

# Aspects of Early Epithelial Ovarian Cancer

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The definition of early ovarian cancer is inevitably difficult and open to several interpretations. With these restrictions in mind early ovarian cancer in this discussion will be limited to epithelial ovarian cancer which is restricted to the pelvis. The FIGO staging classification for gynaecological malignancies stipulates that in this respect stages I and II should be included in this discussion (Table 1).

## Epidemiology

The age adjusted incidence of ovarian cancer has a range of 2 - 4 per 100.000 women in developing countries. In developed countries the incidence may be up to 15 per 100.000. The lower incidence in developing countries may be a result of incomplete reporting, although other factors, including socio-economic factors and diet may play a role.

The age-specific incidence rates range from 2 per 100.000 women between 20 and 29 and increases to 55 per 100.000 women at the age of 70 years.

Borderline epithelial carcinomas tend to be found in younger patients with almost 50% of these tumours occurring in patients younger than 40 years. In contrast, just over 10% of frankly invasive ovarian cancers are found in patients younger than 40 years of age.

## Histopathology

The majority of all primary ovarian cancers arise from the coelomic epithelium or mesothelium. The international histological classification by the World Health Organisation has been universally accepted (Table 2).

## Symptoms and pre-operative evaluation

Abdominal pain and swelling are the two most frequent reported complaints. These are often mild, intermittent chronic and usually persist for months, such that even if the patient consults a doctor, another diagnosis such as irritable bowel syndrome may be entertained. Ovarian cancer has no

unique set of symptoms and can vary considerably at presentation. This often means that patients with rather vague symptoms present late for a diagnosis of ovarian cancer. It is therefore no surprise that by the time the diagnosis is made, almost 50% of patients will have disease that has metastasised from the ovary to the pelvis or the peritoneal cavity.

On clinical examination it is impossible to determine if an adnexal mass is malignant or not. However, ascites and/or a fixed mass with an irregular aspect in the posterior cul-de-sac found on vaginal and rectal examination should be a strong indication of a malignant tumour.

If there is a suspicion for an ovarian cancer the pre-operative evaluation and work-up should be comprehensive (Table 3).

**Table 1.**  
**FIGO Staging Classification for Ovarian Cancer**

<b>I Growth limited to the ovaries</b>
IA Growth limited to one ovary; no ascites. No tumour on the external surface; capsule intact.
IB Growth limited to both ovaries; no ascites. No tumour on the external surfaces; capsules intact.
IC Tumour either Stage IA or IB but with tumour on the surface of one or both ovaries; or with capsule ruptured; or with ascites present containing malignant cells or with positive peritoneal washings.
<b>II Growth involving one or both ovaries with pelvic extension.</b>
IIA Extension and/or metastases to uterus and/or tubes.
IIB Extension to other pelvic tissues.
IIC Tumour either IIA or IIB but with tumour on surface of one or both ovaries; or with capsule(s) ruptured; or with ascites containing malignant cells or with positive peritoneal washings.
<b>III Tumour involving one or both ovaries with peritoneal implants outside the pelvis and/or positive retroperitoneal or inguinal nodes. Superficial liver metastases equal Stage III. Tumour is limited to the true pelvis but with histologically verified malignant extension to small bowel or omentum.</b>
IIIA Tumour grossly limited to the true pelvis with negative nodes but histologically confirmed microscopic seeding of abdominal peritoneal surfaces.
IIIB Tumour of one or both ovaries with histologically confirmed implants of abdominal peritoneal surfaces, none exceeding 2cm in diameter. Nodes negative.
IIIC Abdominal implants >2cm in diameter and/or positive retroperitoneal or inguinal nodes.
<b>IV Growth involving one or both ovaries with distant metastases. If pleural effusion is present there must be a positive cytology result to allot a case to Stage IV. Parenchymal liver metastases equal Stage IV.</b>

## early epithelial ovarian cancer

### Diagnosis, staging and surgical treatment:

The ultimate diagnosis of early ovarian cancer is made at surgery, and even though one may be highly suspicious of the diagnosis pre-operatively, the diagnosis is surgical and not radiological or clinical. A good understanding of the patterns of spread of ovarian cancer is mandatory.

### Epithelial ovarian cancers spread along three patterns:

#### A. Transcoelomic:

Exfoliating cells from the cancer migrate with the circulation of peritoneal fluid along the para-colic gutters to the diaphragm, liver surface and the pouch of Douglas. Malignant cells may spread by migration to the omentum and surfaces of small and large bowel.

#### B. Lymphatic:

Malignant cells may spread via the lymph channels along the infundibulo-pelvic ligaments to the para-aortic lymph node stations. May spread to the iliac and even inguinal lymph node stations

#### C. Haematogenous:

Haematogenous spread is uncommon and may involve spread to the liver and lungs in only up to 5% of cases.

