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## **Management of borderline ovarian tumours during pregnancy: results of a French multi-centre study**

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## ABSTRACT

*Objective:* To assess the diagnostic and prognostic characteristics of borderline ovarian tumours (BOTs) detected during pregnancy, and to establish an inventory of French practices.

*Materials and methods:* A retrospective multi-centre case study of 14 patients treated for BOTs, diagnosed during pregnancy between 2005 and 2017, in five French pelvic cancerology expert centres, including data on clinical characteristics, histological tumour characteristics, surgical procedure, adjuvant treatments, follow-up and fertility.

*Results:* The mean age of patients was 29.3 [standard deviation (SD) 6.2] years. Most BOTs were diagnosed on ultrasonography in the first trimester (85.7%), and most of these cases (78.5%) also underwent magnetic resonance imaging to confirm the diagnosis (true positives 54.5%). Most patients underwent surgery during pregnancy (57%), with complete staging surgery in two cases (14.3%). Laparoscopy was performed more frequently than other procedures (50%), and unilateral adnexectomy was more common than cystectomy (57.5%). Tumour size influenced the surgical approach significantly (mean size 7.5 cm for laparoscopy, 11.9 cm for laparoconversion, 14 cm for primary laparotomy;  $P=0.08$ ), but the type of resection did not. Most patients were initially diagnosed with International Federation of Gynecology and Obstetrics stage IA (92.8%) tumours, but many were upstaged after complete restaging surgery (57.1%). Most BOTs were serous (50%), two cases had a micropapillary component (28.5%), and one case had a micro-invasive implant. BOTs were bilateral in two cases (14.2%). Mean follow-up was 31.4 (SD 14.8) months. Recurrent lesions occurred in two patients (14.2%) and no deaths have been recorded to date among the study population.

*Conclusion:* BOTs remain rare, but this study – despite its small sample size – supports the hypothesis that BOTs during pregnancy have potentially aggressive characteristics.

*Keywords:*

Borderline ovarian tumour

Pregnancy

## 1. Introduction

Borderline ovarian tumours (BOTs) are defined by an histology intermediate between benign and malignant tumours, and account for 15–20% of all ovarian epithelial tumours [1–2]. BOTs differ from ovarian adenocarcinomas in terms of an early age of onset (generally 10 years earlier) and a better prognosis, with a survival rate for all stages confounded of 95% at 5 years and 90% at 10 years [3]. The median age at the time of diagnosis is 45 years, and almost 35% of patients are aged <40 years (i.e. still of childbearing age) [4].

Due to the increasing maternal age at first pregnancy in developed countries, BOTs may be discovered during pregnancy. Routine adnexal screening during obstetric ultrasound in the first trimester [5] is responsible for opportunistic detection of adnexal masses. The overall incidence of these masses remains difficult to estimate, but affects 2–10% of pregnancies [6,7]. Only 2–3% of adnexal masses resected during pregnancy are malignant, and the majority of these malignant masses are, in fact, BOTs [7,8].

If a BOT is suspected during pregnancy, the challenge is two-fold: the preservation of fertility in these patients, who are often young and wish to become pregnant again; and ensuring the appropriate treatment. Basing the treatment strategy around these considerations is more meaningful given that the prognosis for BOTs is excellent [2,3].

Actual literature on BOTs diagnosed during pregnancy remains poor and based essentially on case reports. As such, it is difficult to standardize the management of BOTs [9]. The aim of this study was to assess the diagnostic and prognostic characteristics of BOTs detected during pregnancy, and to establish an inventory of French practices.

## 2. Materials and methods

A retrospective multi-centre case study was conducted of all patients treated for BOTs, diagnosed during pregnancy between 2005 and 2017, in five French pelvic cancerology expert centres [university gynaecology departments in the hospital centres in Poissy, Lille, Lariboisière (Paris), Jean-Verdier (Bondy) and Strasbourg]. All centres had an obstetrics department and a delivery room.

Medical files and data were extracted from a single national database: the French Research Group in Oncological and Gynaecological Surgery (FRANCOGYN<sup>®</sup>) database.

Data included information on clinical characteristics (age; personal, family, gynaecological, obstetric and oncological history), initial tumour characteristics (diagnostic circumstances, size, stage, imaging appearance), initial surgical procedure (surgical approach, excision type, sample sites) and restaging surgery, intra- and postoperative complications (based on the Clavien–Dindo classification), anatomical and pathological tumour characteristics, adjuvant treatments and follow-up.

Histological typing was performed according to the 2003 World Health Organization classification. Histological criteria included: (i) histological type (serous, mucinous, seromucinous); (ii) subtype if appropriate (intestinal, endocervical for mucinous tumours); (iii) degree of differentiation; (iv) presence or absence of micropapillary foci for serous BOTs; (v) presence or absence of vasculolymphatic emboli; (vi) presence or absence of micro-invasive implants; and (vii) locoregional extension stage based on the 2014 classification of the International Federation of Gynecology and Obstetrics (FIGO) [10]. The specialists who examined the samples were pathologists from referring expert centres.

