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Editorial

Borderline ovarian tumors: Guidelines from the French national college of obstetricians and gynecologists (CNGOF)

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ABSTRACT

It is recommended to classify Borderline Ovarian Tumors (BOTs) according to the WHO classification. Transvaginal and suprapubic ultrasonography are recommended for the analysis of an ovarian mass (Grade A). In case of an undetermined ovarian lesion on ultrasonography, it is recommended to perform a pelvic MRI (Grade A) with a score for malignancy (ADNEX MR/O-RADS) (Grade C) included in the report and to formulate a histological hypothesis (Grade C). Pelvic MRI is recommended to characterize a tumor suspected of being BOT (Grade C). It is recommended to evaluate serum levels of HE4 and CA125 and to use the ROMA score for the diagnosis of indeterminate ovarian mass on imaging (grade A). If there is a suspicion of a mucinous BOT on imaging, serum levels of CA 19−9 may be proposed (Grade C). For Early Stages (ES) of BOT, if surgery without risk of tumor rupture is possible, laparoscopy with protected extraction is recommended over laparotomy (Grade C). For treatment of a bilateral serous ES BOT with a strategy to preserve fertility and/or endocrine function, bilateral cystectomy is recommended where possible (Grade B). For mucinous BOTs with a treatment strategy of fertility and/or endocrine function preservation, unilateral salpingo-oophorectomy is recommended (grade C). For mucinous BOTs treated by initial cystectomy, unilateral salpingo-oophorectomy is recommended (grade C). For serous or mucinous ES BOTs, routine hysterectomy is not recommended (Grade C). For ES BOTs, lymphadenectomy is not recommended (Grade C). For ES BOTs, appendectomy is recommended only in case of a macroscopically pathological appendix (Grade C). Restaging surgery is recommended in cases of serous BOTs with micropapillary architecture and an incomplete abdominal cavity inspection during initial surgery (Grade C). Restaging surgery is recommended for mucinous BOTs after initial cystectomy or in cases where the appendix was not examined (Grade C). If restaging surgery is decided for ES BOTs, the following procedures should be performed: peritoneal washing (grade C), omentectomy (grade B), complete exploration of the abdominal cavity with peritoneal biopsies (grade C), visualization of the appendix and appendectomy in case of a pathological macroscopic appearance (grade C) as well as unilateral salpingo-oophorectomy in case of a mucinous BOT initially treated by cystectomy (grade C). In advanced stages (AS) of BOT, it is not recommended to perform a lymphadenectomy as a routine procedure (Grade C). For AS BOT in a patient with a desire to fall pregnant, conservative treatment involving preservation of the uterus and all or part of the ovary may be proposed (Grade C). Restaging surgery aimed at removing all lesions, not performed initially, is recommended for AS BOTs (Grade C). After treatment, follow-up for a duration greater than 5 years is recommended due to the median recurrence time of BOTs (Grade B). It is recommended that a systematic clinical examination be carried out during follow-up of a treated BOT (Grade B). If the determination of tumor markers is normal preoperatively, the routine dosage of tumor markers in BOT follow-up is not recommended (Grade C). In case of an initial elevation in serum CA 125 levels, it is recommended to monitor CA 125 during follow up (Grade B). In case of conservative treatment, it is recommended to use transvaginal and transabdominal ultrasound during follow up of a treated BOT (Grade B). In the event of a BOT recurrence in a woman of childbearing age, a second conservative treatment may be proposed (Grade C). A consultation with a physician specialized in Assisted Reproductive Technique (ART) should be offered in the case of BOTs in women of childbearing age (Grade C). When possible, a conservative surgical strategy is recommended to preserve fertility in women of childbearing age (Grade C). In the case of optimally treated BOT, there is no evidence to contraindicate the use of ART. The use of hormonal contraception after serous or mucinous BOT is not contraindicated (Grade C). After management of mucinous BOT, for women under 45 years, given the benefit of Hormonal Replacement Therapy (HRT) on cardiovascular and bone risks, and the lack of hormone sensitivity of mucinous BOTs, it is recommended to offer HRT (Grade C). Over 45 years of age, HRT can be prescribed in case of a climacteric syndrome after individual benefit to risk assessment (Grade C).

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Introduction

Borderline Ovarian Tumors (BOTs) are believed to account for 10%–20% of all epithelial tumors of the ovary. Their particularity is that they occur on average 10 years earlier and have a much better prognosis than ovarian carcinomas. The two main histological forms of BOTs are serous and mucinous. Survival, all stages combined, is 95 % at 5 years and 90 % at 10 years. The preoperative diagnosis of BOTs is difficult and differentiating between benign and malignant tumors requires precise preoperative examinations. Given the good prognosis of BOTs, the young age of patients at onset and the societal evolution towards later pregnancies, surgical treatment of patients with a desire for pregnancy is evolving to be increasingly conservative.

The French National College of Obstetricians and Gynecologists ("Collège National des Gynécologues et Obstétriciens Français" (CNGOF)) has thus decided to issue guidelines for clinical best practice and management of BOTs with the objective of improving the standard of healthcare. The methodology used in the elaboration of these guidelines followed the standards of the French National Authority for Health (HAS) [1].

These guidelines are intended for healthcare professionals involved in the diagnosis, initial treatment and follow-up of patients with BOT: surgeons, obstetricians and gynecologists, medical oncologists, midwives, anatomo-pathologists, general practitioners and radiologists.

Epidemiology [2,3]

BOTs account for 10%–20% of all epithelial tumors of the ovary. Their particularity is their age at onset, on average 10 years earlier, and their prognosis which is much better than that of ovarian carcinomas. At diagnosis, the median age of patients is 46 years (LE3). Survival, all stages combined, is 95 % at 5 years and 90 % at 10 years. Five-year survival for stages I, II, III, IV is 99.7 % (95 % CI: 96.2–100 %), 99.6 % (95 % CI: 92.6–100 %), 95.3 % (95 % CI: 91.8–97.4 %) and 77.1 % (95 % CI: 58.0–88.3 %) (LE3), respectively. The five-years survival for serous and mucinous tumors is 99.7 % (95 % CI: 99.2–99.9 %) and 98.5 % (95 % CI: 96.9–99.3 %), respectively (LE3).

There is an epidemiological association between individual risk of BOT and family history of BOTs or other cancers (pancreatic, lung, bone and leukemia) (LE3).

