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CJOG CLINICAL JOURNAL OF OBSTETRICS AND GYNECOLOGY
ISSN 2640-2890

Review Article

Laparoscopic staging of borderline ovarian tumours – Technique and results

Klimatsouda M, Donoudis C, Kontopoulos G and Daponte A*

Department of Obstetrics and Gynecology, Faculty of Medicine, School of Health Sciences University of Thessaly, University Hospital of Larisa, Greece

Abstract

Borderline Ovarian Tumors (BOT) tend to present more frequently nowadays, especially in younger women. Furthermore fertility preservation and laparoscopic management is often desired and therefore appropriate counselling is challenging and the treatment selection must be made on evidence based medicine.

Adnexal mass could be a random finding when a typical gynecologic examination is performed. The diagnostic algorithm for possible BOT is the same as for any ovarian tumor, but the treatment options and techniques may vary based on patient's willing to preserve her fertility or not. Laparoscopic or laparotomy approach has similar results although intraoperative findings and frozen section may redirect the primary treatment planning.

When an initial conservative approach is chosen, a secondary approach including total hysterectomy and bilateral salpingo-oophorectomy with staging should be considered. Hence a full counselling is recommended before any primary approach.

More Information

***Address for Correspondence:** Daponte A, Department of Obstetrics and Gynecology, Faculty of Medicine, School of Health Sciences University of Thessaly, University Hospital of Larisa, Greece, Tel: +302413502795; +302413502796; Email: daponte@med.uth.gr; dapontealexandros@gmail.com; maryklim79@gmail.com

Submitted: February 24, 2021
Approved: March 16, 2021
Published: March 17, 2021

How to cite this article: Klimatsouda M, Donoudis C, Kontopoulos G and Daponte A. Laparoscopic staging of borderline ovarian tumours – Technique and results. Clin J Obstet Gynecol. 2021; 4: 020-024.

DOI: 10.29328/journal.cjog.1001081

Keywords: Borderline; Ovarian tumor; Laparoscopy; Staging; Fertility preservation

Abbreviations: BOT: Borderline Ovarian Tumor; Ca 125: Cancer antigen 125; IOTA LR2: International Ovarian; Tumor Analysis LR2 risk model; MRI: Magnetic Resonance Imaging; TAH: Total Abdominal Hysterectomy; BSO: Bilateral Salpingo-oophorectomy; TVS: Transvaginal Sonography

General aspects

Borderline ovarian tumors were first described by Taylor in 1929. The average age of women with Borderline ovarian tumors is 40 years. The percentage of ovarian tumors which are classified histologically as borderline is between 10 to 20%. They are encountered usually in one ovary (unilateral). When found bilateral they are in 30% serous and in 8% mucinous.

The symptoms of BOT are the same as for any adnexal mass and include irregular menses, pain or pressure in the lower abdomen, urinary frequency or constipation and sometimes dyspareunia. Many times, the mass is found incidentally during the routine gynecologic examination.

BOT are usually diagnosed in an early stage and they have a good prognosis -except from the ones with micropapillary or clear cell histology, but they are often misdiagnosed and suboptimal operated, whereas surgical restaging is always required. BOT are associated with age, nulliparity and probably with use of ovarian stimulating drugs [1,2].

In BOT, pathological classification is important, especially for high-risk subtypes.

In order to clarify this possible association ovarian cancer of different histological types and borderline it is recommended that ovarian tumors should be analysed separately to obtain a more reliable difference in incidence between cancer and borderline tumours.

Currently, no 'safe' limits on dose or duration of any of the other drugs used in ovarian stimulation are recommended. One important question for women and practitioners to be determined is whether clomiphene citrate alone is less likely to cause cancer compared with multi-therapy; also, risks associated with the number of IVF stimulation cycles remain to be clarified.

The diagnosis of BOT requires a full medical history, physical examination, pelvic and abdominal imaging and surgical evaluation. The final diagnosis necessitates a histological confirmation.

The diagnosis requires transvaginal ultrasound ideally by an experienced specialist and biomarker Ca 125 [3]. Often the ultrasound's images are similar with benign or invasive tumours. BOT histology is usually associated within a mass with both solid and fluid components, unilocular cyst or with papilla, which could be seen with an invasive tumor. As recently reported, the IOTA LR2 model for the ultrasound has a similar sensitivity to MRI for discriminating between benign and malignant tumors and a higher specificity compared with MRI. Either alone or in conjunction with MRI, the IOTA LR2 model should be included in preoperative evaluation of adnexal masses [4].

