Asian Pacific Journal of Cancer Care
Vol 3 No 4 (2018), 75
Original Research

Epithelial Borderline Ovarian Tumor: Clinicopathological Features, Outcome and Prognostic Factors

Amornrat Temtanakitpaisan Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
Pilaiwan Kleebkaow Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand
Apiwat Aue-aungkul Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand

Objective: To evaluate clinic-pathological characteristics, treatment outcomes, factors affecting survival in patients with borderline ovarian tumors (BOTs).
Methods and Objective: Medical records of patients with BOTs who had been treated at Srinagarind Hospital from 2001 to 2016 were reviewed. Abstracted data included baseline characteristics, clinic-pathologic features, disease-free survival (DFS), and overall survival (OS).
Results: Fifty-two patients with BOTs were included in the study.The mean age+ SD was 41.15+ 15.34 years. Most patients were premenopausal and the most common presenting symptom was adnexal mass. Most patients were in the early stage (90.4%). Thirty-two patients underwent radical surgery (61.5%). Twenty-one patients (40.3%) underwent lymphadenectomy. An appendectomy was performed in 19 (36.5 %) cases. The median follow-up period was 67.5 months (range, 7 to 180 months). The 5-year and 10-year overall survival rates for all stages were 90% and 85%, respectively. The 5-year and 10-year disease-free survival rates for all stages was 87% and 87%, respectively. Seven (13.5 %) patients had the recurrence. Absent residual disease (HR = 0.33; 95 %CI 0.11 – 0.96) and receiving postoperative adjuvant chemotherapy (HR = 0.22; 95 %CI 0.08 – 0.65) were associated factors for DFS.
Conclusion: The majority of patients with BOTs presented at the young age and early stage. Residual lesion and adjuvant chemotherapy are significant factors predicting DFS.

Introduction

Borderline ovarian tumors (BOT) are non-invasive neoplasms with atypical epithelial cell proliferation without destructive stromal invasion. The pathological severity is greater than benign tumor but less than their malignant ovarian tumors [1]. Taylor has first described these type of ovarian tumor in 1929 that was different from both benign and malignant epithelial ovarian tumors [2]. Then, in 1973, the name ‘borderline’ was assigned by the World Health Organization (WHO) with morphological criteria with the absence of stromal invasion [3]. The WHO Classification in 2014 of Tumors of the Female Genital Organs used the term “borderline tumor” interchangeable with “atypical proliferative tumor”—a terminology that was discouraged in the previous WHO classification [4], while the term “tumor of low malignant potential” is no longer use [3].

BOTs have seven types include serous, mucinous, endometrioid, clear cell, Brenner, undifferentiated and mixed tumors. The incidence of BOTs with cysts only is low, approximately 0.6% [5]. Borderline serous ovarian tumors can present at an advanced stage, while borderline ovarian tumors of non-serous types (e.g. endometrioid, mucinous, clear cell, or Brenner) are mostly confined to the ovary [6].

Recently, BOTs are staged according to the International Federation of Gynecology and Obstetrics (FIGO) classification of ovarian cancer. It was reported that 10–15 % of primary epithelial ovarian neoplasms was BOTs [7, 8]. When comparing with epithelial ovarian carcinomas (EOCs), BOTs are more likely to present in premenopausal women with early stages disease. The mainstay of treatment is surgery with excellent prognosis [8]. The 5-year survival rate was 95–97 % and approximately 70 % of these tumors were in stage I at the time of diagnosis [7].

It is difficult to diagnose BOT preoperatively [9]. Cancer antigen 125 (CA-125) might help in advanced stage cases [10]. Regarding the controversy in the surgical management and staging of BOTs, some surgeons prefer to do the surgical staging whereas the others do not perform lymphadenectomy [8, 11]. Women who have completed childbearing and those with advanced stage disease are treated with complete surgical staging that includes total abdominal hysterectomy, bilateral salpingo-oophorectomy, lymphadenectomy and resection of visible peritoneal lesions. Appendectomy may be considered in mucinous BOT subtype [12]. Conservative procedure is preserved for fertility needed patients. The procedure consisting of unilateral salpingo-oophorectomy or ovarian cystectomy in cases of bilateral ovarian involvement [12, 13].

