

Laparoscopic management of unexpected borderline ovarian tumors in women of reproductive age

G. Pados^{1,2}, D. Tsolakidis^{1,2}, H. Bili^{1,2}, D. Athanatos^{1,2}, T. Zamboukas², B. Tarlatzis¹

¹1st Department of Obstetrics & Gynaecology, School of Medicine, Aristotle University of Thessaloniki, "Papageorgiou General Hospital",

²Centre for Endoscopic Surgery "Diavalkaniko" Hospital, Thessaloniki (Greece)

Summary

Purpose of investigation: The aim of this study was to review the clinical features of women with unexpected borderline ovarian tumours. *Methods:* Between October 1992 and December 2010, 1,332 out of 4,016 laparoscopies were performed for adnexal masses in women of reproductive age and 1,838 cysts were removed. When ultrasonographic findings did not meet the criteria for low risk malignancy, tumour markers, colour Doppler and MRI/CT were applied. At laparoscopy any solid component or papilla was sent for rapid frozen section. *Results:* Borderline ovarian tumours were found in eight (0.6%) out of 1,332 patients, two of which were bilateral. The mean age was 28.75 ± 9.27 years and the mean diameter of the cysts was 5.1 ± 1.7 cm. In two cases unexpected malignancy was discovered during the diagnostic and in six cases during the operative phase of the intervention. *Conclusion(s):* Risk of failure to diagnose cancer could be minimised with careful patient selection preoperatively. Adequate training on laparoscopic oncology is the necessary prerequisite for a safe laparoscopic approach.

Key words: Laparoscopy; Ovary; Surgery; Ultrasound; Borderline ovarian tumors.

Introduction

Laparoscopic approach compared with laparotomy is considered the "gold standard" for the management of preoperative diagnosed benign adnexal masses in women of reproductive age [1, 2].

The advances in accurate preoperative diagnosis of suspicious adnexal masses have reduced unnecessary laparotomies without sacrificing the principles of oncologic surgery in cases of unexpected malignancy since the incidence of ovarian cancer is 15.7/100,000 at the age of 40 years [3, 4]. In the reproductive age group, malignancy is found in 7%-13% of cases [5]. In 1973, the term borderline ovarian tumours (BOT) was adopted by the World Health Organization (WHO) and they represent approximately 10-15% of all ovarian tumours. One third of these tumours tend to occur in women younger than 40 years old, who want to preserve their childbearing capacity, and appear in 50-80% of cases at an early stage with a favourable prognosis [6].

However, neither sonographic features nor CA-125 levels are considered as adequate sensitive markers for discriminating a benign from a malignant lesion in premenopausal women [7, 8]. The aim of this study was to review our experience by presenting the clinical features and reproductive outcome of eight cases with unexpected BOT in women of reproductive age, on whom laparoscopic conservative surgery was performed.

Materials and Methods

This is a retrospective review of 1,332 out of 4,016 consecutive operative laparoscopies in women of reproductive age who were treated for adnexal masses; 1,838 cysts were removed at

the Centre for Endoscopic Surgery of 'Diavalkaniko' Hospital during a 17-year period (October 1992-December 2009). All operative laparoscopies and ultrasounds were performed by the same laparoscopist and also, all frozen sections and pathology reports were read by the same pathologist.

In our centre, adnexal masses in women of reproductive age should fit the sonographic criteria listed in Table 1 in order to be characterized preoperatively as non-suspicious and, therefore, to be managed laparoscopically. Magnetic resonance imaging (MRI), due to its high cost, was only ordered in sonographically undetermined ovarian lesions. Finally, as a routine, all patients had a preoperative CA-125 test done, despite its limited usefulness in women of reproductive age. Informed consent was signed by each patient about the possibility of cyst spillage during the intervention, and the possibility of a required staging laparotomy in case of unexpected malignancy confirmed on frozen section, if staging could not be accomplished by laparoscopy.

The protocol for laparoscopic management of adnexal masses followed in our department is depicted in Figure 1.

Results

Eight patients (0.6%) out of 1,332 were discovered to have BOT according to the results of their rapid frozen sections; two (25%) were bilateral. Totally, intraoperative frozen sections were ordered in 69 out of 1,838 cysts (3.7% per cyst) (Table 2). The findings of the preoperative investigation are summarized in Table 3. Of eight cases of unexpected malignancy, two were macroscopically evident during the diagnostic phase of laparoscopy and six were macroscopically recognised during the operative phase of the intervention. No "late" unsuspected ovarian malignancy was encountered. In all patients laparoscopic salpingo-oophorectomy was performed except for one nulliparous woman with a borderline malignancy of both ovaries. In this case, ovarian cystectomy was initially per-

Revised manuscript accepted for publication August 5, 2011

Table 1. — Ultrasonography evaluation of adnexal masses.