The risk of BOTs increases with a personal history of a benign ovarian cyst (LE2) or pelvic infectious disease (LE3).

An epidemiological association exists between exposure to hormones and the risk of BOTs (LE3). The relative risk of BOTs decreases as parity increases, with a relative risk of a BOT at 0.44 (0.26 to 0.75) among multiparous women (LE3).

The overall risk of BOT recurrence is estimated at between 2% and 24 % (LE2). The risk of BOT recurrence with an invasive form ranges from 0.5 % to 3.8 % (LE2). The delay until recurrence can be long sometimes over 10 years after initial treatment (LE2).

An age of under 40 years is a risk factor for recurrence (LE3). An age greater than 50 years is a pejorative prognostic factor associated with lower survival and a higher risk of progression to invasive carcinoma (LE3). The risk of recurrence increases with the initial FIGO stage (LE3).

Conservative BOT treatment is associated with a higher risk of recurrence compared to radical treatment of bilateral salpingo-oophorectomy (LE2), although survival is not impacted (LE2).

For serous BOTs, complete initial surgical staging significantly reduces the risk of recurrence, but with no impact on overall survival (LE2). BOT residue decreases recurrence-free survival (LE4).

Laparoscopy is not associated with a higher risk of recurrence compared to laparotomy (LE2).

An elevation at diagnosis of CA 125 above the norm ($\geq$ 35 IU/mL) for serous BOTs is an independent risk factor of recurrence (LE4).

The score of Ouldamer et al. and the nomogram of Bendifallah et al. are efficient tools for assessing the risk of BOT recurrence after surgical treatment (LE3). The use of these scores and nomograms after surgical treatment of a BOT can therefore be useful to assess the risk of recurrence and to provide information to patients (Grade C).

Biopathology [4]

BOTs include 6 histological subtypes (serous, mucinous, seromucinous, endometrioid, clear cell, Brenner's), of which serous and mucinous are the most frequent (LE2). It is recommended to classify BOTs according to the WHO classification. For serous BOTs, it is recommended to specify the classic histological or micropapillary/cribriform subtype (Grade C). For BOTs, it is recommended that the implant sample be large enough to contain macroscopically normal adjacent tissue (grade C). It is recommended to thoroughly investigate peritoneal implants for invasive potential (Grade B). For bilateral mucinous BOTs and/or peritoneal implants or peritoneal pseudomyxoma, it is recommended to look for a primary digestive or pancreato-biliary cancer with the appropriate examinations (Grade C). For clear cell BOT, it is recommended that the tumor be sampled extensively to rule out the presence of an associated clear cell adenocarcinoma (Grade C). Systematic immunohistochemical analysis is not recommended to search for invasion (Grade C).

In view of the variable reproducibility of both tumor and implant diagnosis and the overall risk of over-diagnosis, it is recommended that a review or double reading by an expert pathologist in gynecology be done in the following situations (INCa guidelines- TMRG Network) (Grade C) [5]:

1 In case of doubt on the borderline nature of the tumor, the histological subtype of BOT, or the invasive nature of an implant.
2 Systematically for non-classical serous BOT and in the presence of peritoneal implants.
3 Systematically for mucinous and clear-cell BOT.

It is recommended that ovarian tumors suspected of being borderline should be sampled extensively in order to rule out an invasion, samples should be directed especially towards solid component and vegetations, to the tumor capsule and to areas with different macroscopic appearances, with at least 1 sample per cm for tumors with a size < 10 cm and 2 per cm for tumors with a size > 10 cm as well as on all papillary and solid areas (Grade C). For serous BOTs with micropapillary patterns (Grade C), it is recommended to sample 2 blocks per cm of tumor (Grade C). In light of the tumor heterogeneity of mucinous BOTs, sampling of 2 blocks per cm of tumor is recommended even if the tumor size is < 10 cm (grade C). In case of microinvasion, or intraepithelial carcinoma, it is recommended that the tumor be further sampled to detect an invasive component (Grade C).

In the absence of macroscopic involvement of the omentum, after careful macroscopic examination, it is recommended that at least 4–6 blocks of systematic sampling be performed on an omentectomy specimen (depending on the size of the epiploic resection) to allow for the detection of the majority of microscopic involvement (Grade C). It is recommended that all lymph nodes and implants be included (Grade C).

It is recommended that a pathologist with an expertise in gynecology should be consulted when extemporaneous histology is required for a suspected BOT (Grade C).

Testing for gene mutations (BRCA, MMR, BRAF, KRAS) in women treated for BOTs is not recommended (grade C).

It is recommended that the pathologic report include the gross examination of tissue samples including a description of the specimens received and their integrity (intact or ruptured ovarian capsule), tumor sites and a description of the omentum (Grade B). It is recommended to specify the histological subtype of the BOT, and for serous BOTs, the presence or absence of micropapillary patterns, the presence of implants (invasive or non-invasive), the presence of microinvasions, other tumor locations, the results of the peritoneal washing and the FIGO classification (Grade B). In case of doubt concerning the BOT histological subtype, it is recommended that an immunohistochemical study with an optimal panel of antibodies be performed (Grade C).

Imaging [6] (Fig. 1)

Ultrasonography is the first-line imaging technique for the diagnosis of adnexal masses and magnetic resonance imaging (MRI) is the most accurate non-invasive technique for the preoperative diagnosis of epithelial tumors of the ovary. The guidelines published jointly by INCa, CNGOF, FRANCOGYN group, and ARCAGY-GINECO for the initial management of epithelial tumors of the ovary are presented below [7]:

1 Transvaginal and suprapubic ultrasonography are recommended for the analysis of an ovarian mass (Grade A).
2 When ultrasonography is performed by an expert, a subjective analysis is recommended (Grade A).
3 In case of ultrasonography performed by a non-expert, the use of simple rules ("Simple Rules") is recommended (Grade A). This approach must be combined with a subjective analysis in order to match the examination quality of an expert sonographer (Grade A).
4 In cases of undetermined ovarian lesions on transvaginal and suprapubic ultrasonography, a pelvic MRI is recommended (Grade A).
5 For adnexal mass, when an MRI is indicated, MRI protocol with T2, T1, T1 sequences with fat saturation, diffusion, injected dynamics, and after gadolinium injection is recommended (Grade B).
6 To characterize an adnexal mass on MRI, it is recommended to include a malignancy risk score (ADNEX MR/O-RADS) (Grade C) in the report and to formulate a histological hypothesis (Grade C).