In the present study, we reviewed the clinic-pathological characteristics, surgical management, and surgical outcomes, and assessed factors affecting survival in patients with borderline ovarian tumors who were had been treated in our institute.

Materials and Methods

After the Ethics Committee for Human Research were approved under protocol number HE581436, the retrospective study was performed in Srinagarind Hospital, Department of Obstetrics and Gynecology, Khon Kaen University, Thailand. All patients with BOTs diagnosed between 1 January 2001 and 31 October 2016 were included. The patient age, gravidity, menopausal status, pre-operative serum CA-125 level, clinical symptoms were collected. Moreover, surgical technique, mean tumor diameter, lymph node status, stage at diagnosis, chemotherapy after surgery and postoperative follow-up periods were evaluated. The histopathological results were re-evaluated and interpreted by only one gynecologic pathologist of Srinagarind Hospital (Kleebkaow P.). Patients with incomplete data were excluded from the analysis.

The International Federation of Gynecology and Obstetrics (FIGO) 2009 staging scheme for epithelial ovarian carcinomas was staged in all patients [14]. Although the FIGO ovarian staging classification was revised on 1 January 2014, we used the previous staging classification for 2014 patients for consistency. Surgical procedures were categorized into two groups: the first group was conservative surgery that for those fertility function is needed. The procedures consisted of unilateral salpingo-oophorectomy(USO) or bilateral salpingo-oophorectomy(BSO) and/or infracolic omentectomy and/or pelvic and/or para-aortic lymphadenectomy (sampling or complete). While the second group was radical surgery that for those with finished childbearing and those with advanced stage disease. It comprised of total hysterectomy and bilateral salpingo-oophorectomy (TAH+BSO) and/or infracolic omentectomy and/or pelvic and/or para-aortic lymphadenectomy (sampling or complete). Additionally, an appendectomy was often performed in case of mucinous BOT. After underwent the surgical procedure, postoperative adjuvant chemotherapy (CT) was administered for FIGO stage IC and more advanced stages or recurrent disease. The postoperative chemotherapy (CT) regimens consisted of carboplatin (AUC5) and paclitaxel (175 mg/m2) every 3 weeks for 6 cycles. After complete primary treatment (surgery or adjuvant chemotherapy), all patients were followed every 3 months for first 24 months and every 6 months up to 5 years. Long-term outcome evaluated at 5 and 10 years was obtained. At each follow-up visit, a patients' history taking, physical and pelvic examinations were performed. Survival analysis was based on the Kaplan-Meier method and results were compared using the log-rank test. Disease-free survival (DFS) was defined as the time from the date of primary surgery to the detection of recurrence or the latest observation. Overall survival (OS) was defined as the time from the date of primary surgery to

death or the latest follow up. The χ2 test and Student's t-test for unpaired data were used for statistical analyses. For predictors with a p-value of less than 0.20 in univariate analysis (log-rank test), Cox proportional hazards regression would be used to determine the independent predictor(s) of survival. All statistical analyses were performed using the SPSS version 22.0. A p-value < 0.05 was considered to indicate statistical significance.

Results A total of 52 patients having a final diagnosis of BOTs between January 1, 2001, and October 31, 2016, in our institution were identified. The mean age+ SD was 41.15 + 15.34 years. Thirty-three patients (63.5%) were premenopausal and 27 patients (51.9%) were nulliparous. The most common symptoms before diagnosis were adnexal mass (100%) followed by GI symptoms (42.3%), abdominal pain (34.6%) and abnormal vaginal bleeding (3.8%). Of 40 patients who had preoperative CA 125 level measurement, mean+ SD of serum preoperative CA 125 level was 335.25+ 1430.63 IU/mL (range 2.0 – 9068.0 IU/mL) (Tabl 1).