	Benign	Suspicious
Size	< 8 cm	> 8 cm
Septum thickness	≤ 3 mm	> 3 mm
Cyst wall thickness	≤ 3 mm	≥ 3 mm
Papillary excrescences projection	≤ 3 mm	> 3 mm
Solid part	Absent	Present
Free fluid	Absent	Present
Doppler RI	> 0.42	< 0.42

Table 2. — Histological types of adnexal cysts.

Type of lesion	Cases	Cysts
Endometriotic cysts	634	917
Dermoid cysts	167	198
Paraovarian-paratubal cysts	189	251
Simple cysts	287	413
Fibroadenomas	3	3
Miscellaneous	44	46
Borderline cysts	8	10
Total	1,332	1,838

Table 3. — Incidence of malignancy during laparoscopic removal of ovarian neoplasms.

Cases	Patient initials	Age	Preoperative diagnosis	Phase of laparoscopy	Final histology of borderline
1	RV	21	R: endometrioma	Diagnostic	Serous cystadenoma
2	BK	32	R: endometrioma	Operative	Endometrioid
3	AV	38	R: 3 simple cysts L: simple cyst	Operative	Serous-papillary
4	TE	16	R: simple cyst L: simple cyst	Operative	Brenner
5	ZN	27	R: endometrioma L: endometrioma	Operative	Endometrioid
6	ZM	42	R: cystadenoma	Diagnostic	Epithelial
7	PM	20	R: dermoid	Operative	Epithelial
8	LZ	34	L: cystadenoma	Operative	Serous-papillary

formed and the patient underwent two IVF trials, the second of which was successful. Three years later the patient underwent bilateral oophorectomy. The disease-free interval ranges from 7-98 months. Regarding the postoperative reproductive outcome, apart from the above described successful IVF, one patient conceived spontaneously and delivered two healthy babies after laparoscopic salpingo-oophorectomy, and another patient has recently been enrolled in an oocyte donation program due to poor ovarian response and advanced reproductive age after two failed IVF trials.

No major intraoperative complications were noted and all procedures were completed laparoscopically with no accidental intraoperative rupture of the borderline adnexal masses. All women were discharged within 24 hours of laparoscopy. In our 1,332 cases, no malignant invasive ovarian tumor was found. The histological types of the adnexal cysts are presented in Table 3.

Discussion

This retrospective study presents 17 years experience of our endoscopic center and according to our protocol the appearance of unsuspected BOT was limited only to eight patients. All of them are alive with favourable prognoses. The rate of unexpected borderline and invasive tumours ranges between 0.4% [9] and 4.2% [10], and our results are one of the lowest compared to the reported outcomes of other experienced endoscopic centres. The strength of this study can be attributed to the fact that all preoperative ultrasound (US) images were personally performed or reviewed in case of referral patients by the laparoscopist. In addition, other studies demonstrated that the risk of malignancy in simple cysts, defined as unilocular with smooth inner wall, rises from 0.8% in premenopausal women to 9.6% in postmenopausal [11]. However, cyst wall papillaries may sometimes be undetected during preoperative workup, especially in cysts with a diameter of > 50 mm because of the larger inner surface that has to be examined. This occurs because small papillary formations of 2-3 mm can easily be missed by US [7] due to poor US penetration and resolution. Taking into consideration the above studies, we can justify our inability to correctly characterise our eight borderline cases. Furthermore, three out of ten BOT were characterised as simple unilocular cysts without any visible papillae or solid mass. Also, four cysts were described preoperatively as endometriomata but histology revealed three of them as endometrioid BOT and the other as borderline serous cystadenoma. Thus, in cases with a previous history of endometriosis a high index of suspicion must always be maintained with strict adherence to pre- and intraoperative protocols.

Laparoscopy or laparotomy, conservative or radical treatment of Stage I BOT are fields of conflict between laparoscopists and oncologists. However, borderline and early ovarian cancers may also be missed after inadequate management by laparotomy [12]. This means that the crucial point is the accuracy of preoperative and intraoperative diagnosis rather than the preferred method of access to the abdominal cavity. In all of our unexpected eight cases, frozen sections were performed due to correct intraoperative laparoscopic diagnosis and were in 100% agreement with the permanent histological results without missing any case of malignancy.