MRI is recommended for indeterminate lesions (Grade A) or for lesions suspected of being BOTs or invasive tumors with ultrasonography (Grade B).

CT scan may be useful in excluding peritoneal carcinomatosis in cases where there is doubt between a BOT and an invasive tumor (Grade C).

The analysis of macroscopic MRI signs should be performed in order to differentiate between the BOT subtypes; serous, seromucinous and mucinous (intestinal type) (Grade C).

Tumor markers [3,8]

For indeterminate ovarian mass on imaging, according to INCa 2018″Guidelines for Patients with Epithelial Ovarian Cancer" [7], it

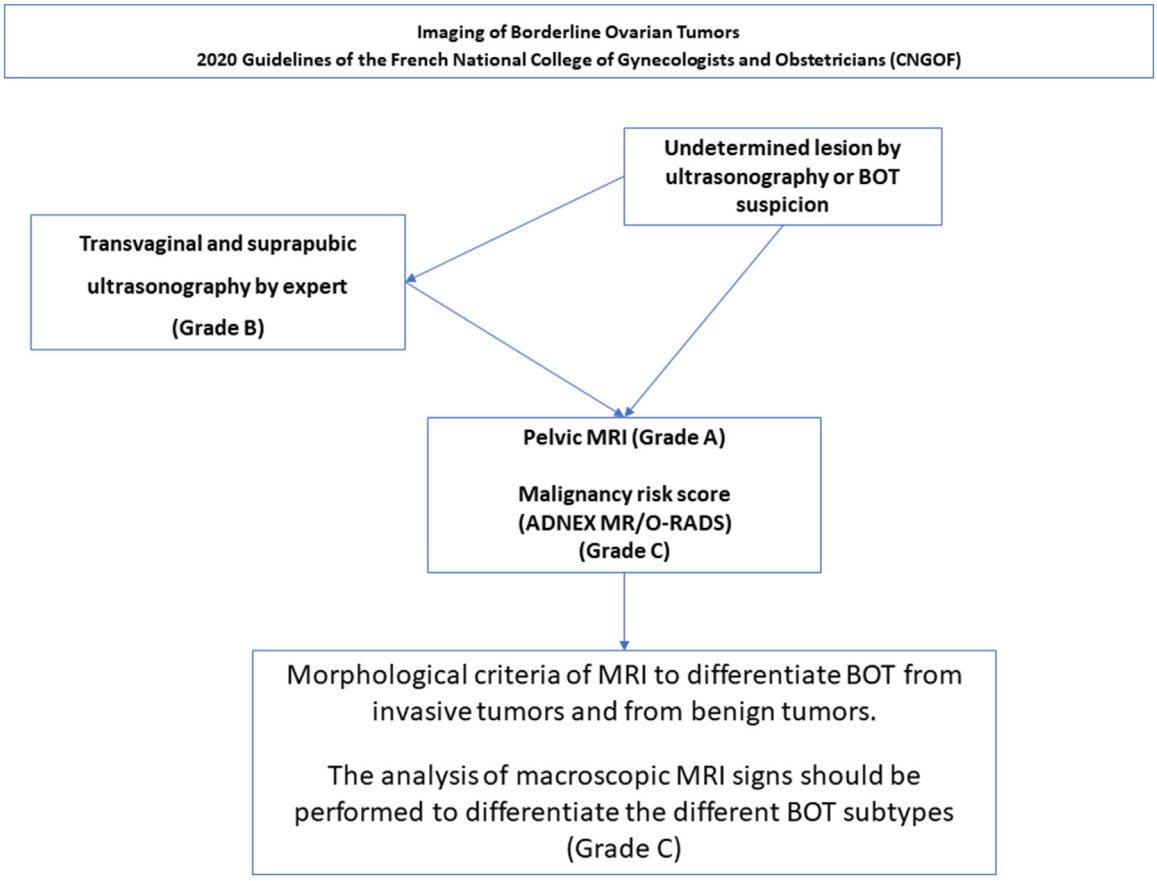

Fig. 1. Imaging of Borderline Ovarian Tumors (BOTs). 2020 Guidelines of the French National College of Obstetricians and Gynecologists (CNGOF).

is recommended that serum HE4 (Grade A) and serum CA125 (Grade A) be measured and that the ROMA score be used (Grade A).

No recommendation can be proposed regarding the use of serum CA125 levels for preoperative differential diagnosis between presumed benign ovarian tumors, BOTs and malignant ovarian tumors.

When a mucinous BOT is suspected on imaging, a CA19 9 assay may be proposed (Grade C).

Surgical Management of early stage (ES) BOT [9]

There is no reason provided in literature to centralize the surgical management of patients with ES BOTs. The role of expert centers is therefore limited to the fields of diagnostic anatomo-pathological confirmation, indications of fertility sparing surgery and expertise for preoperative characterization of ovarian mass on imaging.

1/Initial surgery (Fig. 2)

In the surgical management of ES BOTs, if surgery without risk of tumor rupture is possible, then laparoscopy with a protected extraction is recommended over laparotomy (Grade C). For BOTs, it is recommended that all precautions be taken to avoid tumor rupture, including the intraoperative decision of laparoconversion (Grade C). When surgically treating BOTs, protected extraction of the surgical specimen is recommended (Grade C). It is recommended not to puncture a suspicious ovarian cyst (grade C).

When uni or bilateral ES BOTs are suspected on preoperative imaging in a menopausal patient or when the preservation of fertility or endocrine function are not considered, then bilateral salpingo-oophorectomy (grade B) is recommended. In the case of treatment for bilateral serous ES BOTs with a strategy of fertility or endocrine function preservation, bilateral cystectomy is recommended when possible (grade B). When treating mucinous

