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Accuracy of frozen section in borderline ovarian tumor

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ABSTRACT

Borderline ovarian tumor or low malignant ovarian tumor presents in 10-15% of all ovarian cancers, which usually affects younger women and have favorable prognosis even with conservative surgery, in which fertility can be preserved. Lack of reliable diagnostic tool to indicate the type of malignancy before or at the time of surgery makes the borderline ovarian tumor one of the most controversial topics in gynecology. This might lead to many overtreatment cases with radical surgery or undertreatment with conservative surgery with the higher rate of overtreatment compared to under treatment.

In this review article, we extensively searched for all reported data regarding the accuracy of frozen section in borderline ovarian tumor. Reviewing the results of six studies, which specifically considered the accuracy of frozen section in borderline ovarian tumors, revealed an accuracy of 60% with an agreement between final pathology and frozen section results. Overall, 24.5% of under-diagnosed malignant cases interpreted to be benign and 4.9% overdiagnosed cases with benign tumor considered as a malignant. Frozen section is a reliable tool to exclude benign tumor from borderline and malignant but underdiagnosed percentage is higher. There are limitations in this review including the small number of enrolled cases, different time of diagnosis and different investigated countries and the discrepancies between the studied articles in this review.

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Introduction

For the first time in 1929, Taylor described the borderline ovarian tumor (BOT) or low malignant tumor(1). About 10-15% of all ovarian cancers are BOT. They have very interesting histological behavior. Epithelial cell stratification, increased mitotic activity, and nuclear atypia are some features of malignancy that present in borderline tumors. They lack the invasion into the stroma and they usually affect younger women and have a favorable prognosis (2); however, small percentage of tumors are invasive and classified in advanced stage which are associated with poor prognosis and recurrence rate of about 1-50% (3).

Histologically BOTs are classified based on their epithelial characteristics as serous, mucinous, endometrioid, clear cell or Brenner tumors. Their different histologic type plays an important role in their clinical presentation. Thus, it is very important to determine the cell type before the assessment of BOTs (4-6). Staging is based on International Federation of Gynecology and Obstetrics (FIGO) staging system for ovarian carcinoma.

Review of literature indicated very interesting controversy in distribution of BOTs based on the geographic region. In USA and Europe, the leading histological type of BOTs reported as serous (7-9). Interestingly, studies from Korea and Japan have showed that mucinous type was the most

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common one(10,11). Nevertheless, limited number of patients in these studies did not help to come to the conclusion based on geographic area.

Surgery is a standard of care to treat BOTs. Determinant factors that help to choose the surgical methods including patients' age, fertility status and most importantly the histological characteristic of the tumor. Two standard methods used globally used in order to treat the BOTs, are conservative or radical surgery. Borderline tumors have favorable prognosis even when they are treated with conservative method of surgery. Despite their benign behavior, the treatment of borderline tumors has been more aggressive just because they are regarded as asubset of carcinoma conservatively. Choosing and applying the correct surgery method is vitally important since patient fertility should be preserved when a conservative surgery is chosen as a method of surgery. Patients benefit from conservative surgery, if the tumor has not invaded into the stroma. In contrast, malignant epithelial neoplasms are needed to be treated more aggressively with radical surgery. Therefore, it is critically important to detect the right histology stage of the tumor at the time of surgery. An accurate test will have a golden value in these patients because it can avoid overtreatment by radical surgery and save the patient fertility when it is on early stage. On the other hand, it would not lead to catastrophic underestimation of tumor when it is on advanced stage (12).

Preoperative imaging and tumor markers are usually used to estimate the characteristic of these tumors, but limit information can be obtained from these methods (13,14). Most of the time, the decision should be made at the time of surgery in case of disseminated malignancy. Earlier stage of tumor, FIGO stage 1 and 2, are controversial ones. Preliminary diagnosis can be made based on cytology but tissue biopsy is generally the only definitive available diagnostic tool. Intraoperative frozen section can be an alternative to make the diagnosis intraoperatively. Frozen section, as a diagnostic tool, is widely used to detect the staging of the tumor. Therefore, the right decision on the surgical path with this method not only gives us information about the malignancy but also can report the presence of metastases. Accuracy of frozen section has been reported to be good in terms of diagnosing malignant and benign tumors but its reliability in detecting BOT has not been investigated sufficiently to be statistically significant to be used as a diagnostic tool (15).

In this review article, we extensively searched for all reported data regarding the accuracy of frozen section in BOT and compared the results. We did an extensive search on Medline, preliminary search words were "borderline ovarian tumor and frozen section", "borderline and borderline ovarian tumor". Finally, we found thirty articles, which investigated the accuracy of frozen section in ovarian tumor, but only six of them reviewed in this study(16-21). Studies which did not evaluate the accuracy of frozen section in borderline ovarian tumor or evaluated it in subgroups were excluded from the review. We extracted the accuracy of test in all the studies individually. All data were pooled about overall accuracy, overdiagnosed and underdiagnosed.