Surgical treatment was considered to be conservative if at least part of one ovary and the uterus were conserved. Surgical treatment was radical when bilateral adnexectomy was performed. Staging was conducted following FIGO recommendations [10]: inspection of the

peritoneal cavity, peritoneal cytology, multiple routine and targeted biopsies, infracolic omentectomy, and appendectomy for mucinous tumours. When surgery was not complete, surgical restaging was scheduled post partum, regardless of the initial stage of the disease. There was no indication for performing pelvic or retroperitoneal lymphadenectomy [10].

A descriptive analysis of all included patients was performed. Tumour characteristics, type of resection and surgical approach were compared using Wilcoxon's test for quantitative variables and Chi-squared test for qualitative variables. Data were expressed as percentages for qualitative variables and as means for quantitative data. The significance level was set at 0.05, and the statistical analysis was performed using SAS Studio (SAS Institute, Cary, NC, USA).

### **3. Results**

#### *3.1. General and diagnostic characteristics of the population*

Among 345 cases of BOT, 14 were diagnosed and managed during pregnancy (4%). Initial clinical and diagnostic characteristics are described in Table 1. One patient had previously undergone unilateral adnexectomy of unknown aetiology, and another patient had undergone two unilateral cystectomies for endometriosis. There was no history of BOTs in any of the 14 patients.

**<insert Table 1 near here>**

BOTs were diagnosed more frequently during the first trimester of pregnancy, with only three cases diagnosed during the second trimester (at 20, 23 and 24 weeks of gestation). The exact time of diagnosis was unknown in six cases.

The mean CA125 level, when reported, was 80.4 IU/ml.



### 3.2. Initial surgical characteristics of the population and histological characteristics of BOTs

These characteristics are summarized in Table 2. More than half of the patients underwent surgery during pregnancy ( $n=8$ , 57.1%), and one patient underwent surgery in a single-step postpartum procedure. The delay between ongoing pregnancy and surgery was unknown for five patients (35.7%). Laparoscopy was performed in seven patients (50%), with secondary laparoconversion in five cases (35.7%). Laparotomy was performed in two cases (14.3%). Unilateral adnexectomy was performed in eight cases (57.1%), and cystectomy was performed in five cases (35.7%). One patient underwent bilateral cystectomy (Case 4). Peritoneal lavage with cytological sampling was performed routinely during initial surgery ( $n=14$ , 100%). Multiple peritoneal biopsies were performed in four cases (28.5%), an infracolic omentectomy was performed in two cases (14.3%), and one patient underwent appendectomy (7.1%).

**<insert Table 2 near here>**

Complete surgical staging was performed in two cases (14.3%) during pregnancy. The two cases (Cases 1 and 10) had small (5 and 7 cm) serous BOTs without associated micropapillary components or implants, treated by unilateral adnexectomy, peritoneal cytology, multiple biopsies, infracolic omentectomy and appendectomy. The histology did not detect any malignant cells, and both cases were classified as FIGO stage IA.

Regarding tumour characteristics, the mean lesion size was 10 cm (range 4–17 cm). Lesion size had no impact on the type of resection (adnexectomy or cystectomy, with mean sizes of 10.25 cm and 10.3 cm, respectively;  $p=0.98$ ), but was associated with the surgical approach (laparoscopy, laparoconversion or primary laparotomy, with mean sizes of 7.5 cm,

11.9 cm and 14 cm, respectively;  $p=0.08$ ). Frozen sections were studied in six cases (42.9%), and ascites was observed in three cases (21.4%) (Cases 12, 13 and 14).

The histological type was serous in seven cases (50%), mucinous in six cases (42.9%) and seromucinous in one case (7.1%). Among the serous tumours, there were two cases with an associated micropapillary component ( $n=2$ , 28.5%), including one case with a micro-invasive focus on the contralateral ovary. Among the mucinous tumours, there were five intestinal subtypes, including one case associated with the finding of a mature teratoma, and one case of unknown subtype. The seromucinous case was an endocervical subtype with a non-invasive implant.

There were two cases of bilateral tumours. One had been detected pre-operatively (FIGO stage IB, Case 13), and the other was discovered peri-operatively with histological confirmation on the resected bilateral cystectomy specimen (Case 4).

Pre-operatively, diagnostic staging based on FIGO criteria was stage IA in most cases ( $n=13$ , 92.8%) and stage IB in one case (7.1%). On initial surgery, there were six intra-operative ruptures (42.8%) and one pre-operative rupture, with FIGO stage IA upstaged to IC1 or IC2 (Table 3). Peritoneal cytology was positive with the presence of malignant cells in two cases (14.3%) (Cases 4 and 13), with FIGO stages IA and IB, respectively, upstaged to stage IC3 (Table 3).

**<insert Table 3 near here>**

### *3.3. Restaging surgery*

All characteristics are summarized in Table 3. Restaging surgery was necessary for most patients ( $n=12$ , 85.7%), and routinely included peritoneal cytology, multiple peritoneal biopsies (pouch of Douglas, prevesical space and bilateral pelvic gutters) and infracolic

omentectomy. Appendectomy was performed or had been performed in most cases ( $n=12$ , 85.7%). Treatment was conservative in nine cases (75%) and radical (with contralateral adnexectomy) in three cases (25%). Hysterectomy was performed in two cases (14.3%): one case of mucinous tumour in a 42-year-old patient who did not wish for any subsequent pregnancies, and one case of serous tumour with a micropapillary component and micro-invasive implant in a 25-year-old patient.