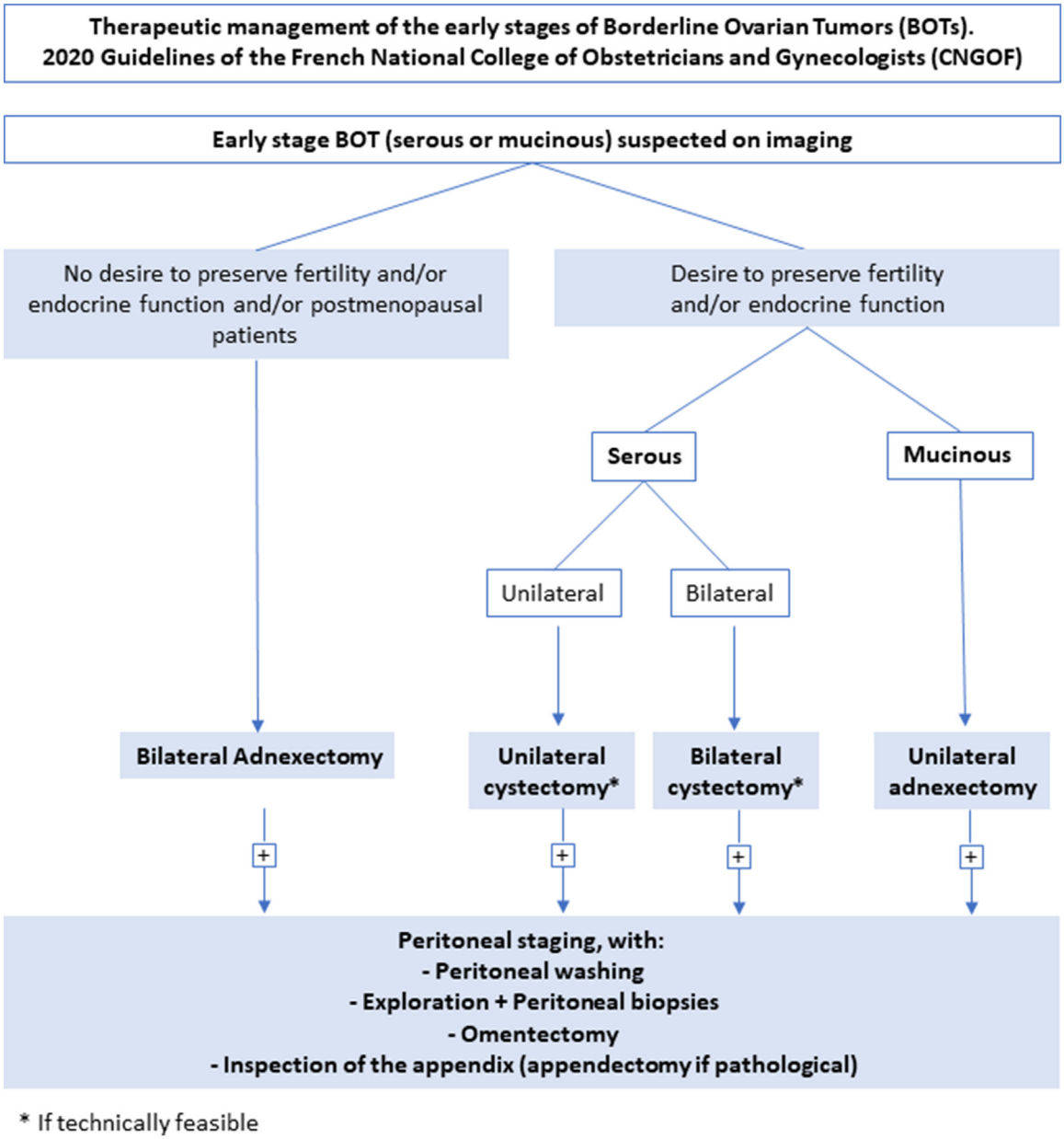

Fig. 2. Therapeutic management of the early stages of serous or mucinous Borderline Ovarian Tumors (BOTs) suspected on imaging. 2020 Guidelines of the French National College of Obstetricians and Gynecologists (CNGOF).

ES BOTs with a strategy of fertility or endocrine function preservation, a unilateral salpingo-oophorectomy is recommended (grade C). No guidelines were possible to issue between cystectomy and unilateral adnexectomy for the treatment of endometrioid ES BOTs with a strategy of fertility or endocrine function preservation.

An omentectomy is recommended to achieve a complete surgical initial staging when a BOT is diagnosed with extemporaneous histology or suspected on the basis of preoperative imagery (Grade B). No guideline on the type of omentectomy to be performed has been issued.

Multiple peritoneal biopsies are recommended in order to achieve a complete surgical initial staging when a BOT is diagnosed following to extemporaneous histology or suspected on preoperative imaging (grade C). Primary peritoneal washing is recommended to achieve a complete surgical initial staging when a BOT is suspected on preoperative imaging (Grade C).

For serous and mucinous ES BOTs, systematic hysterectomy is not recommended (Grade C). For endometrioid ES BOTs (Fig. 3), and in the absence of a treatment strategy aimed at maintaining fertility, hysterectomy is recommended as part of the initial surgery (Grade C). For endometrioid ES-BOTs, if the treatment strategy aims to preserve fertility, then the uterus may be preserved pending a comprehensive evaluation of the endometrium by imaging and endometrial sampling (Grade C).

For ES BOTs, regardless of histological subtype, it is recommended that the macroscopic aspect of the appendix during initial surgery be assessed (Grade B). For ES BOTs, regardless of histological subtype, it is recommended to perform an appendectomy exclusively in the case of a macroscopically pathological appendix (Grade C).

For ES BOTs, regardless of histologic subtype, pelvic and paraaortic lymphadenectomy are not recommended as part of initial surgery (Grade C).

2/Restaging surgery (Fig. 4)

After restaging surgery for presumed ES BOT, the increase in FIGO stage is about 15 % for serous BOTs and less than 5% for mucinous BOTs (LE2).

For BOTs diagnosed with a definitive histology, the indication for restaging surgery should be discussed at a multidisciplinary meeting. For presumed ES BOTs, a laparoscopic approach is recommended for restaging surgery (grade C).

For histological definitive serous ES BOT in a patient treated by initial cystectomy, with a treatment strategy aimed at fertility or endocrine function preservation, restaging surgery for salpingo-oophorectomy is not recommended in the absence of residual lesions at surgery or on postoperative imaging (reference ultrasonography or pelvic MRI) (grade C).

