

DIAGNOSIS AND THERAPEUTIC MANAGEMENT OF OVARIAN CANCER LITERATURE REVIEW

CHAHIRA MAZOUZI

Medical Oncology CHU Bejaia.

RADIA BENYAHIA

Diagnostic Radiology CPMC Algiers.

NADJIA FERRAH

Medical Oncology CHU Bejaia.

BOUALEM BELLOUSE

Gynecology CHU Bejaia.

Abstract

According to the latest WHO data published in 2020, deaths from Ovarian Cancer in Algeria reached 611 or 0.33% of total deaths. Clinically, the ovarian tumor is often cystic but due to the deep location of the ovaries it can reach a significant volume before causing symptoms which can be very varied and are never specific. Ultrasound must be considered as a true extension of the clinical examination. Performed by the suprapubic route with a full bladder and by the transvaginal route with an empty bladder, it must be supplemented at the abdominal and retroperitoneal levels and can benefit from the contribution of color Doppler ultrasound. It is recommended that suspicious adnexal masses or ovarian tumors apparently in early stages be preferentially managed by oncological surgical teams trained in this pathology. Chemotherapy is a weapon that can be used as a first aid in advanced stages or as an adjuvant after a surgical procedure. The aim of our article is to illustrate existing therapies for these malignant tumors.

INTRODUCTION

Ovarian cancer is the sixth most common cancer in women (and the 18th in total of the most common cancers) worldwide. Around 239,000 cases were recorded in 2012, representing almost 4% of all new cases of cancer among women (2% in total), and is the eighth most common cause of cancer death among women worldwide (14th in total) [1]. In Algeria (**Table 1**) it is the third gynecological cancer among woman after breast and cervical cancer [1]. Across the world, age-standardized incidence rates vary more from 11 per 100,000 women in Central and Eastern Europe to less than 5 per 100,000 in parts of Africa. Incidence rates are 11.7 per 100,000 at United Kingdom, 8.0 per 100,000 in the United States, 5.2 per 100,000 in Brazil and 4.1 per 100,000 in China. A global epidemiological assessment shows that ovarian cancer affects especially women between 60 and 70 years old but the possibility of earlier attacks is linked to a hereditary predisposition in patients with family ties to first degree [2]. According to the latest WHO data published in 2020, deaths from Ovarian Cancer in Algeria reached 611 or 0.33% of total deaths. [3, 4] The aim of our article is to illustrate existing therapies for these malignant tumors,

Table 1: Main Locations of Female Cancers in Algiers in 2018

Localisations primitives	Effectifs	Fréquence relative (%)	Incidence brute	Incidence standard
Sein	1525	37,2	82,4	76,5
Colon-rectum	456	11,1	24,6	23,5
Thyroïde	344	8,4	18,6	15,9
Ovaire	174	4,2	9,4	9,3
Système hématopoïétique	142	3,5	7,7	6,8
Col utérin	142	3,5	7,7	7,2
Estomac	124	3	6,7	6,2
Encéphale	95	2,3	5,1	5,2
Ganglion lymphatique	96	2,3	5,2	5,03
Peau (carcinomes basocellulaires exclus)	89	2,2	4,8	5,2

Clinically, the ovarian tumor is often cystic but due to the deep location of the ovaries it can reach a significant volume before causing symptoms which can be very varied and are never specific. We will encounter more or less vague pelvic or abdominopelvic pain radiating into the lower back or inguinal regions; a progressive increase in volume of the abdomen which may be due to the tumor volume and/or ascites;

- Bleeding or abnormal genital discharge
- Disorders due to compression caused by the tumor more or less enclosed in the small pelvis: o intestinal transit disorders, recent constipation, false urges, subocclusion o dysuria or pollakiuria or incontinence by bladder compression o more rarely edema of a limb lower or phlebitis or sciatica due to venous or radicular compression
- Dyspnea may be revealing due to pleural effusion concomitant with ascites. Sometimes, we will encounter a simple abdominal discomfort associated with a discreet alteration of the general condition and often a careful questioning will reveal that these disorders have existed for several months, already indicating a long period of evolution of the disease. Faced with such vague and uncharacteristic symptoms, we must know how to think about ovarian cancer and carry out a careful gynecological examination.

Ultrasound must be considered as a true extension of the clinical examination. Performed by the suprapubic route with a full bladder and by the transvaginal route with an empty bladder, it must be supplemented at the abdominal and retroperitoneal levels and can benefit from the contribution of color Doppler ultrasound. This is an extremely sensitive examination capable of identifying simple follicles on the surface of the ovary. The problem is more one of looking for suspicious signs of malignancy. It is also an operator-dependent examination which benefits from the operator's experience. However, the certainty of benignity or malignancy can only be confirmed by histological analysis. Ultrasound allows exploration of the ovaries, the uterus and its cavity, the peritoneal

cavity, the liver, the kidneys and in favorable circumstances the retroperitoneal lymph node chains. Ultrasound will easily highlight a latero -uterine mass and will make it possible to describe its characteristics:

- side
- size
- echogenicity,

That is to say structure. Most of the time it will make it possible to affirm that it is this is an adnexal mass. These are:

- Either liquid, then they are cysts
- Either solid, more or less homogeneous
- Or mixed, more or less heterogeneous

The simplest appearance is that of an anechoic cyst, that is say pure echo-vacuum and thin-walled fluid associated with no other pelvic abnormality. In women during periods of genital activity, when this cyst remains of modest volume (5 to 6 cm), it suggests above all a functional cyst. It should not be the subject of an aggressive attitude but must be recontrolled after 1 or 2 menstrual cycles because in this case it regresses spontaneously. Its persistence would indicate its organicity and would merit additional exploration because the risk of malignancy cannot be formally excluded even if it is low (1 to 2%). The same cyst after menopause is organic, the risk of malignancy reaches 5 to 7% even in the presence of reassuring characteristics and surgical exploration is essential. Apart from the simple cyst, any complexity of the ultrasound appearance increases the suspicion of malignancy without always confirming it. Thus the cysts can be multiple or multilocular with the presence of septa, the thickness and vascularization of which can be assessed more precisely using Doppler ultrasound. The cysts can be heterogeneous with the presence of more or less fleshy tissue areas or even calcifications. These aspects reinforce the suspicion of malignancy but can also correspond to benign lesions: for example, dermoid cysts which are mature dysembryomas (teratomas) that can be encountered in young women generally contain fatty tissue, sometimes skin appendages.

Or even bone or dental blanks. Mucinous cysts are often large and/or multilocular and endometriotic cysts contain a thick fluid whose sedimentation is sometimes echogenic. The discovery of a homogeneous tissue tumor does not necessarily indicate malignancy but can lead to confusion with a possibly pedunculated subserosal uterine fibroid. Fibroids or fibrotecomas of the ovary exist and reinforce this risk of confusion; presumptive arguments are provided by comparison with the echogenicity of the uterus and the presence or absence of other uterine leiomyomas. Otherwise, surgical exploration will correct the diagnosis. The major sign of malignancy is the irregularities of the internal or external walls of the mass which can take the appearance of more or less thick and more or less confluent vegetations. The presence of a few vegetations (less than 5) is not necessarily a sign of malignancy, but numerous thick and confluent vegetations inside

and outside the mass must be considered malignant without it being possible to decide between true malignancy and attenuated malignancy (“borderline”). Doppler ultrasound is interesting for exploring the vascularization of the cyst of its partitions and/or its vegetations: the neovascularization which accompanies neoplastic lesions is characterized by its richness (hypervascularization) and its rapid circulation speed (decrease in resistivity). The observation of suspicious signs, in particular heterogeneity and vegetations, must complete the exploration at the pelvic and abdominal levels. The other ovary and uterus should be examined because bilateral malignant lesions are common and endometrial metastases are possible, leading to ultrasound thickening of the uterine mucosa. The Douglas must be the subject of particular attention because ascites fluid can accumulate there and we can find the vegetative appearance of carcinomatous nodules. Abdominal exploration must be complete and look for fluid effusion at the upper level (retro- and subhepatic, Morisson space) and carcinomatous nodules at the level of the diaphragmatic domes, the parietal peritoneum and the omentum where they can be particularly bulky.

Contribution of other Imaging Techniques [115 -126]

In fact, from the moment the diagnosis of an organic adnexal mass is raised, surgical exploration at least by laparoscopy is necessary to access the histological diagnosis and eliminate a malignant lesion.

CT and MRI are therefore of limited use in determining the indication for surgery. They may, however, be of interest in advancing the characterization of certain lesions:

- The hematic content of endometriotic cysts would have a fairly characteristic signal on MRI which could thus allow the diagnosis to be made in a suggestive clinical context
- The dermoid cyst can be diagnosed using on the scanner which will easily highlight its characteristic fatty content as well as its calcifications which are visible from the abdomen x-ray without preparation.
- For certain teams, when malignancy is confirmed as well as the presence of peritoneal carcinomatosis, the CT scan would be useful to better appreciate the importance and distribution of peritoneal carcinomatosis, especially at the upper level of the abdomen. This examination is then interesting to better assess the chances of complete resection of the peritoneal disease. CT is also the best examination for exploring the pelvic and lumbo-aortic retroperitoneal lymph node chains. Finally, in cases of peritoneal carcinomatosis and ascites, a chest x-ray is essential to detect possible pleural effusion frequently associated in stages IV of ovarian disease.

