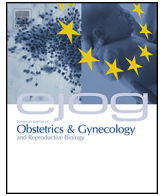


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Frozen section in borderline ovarian tumors: is it reliable?



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ABSTRACT

Objective: We reported the concordance of frozen/section (FS) diagnosis of borderline ovarian tumor (BOT) and identified the factors associated with the concordance.

Study design: FS results of the patients with a final diagnosis of BOT operated between 1990 and 2012 were analyzed. The FS results were reported as benign, rule out borderline tumor, borderline tumor, at least borderline tumor and malign tumor intraoperatively. The concordance of FS diagnosis was determined by comparing the FS result with the final pathological diagnosis. We accepted the FS concordant with the final pathology when the FS result was borderline tumor or at least borderline tumor, since we managed these patients in a similar way intraoperatively. Data regarding histological subtype, tumor size, age of the patients, menopausal status, presence of bilateral disease, preoperative Ca-125 level and the final diagnosis were evaluated.

Results: FS results of 145 patients were analyzed. The concordance of FS analysis for the total group, for the ones with serous and mucinous BOT were 79%, 92% and 62%, respectively. Totally, 29 patients (20%) weren't staged intraoperatively due to inaccurate FS result. Mucinous histology and larger tumor size were associated with lower concordance of FS. Concordance wasn't associated with type of surgery (conservative vs radical), menopausal status, laterality of the tumor, age of the patients and Ca-125 level of the patients.

Conclusion: The high discrepancy rate of FS, especially in mucinous and larger tumors should be kept in mind during intraoperative decision-making based on FS analysis for BOT.

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Introduction

The use of frozen/section (FS) is one of the most important steps in the intraoperative management of adnexal masses. FS helps to select the most appropriate surgical approach for the patients intraoperatively. Therefore, concordance of FS analysis is crucial. A false negative FS analysis may result in re-surgery and the patient may be exposed to the unnecessary morbidity of a comprehensive surgery with a false positive result. An ideal FS would have 100% accuracy for the evaluation of ovarian tumors. The sensitivity and specificity for the FS analysis of ovarian tumors were reported to range between 65–97% and 97–100%, respectively [1]. Large tumor diameter, mucinous histology, borderline tumors were shown to be associated with discrepancy between FS and final pathological result in many studies [1–3].

Borderline tumors are epithelial ovarian tumors different from both benign and malign lesions of the ovaries. Taylor first described this entity in 1929 and it was accepted by WHO as a different type of ovarian tumor in 1973 [4,5]. Borderline ovarian tumor (BOT) is a newer and rarer entity that is still an interesting subject for the studies. While BOT is a challenge for the surgeons in terms of the decision of the extent of the surgery and postoperative management, it is also challenging for the pathologists to diagnose it intraoperatively. It may result from the fact that BOT is an intermediate form having the properties of both benign and malign tumors. Additionally, some tumors may include the areas of both borderline and malign lesions.

We aimed to report the concordance of FS diagnosis of BOT at our institution and to identify the factors associated with the concordance.

Material method

FS results of the patients with a final diagnosis of BOT operated at our institution between 1990 and 2012 were analyzed. The

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patients who were operated at other centers or whose FS analysis of the pathologic specimens was missing were excluded. The pathologic reports, medical records and operation notes of the included patients were obtained from the gynecologic oncology electronic database system. Data regarding histological subtype, tumor size, age of the patients, menopausal status, presence of bilateral disease, preoperative Ca-125 level and the final diagnosis were obtained from these records.

Management of patients with these tumors changed in time during the study period. Staging surgery including abdominal washing, infracolic omentectomy, appendectomy and peritoneal biopsies in the right and left paracolic gutters with or without lymphadenectomy was performed at the discretion of the surgeon and according to the time of the diagnosis of the tumor (intraoperatively vs postoperatively) and according to the histological subtype of the tumor. Fertility-sparing surgery (conservative surgery) was performed in premenopausal women who desired childbearing, most of the other women underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy (radical surgery). Conservative surgery was defined as the conservation of the uterus and at least part of one ovary. This definition includes unilateral oophorectomy (UO), UO with contralateral cystectomy (UO + CC), unilateral cystectomy (UC), and bilateral cystectomy (BC) with or without staging surgery.

All pathological specimens were evaluated by pathologists experienced in gynecological pathology. Specimens were delivered in an unfixed state and were examined grossly by the attending pathologist. Representative samples of suspicious areas, with emphasis on solid, papillary or necrotic regions were submitted for FS evaluation. The frozen section was then placed with the rest of the specimens. At least one section was obtained for every 1 cm of maximal tumor diameter to be fixed in formalin and embedded in paraffin. All of the samples were frozen at -25°C , were cut to 8 μm in thickness and stained with hematoxylin and eosin dye manually. The same pathologist who examined the frozen section made the final pathological diagnosis.