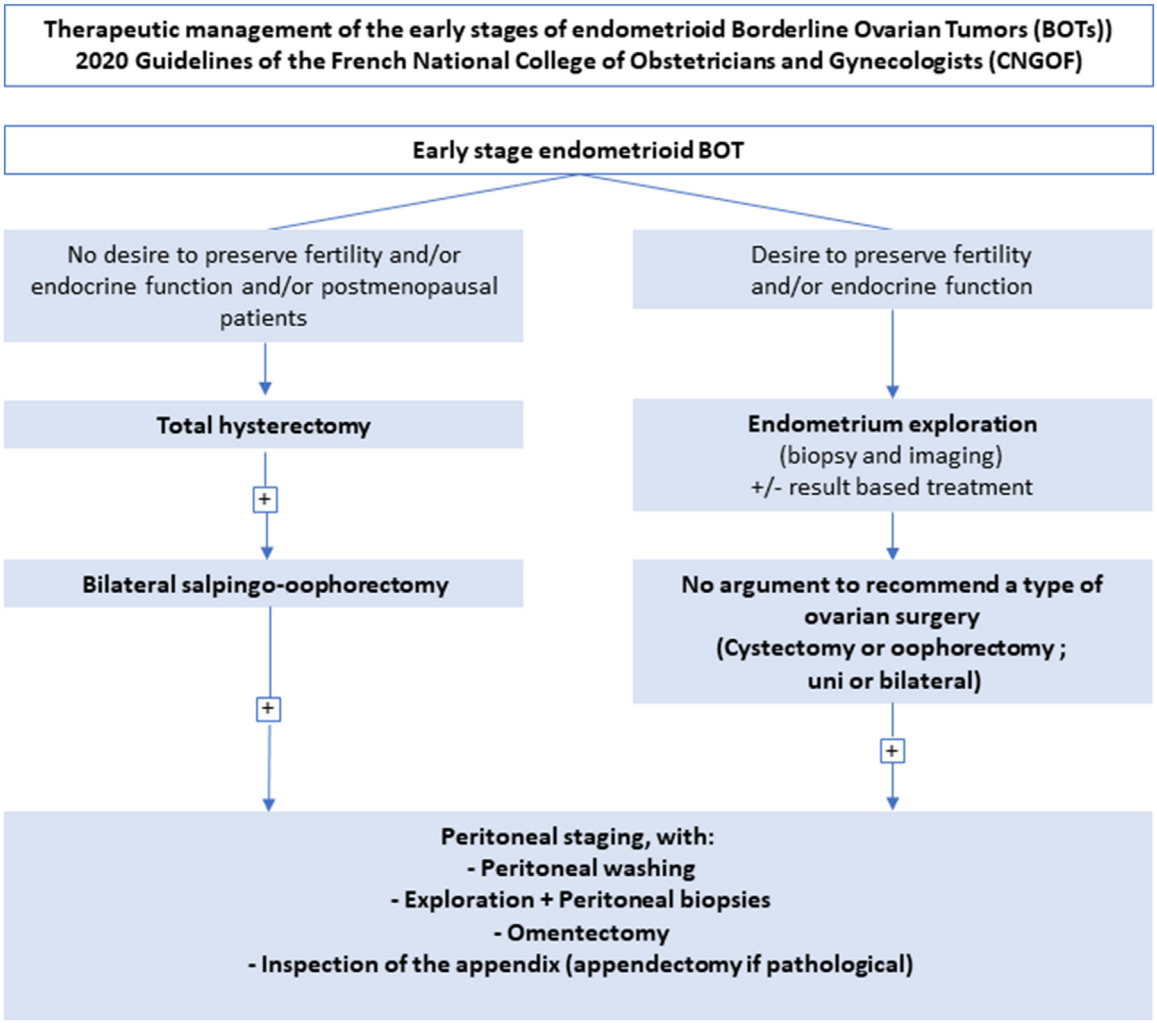

Fig. 3. Therapeutic management of the early stages endometrioid Borderline Ovarian Tumors (BOTs). 2020 Guidelines of the French National College of Obstetricians and Gynecologists (CNGOF).