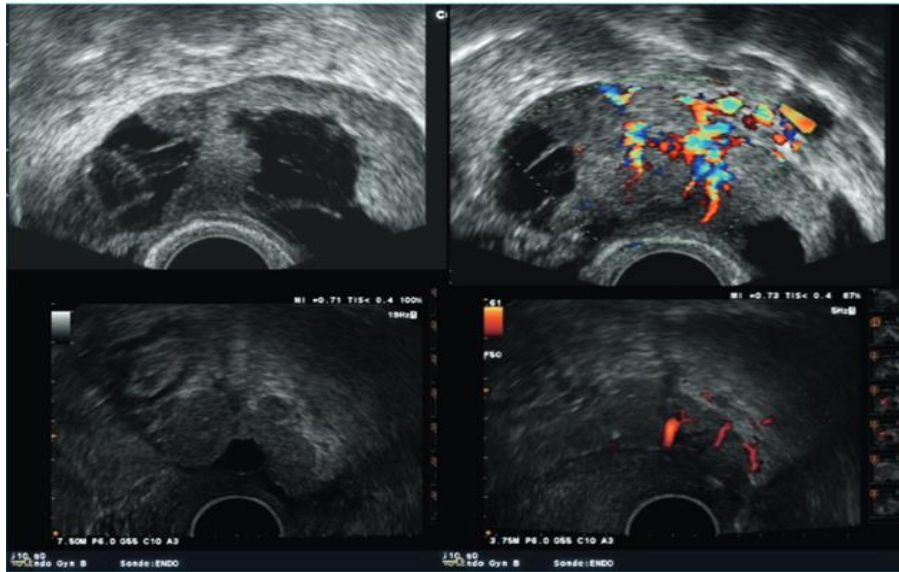


Figure: Typical Appearance of Ovarian Cancer on Endovaginal Ultrasound with Doppler.

It is a semi-solid, semi-cystic tumor with a solid portion that is highly vascularized Doppler. In addition, there is peritoneal thickening made of nodules which are also very vascularized Doppler. This ultrasound appearance is typical of invasive ovarian cancer. The only imaging necessary in these cases is to assess the extent of the disease.

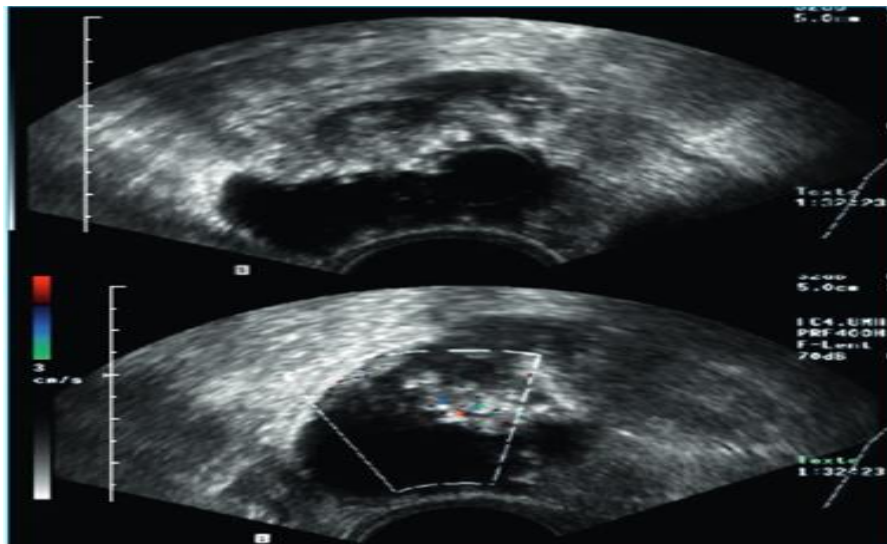


Figure: Ultrasound Appearance of an Ovarian Cystadenofibroma.

This is a tumor presenting a solid Doppler vascularized portion which can easily be confused with ovarian cancer. The optimal course of action when faced with this type of image is to make an ultrasound diagnosis of a complex adnexal mass and to request pelvic magnetic resonance imaging for characterization.

Therapeutic Management

Early Stages: It is recommended that suspicious adnexal masses or ovarian tumors apparently in early stages be preferentially managed by teams trained in this pathology. (See advanced stage recommendations). The pre-therapeutic assessment is the same as that for advanced stages.

- Pelvic MRI is useful for preoperative characterization of the adnexal mass.
- In young women wishing to preserve their fertility, having a priori an early stage, an oncofertility consultation is essential.

This discussion should be added to the other discussions carried out during the CPR (see AP-HP framework: Fertility preservation, April 2016). Standard surgical treatment must include peritoneal cytology, excision of the 2 appendages, hysterectomy, at least infracolic omentectomy, appendectomy, pelvic and aorticacaval lymphadenectomy, as well as multiple peritoneal biopsies performed in each quadrant of the 'abdomen. Young patients wishing to preserve their fertility potential can benefit from conservative treatment. The complete recommendations are detailed in the AP-HP Fertility Preservation standard, April 2016. We simply recall that the intervention must include excision of the affected appendix (stages IA), and all the staging procedures (on the other hand systematic biopsy of the preserved ovary is not recommended). The main indications are:

- Low-grade serous form, stage IA or IC1. Curages are not indicated in cases of stage IA.
- Endometrioid form of grade 1 or 2, stages IA or IC1 (an endometrial curettage must be associated)
- Mucinous form of stage IA, IB, IC1. Curages are not indicated in cases of expansive variety at stage IA. Conversely, grade 3 tumors, clear cell cancers and stages IB, IC2 and IC3 are contraindications
- This intervention can be carried out by laparotomy or laparoscopy, provided that the operator is trained and that the approach does not influence the result of the intervention.