Characteristic	**Number = 52**	**%**
Age (Mean 41.15, SD=15.341)		
Less than 60	47	90.4
60 and more than 60	5	9.6
Parity		
Nulliparous	27	51.9
Multiparous	25	48.1
Menopausal status		
Premenopausal	33	63.5
Postmenopausal	19	36.5
Underlying disease		
DM	3	5.8%
HT	5	9.6
Heart	1	1.9
Presenting symptoms		
Adnexal mass	52	100
Pelvic pain	18	34.6
GI symptom	22	42.3
Vaginal bleeding	2	3.8
Preoperative CA-125 in 40 patients and missing data 12) **Mean (range 2.0 – 9068.0 IU/mL, SD=1430.632**		
≤ 35 IU/mL	21	40.4
> 35 IU/mL	19	36.5

Table 1 Clinical characteristic of the patients with borderline ovarian tumors according to time of diagnosis

Regarding tumor characteristics, the mean+ SD of the diameter of the ovarian mass was 17.35+ 7.76 cm. Forty-eight patients (92.3%) had the tumor size ≥ 10 cm. Half of the BOTs (50%) was found in the right ovary. Bilateral lesions were noted in only 13.5 % of patients. Forty-seven patients (90.4%) presented in early-stage disease, whereas the remaining 5 patients (9.6%) had the advanced stage at the time of diagnosis (Tabl 2). Mucinous type is the most common followed by serous type (75% and 25%, respectively) Only one patient (1.9%) had the serous type with the micro-invasive lesion.

Characteristics	**Number(N)**	**%**
Tumor location		

Left	19	36.5
Right	26	50
Bilateral	7	13.5
Tumor size (range 5-40 cm) mean 17.35, SD=7.757		
Less than 10 cm.	4	7.7
10 cm. and more than	48	92.3
Subtype		
Serous	13	25
Mucinous	39	75
Stage		
Early stage(I-II)	47	90.4
Advanced stage (III-IV)	5	9.6

Table 2 Pathological and surgical characteristics of patients with borderline ovarian tumors

Endometriosis and pseudomyxoma peritonei lesions were found as co-incidental findings in patients with the mucinous group (3.8% and 5.5%, respectively). The surgical procedures are shown in Tabl 3. Twenty patients (38.5%) underwent conservative surgery. Twenty-one patients (40.3%) underwent lymphadenectomy. An appendectomy was performed in 19 (36.5 %) cases. Only one case (1.9%) with mucinous type had appendiceal involvement. After underwent the surgical procedure, twelve patients received postoperative adjuvant chemotherapy (CT).

Treatment	**Number(N)**	**%**
Procedures		
Conservative surgery	20	38.5
Unilateral SO or BSO or tumor biopsy or omental biopsy	14	27.0
Unilateral SO and lymphadenectomy	6	11.5
Radical surgery	32	61.5
TAH+BSO	17	32.7
Complete surgical staging	15	28.8
Lymphadenectomy	21	40.3
Appendectomy	19	36.5
Residual tumor	1	1.9
Postoperative chemotherapy	12	23.1
Response chemotherapy		
Complete	49	94.2
Partial	2	3.8
Stable	0	0
Progression	1	1.9

Table 3: Treatment characteristics of patients with borderline ovarian tumors

The median follow-up period was 67.5 months (range, 7 to 180 months). The 5-year and 10-year overall survival rates for all stages was 90% and 85%, respectively. The 5-year and 10-year disease-free survival rates for all stages were 87% and 87%, respectively. Seven patients (13.5 %) had disease recurrence. Most recurrent patients were the mucinous type (71.4%) and in advanced stage (57.1%). Moreover, of the 7 recurrence patients, 6 patients (85.7%) underwent radical surgery and 5 patients (71.4%) received CT for recurrent disease. No one died during the follow-up period.

According to univariate analysis, absent residual disease and receiving adjuvant chemotherapy for tumor stage ≥ IC were the significant prognostic factors for DFS (HR = 0.33; 95 %CI 0.11 – 0.96; p = 0.04, HR = 0.22; 95 %CI 0.08 – 0.65; p = 0.006, respectively). Menopausal status, radicality of

surgery, lymphadenectomy, and appendectomy were not associated with DFS (Tabl 4).