Nevertheless, only tumor size and high levels of Ca 125 could set the suspicion of ovarian malignancy. Tumor size > 8 cm is associated with 22,4% invasive cancer on final pathology *vs*. 3,2% in tumors < 8 cm [5].

Surgical evaluation – Treatment

The intraabdominal surgical procedure should be the same either with open or laparoscopic surgery and this must be preoperatively explained to the patient.

The surgical evaluation and treatment are based upon age and desire of fertility preservation. In cases where either fertility preservation is not desired or family is completed the surgical approach is staging laparotomy or laparoscopy including total hysterectomy with bilateral salpingo-oophorectomy, omentectomy, peritoneal washing and multiple peritoneal biopsies. Only suspicious lymph nodes should be sampled. Appendectomy may be considered if the histological type reveals mucinous type. This is an additional reason why intraoperative frozen section and histologic examination is always required.

If fertility preservation or endocrine function preservation is required (stage I) cystectomy or unilateral salpingo-oophorectomy could be the surgical option. Still in those cases full staging should be performed; pelvic washings should be sampled with omental biopsy and biopsies of any peritoneal lesions. Appendectomy should be again considered in cases of mucinous type BOT. Furthermore, clear cell should be excluded from conservative management. Intraoperative Frozen section and histologic examination is required.

The dilemma that arises is if simple cystectomy or oophorectomy or unilateral salpingo-oopherectomy (USO), is an appropriate treatment for women with BOTs who wish to preserve fertility. Even a cystectomy could be an acceptable fertility-sparing therapy in certain patients, when a cystectomy is the only surgical option after appropriate extensive counselling. Even in advanced disease with one ovary unaffected, fertility may be retained provided the patient gets full counselling.

In each patient, regardless if fertility preservation is intended or not, thorough abdominal inspection for macroscopic findings should be performed. In particular, the surgeon overviews thoroughly for presence of extraovarian implants, exophytic growth, anarchic vascularization on the surface of the ovary or ascites.

There is an ongoing debate, for more than ten years , whether laparoscopic or open surgery approach is preferable for BOTs treatment.

Criteria for referral to gynaecological oncologist are subcategorized into two groups, premenopausal (< 50 yrs) and postmenopausal (> 50 yrs) as below [6].

Premenopausal	Postmenopausal
CA 125 levels (> 200 iu/ml)	Elevated CA 125 levels
Ascites	Ascites
Evidence of abdominal or distant metastasis	Nodular or fixed pelvic mass
Family history of breast or ovarian Cancer	Evidence of abdominal or distant metastasis
	Family history of breast or ovarian cancer

As far as intraoperative frozen section is concerned sensitivity varies from 71,1% to 75%, positive predictive value ranges from 84,3% to 94,5%. It must be mentioned that BOTs are not only often under diagnosed in 6,6% to 28%, but also over diagnosed in up to 30,6% of BOT patients [5].

When intraoperative frozen section reveals endometrioid or clear cell tumor's histologic subtype reclassification in final histology is obligatory [5].

Tumor size can be associated with the likelihood of invasive cancer on final histopathological examination of the specimen. BOTs over 8 cm are related to invasiveness up to 22,4%. On the other hand, size< 8cm, are less likely to reveal invasive cancer with a reported incidence of 3,2%. Hence, comprehensive surgical staging in BOT > 8 cm in diameter, as well as those with micropapillary serous, endometrioid, and clear cell histology diagnosed at the time of frozen section analysis is essential [5,7].

Intraoperative frozen section is also useful to differentiate BOTs and benign tumors but concerning differential diagnosis between BOTs and epithelial ovarian cancer it must be remembered that it is not always feasible with frozen section!

What about lymph nodes?

Lymph node sampling has low prognostic utility. The overall survival in BOT patients is 98% for 6,5 years [22]. In BOT the involvement of lymph nodes is 17-21%, whereas malignant transformation is about 2%. For advanced stage BOT tumors lymph node involvement can't be used as a prognostic factor [9].

Several studies have shown that we can omit lymphadenectomy, even for the advanced disease because there is no difference in recurrence or survival rate [8,10-12].