The operative report must provide an analytical description of the lesions. Indication for chemotherapy according to the opinion of oncologists:

- 3 to 6 cycles of carboplatin taxol (rather 6 in high-grade serous).
- Formal indication in high grade serous. • To be discussed on a case by case basis in RCP in other cases.

Advanced Stages

The blocking points for initial surgery are as follows:

- Diffuse carcinomatosis reaching the ileal serosa and/or the mesentery, requiring extensive resection (short bowel syndrome)
- Significant and deep infiltration of the root of the mesentery
- Complete resection obtained at a cost a total colectomy and/or a gastrectomy
- Deep infiltration of the hepatic pedicle Referral towards primary surgery or neoadjuvant chemotherapy must be taken during an RCP bringing together the following professionals:
- Surgeon trained in pathology ovarian
- Pathologist trained in ovarian pathology
- Radiologist trained in ovarian pathology
- Medical oncologist trained in ovarian pathology

In case of primary surgery

- The intervention must be carried out on a patient who is informed of the objective of the intervention, the procedures probably necessary, usual risks and the patient circuit.
- The objective of the intervention is the complete macroscopic resection of the lesions.
- The operative report must give an analytical description of the carcinomatosis at the start of the intervention with calculation of the ICP.

It is also necessary to make an analytical description of the residual lesions if necessary using the CCR score.

- The intervention must include at least a complete exploration of the abdomen and pelvis, a non-conservative total hysterectomy, a total infra-gastric omentectomy, an appendectomy, pelvic and aortic - caval dissections in the event of complete peritoneal resection.
- Other procedures such as peritoneal or digestive resections will be carried out in a manner adapted to the extent of the disease. Creating a protective stoma should not be systematic. Early closure (on day 8) of a protective ileostomy must be discussed on a case-by-case basis.
- The intervention must be preceded by a nutritional assessment, correction of malnutrition and pre-operative enteral nutrition. Systematic.
- Anesthesia must be carried out by a professional trained in cancer surgery. The patient must be able to benefit from a systematic passage to surgical intensive care or surgical intensive care.

In the Case of Neoadjuvant Chemotherapy –

Neoadjuvant chemotherapy may be preferred in patients with a medical contraindication to first-line surgery, if the extension of the carcinomatosis does not allow reasonable consideration of complete resection (need for the opinion of a trained team) or in the case of extra-peritoneal location (carcinomatous pleural effusion for example).

- The standard is to carry out 3 or 4 cycles of chemotherapy combining carboplatin (AUC 5) and paclitaxel (175 mg/m²) every 21 days. It is recommended to organize from the start of chemotherapy, the clinical and radiological assessment carried out immediately following the 3rd cycle as well as to organize interval surgery (consultation, operating room, etc.) after the 3rd cycle or after an additional waiting cycle.
- Interval surgery is performed and organized in the same way as the initial surgery.
- An RCP must validate the feasibility and indication of the intervention. It is recommended to perform a laparoscopy at the start of the procedure in order to check the feasibility of a complete procedure.
- For patients undergoing more than 4 cycles of neoadjuvant chemotherapy, it will be necessary to perform at least 2 cycles of chemotherapy after the procedure.
- Anti-angiogenics or other molecules are not recommended before interval surgery.

❖ Post-operative Treatments for Advanced Stages

Primary surgery with complete resection:

- Chemotherapy comprising carboplatin (AUC5 or 6) and paclitaxel (175 mg/m² 3 hours) will be delivered up to a total of 6 cycles. Bevacizumab (15 mg/kg, continued for 12 months as monotherapy) may be combined (delay the initiation of bevacizumab to cycle 2 or even 3 in the event of surgery with resection of hollow organs or parietal healing disorder).
- The time for initiation of chemotherapy must be as short as possible and take into account the surgical procedures performed. - Additional administration of chemotherapy intraperitoneally constitutes an option which will be discussed in the RCP (4-5). Weekly administration of paclitaxel (80 mg/m² without interruption) is an option.

Initial Surgery Including a Macroscopic Tumor Remnant:

- We will use a combination of carboplatin , paclitaxel and bevacizumab with the same recommendations as previously, First surgery with complete resection) (delay the initiation of bevacizumab to cycle 2 or even 3 in the case of surgery with resection hollow organs or parietal healing disorder).

3) In case of neoadjuvant chemotherapy:

- After interval surgery, chemotherapy comprising paclitaxel and carboplatin is resumed up to a total of 6 cycles

1) Primary surgery with complete resection)

- Bevacizumab is added with the same recommendations as previously (28 days after surgery, this period being extended in the case of digestive anastomosis).