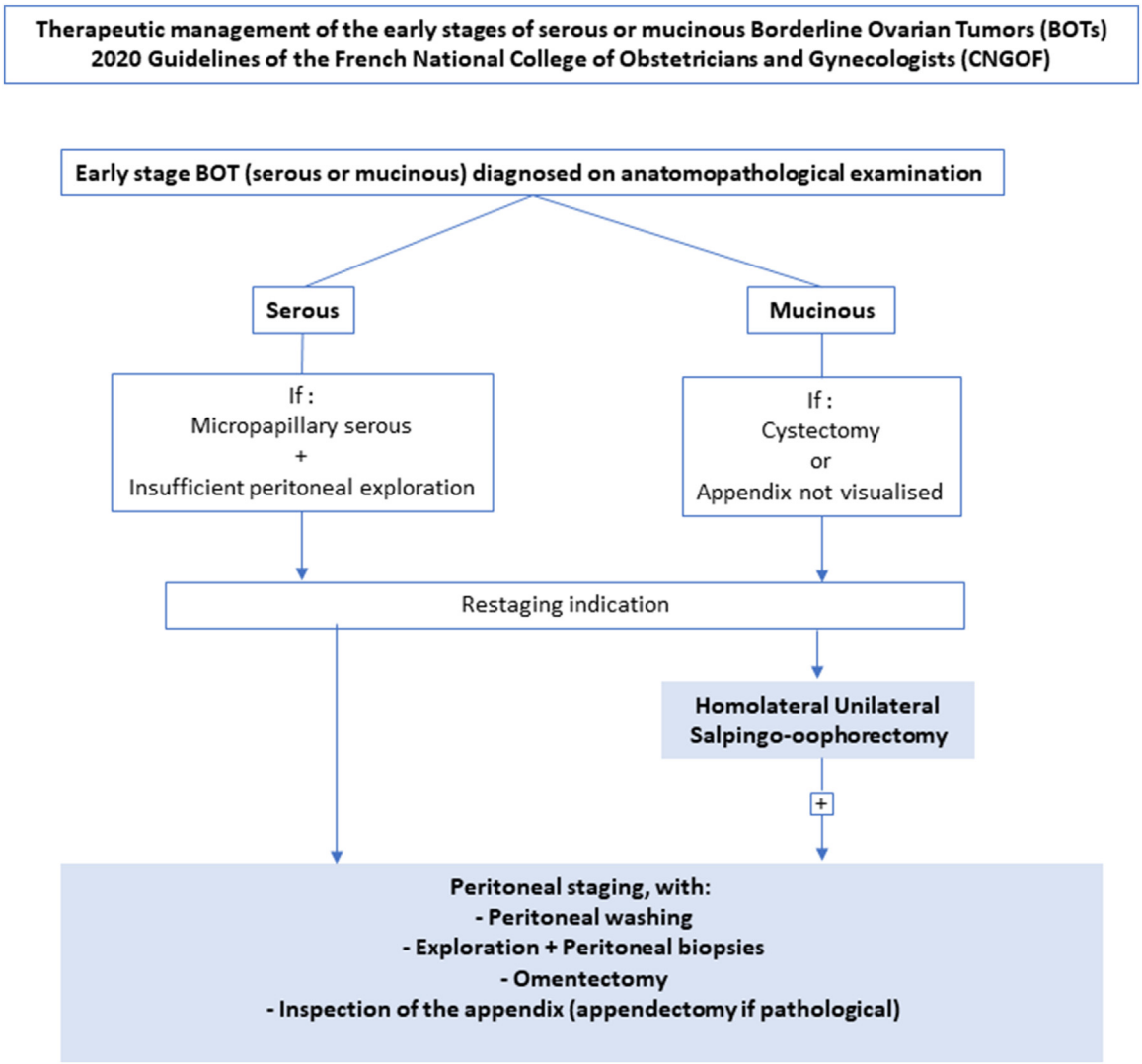

Fig. 4. Therapeutic management of the early stages of serous or mucinous Borderline Ovarian Tumors (BOTs) diagnosed on an anatomopathological examination. 2020 Guidelines of the French National College of Obstetricians and Gynecologists (CNGOF).

Restaging surgery is recommended for serous BOTs with a micropapillary patterns or following to an incomplete inspection of the abdominal cavity during initial surgery (grade C). Restaging surgery is recommended for mucinous BOT in cases where the appendix was not visualized or where an initial cystectomy has been performed imposing a unilateral salpingo-oophorectomy (grade C). When a restaging surgery is indicated for a presumed ES BOT, the procedure should include peritoneal washing (grade C), an omentectomy (no guidelines could have been issued on the type of omentectomy) (grade B), a complete exploration of the abdominal cavity with peritoneal biopsies of suspicious areas or systematically (grade C), exploration of the appendix (Grade B) with an appendectomy in case of a pathological macroscopic appearance (grade C). In cases of mucinous BOTs restaging surgery should also include unilateral salpingo-oophorectomy for mucinous BOTs treated initially by cystectomy (grade C).

For endometrioid ES BOTs, in the absence of a strategy to maintain fertility, hysterectomy is recommended (Grade C).

For ES BOT, regardless histological subtype, pelvic and para-aortic lymphadenectomy is not recommended as part of restaging surgery (Grade C).

Surgical Management of advanced stage (AS) BOT [10]

Advanced stage BOTs are defined by a FIGO stage $\geq$ II. Following to a preoperative suspicion (after imaging) or a postoperative diagnosis of AS BOT, patients should be referred to an expert center in ovarian cancer treatment (Grade C).

Data in literature does not provide sufficient proof to establish a preferred surgical approach for AS BOTs. Literature does not provide sufficient data to conclude that hysterectomy should be routinely performed for serous and mucinous AS BOTs, the goal of the surgery being no tumor residue.

For AS BOTs, lymphadenectomy is not recommended as a routine procedure (Grade C).

For AS BOTs, and by analogy to epithelial ovarian cancers [7], it is recommended that peritoneal carcinomatosis be described before any cytoreduction and that tumor residue be noted at the end of surgery (size, location and reason for non-extirpation). For AS BOTs, the use of a peritoneal carcinosis score to objectively assess the tumor burden such as the "Peritoneal Cancer Index" (PCI) is recommended (Grade C). For AS BOTs, and in patients with a desire to fall pregnant, conservative treatment with uterine

preservation and all or part of the ovary may be proposed after a multidisciplinary meeting (Grade C). For AS BOTs, in case of conservative treatment for fertility preservation, a biopsy of the contralateral ovary is not recommended (Grade C). Restaging surgery aimed at the removal of all lesions, if not performed initially, is recommended for AS BOTs (Grade C).

For AS BOT, guidelines could have not been issued regarding an indication for chemotherapy, even in the case of invasive implants.

Completion surgery [3]

For serous BOT, it is not recommended to perform completion surgery following to pregnancy and childbirth after conservative treatment (preservation of ovaries and uterus) (Grade B). There are no guidelines for mucinous BOTs on completion surgery.

Follow-up [3,8,11]

After treatment, follow-up beyond 5 years is recommended, this time frame takes into account the median time to recurrence of a BOT (Grade B). It is recommended that a systematic clinical examination be carried out during the follow-up of a treated BOT (Grade B). In case of an initial elevation of CA 125 levels, it is recommended to use CA 125 measurement during the follow-up after BOT treatment (Grade B). After initial conservative treatment, and even in case of a normal clinical examination, transvaginal and suprapubic ultrasonography are recommended during follow-up to detect recurrences (Grade B). There is insufficient data in literature to specify the timing of these examinations (clinical examination, ultrasonography and CA 125) for the follow-up of BOTs.

For BOTs, when tumor markers are normal preoperatively, their evaluation is not recommended during follow-up (Grade C).

Recurrence of BOT [3,11] (Fig. 5)

In case of ovarian preservation, recurrences are most often observed on the preserved ovary(ies) (LE2). Serous BOT recurrences usually appear as thin-walled, fluid cysts with vegetations, which corresponds in the IOTA classification to a solid unilocular cyst (LE2). In this case, a cyst size of less than 20 mm is not sufficient to eliminate the diagnosis of a BOT recurrence (LE2). Mucinous BOT recurrences mostly appear as multilocular or solid multilocular cysts (LE4). The « ovarian crescent sign » is a criterion in favor of a non-invasive recurrence in the case of a complex mass (LE4).

Because of its low sensitivity, the normality of the CA 125 assay does not rule out the diagnosis of a BOT recurrence (LE2).

In case of a BOT recurrence, in a woman of childbearing age, a second line of conservative treatment (Fig. 5) can be proposed after informing the patient of the risk of additional recurrences (Grade C). It is not possible to issue guidelines on operative strategy (uni or bilateral cystectomy and/or salpingo-oophorectomy) depending on the initial management and the characteristics of the recurrence. In the presence of non-invasive BOT implants, conservative treatment may be offered after a first non-invasive recurrence in women wishing to preserve their fertility (Grade C).

In the absence of an invasive tumor at the time of a BOT recurrence, chemotherapy is not indicated. In case of ovarian or peritoneal infiltration at recurrence, chemotherapy should be discussed at a multidisciplinary meeting.