When an unexpected malignancy is encountered in case of a presumed benign cyst based on the findings of preoperative investigation and laparoscopic inspection, three completely different subgroups with different implications for prognosis can be distinguished: a) the malignancy is macroscopically evident during the diagnostic phase of laparoscopy and no operative maneuver is considered on the cyst, b) the malignancy is macroscopically evident during the operative phase of laparoscopy, when the cyst wall is opened, and c) no macroscopic evidence has been found either in the diagnostic or operative phase, and no frozen section has been performed or in case of a false negative frozen section the operative procedure is completed by laparoscopy. In the first subgroup no adverse

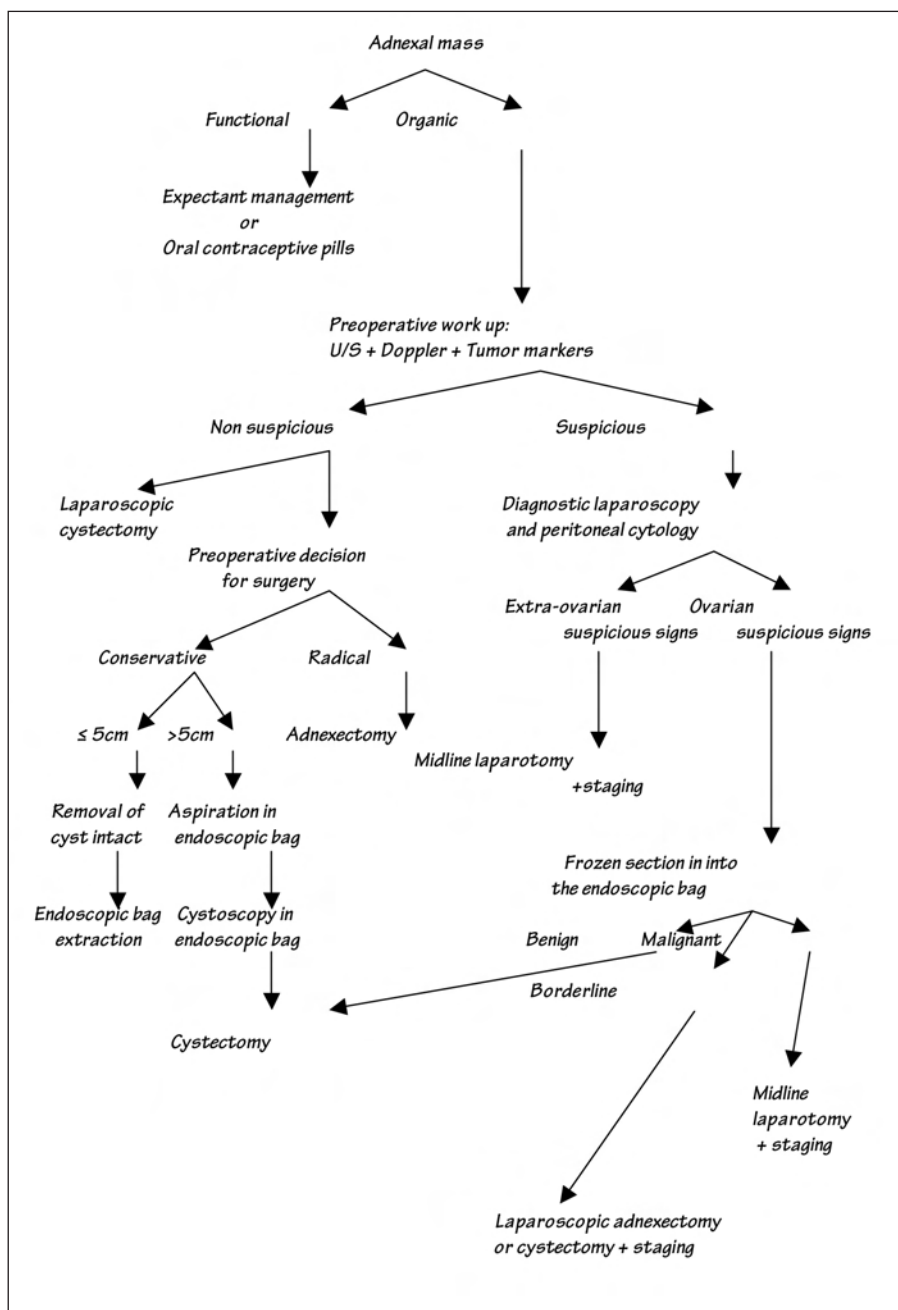


Figure 1. — Our protocol for laparoscopic management of adnexal masses.

effect on prognosis from the surgical approach can be expected, except for the theoretical negative effect from the increased intraperitoneal pressure. In the second subgroup, when an accidental rupture of the cyst occurs, the patient is upstaged from Stage IA to IC. For this reason in suspicious cysts all operative maneuvers should take place using an endoscopic bag. In the third subgroup, since there is a delay until the final pathology which has a detrimental effect on the prognosis. From the eight cases of unexpected malignancy of our study, two were macroscopically evident during the diagnostic phase of

laparoscopy and six were macroscopically recognized during the operative phase of the intervention. No “late” unsuspected ovarian malignancy was encountered.