F. Inoperable patient, including after neoadjuvant chemotherapy Continuation of chemotherapy with possible addition of bevacizumab to be discussed in CPR.

Monitoring after Treatment

During the first year, a clinical examination with dosage of appropriate markers (CA 125) must be carried out every 3 months. It is wise to alternate consultations with the oncologist and the referring surgeon and gynecologist. There is no indication for systematic imaging unless there is residual lesion.

Diagnosis and Treatment of a Biological Relapse

Relapse is suspected clinically and/or confirmed in the event of a doubling of the CA 125 level (confirmed on a 3rd sample) and on imaging. The assessment must include a complete clinical examination and a thoraco- abdomino- pelvic CT scan. A PET CT scan can be associated in the event of a normal scan.

Treatment of Relapse

Treatment must be decided during an RCP comprising at least a surgeon, a medical oncologist, a radiologist and a pathologist, trained in ovarian pathology. It is recommended not to initiate treatment before the appearance of symptoms or at least lesions visible on imaging if the time between the end of initial treatment and relapse is greater than 12 months. Platinum-resistant relapse (less than 6 months after the end of treatment) or refractory (progression under treatment)

- There is no surgical indication, except for patients who have not received surgery meeting quality criteria aforementioned.
- It is recommended to use mono-chemotherapy with doxorubicin liposomal pegylated (40 mg/m² every 4 weeks), or weekly paclitaxel (80 mg/m², 3 weeks out of 4) or topotecan (1.25 mg/m² D1 to D5 every 21 days to be adapted to renal function , or 4 mg/m² weekly), or gemcitabine (1 g/m² weekly).
- Bevacizumab (15 mg/kg) can be given in combination with monochemotherapy if the patient has not already received bevacizumab and if the resistant relapse occurs in the 1st or 2nd ^{relapse} (AMM).

Intermediate platinum relapse (6 to 12 months after the end of treatment)

- The benefit of surgical intervention should be discussed. The AGO score must be calculated.
- In the event of a decision for chemotherapy, it is recommended to use carboplatin (AUC 5) combined with doxorubicin liposomal pegylated (30 mg/m²) every 4 weeks, or carboplatin (AUC4) combined with gemcitabine (1 g/m² D1 and D8) every 3 weeks, or carboplatin combined with paclitaxel or doxorubicin liposomal pegylated (30 mg/m²), combined with trabectedin (1.1 mg/m²) every 3 weeks.
- Bevacizumab (15 mg/kg) may be given in addition to platinum-based chemotherapy if the patient has not already received it and in the event of a first relapse.

1 Sensitive platinum relapse (more than 12 months after the end of the treatments)

- The treatment must be decided during an RCP comprising at least a surgeon, a medical oncologist, a radiologist and a pathologist, all trained in ovarian pathology. It is recommended not to initiate treatment before the appearance of symptoms or at least lesions visible on imaging.
- The benefit of surgical intervention must be discussed. The AGO score must be calculated.
- If chemotherapy is decided, it is recommended to use carboplatin combined with doxorubicin liposomal pegylated, or carboplatin combined with gemcitabine , or carboplatin combined with paclitaxel or doxorubicin liposomal pegylated , associated with trabectedin .
- Bevacizumab may be given in addition to platinum-based chemotherapy if the patient has not already received it and in the event of a first relapse.
- Olaparib is indicated for maintenance of platinum-based chemotherapy for patients with constitutional or tumor mutation of BRCA1 or BRCA2:

o when the constitutional BRCA status is unknown, a rapid coordinated circuit is activated, which involves consultations, RCPs and the corresponding laboratories, with results expected in 6 to 8 weeks:

- An oncogenetics consultation must take place within 15 days with implementation of an emergency constitutional test. This test can be initiated by the oncologist who ensures the intervention of an oncogenetics consultation.
- In parallel, the search for a BRCA 1/2 tumor mutation can be initiated by the oncologist or oncogeneticist ,
- The results which determine the treatment are reported by the oncologist who ensures that a prior oncogenetic consultation has taken place and plans the next one for the result. In the event of no family history and a negative result for the BRCA

mutation search, the question is asked to the oncogeneticist about the need for a second oncogenetics consultation.

o In the absence of a constitutional mutation of BRCA1/2, the search for a tumor mutation of BRCA 1/2 is initiated by the oncologist who returns the results, transmits them to the oncogeneticist and, if possible, to the laboratory who carried out the constitutional test.

I - Elderly patients (>75 years)

The care of elderly patients is generally comparable to that of other patients. It will simply be necessary to add a systematic consultation with an oncogeriatrician . The surgical intervention, whether carried out as first intention or after neoadjuvant chemotherapy, must take into account the fragility of the patient.

