International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Jolly RS et al. Int J Reprod Contracept Obstet Gynecol. 2024 Dec;13(12):3466-3471
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20243575

Original Research Article

Role of frozen section biopsy in the diagnosis of ovarian masses

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Received: 10 October 2024
Accepted: 07 November 2024

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ABSTRACT

Background: Ovarian malignancy is an important cause of mortality among women with most cases being diagnosed late and requiring aggressive management. The association between the final diagnosis on standard conventional histopathological sections and the examination of intraoperative frozen sections is an important tool for quality control. Therefore, this study aimed to assess the role of frozen section biopsy in diagnosing ovarian masses.
Methods: This was a cross-sectional study conducted in the department of obstetrics and gynecology, Dhaka Medical College Hospital, Dhaka, Bangladesh during the period from January 2020 to December 2020. In our study, we included 50 diagnosed cases of ovarian masses who attended the department of obstetrics and gynecology in Dhaka Medical College Hospital for surgery.
Results: The mean age of the patients was 31.68±11.04 years. On the frozen section, forty-one patients (82%) were diagnosed as benign cases while nine patients (18%) were identified as malignant. The final histopathologic diagnosis revealed 38 (76%) as benign tumors and 12 (24%) as malignant tumors. Frozen section biopsy (FSB) was found to be 75% sensitive and it showed 100% specificity. The PPV, NPV, and diagnostic accuracy of FSB were found to be 100%, 92.6%, and 94% respectively. Among the three discordant cases, two were mucinous adenocarcinoma and one was papillary serous cyst adenocarcinoma.
Conclusions: This study showed a diagnostic accuracy of 94%, which is an eye-opener for gynecological oncologists regarding the usefulness of frozen section biopsy. Frozen section diagnoses can be extremely helpful in the clinical management of ovarian cancers.

Keywords: Accuracy, Frozen section, Histopathology, Ovarian tumor

INTRODUCTION

Ovarian tumors constitute a heterogeneous group of lesions that include benign, borderline, and malignant tumors.[1] Ovarian malignancy is an important cause of mortality among women with most cases being diagnosed late and requiring aggressive management. However, in the early stages of surface epithelial cancers, borderline tumors, and germ cell tumors, conservative management is usually followed. Hence, intraoperative frozen section analysis is of utmost importance for planning proper surgical management.[2]

A diagnostic tool that helps to identify various ovarian lesions with a high degree of accuracy helps the surgeon choose the appropriate operating procedure.[3] Preoperative diagnostic modalities include serum tumor marker level estimation and imaging. The serum tumor marker CA-125

is not specific. CA-125 level can be normal in the early stages of ovarian carcinoma and can be raised in nonneoplastic gynecological conditions like endometriosis and pelvic inflammatory disease.[4]

Ovarian cancer has often been called the "silent killer" because of nonspecific symptoms and a lack of trustworthy screening for early-stage cancer detection. Most cases are diagnosed in the advanced stages and require aggressive surgical management.[2]

In the early stages of epithelial ovarian cancer, borderline tumors, and germ cell tumors a conservative approach may be followed particularly in women of reproductive age group whereas in cases of advanced stage malignant ovarian neoplasms a radical surgery is undertaken. Therefore, an intraoperative diagnosis is crucial in planning for the appropriate surgical management.

Pre-operative biopsy is not an option for ovarian masses, and is the only cytological sample available for an effusion-related fluid evaluation. Furthermore, a frozen section is a more accurate diagnosis than a preoperative evaluation that includes a history, physical examination, several imaging examinations, and tumor markers, or an intraoperative diagnosis made using cytological techniques like imprint and scrape cytology.[5]

Although the histopathological diagnosis remains the gold standard technique, an intraoperative diagnosis by frozen section becomes a valuable tool that provides a primary diagnosis of tumors as benign, borderline and malignant and thus guides the operating surgeon in a direction toward the extent of the surgery and also determines the need for a further workup.[6]

According to many studies in the literature, the overall accuracy of intraoperative frozen section diagnosis for ovarian tumors ranges between 73% and 98%.[5]

Periodic review of the association between frozen section diagnosis and final histopathological diagnosis is useful to identify the potential causes of errors and thus measures can be implemented to help prevent similar occurrences.[7]

When it comes to young women whose ovarian cancers may be treated conservatively while maintaining fertility, the precision of the frozen section diagnosis is crucial. In surgical pathology laboratories, the association between the final diagnosis on standard conventional histopathological sections and the examination of intraoperative frozen sections is an important tool for quality control. Therefore, in this study, we aimed to assess the role of frozen section biopsy in diagnosing ovarian masses.

METHODS

This was a cross-sectional study conducted in the department of obstetrics and gynecology, Dhaka Medical College Hospital, Dhaka, Bangladesh during the period from January 2020 to December 2020. In our study, we included 50 diagnosed cases of ovarian masses who attended the department of obstetrics and gynecology in Dhaka Medical College Hospital for surgery.

These are the following criteria to be eligible for enrolment as our study participants:

Inclusion criteria

Patients aged more than 18 years; patients diagnosed with ovarian tumor by clinical examination and radiologically; patients who were willing to participate.

Exclusion criteria

Patients diagnosed case of ovarian tumor with enlarged supraclavicular or inguinal lymph node; patients diagnosed case of ovarian tumor with features of liver, omentum, or lung metastasis; patients diagnosed case of ovarian tumor with pleural effusion or ascites.