On completion of this restaging surgery, for the total sample population, six cases retained the same FIGO stage (IA; 42.9%), six cases were reclassified as stage IC1 or IC2 (intra- or pre-operative extracapsular rupture,  $n=5$  and  $n=1$ , respectively) (42.9%), one case was reclassified as stage IC3 (peritoneal cytology positive) (7.1%), and one case was reclassified as stage IIB (Case 13) (7.1%).

Ovarian involvement was bilateral in two cases, with positive peritoneal cytology in both patients. Implants were also detected, being non-invasive in Case 4 and invasive in Case 13. Case 13 had a serous BOT with a unilateral micropapillary component, and underwent unilateral adnexectomy with contralateral ovarian biopsy; this revealed the presence of a micro-invasive implant measuring 6 mm. During staging surgery, peritoneal cytology demonstrated the presence of malignant tumour cells, and the disease was reclassified as FIGO stage IIB. There was no intra-operative cystic rupture. Treatment was radical with contralateral adnexectomy, hysterectomy, omentectomy, multiple peritoneal biopsies, appendectomy, para-aortic lymphadenectomy and pelvic curettage. Definitive histology also detected an isolated micro-invasive parietal implant in the left pelvic gutter. No lymph node invasion was found in the dissected nodes (pelvic: N0/7; para-aortic: N0/20). Treatment was followed up by adjuvant chemotherapy with carboplatin-taxol.

The mean follow-up was 31.4 [standard deviation (SD) 14.8] months. To date, no deaths have been recorded among the study patients. Recurrent lesions have occurred in two

patients (14.3%) (Cases 3 and 4). In Case 3, the recurrence was particularly severe, with an intestinal mucinous BOT, initially FIGO stage IA, measuring 6 cm, which underwent unilateral adnexectomy, with secondary staging surgery (peritoneal cytology, multiple biopsies and infracolic omentectomy) upstaging the tumour to stage IC2 due to pre-operative cyst rupture. No implants were identified. The patient had undergone appendectomy in the past. Recurrence occurred 30 months after initial surgery, with a clinical picture of adnexal torsion accompanied by major peritoneal carcinosis, ascites, extensive intestinal nodules and pleural metastases, upstaging the disease to FIGO stage IV. After left adnexectomy and detorsion, treatment included six courses of chemotherapy with carboplatin-taxol, followed by closure surgery including omentectomy, total colectomy, splenectomy, cholecystectomy, and para-aortic and pelvic lymphadenectomies which revealed lymph node metastases, but without hysterectomy. The second case (Case 4) had a bilateral endocervical seromucinous BOT, and initially underwent conservative treatment with bilateral cystectomy. This case was initially classed as FIGO stage IC3 due to intra-operative rupture of the cyst and positive peritoneal cytology. Complete staging surgery was performed subsequently (peritoneal cytology, multiple biopsies, infracolic omentectomy and appendectomy), and revealed the presence of non-invasive peritoneal implants. Recurrence occurred unilaterally (FIGO stage I), indicating that unilateral adnexectomy was necessary without any additional surgical procedures.

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#### **4. Discussion**

This study presents an original multi-centre series of BOTs diagnosed and treated during pregnancy. After the series published by Fauvet et al. in 2012 [9], this is the second multi-centre study devoted to the diagnosis and management of BOTs during pregnancy. A review of the current literature highlights several studies on the impact of treating these tumours on

subsequent fertility, but only case reports have been published to date on their management during pregnancy.

The FRANCOGYN database is a multi-centre national database integrating data from French expert centres in pelvic cancerological diseases. This database pools patients from five centres (Poissy, Lariboisiere and Jean Verdier in Paris; Lille CHU and Strasbourg CHU) and includes 345 cases registered between 2005 and 2017.

#### *4.1. Results*

BOTs are set apart from other ovarian cancers in terms of the age of onset, and generally occur 10 years earlier than other ovarian adenocarcinomas [3]. This study confirmed this tendency with a mean recorded age of 29.8 years in the study population. The two main problems caused by the early age of onset are preservation of fertility, and a potential increase in the number of cases occurring during pregnancy, especially in view of the advancing maternal age in France.

Furthermore, routine ultrasound screening in the first trimester of pregnancy and the improving performance of diagnostic methods supports the hypothesis of a potential increase in the number of cases of BOT diagnosed during pregnancy.