The options are:

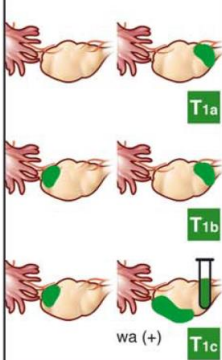
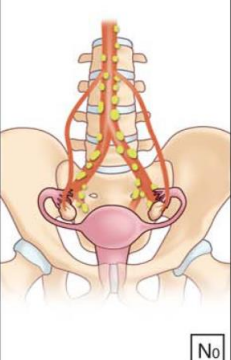
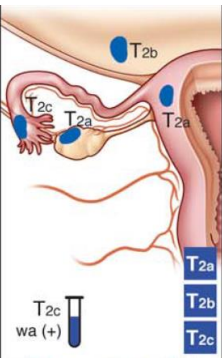
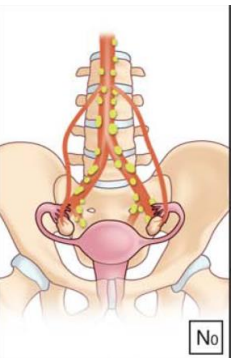
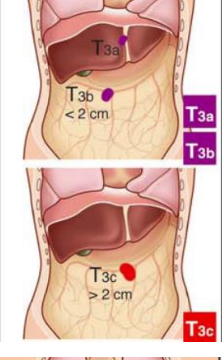
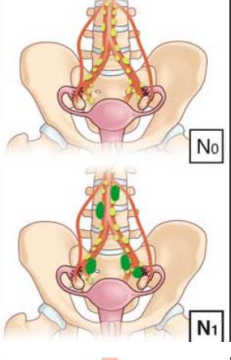
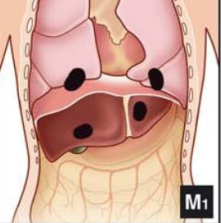
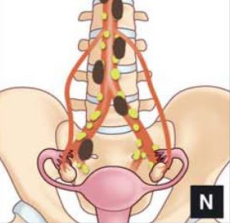
- monotherapy with carboplatin AUC 5 q3 to 4 s
- carboplatin - fractionated paclitaxel (carboplatin AUC 5, D1 and paclitaxel 80 to 90 mg/m² D1&8, q3s)
- carboplatin -paclitaxel weekly (carboplatin AUC 2, combined with paclitaxel 60 mg/m² every week)
- Carboplatin AUC 5, combined with paclitaxel 175 mg/m² every 3 weeks. Bevacizumab may be used after verifying the absence of contraindications.

Oncogenetic Consultation

Patients must benefit from an oncogenetic consultation from the initial treatment, apart from mucinous or non-epithelial histology, regardless of the age at which the diagnosis is revealed. Information relating to a search for constitutional mutation is delivered with a proposal for this search and signature of an ad hoc informed consent. In a first step, the result of the search for mutations on the BRCA1 or BRCA2 genes must occur within 5 to 6 months following diagnosis. In a second step, in particular in the case of a suggestive family history, a search for mutations in PANEL multigenes may be recommended by the oncogeneticist. The implementation, at the tumor level, of somatic orientation tests in favor of Lynch syndrome is recommended in particular in cases of suggestive histology or a family history of colon or endometrial cancers, with:

- **(i)** Immunohistochemistry looking for silencing of MMR gene expression;
- **(ii) Molecular test looking for** micro-satellite instability: RER test analyzing the status, i.e. MSS, not suggestive; or MSI, i.e. unstable which leads to the search for a constitutional mutation of the MMR genes.

Table 4: Equivalence of the International Federation of Obstetrician-Gynecologists (FIGO) and Tumor-nodes-metastasis (TNM) Classifications for Ovarian Tumors.

	Définition			Description
	FIGO	TNM		
	I	T1N0M0		Tumeur limitée aux ovaires ; pas de cellules malignes ganglionnaires régionales
	IA	T1aN0M0		Tumeur limitée à un seul ovaire ; capsule intacte ; pas de tumeur à la surface de l'ovaire ; pas de cellules malignes dans l'ascite ou le lavage péritonéal
	IB	T1bN0M0		Tumeurs des deux ovaires ; capsules intactes ; pas de tumeur à la surface des ovaires, pas de cellules malignes dans l'ascite ou le lavage péritonéal
	IC	T1cN0M0		Tumeur d'un ou deux ovaires avec rupture capsulaire ou tumeur à la surface ovarienne ; ou cellules malignes dans le liquide d'ascite ou de lavage péritonéal
	II	T2N0M0		Tumeur d'un ou deux ovaires étendue au pelvis avec ou sans implants
	IIA	T2aN0M0		Extension et/ou implants sur l'utérus et/ou aux trompes ; pas de cellule maligne dans l'ascite ou le lavage péritonéal
	IIB	T2bN0M0		Extension aux autres tissus pelviens, pas de cellule maligne dans l'ascite ou le lavage péritonéal
	IIC	T2cN0M0		Extension pelvienne (T2a ou T2b) avec cellules malignes dans le liquide d'ascite ou de lavage péritonéal
	III	T3		Tumeur d'un ou deux ovaires avec métastase péritonéale confirmée au microscope au-delà du pelvis et/ou adénopathie métastatique régionale
	IIIA	T3aN0M0		Métastase péritonéale microscopique au-delà du pelvis
	IIIB	T3bN0M0		Métastase macroscopique au-delà du pelvis de 2 cm ou moins en plus grande dimension
	IIIC	T3c et/ou N1		Métastase macroscopique de plus de 2 cm en plus grande dimension et/ou adénopathie métastatique régionale
	IV	M1		Métastase à distance (autre que métastase péritonéale)