Risk factors	Hazard ratio	95%CI	P-value
Menopausal status			
Premenopausal	Reference category		
Postmenopausal	0.72	0.32 – 1.60	0.42
Preoperative serum CA-125			
≤ 35 IU/mL	Reference category		
> 35 IU/mL	0.02	0 – 50.99	0.32
Procedure			
Conservative surgery	Reference category		
Radical surgery	0.14	0.005 – 4.12	0.26
Appendectomy			
Not performed	Reference category		
Appendectomy	0.77	0.35 – 1.72	0.53
Lymphadenectomy			
Not performed	Reference category		
Lymphadenectomy	0.78	0.14 – 4.29	0.78
FIGO stage			
Early stage (I-II)	Reference category		
Advanced stage (III-IV)	0.97	0.13 – 7.11	0.97
Residual tumor			
Present	Reference category		
Absent	0.33	0.11 – 0.96	0.04
Postoperative chemotherapy			
None	Reference category		
Postoperative chemotherapy	0.22	0.08 – 0.65	0.006

Table 4: Univariate analyses of risk factors in patients with borderline ovarian tumors-specific disease free survival (DFS)

Discussion

In this study, we reviewed 52 patients with BOTs who were treated with surgery in Srinagarind Hospital, Khon Kaen, Thailand. BOTs represent approximately 10% of EOC. However, their prognosis is more favorable. These tumors are detected at the younger age and at lower stages [8] that is similar to our study. That is most patients in our review were in premenopausal status and presented in the early stage of the disease. The presenting symptoms varied between studies. Comert et al. [15] found that the most common symptoms were the pelvic pain (42.7%), and followed by bloating sensation (25.3%). While the adnexal mass is the most common leading symptoms that found in our study and followed by GI symptoms, abdominal pain, and abnormal vaginal bleeding.

Regarding histopathologic types of BOTs, Aure JC et al. [16] reported the most common histopathological types were serous (65%) and followed by the mucinous (35%). In addition, Link et al. [17] showed that 50% of the borderline ovarian tumors patients presented with serous histology, 46% were mucinous, and 3.9% were mixed, endometrioid, clear cell or Brenner tumors. Whereas our study found mucinous type was the predominant type (75%) and followed by serous type (25%). The differences might be the geographic and cultural variation.

BOTs are staged using the FIGO criteria that have been developed and applied to invasive ovarian carcinomas. Russell P et al. [18] reported that most BOTs presented at stage I (50% to 80%) that is

similar to our findings. It was found 90.4% had the early stage of the disease. Furthermore, Massad et al. [19] showed the recurrence or persistence rate after surgery in each stage. The recurrent rates were 2.1% in stage I was 2.1%, 7.1% in stage II nd 14.4% in stage III/IV. These findings are in line with our study. The recurrent rates in stage I-II and III-IV BOTs in the present study were approximately 5.8% and 7.7%, respectively.

There is an important and controversial issue regarding surgical approaches in diagnosed BOT patients, especially in women who wish to preserve their reproductive status. As has already been mentioned, patients with borderline ovarian tumors tend to be younger than women with invasive ovarian cancer. Therefore, the fertility issue is taken to be the account in younger women [20]. In our study, more than half of patients were radical surgery similar to the ovarian cancer surgery situation. However, we found no difference between the survival rates of radical and conservative surgery patients. Many previous studies [21, 22] have suggested that patients who had undergone conservative surgery had higher recurrence rates than the radical surgery group. Furthermore, Boran et al. [21] reported that no recurrence was found after radical surgery, Whereas, the recurrent rate was 6.5% after conservative surgery. In contrast, we found that 7 patients (13.5%) experienced the recurrence of the disease. Six patients (85.7%) underwent radical surgery. Moreover, no difference was found between completely and incompletely staged patients. Thus, surgical procedural types not reduced the recurrence of the disease.

Our data found that lymphadenectomy did not show statistically significant improvement in DFS and OS. These results were similar to those previously reported [23].

Furthermore, we found that radical surgery was not an independent prognostic factor for DFS or OS. These findings were similar to the previous studies [21, 22]. We also demonstrated that hysterectomy had no impact on survival in BOT patients, that similar to Menczer et al.'s study [24].

Coincidental appendectomy to surgical staging procedures has been recommended for mucinous tumors [8].In our study, 36.5% of all cases underwent appendectomies, 38.5% of mucinous type underwent appendectomies and 30.8% of serous type underwent appendectomies. However, coincidental appendectomy had no impact on overall survival rate (HR = 0.45; 95 % CI = 0.08 – 2.71; $p = 0.38$) and disease-free survival rate (HR = 0.43; 95 % CI = 0.07 – 2.56; $p = 0.35$) in the mucinous type of BOTs. Thus, it is not necessary to perform appendectomy routinely in patients with mucinous BOTs. According to our findings, Kleppe et al.'s [25] and Lin et al.'s studies [26] reached the same conclusion.