In this study, BOTs detected during pregnancy accounted for 4% of all BOTs, but this is probably an underestimate. In most cases, a suspicion of ovarian tumour had already been raised on routine ultrasonography, usually during first trimester ultrasonography (85.7% of cases). Ultrasonography is the gold standard to characterize adnexal masses during pregnancy. In order to standardize the diagnosis, Timmerman et al. established ‘simple rules’ for endovaginal ultrasonography with very high sensitivity (95%) and specificity (91%) [11]. Recent French recommendations indicate pelvic magnetic resonance imaging (MRI) from 12 weeks of gestation onwards in the event of an indeterminate adnexal mass [12]. Most

patients underwent additional pelvic MRI in order to confirm the diagnosis (78.5%), a technique with moderate sensitivity and specificity (54.5% true positives, 18.2% overestimation of suspected malignancy, 27.3% underestimation of suspected benignity). Postsurgical obstetric outcomes were unknown due to the prospective collection of data.

Initial surgery was performed during pregnancy for most patients, but data on the gestational age at the time of surgery were missing in several cases ( $n=5$ , 35.7%). Only two patients underwent single-step staging surgery: one during pregnancy and another in the immediate post partum, which is similar to data in the literature [9,13–15]. This can be explained by the difficulties of operating on these patients due to the volume of the cyst as well as the uterine volume, as surgery is most commonly performed in the second trimester of pregnancy [12,16]. The initial surgical approach chosen was usually laparoscopy, although laparoconversion was common due to tumour size; this follows current treatment recommendations (Observatory on Rare Malignant Gynecological Tumors) [17]. Whenever possible, the preferred surgical approach should be laparoscopy given its minimally invasive nature [18–20]. However, surgeons generally elect to perform laparotomy for large tumours in order to avoid intra-operative rupture of the tumour capsule, which seems to be a prognostic factor in the risk of recurrence [17,21,22] although this is still under debate [23].

All the cases in this study benefited from conservative surgery. This strategy has been proven to be safe and efficient to enable further pregnancy, as shown by Candotti et al. [24]. They reported a recurrence rate of 19%, a survival rate of 100%, and spontaneous pregnancies were achieved by 73% of patients who wanted another baby.

In the present study, frozen sections were used in six cases, including the two cases who underwent single-step staging surgery (Cases 1 and 10), but histology was not available

for these examinations. As such, it was not possible to draw any conclusions regarding the sensitivity and specificity of this procedure.

During initial surgery, 92.8% of BOTs were classified as FIGO stage IA with involvement of an isolated unilateral ovary ( $n=13$ ), which concurs with data in the literature showing that 90% of BOTs diagnosed in pregnant women are stage I [25]. The tumour profile was bilateral from the outset in a single case (Case 13), and became bilateral in another case when it was decided intra-operatively to perform bilateral cystectomy (Case 4).

The histological type found was similar to the results of other recent studies, with a predominance of serous tumours (50%) and a tendency toward an increase in mucinous tumours (42.8%) [9,13,26]; in addition, there was one case with a seromucinous tumour.

In their work on the diagnostic and therapeutic management of BOTs during pregnancy, Fauvet et al. demonstrated a high incidence of aggressive BOTs when they occur during pregnancy [9]. Almost 41.2% of BOTs exhibited a micropapillary component. In the present study, the micropapillary component associated with serous tumours was 28.5% ( $n=2/7$ ), although this result cannot be extrapolated due to the small patient population. Nevertheless, this is a crucial histological feature in the prognosis as it has been shown that the micropapillary component of serous BOTs is often associated with bilateral tumours and invasive implants [27,28]. In this study, one of the two cases of serous BOT with a micropapillary component presented with micro-invasive implants on the contralateral ovary along with the presence of tumour cells on peritoneal cytology, upstaging the tumour from FIGO stage IA to stage IIB, and requiring adjuvant treatment by chemotherapy. This was the only case of invasive implant in this series.

Intra- or pre-operative capsular rupture was common in this study ( $n=7$ , 50%), and involved both cases presenting with recurrence (Cases 3 and 4). It occurred more frequently in cases who underwent primary laparoscopy ( $n=3$ , 42.9%) or laparoconversion ( $n=3$ , 42.9%)

than in cases where laparotomy was performed from the outset ( $n=1$ , 14.2%), which corresponds with data in the literature [21]. The impact of intra-operative cyst rupture on the prognosis of BOTs is controversial, but it seems that intra-operative rupture increases the rate of recurrence according to the most recent data in the literature [22].

Restaging surgery was performed in all patients who did not initially undergo complete surgery ( $n=12$ ; 85.7%). The use of this staging surgery is debatable, especially in those cases of FIGO stage IA serous BOT in whom staging remained identical following surgery and recurrence was not observed.

The literature reports a low rate of BOT upstaging, with a minor impact on the recurrence rate [15,29]. Upstaging appears to be more common in cases of serous BOT treated by cystectomy [15]. In the present study, BOTs were commonly reclassified due to the frequent occurrence of intra- or pre-operative rupture ( $n=7$ , 50% of cases), but remained FIGO stage I. Only one case was upstaged to FIGO stage IIB; this was a micropapillary serous BOT with a micro-invasive implant (Case 13). Therefore, few cases in this study required upstaging, which is consistent with the literature [15,30].

In addition to the micropapillary component, other prognostic factors have been identified recently in the risk of recurrence for FIGO stage I serous BOTs (i.e. most BOTs detected during pregnancy), such as young age (<30 years), conservative treatment by cystectomy, and bilateral character [31]. The observation of aggressive treatment regimens in pregnant women who meet these criteria is therefore readily comprehensible.