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The operation for ovarian cancer which ultimately incorporates the definitive surgery and at the same time a staging laparotomy, should start with entry into the abdominal cavity through a vertical incision which will allow for adequate access to both the pelvis as well as the upper abdomen. After clinical assessment that the cancer

is confined to the pelvis and thus seemingly is an early ovarian cancer, fluid is aspirated from POD and para-colic gutters and wipes from diaphragm (right and left) for cytological assessment. If no fluid is found, washings should be performed by instilling and recovering up to 100 ml of saline from these sites. This is followed by random peritoneal biopsies from the same sites. These procedures are important as positive washings in an ovarian cancer seemingly confined to the ovary or ovaries places the patient in a prognostically unfavourable stage IIC (Table 1). Moreover, in case of positive random biopsies from extra-pelvic sites the patient is deemed to have at least stage III disease (Table 1) with far reaching consequences for post-operative treatment and ultimately prognosis. A careful exploration of the pelvis and abdomen must then take place to primarily exclude spread of disease from the pelvis. Any suspicious areas or adhesions should be biopsied.

The surgical treatment of early ovarian cancer should include a total abdominal hysterectomy and bilateral salpingo-oophorectomy followed by an infracolic omentectomy. If a solitary ovarian cancer is found the tumour should be removed intact to avoid the occurrence of surgical spill. A frozen section may be helpful if there is uncertain-

**Table 2.**

### Histological classification of Epithelial Ovarian Cancer

1. Serous
2. Mucinous
3. Endometrioid
4. Brenner tumour
5. Mixed epithelial
6. Undifferentiated
7. Unclassified

ty if the tumour is malignant or not. Careful notes should be made of size and site of any residual tumour.

The retroperitoneal spaces should be dissected and explored to evaluate the pelvic lymph nodes. Palpation of these nodes through the peritoneum is notoriously inaccurate. Any enlarged nodes should be resected and submitted separately for histological evaluation. Similarly, the para-aortic nodes should be palpated and, if indicated fine needle aspiration and/or excision of suspicious para-aortic nodes should be carried out.

The presence of a gynaecologic oncology specialist during surgery is relevant in order to perform appropriate staging procedures as well as surgical treatment. In patients where such a specialist is not present, understaging may be a problem. Up to 30% of patients presumed to have early stage ovarian cancer as a result of inadequate primary operation will be upstaged after a second thorough exploration with the omentum, pelvic and para aortic lymph nodes and diaphragm being the sites where metastases are commonly missed, if not looked out for.

The role of conservative surgery may be considered in patients who desire to preserve fertility. Conservative surgery in this context should include careful surgical staging and removal of the affected ovary and an adequate infra-colic omentectomy. Ideally, the histology should indicate either a borderline carcinoma or at most a well differentiated epithelial malignancy. These patients should be followed carefully with routine pelvic

**Table 3: Standard pre-operative evaluation**

- Full Blood Count, Renal/liver function test.
- Tumour markers: CA125.
- If significant bowel symptoms or occult blood positive: gastroscopy/colonoscopy or barium studies.
- Careful breast palpation (mammography if indicated).
- CXR. U/S of liver and/or CT scan for liver metastases if suggested by radiologist. CT scan or MRI to be performed on an individualised basis.
- Diagnostic ascitic tap ñ fluid for micro/ cytology/ chemistry.
- Refer gynaecological oncology specialist.
- Book frozen section.
- Start anti-coagulative measures.
- Intermittent pneumatic compression/ or TED stockings.

examinations, ultrasound and serial CA 125 serum levels. The presence of a gynaecological oncologist may be helpful in case of an ensuing Caesarian section to assess the possibility of unsuspected existence of malignant tissue or cells. Generally, the other ovary and uterus are removed at the completion of childbearing.

### Adjuvant treatment

The long term prognosis of ovarian cancer with disease limited to ovaries and/or pelvis (10 year survival up to 70%) is better than that of patients with advanced ovarian cancer (10 year survival up to 25%). Nevertheless, up to 50% of women with early stage epithelial ovarian cancer eventually develop a recurrence and die from the disease.

The most active agent for adjuvant treatment for epithelial ovarian cancer is a platinum compound administered either as a single agent or in combination with other cytotoxics and given cyclically with 3 or 4 weeks intervals.

It is generally accepted that patients with stage II disease with extra ovarian disease, but confined to the pelvis, require 6 cycles of adjuvant chemotherapy. Secondly, it is common practice to treat patients with tumour on the surface of the ovary or ovaries (Stage IC)

with 4 cycles of adjuvant chemotherapy. Similarly, patients with stage I disease where the histology indicates a poorly differentiated tumour should be treated with 4 cycles of adjuvant chemotherapy.

### Conclusions:

- Early epithelial ovarian cancer has the same age distribution as advanced ovarian cancer. Borderline ovarian cancer is however found in younger patients.
- Comprehensive staging is imperative in patients with seemingly early ovarian cancer.
- Patients with either a poorly differentiated epithelial cancer and/or ovarian surface involvement or with spread to the pelvis should have adjuvant treatment.
- Up to 50% of patients with early ovarian cancer will develop recurrent disease.

### References on request

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