The FS results were reported as benign, rule out borderline tumor, borderline tumor, at least borderline tumor and malign tumor intraoperatively. The concordance of FS diagnosis was determined by comparing the FS result with the final pathological diagnosis. We accepted the FS concordant with the final pathology when the FS result was borderline tumor or at least borderline tumor, since we managed these patients in a similar way intraoperatively. For the patients with a FS result of borderline tumor or at least borderline tumor, we generally performed staging surgery with or without lymphadenectomy depending on the histological subtype of the tumor. There was a tendency not to perform lymphadenectomy in the patients with mucinous borderline tumor and patients with all other subtypes usually underwent lymphadenectomy depending on the attending surgeon. All the other FS results were categorized as discordant.

Statistics

The concordance of the results of FS and the results of paraffin sections were analyzed in terms of the presence of borderline tumor. Descriptive statistics were calculated by using the SPSS (Statistical Package for Social Sciences) 17.0 package program. Chi-square and ANOVA Table tests were used to analyze the differences between mean values and percentages. The cut-off value for statistical significance was set at $p < 0.05$.

Results

A total of 239 patients who were diagnosed with BOT between 1990 and 2012 were identified. Seventy-eight patients were

excluded, since they weren't operated in our institution and 16 patients were excluded, since results of FS analysis were missing. Therefore, FS results of 145 patients with a final diagnosis of ovarian borderline tumor operated in our institution in the mentioned time period were analyzed.

Median age of the patients was 42 years (range, 16–77). Among these, 75% of the patients were premenopausal. Seventy-two patients had conservative surgery. Median preoperative Ca-125 level was 44 IU/ml (range, 1–841 IU/ml). Median tumor size was 100 mm (range, 15–400 mm). Median size was then categorized by histology. Mucinous tumors had the largest median size of 200 mm (range, 40–400 mm). It was 95 mm (range, 15–350 mm) for serous tumors ($p < 0.001$). Of the 88 patients whose both ovaries were evaluated, 26 patients (30%) had bilateral tumors. In the final diagnosis, histological cell types were serous for 87 patients (60%), mucinous for 47 patients (32%), endometrioid for six patients, mixed type for four patients and Brenner for one patient.

Intraoperatively, 99 patients were reported to have borderline tumor, 18 patients were reported to have benign disease, 11 patients were reported to have rule out borderline tumor and the FS result for 16 patients and one patient were at least borderline tumor and invasive cancer, respectively. According to the paraffin block results, FS analysis was concordant for 115 (79%) of 145 patients with BOT. FS analysis detected 80 (92%) of 87 patients and 29 (62%) of 47 patients with a final diagnosis of serous and mucinous borderline tumor, respectively. In other words, the sensitivity (concordance) of FS analysis for the total group, for the ones with serous and mucinous borderline tumor were 79%, 92% and 62%, respectively. In terms of sensitivity of FS, the difference between serous and mucinous tumors was statistically significant ($p < 0.001$). The FS analysis was correct for three of six endometrioid tumor, two of four mixed tumors and for the one Brenner tumor.

Among 30 discordant FS results, 18 FS were reported as benign, 11 were reported as rule out borderline tumor and one FS was reported as invasive cancer intraoperatively. The patient with the FS result as invasive cancer was 65 years-old and had mixed tumor and she underwent staging surgery intraoperatively. Final diagnosis of 18 patients with discordant FS was mucinous borderline tumor. Three of these 18 patients underwent restaging surgery with lymphadenectomy and remaining 15 patients didn't have reoperation and were followed-up conservatively. Final diagnosis of seven patients with discordant FS results was serous borderline tumor. All but two patients underwent restaging surgery. Final diagnosis of three patients with discordant FS was endometrioid borderline tumor. Only one of these patients had restaging surgery. Final diagnosis of the last patient with discordant FS was mixed borderline tumor and she underwent restaging surgery. Totally, 29 patients (20%) weren't staged intraoperatively due to inaccurate FS result. This ratio was 8.1% (7/87) for serous tumors. None of the patients having re-surgery was upstaged.

Only histological subtypes of two patients changed in the paraffin blocks. These patients were reported to have serous borderline tumor intraoperatively. However, one of these patients was detected to have mixed type borderline tumor and the other patient had endometrioid borderline tumor in the final diagnosis.

In the study population, there was recurrence in only one patient. The patient with recurrence had had benign FS result and had had serous borderline tumor as the final diagnosis. She had undergone unilateral oophorectomy intraoperatively. The abdominal cytology was positive. She hadn't accepted re-surgery. After 24 months of the first operation, she had recurrence in the contralateral ovary. She had right salpingo-oophorectomy + bilateral pelvic and paraaortic lymphadenectomy + appendectomy + omentectomy and she has been free of disease for 97 months.

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