The literature only reports one study with more important aggressiveness criteria for BOTs during pregnancy [9]. Thus, there are insufficient data for the French recommendations to recommend a type of surgical treatment or surgical approach [12]. The management of these patients must be discussed in multi-disciplinary meetings on a case-by-case basis, taking



into account the obstetric term, tumour type and size, and desire for subsequent pregnancy [12].

In this study, the common finding in the two cases of recurrence (Cases 3 and 4) was a mucinous component (mucinous and seromucinous) in patients aged  $\leq 30$  years (23 and 30 years, respectively) who had undergone initial surgery by laparoscopy (laparoscopy and laparoconversion, respectively) during which cyst rupture had occurred. Treatment was conservative (unilateral adnexectomy and bilateral cystectomy, respectively) and the tumour was bilateral in the latter case. These results cannot be extrapolated in view of the small number represented, although they concur, in part, with data in the literature.

#### *4.2. Limitations*

This study had several limitations. Most importantly, this was a retrospective study with a significant amount of missing data. The sample size was very small ( $n=14$ ) despite the duration of the study and its multi-centre nature. There was significant classification bias in conceptualization of the database, which made it difficult to identify cases of pregnancy and data relative to this event (weeks of gestation at diagnosis, weeks of gestation at initial surgery, interval between initial surgery and restaging, obstetric issues etc.). This can be explained by the fact that the occurrence of malignant ovarian tumours in pregnant women remains rare, and was not considered when the database was built. The lack of data concerning pregnancy contrasts with the very large amount of data included in this database.

The diversity of practices applied at the different centres also made it difficult to define a management algorithm.

Another bias could be the short mean follow-up time [31.4 (SD 14.8) months]. The recent literature indicates a higher median time for recurrence; for example, 48 months for Candotti et al. [24]. This short mean follow-up time is ascribed to the conception of the

database, and is probably related to loss to follow-up in this small series. Despite the lack of data, the length of follow-up complies with the data from recent French recommendations on the management of BOTs, which find a recurrence rate, mean or median, always superior to 2 years of follow-up [32].

## **5. Conclusion**

Despite the small sample size, this study complements the scant existing literature on BOTs during pregnancy. These tumours remain rare but management is important, requiring a balance between optimal treatment and preservation of subsequent fertility. There is very little standardization of the management strategy during pregnancy, although it is based on the gold standard treatment in non-pregnant women (i.e. initial surgery with complete staging). Recently, French experts have tried to issue recommendations on the topic, but larger-scale projects are needed to confirm the current hypotheses regarding BOTs during pregnancy.

### **Conflict of interest**

None declared.

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None.

### **References**

- [1] Hart WR. Borderline epithelial tumors of the ovary. *Mod Pathol Off J U S Can Acad Pathol Inc* 2005;18(Suppl. 2):S33–50.
- [2] Daraï E, Fauvet R, Uzan C, Gouy S, Duvillard P, Morice P. Fertility and borderline ovarian tumor: a systematic review of conservative management, risk of recurrence and alternative options. *Hum Reprod Update* 2013;19:151–66.
- [3] Tulpin L, Akerman G, Morel O, Desfeux P, Malartic C, Barranger E. [Management of borderline tumors of the ovary]. *J Gynecol Obstet Biol Reprod (Paris)* 2008;37:F69–76.
- [4] Skírnisdóttir I, Garmo H, Wilander E, Holmberg L. Borderline ovarian tumors in Sweden 1960–2005: trends in incidence and age at diagnosis compared to ovarian cancer. *Int J Cancer*

2008;123:1897–901.

[5] Recommandations du CFEF (Collège Français d’Echographie Foetale) 2016 – éléments devant figurer dans le compte rendu d’échographie. CFEF; 2016. Available at: <http://www.cfef.org/archives/bricabrac/cneof/compte-renducneof2016.pdf> (last accessed 10 November 2020).

[6] Schwartz N, Timor-Tritsch IE, Wang E. Adnexal masses in pregnancy. *Clin Obstet Gynecol* 2009;52:570–85.

[7] Sherard GB, Hodson CA, Williams HJ, Semer DA, Hadi HA, Tait DL. Adnexal masses and pregnancy: a 12-year experience. *Am J Obstet Gynecol* 2003;189:358–62, discussion 362–3.

[8] Casanova J, Maciel R, Ferreira V, Fernandes E, Rodrigues RM. Borderline ovarian tumor during pregnancy: a case report. *Case Rep Obstet Gynecol* 2013;2013:160319.

[9] Fauvet R, Brzakowski M, Morice P, Resch B, Marret H, Graesslin O, et al. Borderline ovarian tumors diagnosed during pregnancy exhibit a high incidence of aggressive features: results of a French multicenter study. *Ann Oncol Off J Eur Soc Med Oncol* 2012;23:1481–7.

[10] FIGO (International Federation of Gynecology and Obstetrics) 26th Annual Report on the Results of Treatment in Gynecological Cancer. *Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet* 2006;95(Suppl. 1):S1–257.