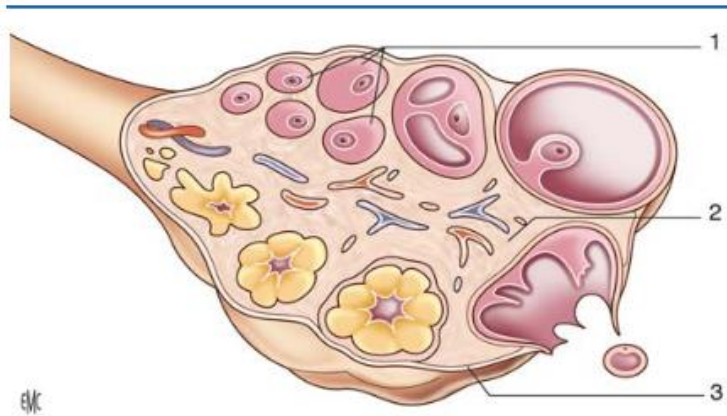


Figure: Histogenesis of ovarian tissue. Different histological types: constituents of the undifferentiated gonad (5th week of gestation).

Presence of more specific elements of the male gonad (undifferentiated gonad up to 4 months of gestation) . Identical histological types for ovary and testis.

1. Germ cells;
2. Mesonephros/mesenchyme;
3. Coelomic epithelium.

CONCLUSION

Ovarian cancer affects one in 70 women. It is a severe disease whose diagnosis is made in the majority of cases at an advanced stage, that is to say with peritoneal involvement beyond ovaries. This gives this cancer a poor prognosis. The standard treatment is surgery combined with chemotherapy. Surgery has a central place in the management of this cancer. The surgical procedure must be complete, with no tumor residue at the end of the procedure. The benefit in terms of patient survival depends on this criterion. Surgery is primary or interval after neoadjuvant chemotherapy. Finally, in the carcinogenesis of these cancers, particularly high-grade serous cancers (majority histological diagnosis), a deficiency in homologous repair of deoxyribonucleic acid (DNA) (HRD), acquired or constitutional, allows the use of a new therapy based on PARP (poly[adenosine diphosphate-ribose] polymerase) inhibitors and changing the prognosis of this subgroup of patients.

Bibliography

- 1) Globocan 2008 (IARC). Section of Cancer Information. <http://globocan.iarc.fr>.
- 2) Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; 127:2893–917.
- 3) Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2020. *CA Cancer J Clin* 2020; 59:225–49.

- 4) Ménégoz F, Chérié -Challine L. Cancer in France: incidence and mortality. - Evolution. French cancer registers (FRANCIM) and the Ministry of Employment and Solidarity. Paris: French Documentation; 2020.
- 5) Goff BA, Mandel LS, Melancon CH, Muntz HG. Frequency of symptoms of ovarian cancer in women presenting to primary care clinics. *JAMA* 2004; 291:2705-12.
- 6) Andersen MR, Goff BA, Lowe KA, et al. Use of a Symptom Index, CA125, and HE4 to predict ovarian cancer. *Gynecol Oncol* ; 116:378-83.
- 7) Andersen MR, Goff BA, Lowe KA, et al. combining a symptoms index with CA 125 to improve detection of ovarian cancer. *Cancer* 2008; 113:484-9.
- 8) Goff BA, Matthews B, Andrilla CH, et al. How are symptoms of ovarian cancer managed? A study of primary care physicians. *Cancer* 2010; 117:4414-23.
- 9) Sharma A, Gentry-Maharaj A, Burnell M, et al. assessing the malignant potential of ovarian inclusion cysts in postmenopausal women within the UK Collaborative Trial of Ovarian Cancer Screening (UKC-TOCS): a prospective cohort study. *BJOG* 2012; 119:207-19.
- 10) Van Holsbeke C, Daemen A, Yazbek J, et al. Ultrasound methods to distinguish between malignant and benign adnexal masses in the hands of examiners with different levels of experience. *Ultrasound Obstet Gynecol* 2009; 34:454-61.
- 11) Bazot M, Nassar-Slaba J, Thomassin- Naggara I, Cortez A, Uzan S, Darai E. MR imaging compared with intraoperative frozen -section examination for the diagnosis of adnexal tumors ; correlation with final histology . *Euro Radiol* 2006; 16:2687-99.
- 12) Kinkel K, Lu Y, Mehdizade A, Pelte MF, Hricak H. Indeterminate ovarian mass at US: incremental value of second imaging test for characterization – meta-analysis and Bayesian analysis. *Radiology* 2005; 236:85-94. [118]. Siegelman ES, Outwater EK. Tissue characterization in the female pelvis by means of MR imaging. *Radiology* 1999; 212:5-18.
- 13) Outwater EK, Siegelman ES, Talerman A, Dunton C. Ovarian fibromas and cystadenofibromas: MRI features of the fibrous component. *J Magn Reson Imaging* 1997; 7:465-71.
- 14) Thomassin- Naggara I, Darai E, Cuenod CA, et al. Contribution of diffusion- weighted MR imaging for prediction benignity of complexadnexal masses. *Euro Radiol* 2009; 19:1544-52.
- 15) Thomassin- Naggara I, Bazot M, Darai E, Callard P, Thomassin J, Cuenod CA. Epithelial ovary tumors: value of dynamic contrast-enhanced MR imaging and correlation with tumor angiogenesis. *Radiology* 2008; 248:148-59.
- 16) Thomassin- Naggara I, Darai E, Cuenod CA, Rouzier R, Callard P, Bazot M. Dynamic contrast-enhanced magnetic resonance imaging: has useful tool for characterizing ovary epithelial tumors. *J MagnReson Imaging* 2008; 28:111-20.
- 17) Thomassin- Naggara I, Cuenod CA, Darai E, Marsault C, BazotM . Dynamic contrast-enhanced MR imaging of ovarian neoplasms:current status and future perspectives. *Magn Reson Imaging Clin N Am* 2008; 16:661-72 (ix).
- 18) Takeuchi M, Matsuzaki K, Harada M. Preliminary observations and clinical value of N- acetyl resonances in ovarian tumors using in-vivo proton MR spectroscopy at 3T. *Euro Radiol* 2011; 21:2640-6.
- 19) Tempany CM, Zou KH, Silverman SG, Brown DL, Kurtz AB, McNeil BJ. Staging of advanced ovary cancer: comparison of imaging modalities – report from the Radiological Diagnostic Oncology Group. *Radiology* 2000; 215:761-7.