Pregnancy and BOT [12]

Pelvic ultrasonography remains the first-line examination for the detection and characterization of adnexal masses during

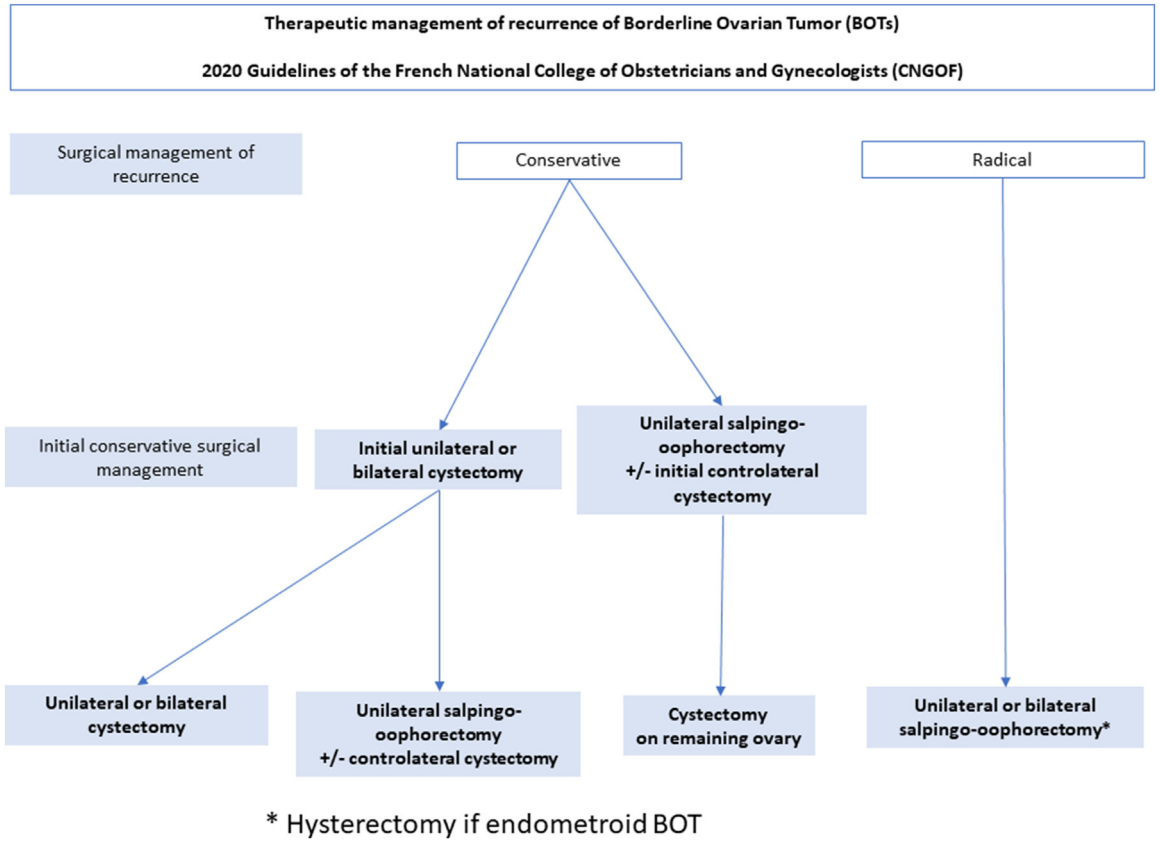

Fig. 5. Therapeutic management of recurrence of Borderline Ovarian Tumors (BOTs) Guidelines of the French National College of Obstetricians and Gynecologists (CNGOF).

pregnancy (Grade C). Pelvic MRI is recommended from the 12th week of gestation in case of indeterminate adnexal masses and should be concluded with a diagnostic score (ADNEX MR/O-RADS) (Grade C). The injection of gadolinium should be restricted due to the proven risks to the fetus and should be discussed on a case-by-case basis after informing the patient (Grade C).

In the absence of data in literature, no guidelines have been issued regarding the use of tumor markers for the diagnosis of BOTs.

There is insufficient evidence to recommend cystectomy or adnexectomy for the treatment of BOTs during pregnancy. For treatment of BOTs during pregnancy, the laparoscopic route should be preferred if feasible (Grade C). The approach and type of surgical treatment should be appropriate with respect to the size of the lesion, the obstetrical term, and the subsequent desire for pregnancy as advised in a multidisciplinary meeting. With regard to expectant management: in the absence of sufficient data in literature, no guidelines have been issued regarding the follow-up of suspicious non-operated BOTs during pregnancy.

Management of infertility and preservation of fertility in case of BOT [13]

One third of patients treated for a BOT is of childbearing age, and their prognosis is excellent (LE3). Infertile patients have an excess risk of developing a BOT (LE3). The use of conservative surgical treatment may be the first step in preserving fertility in the event of a BOT (LE2). Pregnancy rates (spontaneous and/or induced) vary from 40 % to 80 % depending on the study. Ovarian stimulation as part of ART in patients who have been treated conservatively for BOTs does not increase the risk of recurrence (LE2).

A consultation with a physician specialized in ART should be offered in case of a BOT in a woman of childbearing age (Grade C). It is recommended that patients be provided with full information on the risk of a decrease in ovarian reserve associated with surgical treatment of BOTs (Grade C). It is recommended that ovarian reserve be assessed prior to surgical management of suspected BOTs (Grade C). Where possible, a conservative surgical strategy is recommended to preserve fertility in women of childbearing age in the event of a BOT (Grade C). There is no specific data on how to manage infertility following to conservative treatment for BOT. In the case of infertility after conservative treatment for a BOT, a consultation with a physician specialized in ART is required (Grade C). In the case of a history of optimally treated BOT, there is no evidence in literature to contraindicate the use of ART. In the presence of pejorative prognostic criteria (implants), the use of ART should be discussed on a case-by-case basis in the context of a multidisciplinary meeting. In the case of infertility after conservative treatment of a BOT, there is no data to justify a delay between surgical treatment and ART. There is insufficient data on cases of conservative treatment for BOT recurrence to establish guidelines on fertility management. After treatment of a BOT recurrence, indications of ovarian stimulation should be discussed in a multidisciplinary meeting. In case of conservative treatment, there is no contraindication to ovarian stimulation for oocyte vitrification after complete surgery (LE4). In the case of pejorative prognostic criteria (implants), the possibility of ovarian stimulation should be discussed on a case-by-case basis in multidisciplinary meeting. For women who cannot have conservative treatment of the adnexa or for patients with a BOT recurrence on a single ovary, several fertility preservation techniques are described (cryopreservation of the ovarian cortex, puncture of immature oocytes and, in particular, In Vitro Maturation before cryopreservation) but with insufficient levels of evidence to draw a recommendation.