[11] Timmerman D, Testa AC, Bourne T, Ameye L, Jurkovic D, Van Holsbeke C, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol Off J Int Soc Ultrasound Obstet Gynecol* 2008;31:681–90.

[12] Zilliox M, Lallemand M, Thomassin-Naggara I, Ramanah R. [Borderline ovarian tumours: CNGOF guidelines for clinical practice – pregnancy]. *Gynecol Obstet Fertil Senol* 2020;48:322–9.

[13] Fauvet R, Boccara J, Dufournet C, Poncelet C, Daraï E. Laparoscopic management of

borderline ovarian tumors: results of a French multicenter study. *Ann Oncol Off J Eur Soc Med Oncol* 2005;16:403–10.

[14] Fauvet R, Poncelet C, Darai E. [Feasibility and limits of laparoscopic treatment of borderline ovarian tumours]. *Gynecol Obstet Fertil* 2006;34:470–8.

[15] Fauvet R, Boccara J, Dufournet C, David-Montefiore E, Poncelet C, Darai E. Restaging surgery for women with borderline ovarian tumors: results of a French multicenter study. *Cancer* 2004;100:1145–51.

[16] Malek-mellouli M, Taamallah N, Ben Amara F, Reziga H. [Laparoscopic management of ovarian masses during pregnancy]. *Tunis Med* 2013;91:534–8.

[17] Référentiel de la prise en charge des tumeurs borderline de l’ovaire. Observatoire des Tumeurs Malignes Rares Gynécologiques; 2018. Available at: <http://www.ovaire-rare.org/TMRG/upload/howto/ReferentielBorderline.pdf>

[18] Hakoun AM, AbouAl-Shaar I, Zaza KJ, Abou-Al-Shaar H, A Salloum MN. Adnexal masses in pregnancy: an updated review. *Avicenna J Med* 2017;7:153–7.

[19] Hoover K, Jenkins TR. Evaluation and management of adnexal mass in pregnancy. *Am J Obstet Gynecol* 2011;205:97–102.

[20] Guidelines Committee of the Society of American Gastrointestinal and Endoscopic Surgeons, Yumi H. Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy: this statement was reviewed and approved by the Board of Governors of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), September 2007. It was prepared by the SAGES Guidelines Committee. *Surg Endosc* 2008;22:849–61.

[21] Maneo A, Vignali M, Chiari S, Colombo A, Mangioni C, Landoni F. Are borderline tumors of the ovary safely treated by laparoscopy? *Gynecol Oncol* 2004;94:387–92.

[22] Poncelet C, Fauvet R, Boccara J, Darai E. Recurrence after cystectomy for borderline

ovarian tumors: results of a French multicenter study. *Ann Surg Oncol* 2006;13:565–71.

[23] Bourdel N, Huchon C, Cendos AW, Azais H, Bendifallah S, Bolze PA, et al. [Borderline ovarian tumours: CNGOF guidelines for clinical practice – short text]. *Gynecol Obstet Fertil Senol* 2020;48:223–35.

[24] Candotti G, Peiretti M, Mangili G, Bergamini A, Candiani M, Cioffi R, et al. What women want: fertility sparing surgery in borderline ovarian tumours patients and pregnancy outcome. *Eur J Surg Oncol* 2020;46:888–92.

[25] Trimble EL, Trimble CL. Ovarian tumors of low malignant potential. *Curr Treat Options Oncol* 2001;2:103–8.

[26] Bonnamy L, Fignon A, Fetissof F, Berger C, Body G, Lansac J. [Borderline tumors of the ovary: a multicenter study in 137 patients]. *J Gynecol Obstet Biol Reprod (Paris)* 2001;30:272–81.

[27] Seidman JD, Kurman RJ. Ovarian serous borderline tumors: a critical review of the literature with emphasis on prognostic indicators. *Hum Pathol* 2000;31:539–57.

[28] Laurent I, Uzan C, Gouy S, Pautier P, Duvillard P, Morice P. Results after conservative treatment of serous borderline tumors of the ovary with a micropapillary pattern. *Ann Surg Oncol* 2008;15:3561–6.

[29] Querleu D, Papageorgiou T, Lambaudie E, Sonoda Y, Narducci F, LeBlanc E. Laparoscopic restaging of borderline ovarian tumours: results of 30 cases initially presumed as stage IA borderline ovarian tumours. *BJOG* 2003;110:201–4.

[30] Zapardiel I, Rosenberg P, Peiretti M, Zanagnolo V, Sanguineti F, Aletti G, et al. The role of restaging borderline ovarian tumors: single institution experience and review of the literature. *Gynecol Oncol* 2010;119:274–7.

[31] Uzan C, Muller E, Kane A, Rey A, Gouy S, Bendifallah S, et al. Prognostic factors for recurrence after conservative treatment in a series of 119 patients with stage I serous

borderline tumors of the ovary. *Ann Oncol* 2014;25:166–71.

[32] 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;48:314–21.