The use of adjuvant chemotherapy for BOTs remains controversial [27]. According to the last version of the National Comprehensive Cancer Network (NCCN), the treatment recommendation after comprehensive staging depends on the presence or absence of invasive implants. The initial therapeutic approach in patients with invasive implants may include observation as well as alternative to consider adjuvant chemotherapy (Category 2B) [28]. Trope et al. [29] and Gokcu et al. [27] reported that surgery followed by chemotherapy did not show a different survival rate compared to no adjuvant chemotherapy in advanced-stage BOTs. Contrast with our study that chemotherapy after surgical procedure given in FIGO stage IC and more advanced stages improved overall survival (OS) and disease-free survival (DFS) significantly.

The previous studies [22, 27, 30] noted that the age more than 40 years, menopausal status, FIGO stage, surgical staging, radical surgery, lymph node dissection, appendectomy and undergoing adjuvant chemotherapy for a tumor of stage ≥ IC were not independent prognostic factors for DFS or OS. While our study found that absent residual disease and adjuvant chemotherapy for tumor stage ≥ IC on disease-free survival (DFS) were the significant associated prognostic factors for DFS (HR = 0.33; 95 %CI 0.11 – 0.96; $p = 0.04$, HR = 0.22; 95 %CI 0.08 – 0.65; $p = 0.006$, respectively). This is a retrospective study to evaluate the clinicopathological features, outcomes and prognostic factors affecting the overall survival and disease-free survival in women with borderline ovarian tumors with only one gynecologic pathologist interpreted histopathology. Therefore, this is the

strength of the study. However, due to the rarity of these tumors and limitation of sample size with retrospective data in only one institute so this is the weakness of our study. For more promising data, multicenter prospective randomized controlled trials data should be conducted.

In Conclusion, The majority of patients with BOTs presented in young age and early stage. Residual disease and postoperative adjuvant chemotherapy were associated factors for DFS.

Funding Statement: None

References

[1]. Silverberg SG, Bell DA, Kurman RJ, Seidman JD, Prat J, Ronnett BM, et al. Borderline ovarian tumors: key points and workshop summary. Human pathology. 2004;35(8):910-7.

[2]. Taylor H. Malignant and semi-malignant tumors of the ovary. Surg Gynecol Obstet. 1929;48:204-30.

[3]. Hart WR, Norris HJ. Borderline and malignant mucinous tumors of the ovary. Histologic criteria and clinical behavior. Cancer. 1973;31(5):1031-45.

[4]. Hauptmann S, Friedrich K, Redline R, Avril S. Ovarian borderline tumors in the 2014 WHO classification: evolving concepts and diagnostic criteria. Virchows Arch. 2017;470(2):125-42.

[5]. Pados G, Tsolakidis D, Bili H, Athanatos D, Zaramboukas T, Tarlatzis B. Laparoscopic management of unexpected borderline ovarian tumors in women of reproductive age. European journal of gynecological oncology. 2012;33(2):174-7.

[6]. Denny L, Quinn M. FIGO Cancer Report 2015. International journal of gynecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2015;131(2): S75.

[7]. Tinelli R, Tinelli A, Tinelli FG, Cicinelli E, Malvasi A. Conservative surgery for borderline ovarian tumors: a review. Gynecologic oncology. 2006;100(1):185-91.

[8]. Gershenson DM. Clinical management potential tumours of low malignancy. Best practice & research Clinical obstetrics & gynecology. 2002;16(4):513-27.

[9]. Medeiros LR, Rosa DD, da Rosa MI, Bozzetti MC. The accuracy of CA 125 in the diagnosis of ovarian tumors: a quantitative systematic review. European journal of obstetrics, gynecology, and reproductive biology. 2009;142(2):99-105.

[10]. Timmerman D, Van Calster B, Testa AC, Guerriero S, Fischerova D, Lissoni AA, et al. Ovarian cancer prediction in adnexal masses using ultrasound-based logistic regression models: a temporal and external validation study by the IOTA group. Ultrasound in obstetrics & gynecology: the official journal of the International Society of Ultrasound in Obstetrics and Gynecology. 2010;36(2):226-34.

[11]. 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(6):1145-51.

