

Diagnostic accuracy of frozen section in ovarian masses: an experience at tertiary care hospital

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ABSTRACT

Background: Frozen section is quick and reliable technique for urgent tissue diagnosis i.e. on table diagnosis. In ovarian neoplasms different categories i.e. benign, borderline and malignant tumors are surgically treated differently. In such situations, frozen section is very helpful and can changes the surgical management of patients. In the present study we evaluate diagnostic accuracy of frozen section in ovarian neoplasms.

Patients and methods: This was a comparative cross-sectional study conducted at department of pathology of Fatima Jinnah Medical University, Lahore, from 01-06-2013 to 31-05-2015. This study comprised of 70 patients having ovarian masses on abdominal ultrasonography and planned to undergo surgery. The participants were operated and frozen sections of all the fresh specimens were performed at Pathology Department. The specimens were then fixed and paraffin sections were prepared for evaluation of histopathological changes.

Results: Out of total 70 cases (patient age range 10-82 years) 25 (35.7%) were malignant, 3 (4.3%) were borderline and 42 (60%) were benign. In FS analysis, 24 (34.3%) cases were diagnosed as malignant, 5 (7.1%) as borderline and 41 (58.6%) as benign. There were disagreements between diagnoses of frozen section and permanent paraffin sections in 04 (5.71%) cases. The overall accuracy of frozen section diagnosis was 97.10 %. The sensitivity of FS for all three categories i.e. benign, borderline and malignant lesions was 100%, 75% and 96%; and specificities were 97.6%, 100% and 100% respectively.

Conclusion: Frozen section is a reliable and precise technique in the intraoperative evaluation of patients with suspicious ovarian masses.

Keywords:

Frozen section, ovarian masses, intraoperative evaluation.

INTRODUCTION

Ovarian tumors are common forms of neoplasia in women and ranked as the eighth most common malignancy in females, accounting for approximately 4% of all women's cancers.¹ The mortality among patients with ovarian cancer is very high as compared to other gynaecological malignancies because patients are usually diagnosed at very late stage. Majority of females i.e. about 60% are diagnosed at stage III- IV at the time of diagnosis.¹⁻⁶ Ovarian tumors classification is complex and is divided into three broad categories i.e. surface epithelial tumors, sex cord stromal tumors and germ cell tumors. The most common are the surface epithelial tumors which comprises of about 60-70 % of all ovarian tumors.⁴⁻⁶ These are derived from surface epithelium and are more common in females older than 40 year. Germ cell tumors arise from germ cells

and consist of 30% of all ovarian tumors. These are more common in young females. Sex cord stromal tumors derived from ovarian stroma, comprised of approx. 6% of all ovarian neoplasms and are more commonly found in postmenopausal women.^{6,7} Surface epithelial tumors are further categorized into benign, borderline and malignant neoplasms. Surgical management of each category is different so precise and correct diagnosis is very important.⁷

These neoplasms are usually diagnosed by correlation of general physical examination (especially pelvic examination), serological markers (Alpha fetoproteins, Beta HCG, CA 125), and ultrasonography but these tools are insufficient and can miss the cancer in its early stage.^{8,9} The diagnosis is only confirmed with histopathological examination of tissue specimen obtained during surgery. In the last few decades a new diagnostic tool, intraoperative frozen section (FS) has been introduced for diagnosis of suspicious ovarian masses.^{10,11} It is found to be an accurate and precise technique for the surgical management of suspicious ovarian tumors and has been used intra-operatively to verify microscopic diagnosis (benign, borderline or malignant) before planning for definitive surgery.¹⁰⁻¹² Benign tumors are managed conservatively i.e. ovarian cystectomy, however the management of the borderline tumors is variable

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depending on the age or fertility of the patient. Intraoperative frozen section helps to prevent over or under treatment of patients with suspicious ovarian masses.^{13,14} This study was conducted to assess the diagnostic accuracy of frozen section taking histopathology as gold standard.

PATIENTS AND METHODS

This comparative cross-sectional study was carried out at the Department of Pathology, Fatima Jinnah Medical College, Lahore, from 01-06-2013 to 31-05-2015 after the approval of ethical review committee, Fatima Jinnah Medical University, Lahore. The study comprised 70 patients with suspicious ovarian masses. Females of all ages with suspicious ovarian masses on abdominal ultrasonography were included. Females with inflammatory adnexal mass assessed on physical examination, diagnosed cases of endometriosis and patients with previous history of ovarian malignancy were excluded. These subjects were selected for surgery and frozen section by the Gynecology Department of Sir Ganga Ram Hospital Lahore. The demographic information was recorded in the predesigned research proforma. A specimen of the ovarian mass was taken by the gynecologist during laparotomy and sent to Pathology Department Fatimah Jinnah Medical College without formalin, for frozen section. A thorough gross examination including color, size of tumor, capsular integrity, solid and cystic areas, necrosis and hemorrhage was done. After that small representative tissue sections from the specimen were placed in Cryostat and frozen up to -8°C, cut, stained and then examined by senior consultant pathologists having more than ten years' experience of histopathology reporting. Three categories (benign, borderline and malignant) were made on the basis of morphology. The final results of frozen section and histopathology were compared taking histopathology as 'gold standard'. The tumors that are benign both in frozen and permanent sections are considered as true negatives and that are malignant in both sections are considered as true positives. The tumors that are reported as malignant/ borderline on frozen section and proved to be benign on permanent sections are labeled as false positive and the tumors that are reported as benign/borderline on FS and malignant on permanent sections are labeled as false negative. Then specificity, sensitivity, negative and positive predictive values and diagnostic accuracy of each category (benign

borderline and malignant) were calculated individually using 2x2 tables.