Technique

Omentectomy is a standard procedure for the surgical management of BOTs. The performance of a laparoscopic omentectomy includes in laparoscopic staging the set of 3 ports. The usual position of these ports are a 5 mm port in the right side of the abdomen, a 10 mm camera port usually in the umbilicus and a 10 mm port in the left side of the abdomen. When we perform a partial omentectomy, we remove only certain part of the omentum. More specifically for laparoscopic staging in BOT cases, we prefer infracolic omentectomy; arcades of the gastroepiploic vessels are preserved and the range of resection is bellow gastroepiploic arcades and the rest of the gastrocolic ligament. We make a dissection line 4-5 cm apart from the greater curvature of the stomach. The omentum is divided 2-3 cm distance from the gastroepiploic vessels. We make a window at 2–3 cm apart from the arc of the gastroepiploic vessels near lower to mid body of the stomach. Operator's left hand grasps the greater curvature of the stomach and lifts upward direction, while operator's right hand divides omentum following the gastroepiploic vessels towards the left side to the lower pole of the spleen. It is important to identify the colon to prevent its injury and make sure that the colon wall is not in the way of the dissecting plane. The left gastroepiploic vessels are ligated as the same method as used for total omentectomy [13].

The requirements for a successful laparoscopic surgery are a skilled surgeon, mass < 5 cm, removal of the affected ovary (if conservative therapy desired), cystectomy if fertility is desired in cases of bilateral neoplasia. It must be remembered that cystectomy is reported with a higher risk of relapse [14].

The advantages of laparoscopic techniques include; the use of magnification enables a thorough complete examination of the abdominal cavity to confirm diagnosis and facilitate appropriate staging, facilitation of aspiration and washing of the peritoneum, minimization of surgical invasiveness, postoperative pain and wound - related complications [15,16].

On the other hand, complications of laparoscopic techniques are; possibility of undertreatment (reported associations with higher risk of recurrence and lower survival rates), port site metastasis and most important rupture of the cyst.

Concerns

Fertility sparing surgery should be recommended with caution.

Advanced stage (≥ stage II), a serous type, and the presence of bilateral and micropapillary lesions were associated with a higher recurrence rate and a shorter recurrence interval after conservative surgery.

Treating physicians must be careful in choosing fertility sparing surgery patients and pregnancy should be advised as soon as possible after the surgery. Patients that are not yet ready to conceive can be referred to reproductive endocrinology and infertility clinics for other fertility options, including the freezing of embryos and oocytes.

Adnexectomy (unilateral salpingo-oophorectomy) is preferable for patients with unilateral borderline ovarian tumors to achieve ideal oncological outcomes and a satisfactory pregnancy rate.

Bilateral cystectomy is preferably chosen for patients with bilateral borderline ovarian tumors, since no statistically significant difference in terms of recurrence rate, DFS or pregnancy outcome was observed between bilateral cystectomy and unilateral salpingo-oophorectomy + contra lateral cystectomy groups [14].

Short follow-up periods should be advised, in order to investigate the outcomes of borderline ovarian tumor patients undergoing fertility sparing surgery [14].

Surgical restaging after final histology - exceptions

Surgical restaging is required when initial staging is missing. Laparoscopy in expert hands could still be a valuable surgical option. A selected group of patients could be exempted from restaging; age > 30 yrs, radical treatment, stage IA, negative peritoneal cytology, mucinous- diploid- non micropapillary BOT [17].

In conclusion, the management of BOT could be summarized in the following figure 1.

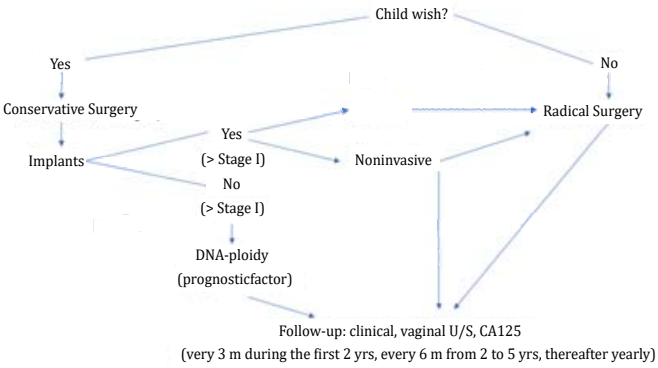

Figure 1

Conservative*: Preferable unilateral Salpingo-oophorectomy or cystectomy when Bilateral tumor/Unilateral salpingo – oophorectomy in Medical History.*

Radical*: TAH+ BSO*

Common Steps*: Peritoneal washings, Omentectomy, Multiple peritoneal biopsies and resection of implants. Appendectomy (mucinous).*

In summary, we present the following practice points which should be considered by gynecology-oncologists, as far as BOTs are concerned.