[12]. Cadron I, Leunen K, Van Gorp T, Amant F, Neven P, Vergote I. Management of borderline ovarian neoplasms. Journal of clinical oncology: official journal of the American Society of Clinical Oncology. 2007;25(20):2928-37.

[13]. Kristensen GS, Schledermann D, Mogensen O, Jochumsen KM. The value of random biopsies, omentectomy, and hysterectomy in operations for borderline ovarian tumors. International journal of gynecological cancer: official journal of the International Gynecological Cancer Society. 2014;24(5):874-9.

[14]. Benedet JL, Bender H, Jones H, 3rd, Ngan HY, Pecorelli S. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO Committee on Gynecologic Oncology. International journal of gynecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2000;70(2):209-62.

[15]. Comert DK, Ureyen I, Karalok A, Tasci T, Turkmen O, Ocalan R, et al. Mucinous borderline ovarian tumors: Analysis of 75 patients from a single center. Journal of the Turkish German Gynecological Association. 2016;17(2):96-100.

[16]. Aure JC, Hoeg K, Kolstad P. Clinical and histologic studies of ovarian carcinoma. Long-term follow-up of 990 cases. Obstetrics and Gynecology. 1971;37(1):1-9.

[17]. Link CJ, Jr., Reed E, Sarosy G, Kohn EC. Borderline ovarian tumors. The American journal of medicine. 1996;101(2):217-25.

[18]. Russell P. The pathological assessment of ovarian neoplasms. II: The proliferating 'epithelial' tumours. Pathology. 1979;11(2):251-82.

[19]. Segal GH, Hart WR. Ovarian serous tumors of low malignant potential (serous borderline tumors). The relationship of the exophytic surface tumor to peritoneal "implants". The American journal of surgical pathology. 1992;16(6):577-83.

[20]. Fox H. The concept of borderline malignancy in ovarian tumours: a reappraisal. Current topics in pathology Ergebnisse der Pathologie. 1989;78:111-34.

[21]. Boran N, Cil AP, Tulunay G, Ozturkoglu E, Koc S, Bulbul D, et al. Fertility and recurrence results of conservative surgery for borderline ovarian tumors. Gynecologic oncology. 2005;97(3):845-51.

[22]. Guvenal T, Dursun P, Hasdemir PS, Hanhan M, Guven S, Yetimalar H, et al. Effect of surgical staging on 539 patients with borderline ovarian tumors: a Turkish Gynecologic Oncology Group study. Gynecologic oncology. 2013;131(3):546-50.

[23]. Tinelli R, Malzoni M, Cosentino F, Perone C, Tinelli A, Malvasi A, et al. Feasibility, safety, and efficacy of conservative laparoscopic treatment of borderline ovarian tumors. Fertility and sterility. 2009;92(2):736-41.

[24]. Menczer J, Chetrit A, Sadetzki S. The effect of hysterectomy on the survival of patients with borderline ovarian tumors. Gynecologic oncology. 2012;125(2):372-5.

[25]. Kleppe M, Bruls J, Van Gorp T, Massuger L, Slangen BF, Van de Vijver KK, et al. Mucinous borderline tumours of the ovary and the appendix: a retrospective study and overview of the literature. Gynecologic oncology. 2014;133(2):155-8.

[26]. Lin JE, Seo S, Kushner DM, Rose SL. The role of appendectomy for mucinous ovarian neoplasms. American journal of obstetrics and gynecology. 2013;208(1):46.e1-4.

[27]. Gokcu M, Gungorduk K, Asicioglu O, Cetinkaya N, Gungor T, Pakay G, et al. Borderline ovarian tumors: clinical characteristics, management, and outcomes - a multicenter study. Journal of ovarian research. 2016;9(1):66.

[28]. NCCN. Clinical Practice Guidelines in Oncology Ovarian Cancer. Including Fallopian Tube Cancer and Primary Peritoneal Cancer Version 1. 2016.

[29]. Trope CG, Kaern J, Davidson B. Borderline ovarian tumours. Best practice & research Clinical obstetrics & gynecology. 2012;26(3):325-36.

[30]. Winter WE, 3rd, Kucera PR, Rodgers W, McBroom JW, Olsen C, Maxwell GL. Surgical staging in patients with ovarian tumors of low malignant potential. Obstetrics and Gynecology. 2002;100(4):671-6.

References