RESULTS

A total 70 biopsies of ovarian masses, (age range 10-82 year) mean age 45.98 ± 12.46 were assessed in Fatima Jinnah Medical College Pathology Department. Overall, 35.7% (n=25) of cases were malignant, 4.3% (n=3) borderline and 60% (n=42) benign neoplasms on paraffin section diagnosis. In FS analysis, 34.3% (n=24) were malignant, 7.1% (n=5) borderline and 58.6% (n=41) benign lesions (Table 1).

There was complete concordance in 94.3% of the cases; partial concordance in 2.8% cases whereas 2.8% showed no concordance. There were disagreements between the diagnoses of frozen sections and permanent paraffin sections in 04 cases (Figure 1). One border line mucinous tumor on frozen sections (Figure 2) was found to be mucinous cyst adenocarcinoma (Figure 3) in the paraffin embedded tissue sections. One borderline serous tumor on frozen sections turned out to be serous cystadenoma on permanent section. One endometrioid tumor on frozen section turned out to be metastatic Krukenberg's on permanent section. One yolk sac tumor on frozen section turned out to be mixed germ cell tumor on permanent section.

In 41 cases (58.6 %) diagnosis of benign neoplasm was made on frozen section which was then confirmed by paraffin sections. These 41 cases, therefore, were regarded as true negatives. In malignant category frozen section was able to identify 24 (34.3 %) out of 25 (35.7 %) malignant neoplasms, confirmed on paraffin sections and these were labeled as true positives. As for the remainder, 1 (1.42%) case was represented as false negative (under diagnosis) and 1 (1.42 %) case was false positive (over diagnosis).

The probability that patient having malignant neoplasm was diagnosed by frozen section is defined as its sensitivity and in this study, it was 96 % while the ability of frozen section to assess the negative result in benign cases is defined as its specificity which was 100% in the current study. Positive predictive value of a positive (i.e. malignant) frozen section was 100% and negative predictive value of negative (i.e. benign) frozen section was also 100%.

The frozen section was 96% sensitive and 100% specific in malignant tumors. Positive and negative predictive values of 100% each was calculated in this category of malignant neoplasm. Overall, the sensitivity

Table 1. Comparison of frozen section diagnosis and permanent section diagnosis

Diagnosis	Frozen section		Permanent section	
	No.	%	No.	%
Benign	41	58.6	42	60
Borderline	05	7.1	03	4.3
Malignant	24	34.3	25	35.7

Table 2: Diagnostic value of frozen section for ovarian tumor of various histologic types.

Sensitivity %	Specificity %	PPV %	NPV %	Diagnostic accuracy %
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Benign	100	97.6	100	100	95.3
Borderline	75	100	75	100	60
Malignant	96	100	100	100	92.3

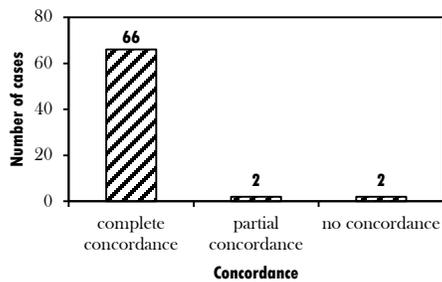


Figure 1. Concordance between frozen and paraffin section diagnosis

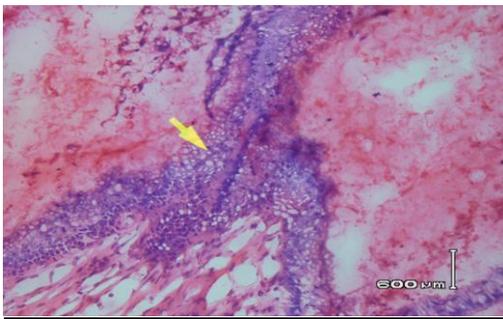


Figure 2: Photomicrograph of borderline mucinous tumor (frozen section) (20x) H & E stain. Frozen section of borderline mucinous tumor showing multilayering and mucin in the epithelium. (arrow)