Hormonal contraception and Hormonal replacement therapy [14]

Literature does not provide data on the use of hormonal contraception after BOT. All data concerning the risk of developing a BOT in oral contraceptive users is reassuring and shows a tendency to reduce the risk of serous BOTs (LE2), and a less marked or neutral impact on the risk of mucinous BOTs (LE2). The use of hormonal contraception after serous or mucinous BOT is not contraindicated (Grade C).

After management of a mucinous BOT, for women under 45 years of age, given the benefit of HRT on cardiovascular and bone risks, and the absence of hormone sensitivity of mucinous BOTs, it is recommended to propose HRT (grade C). After management of a mucinous BOT, for women over 45 years of age, there is no reason to contraindicate the use of HRT. In case of a climacteric syndrome, and as part of an individual assessment of the benefit to risk balance, HRT may be prescribed (Grade C). After management of a serous BOT, with pejorative histological criteria (implants): given the increased risk of recurrence in an invasive hormone-sensitive form, no recommendation on the use of an HRT can be made. The prescription of HRT must be considered with caution, according to an individual risk to benefit balance, as part of a shared medical decision and after discussion in a multidisciplinary meeting including surgeons, pathologists and gynecologists. The elements that could guide the prescription could be the type of implant (invasive or not), the association with other pejorative histological criteria (micropapillary, micro-invasion), the precocity of the menopause. In case of an unfavourable benefit –risk balance for HRT, vaginal local estrogens and/or non-hormonal management of the climacteric syndrome should be proposed, using selective serotonine recapture inhibitors, gabapentine, prégabaline or clonidine. After management of a serous BOT, and in the absence of pejorative histological criteria, there is no reason to contraindicate the use of HRT. In women under 45 years of age without a climacteric syndrome, or in women over 45 years of age with a climacteric syndrome, HRT may be prescribed with regular reassessment of the risk to benefit balance (grade C).

Promotor of the guidelines

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Declaration of Competing Interest

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References

[1] Huchon C, Bourdel N, Daraï E. [Borderline Ovarian tumours: CNGOF guidelines for Clinical Practice - Methods & Organization]. Gynecol Obstet Fertil Senol 2020;48(3 March)236–8, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.023 Epub 2020 Jan 28.

[2] Ouldamer L, Body G, Daraï E, Bendifallah S. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - epidemiological aspects and risk factors]. Gynecol Obstet Fertil Senol 2020;48(3 March)239–47, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.012 Epub 2020 Jan 28.

[3] Margueritte F, Sallee C, Lacorre A, Gauroy E, Larouzee E, Chereau E, et al. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - epidemiology and risk factors of relapse, follow-up and interest of a completion surgery]. Gynecol Obstet Fertil Senol 2020;48(3 March)248–59, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.013 Epub 2020 Jan 28.

[4] Eymerit-Morin C, Brun JL, Vabret O, Devouassoux-Shisheboran M. [Borderline ovarian tumours: CNGOF Guidelines for clinical practice - Biopathology of ovarian borderline tumors]. Gynecol Obstet Fertil Senol 2020;16(May), doi:http://dx.doi.org/10.1016/j.gofs.2020.05.007 S2468-7189(20)30187-2.

[5] « Référentiel de l'observatoire des tumeurs rares gynécologiques: les tumeurs ovariennes borderline, Mai. 2019. https://www.ovaire-rare.org.

[6] Abdel Wahab C, Rousset P, Bolze PA, Thomassin-Naggara I. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - imaging]. Gynecol Obstet Fertil Senol 2020;48(3 March)260–76, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.014 Epub 2020 Jan 28.

[7] Lavoue V, Huchon C, Akladios C, Alfonsi P, Bakrin N, Ballester M, et al. Management of epithelial cancer of the ovary, fallopian tube, and primary peritoneum. Short text of the French Clinical Practice Guidelines issued by FRANCOGYN, CNGOF, SFOG, and GINECO-ARCAGY, and endorsed by INCa. Eur J Obstet Gynecol Reprod Biol 2019;236(May):214–23.

[8] Nyangoh-Timoh K, Bendifallah S, Dion L, Ouldamer L, Levêque J. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - value of tumor markers]. Gynecol Obstet Fertil Senol 2020;48(3 March)277–86, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.015 Epub 2020 Jan 28.

[9] Canlorbe G, Lecointre L, Chauvet P, Azaïs H, Fauvet R, Uzan C. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - therapeutic management of early stages]. Gynecol Obstet Fertil Senol 2020;48(3 March) 287–303, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.016 Epub 2020 Jan 28.

[10] Raimond E, Bourdel N. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - surgical management of advanced stages of borderline ovarian tumours]. Gynecol Obstet Fertil Senol 2020;48(3 March)304–13, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.017 Epub 2020 Jan 28.

[11] Gauroy E, Larouzée E, Chéreau E, De La Motte Rouge T, Margueritte F, Sallée C, et al. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - diagnosis and management of recurrent borderline ovarian tumours]. Gynecol Obstet Fertil Senol 2020;48(3 March)314–21, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.019 Epub 2020 Jan 28.

[12] Zilliox M, Lallemant M, Thomassin-Naggara I, Ramanah R. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - pregnancy]. Gynecol Obstet Fertil Senol 2020;48(3 March)322–9, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.018 Epub 2020 Jan 28.

[13] Raad J, Rolland L, Grynberg M, Courbiere B. Mathieu d'Argent E. [Borderline ovarian tumours: CNGOF guidelines for clinical practice - fertility]. Gynecol Obstet Fertil Senol 2020;48(3 March)330–6, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.020 Epub 2020 Jan 28.

[14] Rousset-Jablonski C, Pautier P, Chopin N. [Borderline Ovarian Tumours: CNGOFS Guidelines for Clinical Practice - Hormonal Contraception and MHT/HRT after Borderline Ovarian Tumour]. Gynecol Obstet Fertil Senol 2020;48(3 March)337–40, doi:http://dx.doi.org/10.1016/j.gofs.2020.01.021 Epub 2020 Jan 28.

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