Literature review

Gultekin and colleagues retrospectively evaluated 82 cases diagnosed with BOT between 1995 and 2007. They compared the result of frozen sections with permanent paraffin sections. Their data showed the 69.5% rate of correct diagnosis, 1.2% overdiagnostic rate and 29.3% underdiagnostic rate (16).

Tempfer et al. investigated 96 cases of BOT between 1995 and 2007. The result of frozen section (FS) and paraffin section were compared in 71.9% of cases, which accounted for 69 of 96 and the result of FS and definitive histology were the same. Results showed an overall sensitivity of 75% and positive predictive value (PPV) of 94.5%. Twenty-eight percent (27 out of 96) were underdiagnosed and none overdiagnosed (17).

Kayikcioglu and colleagues conducted their study on thirty-three patients evaluated based on frozen sections between February 1992 and December 1997. The correlation between frozen section diagnosis and final pathological examination was 72.7% (24/33). Nine percent (2/22) of cases had inaccurate results in the serous type and 36.6% (4/11) in the mucinous type. They found that the sensitivity and specificity of frozen section diagnosis were 86.95 and 57.14%, respectively. They concluded that the frozen section evaluation in identifying a borderline ovarian malignancy was accurate enough to be used(18).

K. Houck, et al studied 140 cases in their study at Massachusetts General Hospital between 1980 and 1998 and revealed 60% consistency between frozen section and final pathology results. Moreover, they reported 10.7% overdiagnosed and 29.3% underdiagnosed cases in their study whereas the positive predictive value of borderline by frozen section was 89.3% (19).

Another study conducted at University of Pennsylvania by Menzin and colleagues evaluating frozen section and final pathology results of 48 patients between 1986 and 1993. In all 48 cases, frozen section was suggestive of BOT. Their analysis showed 27.1% underdiagnosed and none of

Table 1. Comparison of the accuracy and the rate of underdiagnosed and overdiagnosed frozen sections on borderline ovarian tumor

Author	Accuracy		Underdiagnosed		Overdiagnosed	
Reference	Number	percentage	Number	Percentage	Number	percentage
Gultekin (16)	(57/82)	59.60%	(24/82)	29.30%	(1/82)	1.90%
Tempfer (17)	(69/96)	71.90%	(27/96)	28%	(0/96)	0%
Kayikcioglu(18)	(24/33)	72.70%	(6/33)	18.20%	(3/33)	9%
Houck (19)	(84/140)	60%	(41/140)	29.30%	(15/140)	10.70%
Menzin (20)	(33/48)	27%	(13/48)	27%	(0/48)	0%
Kim (21)	(63/76)	82.90%	(8/76)	10.50%	(5/76)	6.60%
overall	(330/485)	68.00%	(119/485)	24.50%	(24/485)	4.90%

the final pathology results was benign while frozen sections suggested borderline. They concluded that frozen section was accurate in excluding the benign tumor but when it came to distinguish between borderline and invasive tumor it was not reliable (20).

Kim and colleagues reviewed all pathology reports of BTO in both frozen section and permanent histology analyses between 1994 and 2008 at Seoul St. Mary's Hospital. Similar to other studies, they compared the results of frozen section and permanent histology. They showed 62.4% agreement between frozen section and permanent histology results, which accounted for 63 of 76 cases. They had 76 cases of BOT diagnosed by frozen section. Eight has been underdiagnosed and five overdiagnosed, which were 10.5% and 6.6%, respectively. Fifty percent sensitivity and 80% specificity were reported in mentioned study (21).

Summary of all above mentioned studies and pooled data are shown on Table 1.

In addition to the accuracy of frozen section compared to the permanent histology results, some other variables have been also evaluated in some of these studies. Some of them examined serous and mucinous types of the tumors. One concluded that serous type had more missing diagnosed cases (18) while other results showed that tumors other than serous were more likely to be missed (19).

Expert pathologist was another controversial variable expressed in the study of Gultekin et al and some other retrospective reviews. They showed that expert pathologist and accuracy of frozen section diagnosis were parallel (16). Menzin and Tempfer studies have shown no difference in expertise of pathologist regarding accuracy of frozen section (17,20).

Conclusion

It is important to choose the right surgical policy at pelvic mass operation, especially when it comes to BOT, which has favorable prognosis even with conservative surgery due to preservation of fertility in younger women. There is no accurate diagnostic method to evaluate the ovarian tumor before or at the time of surgery. Frozen section analysis can provide some valuable histological information in term of malignant ovarian mass. However, the overall diagnostic performance of BOTs has not been reported satisfaction in different studies. According to previous published, data frozen section had a underdiagnostic rate of 24.5%. It showed an excellent result in term of excluding the benign tumor.

This study has its own limitations. All the published data were based on retrospective studies performed on different time frame with different diagnostic criteria and various recommendations. Moreover, they were from different areas, which might cause some bias. Number of enrolled cases were limited in addition to different inclusion and exclusion criteria in each study. Although most of the results were statistically acceptable with p-value of <0.05, broad multicentral prospective studies are needed in order to either accept or reject the frozen section as a golden diagnostic tool in BOT.

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Conflict of Interest

The authors declare no conflict of interest.

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