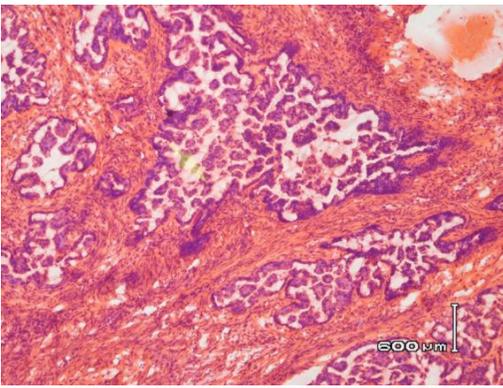


Figure 3: Photomicrograph of Mucinous cyst adenocarcinoma (paraffin section) (10x) H & E stain. Mucinous cyst adenocarcinoma showing stromal invasion. (arrow)

of borderline tumors was 75% and the specificity was 100%. The positive and negative predictive values of frozen sections for borderline malignancies were 75% and 100% respectively. For benign ovarian tumors, the sensitivity, specificity positive and negative predictive values are 100%, 97.6%, 100% and 100% respectively (Table 2). The overall accuracy of frozen section diagnosis was 97.10%.

DISCUSSION

Intraoperative frozen section is being used more frequently for the diagnosis of ovarian masses due to its good diagnostic accuracy (more than 96 %),^{7,8} because precise intraoperative diagnosis of an ovarian malignancy is of great importance to plan most suitable and proper surgical procedure in order to avoid over and under treatment of the patients.¹⁵ As majority of females with ovarian masses do not have definitive diagnosis prior to surgery, the plan and extent of surgery as well as diagnosis is mainly dependent on intraoperative frozen section. In cases which turn out to be benign, conservative surgeries are performed however, in borderline and malignant neoplasms radical surgeries are performed during the same surgical procedure and the patient do not have to undergo multiple surgeries. Furthermore, young females with borderline tumors may have more conservative procedures to preserve the fertility of the patient. Hence accurate and precise intraoperative diagnosis remains the backbone of surgical planning and management of patient in suspicious ovarian masses.¹⁶⁻¹⁸

Number of studies have been conducted to calculate the accuracy of intraoperative frozen section in ovarian neoplasm and it turned out to be a precise and reliable technique in benign and borderline cases however, in borderline epithelial tumors it is less reliable and major diagnostic errors in frozen section fall in this category.^{19, 20}

Basaran and coauthors reviewed 44 borderline ovarian tumors over a period of 5 years. There was complete concordance between frozen section and permanent sections in 37/44 cases (84.1%). In 01 out of 44 cases (2.3 %) frozen section diagnosed benign neoplasms as borderline ovarian tumor (false positive) and in 6 out of 44 cases (13.6%) there was underdiagnosis i.e. malignant tumor diagnosed as BOT (false negative).²¹

Yildirim and associates reviewed 192 ovarian tumors including all types. Their 188 out of 192 cases completely agreed with the permanent sections. The overall accuracy was 97.9%. The sensitivity of frozen section for benign, borderline and malignant tumors was 98.8%, 90% and 93.8% respectively whereas specificity was 92.8%, 98.9% and 100% respectively. Over as well as under diagnosis, i.e. false positive and false negative, was reported in 2/192 cases (1.07%) each.²²

In another study carried out by Acikalin and colleagues in 2014 overall accuracy was reported to be 96.5% and the sensitivity of frozen section in benign, borderline and malignant tumors was 97.5%, 95.8% and 95.6% respectively whereas specificities were 97.5%, 97.6% and 100% respectively.⁸

In this study, the overall accuracy was 97.10% which concurs with the previous reports.^{7-9,21,22} Sensitivity of frozen section diagnosis of benign, borderline, and malignant lesions was 100%, 75% and 96%; and the

specificities were 97.6%, 100% and 100%, respectively. The diagnostic accuracy of benign, borderline and malignant tumors was 95.3%, 60% and 92.3% respectively, which is in concordance with all the previous studies conducted on ovarian masses.^{7-9,21,22}

Major reasons of discrepancies in the diagnosis of frozen section in different studies include sampling error and pathologist misinterpretation. The tumors with large sizes like mucinous tumors have less sensitivity of frozen section. Discrepancies in these tumors can be decreased by taking more sections in larger tumors (>10 cm).²¹ Proper sampling, expert pathologist and good communication between surgeon and pathologist are very important factors for accurate FS diagnosis. Under diagnosis was made in cases where the error was in taking samples from large masses. Diagnostic reliability of FS was very high in small serous epithelial tumors. Majority of discrepancies in FS diagnosis fall in the category of borderline mucinous tumors because these tumors may be very large and may have benign, borderline, and malignant areas in the same tumor. These discrepancies can be avoided by taking more sections from different sites. Therefore, large tumors and mucinous histology are the major predictors of wrong diagnosis.

CONCLUSION

This study concludes that frozen section is a reliable technique for interpretation of suspicious ovarian masses intra-operatively. In institutions where the facility is available and expert pathologists are present for frozen section reporting, it is of great help and can be utilized to plan the extent of surgery. Frozen section is very accurate for benign and malignant tumors, however its accuracy is relatively low in borderline tumors and requires careful judgement and operative decision by the gynecologist to avoid under- or over treatment.

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