**Table 1**

General and initial diagnostic characteristics of 14 cases of borderline ovarian tumour during pregnancy.

|  | <i>n</i> =14 (%) |
|--|------------------|
| Age, mean (standard deviation), years                                | 29.3 (6.2)       |
| Body mass index, mean (range), kg/m <sup>2</sup>                     | 23.8 (17–34)     |
| Parity, mean (range), <i>n</i> (%)                                   | 1 (0–3)          |
| Primiparous  | 7 (50%)          |
| Nulliparous  | 4 (28.5%)        |
| Family history of gynaecological cancer, <i>n</i> (%)                | 1 (7.1%)         |
| Time of diagnosis during pregnancy, mean (range), weeks of gestation | 13.8 (6–24)      |
| Missing data   | 6 (42.8%)        |
| Diagnostic circumstances   |                  |
| Opportunistic on T1 ultrasonography                                  | 12 (85.7%)       |
| Abdominal pains  | 1 (7.1%)         |
| Suspected adnexal torsion  | 1 (7.1%)         |
| CA125, IU/ml   |                  |
| <35 (normal)   | 5 (35.7%)        |
| ≥35  | 6 (42.9%)        |
| Missing data   | 3 (21.4%)        |
| Ultrasonography  | 14 (100%)        |
| Tumour size, mean (range), cm  | 10 (4–17)        |
| Bilateral from outset  | 1 (7.1%)         |
| Initial MRI  | 11 (78.5%)       |
| Suspected borderline tumour  | 6 (54.5%)        |
| Suspected malignant tumour   | 2 (18.2%)        |
| Suspected benign tumour  | 3 (27.3%)        |

T1, first trimester; MRI, magnetic resonance imaging.



**Table 2**

Initial surgical and histological characteristics of 14 cases of borderline ovarian tumour during pregnancy.

| Case | Tumour size (cm)        | FIGO stage on diagnosis pre-operatively | Surgical approach | Type of surgery         | Histological type | Additional histological factors  |
|------|-------------------------|---|-------------------|-------------------------|-------------------|--|
| 1    | 5                       | IA                                      | Laparoscopy       | UA + PC + MB + OM + APP | Serous            |  |
| 2    | 4                       | IA                                      | Laparoscopy       | UC + PC                 | Serous            | Micropapillary   |
| 3    | 6                       | IA                                      | Laparoscopy       | UA + PC                 | Mucinous          | Intestinal   |
| 4    | 7                       | IA                                      | Laparoconversion  | BC + PC                 | Seromucinous      | Endocervical, non-invasive implant   |
| 5    | 13                      | IA                                      | Laparotomy        | UA + PC                 | Mucinous          | Intestinal   |
| 6    | 6.5                     | IA                                      | Laparoconversion  | UC + PC                 | Serous            |  |
| 7    | 9                       | IA                                      | Laparoscopy       | UA + PC + MB            | Mucinous          | Intestinal   |
| 8    | 12                      | IA                                      | Laparoscopy       | UC + PC                 | Mucinous          | NK   |
| 9    | 14                      | IA                                      | Laparoconversion  | UC + PC                 | Serous            |  |
| 10   | 7                       | IA                                      | Laparoscopy       | UA + PC + MB + OM       | Serous            |  |
| 11   | 15                      | IA                                      | Laparotomy        | UC + PC                 | Mucinous          | Intestinal with foci of endometriosis, and associated with a mature teratoma |
| 12   | 15                      | IA                                      | Laparoconversion  | UA + PC + MB            | Mucinous          | Intestinal   |
| 13   | 10 (left) and 5 (right) | IB                                      | Laparoscopy       | UA + COB + PC           | Serous            | Micropapillary, micro-invasive focus on the contralateral ovary              |
| 14   | 17                      | IA                                      | Laparoconversion  | UA + PC                 | Serous            |  |

FIGO, International Federation of Gynecology and Obstetrics; UC, unilateral cystectomy; BC, bilateral cystectomy; UA, unilateral adnexectomy; COB, contralateral ovarian biopsy; PC, peritoneal cytology; MB, multiple biopsies; OM, omentectomy; APP, appendectomy; NK, not known.

**Table 3**

Results of restaging surgery.

| Case | Histological type  | Type of surgery               | Definitive<br>FIGO stage | Recurrence   |
|------|--|-------------------------------|--------------------------|--|
| 1    | Serous   | ∅                             | IA                       | No   |
| 2    | Micropapillary serous  | IUA + CC + PC + OM + MB       | IC1                      | No   |
| 3    | Intestinal mucinous  | PC + OM + MB                  | IC2                      | Invasive stage IV<br>mucinous adenocarcinoma<br>(peritoneal carcinosis, pleural<br>and splenic metastases) |
| 4    | Endocervical seromucinous<br>Non-invasive implant  | PC + OM + MB                  | IC3                      | Stage IA mucinous BOT  |
| 5    | Intestinal mucinous  | PC + OM + MB                  | IA                       | No   |
| 6    | Serous   | IUA + PC + OM + MB            | IC1                      | No   |
| 7    | Intestinal mucinous  | CUA + UIR + PC + OM + MB      | IA                       | No   |
| 8    | Mucinous   | IUA + CC + PC + OM + MB       | IC1                      | No   |
| 9    | Serous   | PC + OM + MB                  | IC1                      | No   |
| 10   | Serous   | ∅                             | IA                       |  |
| 11   | Intestinal mucinous with<br>endometriosis foci, and associated<br>with a mature teratoma | PC + OM + MB                  | IC1                      | No   |
| 12   | Mucinous   | HRT + CUA + PC + OM + MB      | IA                       | No   |
| 13   | Micropapillary serous, micro-<br>invasive focus over contralateral<br>ovary              | HRT + CUA + CC + PC + OM + MB | IIB                      | No   |
| 14   | Serous   | PC + OM + MB                  | IA                       | No   |