After correct diagnosis, the next important step is the appropriate management of a borderline adnexal mass, which depends on the laparoscopist’s experience and patient’s expectations with regard to the maintenance of fertility capacity in case of unexpected borderline or malignant tumour. In favour of fertility sparing treatment is a recent Gynaecologic Oncology Group (GOG) study suggesting that even cystectomy may be adequate thera-

py for women of reproductive age considering an the eventual relapse may be successfully managed by reoperation [13]. Seven out of our eight patients chose salpingo-oophorectomy in case of unexpected BOT and the other one of our nulliparous patients initially gave her consent for cystectomy, but later, after two successful IVF cycles and pregnancy, underwent bilateral oophorectomy.

In the absence of prospective clinical trials with regard to the spillage of the cyst content after intentional or no cyst perforation, the prognostic value of intraoperative rupture of cysts in Stage IA BOT or invasive cancer is a controversial topic. However, spilling should be avoided until otherwise confirmed.

In conclusion, in women of reproductive age, pre-laparoscopic evaluation and selection for the endoscopic approach are of utmost importance in the reduction of cases of unrecognised borderline or malignant ovarian cysts. Finally, in young women wishing to preserve their fertility, a conservative approach is reasonable followed by definitive surgery after successful pregnancies or by recurrence or malignant invasion at an early stage.

References

- [1] Canis M., Rabischong B., Houille C., Botchorishvili R., Jardon K., Safi A., Wattiez A., Mage G., Pouly J.L., Bruhat M.A.: "Laparoscopic management of adnexal masses: a gold standard?". *Curr. Opin. Obstet. Gynecol.*, 2002, 14, 423.
- [2] Pados G., Tsolakidis D., Bontis J.: "Laparoscopic management of the adnexal mass". *Ann. N.Y. Acad. Sci.*, 2006, 1092, 211.
- [3] Canis M., Pouly J.L., Wattiez A., Mage G., Manhes H., Bruhat M.A.: "Laparoscopic management of adnexal masses suspicious at ultrasound". *Obstet. Gynecol.*, 1997, 89, 679.
- [4] Yancik R.: "Ovarian cancer. Age contrasts in incidence, histology, disease stage at diagnosis, and mortality". *Cancer*, 1993, 71, 517.
- [5] DiSaia P.J., Creasman W.T.: "The adnexal mass and early ovarian cancer". In: *Clinical Gynecologic Oncology*, 5th edition, 1997, St. Louis, Mosby, 253.
- [6] Tinelli R., Tinelli A., Tinelli F., Cicinelli E., Malvasi A.: "Conservative surgery for borderline ovarian tumors: A review". *Gynecol. Oncol.*, 2006, 100, 185.
- [7] Exacoustos C., Romanini M.E., Rinaldo D., Amoroso C., Szabolcs B., Zupi E., Arduini D.: "Preoperative sonographic features of borderline ovarian tumors". *Ultrasound Obstet. Gynecol.*, 2005, 25, 50.
- [8] Timmerman D., Van Calster B., Jurkovic D., Valentin L., Testa A.C., Bernard J.P., Van Holsbeke C., Van Huffel S., Vergote I., Bourne T.: "Inclusion of CA-125 does not improve mathematical models developed to distinguish between benign and malignant adnexal tumors". *J. Clin. Oncol.*, 2007, 25, 4194.
- [9] Nezhat F., Nezhat C., Welander C., Benigno B.: "Four ovarian cancers diagnosed during laparoscopic management of 1011 women with adnexal masses". *Am. J. Obstet. Gynecol.*, 1992, 167, 790.
- [10] Guglielmina J.N., Pennehonat G., Deval B., Benifla J.L., Darai E., Crequat J., Walker-Combrouze F., Madelenat P.: "Treatment of ovarian cysts by laparoscopy". *Contracept. Fertil. Sex.*, 1997, 25, 218.
- [11] Osmers R.G., Osmers M., Von Maydell B., Wagner B., Kuhn W.: "Preoperative evaluation of ovarian tumors in the premenopause by transvaginosonography". *Am. J. Obstet. Gynecol.*, 1996, 175, 428.
- [12] Heleva M.E., Krepart G.V., Lotocki R.: "Staging laparotomy in early epithelial ovarian carcinoma". *Am. J. Obstet. Gynecol.*, 1986, 154, 282.
- [13] Romagnolo C., Gadducci A., Sartori E., Zola P., Maggino T.: "Management of borderline ovarian tumors: Results of an Italian multicenter study". *Gynecol. Oncol.*, 2006, 101, 255.

Address reprint requests to:
G. PADOS, M.D.
40, Mitropoleos Street
Thessaloniki 54623 (Greece)
e-mail: padosgyn@hol.gr