- 20) Hanbidge AE, Lynch D, Wilson SR. US of the peritoneum. *Radiographics* 2003; 23: 663-84 (discussion 84-5).
- 21) D.Querleu , I.Ray -Coquard, JMClasse , JSAucouturier , F.Bonnet , P.Bonnier , E. Darai , M.Devouassoux L.Gladiëff , O.Glehen , C.Haie-Meder , F.Joly , F.Lécuru , JPLefranc , C.Lhommé , P.Morice , A.Salengro , E Stoeckle , S.Taieb , ZXZeng & E.Leblanc . Quality indicators in ovarian cancer surgery: Report from the French Society of Gynecologic Oncology (French Society of Gynecological Oncology, SFOG) *Year Oncol* 2013; 24:2732-2739.
- 22) Namer M, Pujade-Lauraine E, Ray-Coquard I, Freyer G, Lecuru F. First recommendations on ovarian cancer. Nice – St Paul de Vence 2012. *Onko +* 2013; 41:3-38
- 23) Prat J. Staging classification for cancer of the ovary, fallopian tube and peritoneum. *Int J Gynecol Cancer* 2014; 124:1-5. [138] Harmon R, Sugarbaker P. Prognosis indicators in peritoneal carcinomatosis from gastrointestinal cancer. *Int Sem Surg Oncol* 2005; 2:3
- 24) du Bois A, Quinn M, Thigpen T, et al. 2004 Consensus statements on the management of ovarian cancer: final document of the 3rd International Gynecologic Cancer Intergroup Ovarian Cancer Consensus Conference (GCIG OCCC 2004). *Ann Oncol* 2005; 16 Suppl 8:viii7.
- 25) NCCN Guidelines Version 2.2012: Epithelial ovarian cancer/ fallopian tube cancer/ primary peritoneal cancer. http://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf (Accessed on November 30, 2011).
- 26) Katsumata N, Yasuda M, Takahashi F, et al. Dose-dense paclitaxel once a week in combination with carboplatin every 3 weeks for advanced ovary cancer: a phase 3, open-label, randomized controlled trial. *Lancet* 2009; 374:1331.
- 27) Katsumata N, Yasuda M, Isonishi S, et al. Long term results of dose-dense paclitaxel and carboplatin versus conventional paclitaxel and carboplatin for treatment of advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer (JGOG 3016): has randomized, controlled, open-label trial. *Lance Oncol* 2013; 14:1020.
- 28) Chan J, Brady M, Penson R, et al. Phase III trial of every-3-weeks paclitaxel versus dose dense weekly paclitaxel with carboplatin +/- bevacizumab in epithelial ovarian , peritoneal , fallopian tube cancer: GOG 262 (NCT0116712). Oral presentation at the 2013 European Society of Gynecological Oncology Annual Meeting, Liverpool.
- 29) Pignata S, Scambia G, Katsaros D, et al. Carboplatin plus paclitaxel once a week versus every 3 weeks phase 3 trial. *Lancet Oncol* 2014; 15:396 Rare ovarian cancers