- Borderline ovarian tumours present similarly to other types of adnexal masses.
- Surgery is the primary treatment, and the surgical approach—open versus minimally invasive—should be individualized.
- For women in the reproductive age group, preoperative fertility preservation counselling is recommended.
- Since most borderline tumours are confined to the ovary (ies) and may involve one ovary, fertility-sparing surgery is feasible in a high proportion of women in the reproductive age group.
- Even if bilateral ovarian involvement is noted, fertility-sparing surgery may still be feasible with bilateral ovarian cystectomies or ovarian cystectomy plus unilateral salpingo-oophorectomy.

If borderline ovarian tumor is diagnosed on frozen section examination, surgical staging should include cytologic washings, omentectomy and peritoneal biopsies.

Routine lymphadenectomy is not recommended as part of surgical staging.

If extra-ovarian spread is noted at surgery, maximum cytoreductive surgery with no gross residual should be the objective.

Postoperative treatment is recommended only for those patients with serous borderline tumours and invasive peritoneal implants.

If relapse with borderline tumor occurs, standard treatment consists of surgery alone.

If relapse with invasive carcinoma occurs, treatment may include secondary surgery and chemotherapy [18-25].

Discussion

BOTs are more likely to present in younger women; therefore, it is important to choose the best treatment whether fertility preservation is desired.

Borderline ovarian epithelial neoplasms are noninvasive neoplasms that occasionally have intraperitoneal spread. The majority of cases are serous or mucinous. If early diagnosed in stage 1, the five-year survival rate approaches 99%. The clinical presentation of Borderline Ovarian Tumors is the same as it is for other adnexal masses, while occasionally could be a random ultrasound finding in examination per year. The diagnostic approach includes a thorough medical history, oncology family history, infertility treatments, a physical examination, pelvic and abdominal imaging and surgical evaluation. Tumor size and serum CA 125 have a diagnostic value, but are not pathognomonic with low positive predictive value. The complete staging procedure for any suspicious ovarian mass is the same and can be carried out laparoscopically or by laparotomy dependent on the surgeons skill and preference to achieve optimal treatment and staging for his patient [26]. The surgical treatment of BOTs depends on the age of the patient, their reproductive status, the surgical findings (stage, frozen section's results etc.) and fertility preservation. In postmenopausal women and when fertility preservation is not desired a full staging procedure with Total Abdominal Hysterectomy and Bilateral Salpingo- Oophorectomy (TAH-BSO), omentectomy and peritoneal washings is performed. In women who wish fertility preservation, a conservative treatment approach can be done when results demonstrate disease stage I and patients are willing to close follow up by the gynecologist. Frozen section must be performed intraoperative and the results are used to determine the surgical approach. Lymphadenectomy has a low prognostic or therapeutic utility in patients with borderline tumors. The overall risk of recurrence after conservative surgery ranges from 7% to 30%. Even in conservative surgery for fertility preservation, omentectomy retains its significance for prognosis and incomplete surgical staging has been recently confirmed to be an independent negative prognostic factor for disease recurrence [27-29]. The recurrence rate is higher after cystectomy as well as after laparoscopic approach, although there is no difference between laparotomy and laparoscopy in a 20-year follow up. Chemotherapy is rarely indicated for women with borderline ovarian tumors. Follow-up program includes clinical examination, TVS, levels of CA 125, primarily every 3 months during the first 2 years, every 6 months from 2 to 5 years and thereafter yearly [31].

The consultant should counsel the patient about different surgical approaches laparoscopy versus laparotomy, risks, the influence of radicality in surgery and possible recurrence rates, fertility preservation treatment options, additional measures for malignancy should include chemotherapy, follow up schedule and secondary surgical procedures after family planning is completed [30]. The primary treatment planning could be redirected due to surgical findings, frozen section's results etc. That could include surgical restaging and oncological counselling. Therefore, patient's full consent is necessary for treatment planning. A concession form should be signed.

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