FIGO, International Federation of Gynecology and Obstetrics; ∅, no restaging surgery; IUA, ipsilateral unilateral adnexectomy; CUA, contralateral unilateral adnexectomy; CC, contralateral cystectomy; UIR, uterine implant resection; PC, peritoneal cytology; MB, multiple biopsies; OM, omentectomy; APP, appendectomy; BOT, borderline ovarian tumour; IC1, surgical spill intra-operatively; IC2, capsule ruptured before surgery or tumour on ovarian or fallopian tube surface; IC3, malignant cells present in ascites or peritoneal washings.

**Figure 1.** 2014 International Federation of Gynecology and Obstetrics ovarian, fallopian tube and peritoneal cancer staging system and corresponding TNM staging.

|   |   |   |
|---|---|---|
| <b>I</b>  | <b>Tumour confined to ovaries or fallopian tube(s)</b>  | <b>T1</b>   |
| IA  | Tumour limited to one ovary (capsule intact) or fallopian tube.<br>No tumour on ovarian or fallopian tube surface.<br>No malignant cells in the ascites or peritoneal washings.   | T1a   |
| IB  | Tumour limited to both ovaries (capsules intact) or fallopian tubes.<br>No tumour on ovarian or fallopian tube surface.<br>No malignant cells in the ascites or peritoneal washings   | T1b   |
| IC<br>IC1<br>IC2<br>IC3   | Tumour limited to one or both ovaries or fallopian tubes, with any of the following:<br>Surgical spill intraoperatively<br>Capsule ruptured before surgery or tumour on ovarian or fallopian tube surface<br>Malignant cells present in the ascites or peritoneal washings  | T1c   |
| <b>II</b>   | <b>Tumour involves one or both ovaries or fallopian tubes with pelvic extension (below pelvic brim) or peritoneal cancer (Tp)</b>   | <b>T2</b>   |
| IIA<br>IIB  | Extension and/or implants on the uterus and/or fallopian tubes/and/or ovaries<br>Extension to other pelvic intraperitoneal tissues  | T2a<br>T2b  |
| <b>III</b>  | <b>Tumour involves one or both ovaries, or fallopian tubes, or primary peritoneal cancer, with cytologically or histologically confirmed spread to the peritoneum outside the pelvis and/or metastasis to the retroperitoneal lymph nodes</b>   | <b>T3</b>   |
| IIIA<br>IIIA1<br>IIIA1(i)<br>IIIA1(ii)<br>IIIA 2<br>IIIB<br>III C | Metastasis to the retroperitoneal lymph nodes with or without microscopic peritoneal involvement beyond the pelvis<br>Positive retroperitoneal lymph nodes only (cytologically or histologically proven)<br>Metastasis $\leq$ 10 mm in greatest dimension (note this is tumour dimension and not lymph node dimension)<br>Metastasis $>$ 10 mm in greatest dimension<br>Microscopic extrapelvic (above the pelvic brim) peritoneal involvement with or without positive retroperitoneal lymph nodes<br>Macroscopic peritoneal metastases beyond the pelvic brim $\leq$ 2 cm in greatest dimension, with or without metastasis to the retroperitoneal lymph nodes<br>Macroscopic peritoneal metastases beyond the pelvic brim $>$ 2 cm in greatest dimension, with or without metastases to the retroperitoneal nodes (Note 1) | T1, T2, T3aN1<br><br>T3a/T3aN1<br><br>T3a/T3aN1<br>T3b/T3bN1<br><br>T3c/T3cN1 |
| <b>IV</b>   | <b>Distant metastasis excluding peritoneal metastases</b>   | <b>Any T, Any N, M1</b>   |
| Stage IV A<br>Stage IV B  | Pleural effusion with positive cytology<br>Metastases to extra-abdominal organs (including inguinal lymph nodes and lymph nodes outside of abdominal cavity) (Note 2)   | Any T, Any N, M1  |

Based on 'DG Mutch and J Prat. 2014 FIGO staging for ovarian, fallopian tube and peritoneal cancer. Gynecologic Oncology 2014;133:401-04'

**Notes:**

1. Includes extension of tumour to the capsule of liver and spleen without parenchymal involvement of either organ.
2. Parenchymal metastases are Stage IV B.

**Author queries**

This article has been edited extensively – please check the proofs carefully to ensure that your meaning has not been altered

Section 4.2: ‘which find a recurrence rate, mean or median, always superior to 2 years of follow-up’ – please clarify

Ref 5 – need author and city

Ref 17 – need author and city. The web link does not work. Please check and supply date when this website was last accessed