metastases,
- Capsular liver metastases,
- Single deep liver metastasis, depending on the location.

MINIMUM REQUIRED INFORMATION

✓	All necessary information about sites and size of the disease, tumour dissemination patterns, resections performed, and residual disease should be available in the operation protocol.
✓	The operation protocol should be systematically structured. Tumour dissemination patterns with site and size of the tumour lesions should be described at the beginning of the operation protocol.
✓	All areas of the abdominal and pelvic cavity should be evaluated and described.
✓	All the completed surgical procedures should be mentioned.
✓	If any, the size and location of residual disease should be described at the end of the operation protocol. Reasons for not achieving complete cytoreduction must be defined.
✓	At the minimum, the information contained in the ESGO operative report must be present.
✓	The pathology report should contain all necessary information.
✓	Surgical morbidity and mortality should be assessed and recorded, and selected cases should be discussed at morbidity and mortality conferences.

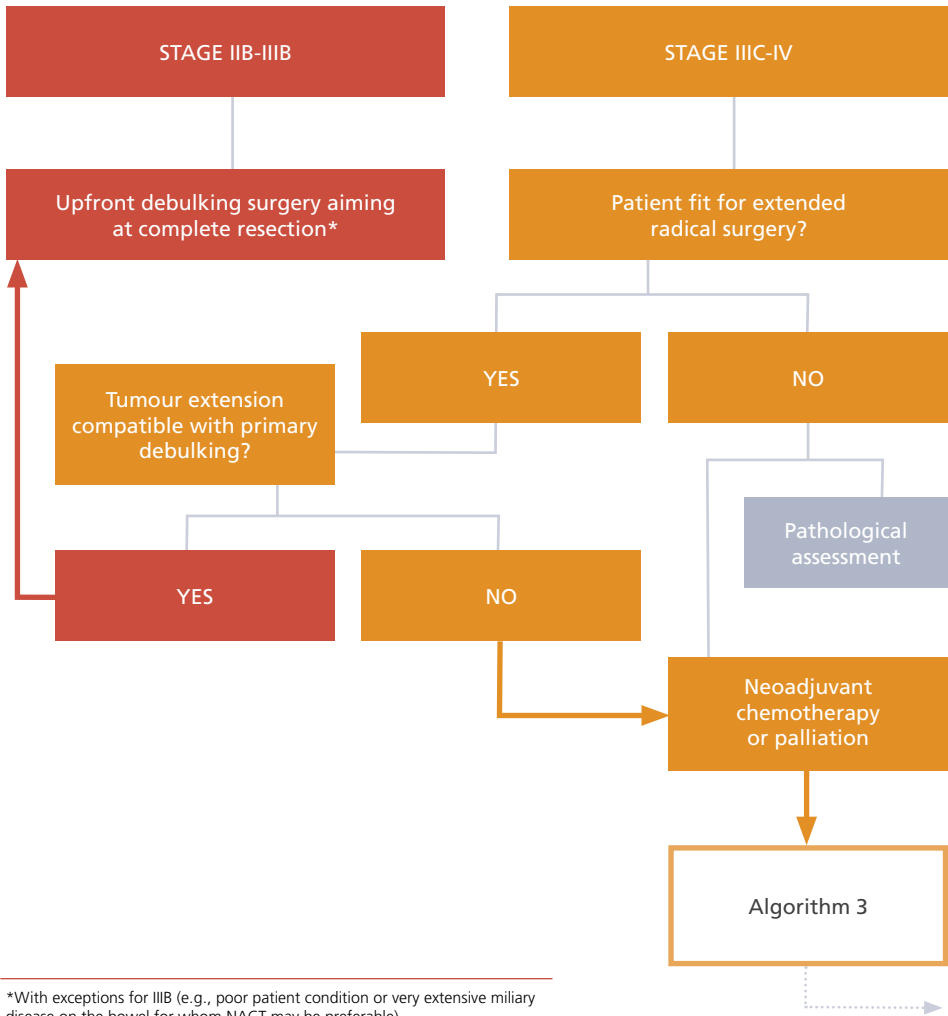
⁵ Pathologic type and grade, performance status, nutritional status, albumin level, comorbidities, when applicable oncogeriatric assessment, imaging and/or exploratory laparoscopy or laparotomy, location of disease, number of bowel anastomoses.

ALGORITHM 1 FOR EPITHELIAL OVARIAN CANCER SURGERY



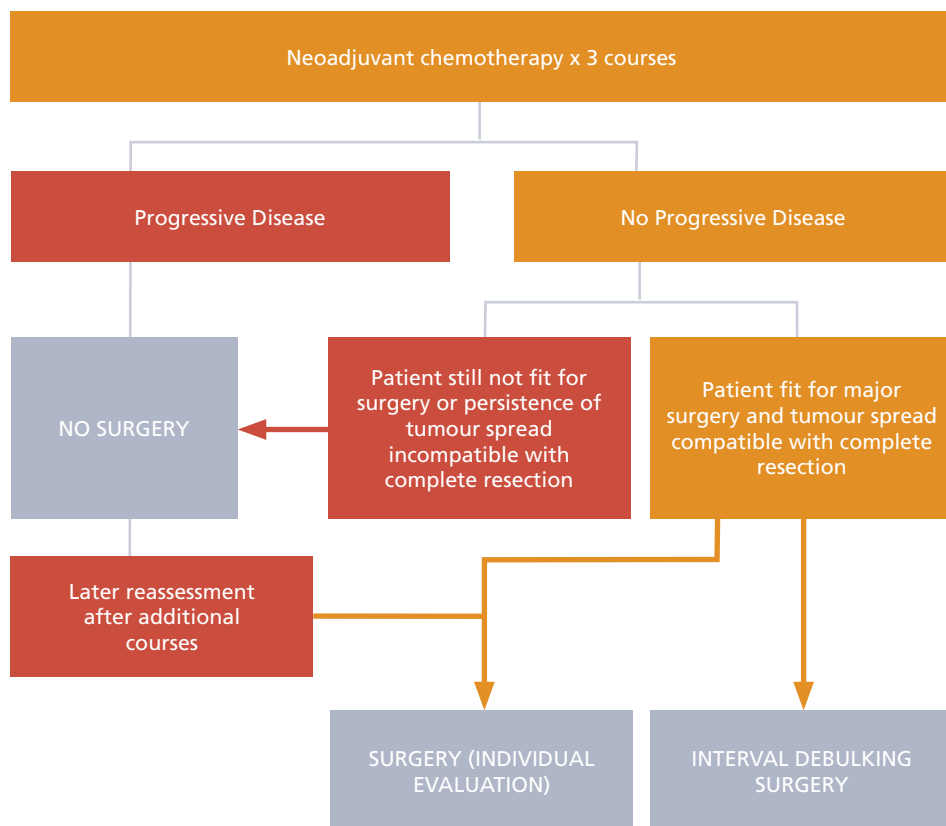
* Consider fertility preservation in selected young patients,
 ** With exceptions for retroperitoneal staging (see specific recommendations on surgery of early-stage ovarian cancer)

ALGORITHM 2 FOR EPITHELIAL OVARIAN CANCER SURGERY



*With exceptions for IIB (e.g., poor patient condition or very extensive miliary disease on the bowel for whom NACT may be preferable)

ALGORITHM 3 FOR EPITHELIAL OVARIAN CANCER SURGERY



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