

# Accuracy of frozen section in borderline ovarian tumor



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**Abstract**

Borderline ovarian tumor or low malignant tumor present in 10-15% of all ovarian cancers, they usually affect younger women and they 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 surgery or at the time of surgery make the borderline ovarian tumor one of the most controversial topics of gynecology malignancy. This leads to many overtreatment cases with radical surgery or undertreatment with conservative surgery with the higher rate of overtreatment compared to undertreatment.

In this review article, we extensively searched for all reported data regarding the accuracy of frozen section in borderline ovarian tumor and compared the results. Our literature search and reviewing the result of 6 studies, which specifically considered the accuracy of frozen section in borderline ovarian tumors, gave us an accuracy of 60% with an agreement between final pathology and frozen section results. 24. 5% of under-diagnosed cases where malignant interpreted to benign and 4. 9% over-diagnosed cases where benign tumor considered as a malignant. Frozen section is a reliable tool to exclude benign tumor from borderline and malignant but under-diagnosed percentage is higher than to be accepted for a reliable diagnostic method. There are limitations in this review included the low number of enrolled cases, different time of diagnosis and different countries, which did not have similar criteria and classification.

## 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 tumor. They lack the invasion into the stroma and they usually affect younger women and have a favorable prognosis (2). However small percentage, which are invasive and classified in advanced stage 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 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 western country 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 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 worldwide are used in order to treat the BOTs, 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 tumor has been more aggressive just because they are regarded as a subset 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 neoplasm 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 what is obtained from these methods are limited (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, 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 intra-operatively. 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 presence of metastases. Accuracy of frozen section has been reported to be good in terms of malignant and benign tumors but its reliability in BOT has not been investigated sufficiently to be statically significant to be used as a diagnostic tool (15).

## **Material and methods**

In this review article, we extensively search for all reported data regarding the accuracy of frozen section in BOT and compared the results.

In order to write this review, 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 30 articles, which investigated the accuracy of frozen section in ovarian tumor, but only 6 of them reviewed in this study (18-23) because other studies was not evaluated the accuracy of frozen section in borderline ovarian tumor or it was evaluated in subgroups.

We looked at accuracy of test in all the studies individually. All data were pooled and overall accuracy, over-diagnosed and under-diagnosed then calculated.

## **Discussion**

Gultekin and colleagues retrospectively evaluated the 82 cases diagnosed with BOT at their clinic in Izmir, Turkey between 1995 and 2007. They compared the result of frozen sections with permanent paraffin section. Their

data showed the 69.5% rate of correct diagnosis, 1.2% over-diagnostic rate and 29.3% under-diagnostic rate (18)

Tempfer et al. were looked at 96 cases of BOT between 1995 and 2007. The result of frozen section and paraffin were compared in 71.9% of cases, which accounted for 69 of 96 the result of FS and definitive histology were the same. Results showed an overall sensitivity of 75% and PPV of 94.5%. Twenty-eight percentage (27 out of 96) were under-diagnosed and none over-diagnosed has reported (19).

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 percentage (2/22) 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 frozen section evaluation in identifying a borderline ovarian malignancy was accurate enough to exclude the(20)

K. Houck, et al review between 1980 and 1998 at Massachusetts General Hospital found by reviewing 140 cases in their study, which had 60% consistency with frozen section and final pathology results. 10.7% over-diagnosed and 29.3% under-diagnosed cases were reported in their study whereas the positive predictive value of borderline by frozen section was 89.3%.

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 of these 48 cases, frozen section was suggested the BOT. Their analysis showed 27. 1% under-diagnosed and none of the final pathology results was benign while frozen section 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 (22).

Kim and colleagues reviewed all pathology reports with BTO in both frozen and permanent section analyses between 1994 and 2008 at Seoul St. Mary's Hospital. Similar to other studies, they have 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 under-diagnosed and 5 over-diagnosed, which was 10. 5% and 6. 6% respectively. 50% sensitivity and 80% specificity was reported in mentioned study (23).

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 evaluated in some of these studies. Some of them examined serous type and mucinous type of the tumor despite the controversial result. One concluded that serous type

had more missing diagnosed cases (20) while other results showed that tumors other than serous were more likely to be missed (21).

Expert pathologist was another controversial variable expressed in Gultekin et al in their research and some other retrospective reviews showed that expert pathologist and accuracy of frozen section diagnosis were parallel (18). Menzin and Tempfer studies have shown no difference in expertise of pathologist regarding accuracy of frozen section.(19, 22)

## **Conclusion**

It is important to choose the right surgical policy at pelvic mass operation, especially when it comes to BOT, which have the 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 valuable histological information in term of malignant ovarian mass. However, the overall diagnostic performance for BOTs has not been reported satisfactory in any study. As it is shown in table 1, according to previous published data FS has under-diagnostic rate of 24. 5%. It showed an excellent result in term of excluding the benign tumor.

These result have 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 area, 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 result were statistically acceptable with p-value of <0.



05, a broad multicentral prospective study is needed in order to either accept or reject the frozen section as a golden diagnostic tool in BOT.