Frozen section procedure

The frozen section procedure is a pathological laboratory procedure to perform rapid microscopic analysis of a specimen. It is used most often in oncological surgery. A frozen section is conducted during gynecological surgery on patients with ovarian and pelvic masses while patients are under anesthesia. The surgeon removes the ovarian tumor very gently and without any delay, this fresh specimen is put in a jar without any formalin and sent to a pathologist. The pathologist freezes the tissue with liquid nitrogen, cuts it, and then stains it with special staining solutions so that it can be viewed under a microscope. Time is important in performing a frozen section to reduce the amount of time that the patient is under general anesthesia. A frozen section usually takes between 30 and 45 minutes. They inform the report to surgeon over the telephone.

Data collection procedure

The pre-operative data regarding age, parity, menopausal status, clinical history, general and physical examination findings, clinical diagnosis, imaging studies, radiological diagnosis, and serum tumor markers, i.e., CA-125, CA19-9, CEA, S. β HCG, LDH, α fetoprotein levels were obtained from the case records. Before laparotomy, comorbidities, nutritional status, and anemia were corrected, and bowel preparation was given. In the pathology department, the gross morphology of the specimen was observed and recorded. Representative bits from the ovarian tumor included bits from cystic areas, i.e., cyst wall, and bits from solid areas as well. For tumors <10 cm in size, two bits were given which included the cyst wall and solid areas if present, whereas for tumors greater than 10 cm in greatest dimension four bits, i.e., two bits from the cyst wall and two bits from solid areas were

given. A frozen section report was given with a specific histologic diagnosis. The final histopathologic diagnosis of ovarian masses was based on the WHO classification.

Statistical analysis

All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of frozen section biopsy for ovarian tumor were calculated by constructing a 2×2 table. A p value <0.05 was considered as significant. Statistical analysis was performed by using SPSS 25 (Statistical Package for Social Sciences) for Windows version 10. The study was approved by the Ethical Review Committee of Dhaka Medical College Hospital.

RESULTS

This cross-sectional observational study was done to assess the role of frozen section biopsy in diagnosing ovarian masses. For this purpose, 50 patients were selected as per inclusion criteria who underwent laparotomy, during which, the tumor was sent for frozen section biopsy and reports were subsequently compared with the final histopathology report. Data were analyzed and the findings derived from the data analysis are given below.

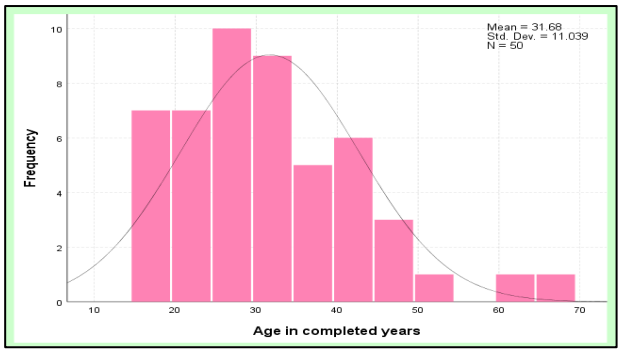

Figure 1: Age distribution of our study patients.

Table 1: Distribution of the patients by obstetric history (n=50).

Variables	Frequency	Percentage
Use of OCP		
Yes	15	30.0
No	35	70.0
Parity		
Nullipara	19	38.0
Multipara	17	34.0
Primipara	13	26.0
Grand multipara	1	2.0

Figure 1 shows the age distribution of study participants. Maximum number of patients were in the age group of 21-30 years (34%), followed by 14 (28%) patients were aged 31-40 years. The mean age of the patients was 31.68±11.04 years and their age ranged from 17 to 65 years.

Table 1 shows that among all respondents, fifteen (30%) of them were using OCP. Most of the respondents were nullipara (38%), followed by multipara (34%) and primipara (26%). There was only 1 patient of grand multipara.

Table 2: Distribution of the patients by tumor-related parameters (n=50).

Parameters	Frequency	Percentage
Lump in abdomen		
Present	44	88.0
Absent	6	12.0
Consistency of the lump (n=44)		
Solid	3	6.8
Cystic	22	50.0
Mixed	19	43.2
Site of the lump (n=44)		
Unilateral	40	90.09
Bilateral	4	9.09
Mobility of the lump (n=44)		
Fixed	22	50.0
Mobile	22	50.0
Size of the tumor (n=44)		
<10 cm	8	18.18
10-20 cm	30	68.18
>20cm	6	13.6

Table 2 shows the distribution of the patients by tumor-related parameters based on the abdominal examination findings. Forty-four respondents (88%) had lump in the abdomen and six patients (12%) had none by per abdominal examination. Most of the lumps were cystic in consistency (22, 50%) and three patients (6.8%) had solid lumps while 19 patients (43.2%) had mixed type lumps. 90.09% lumps were unilateral and the 9.09% were bilateral. Half of the lumps were fixed and half were mobile. The majority (68.18%) of patients had tumor size 10-20 cm.

Table 3: Mean and SD of tumor markers (n=50).

Tumor marker	Mean	SD	Normal value
CA125	295.35	±588.24	0-35 U/ml
CA19-9	158.71	±370.58	0-37 U/ml
CEA	9.59	±29.34	<5 ng/ml
βHCG	2.34	±1.18	<5 mIU/ml
LDH	262.44	±489.17	140-280 U/l
Alpha-fetoprotein	58.95	±222.17	10-20 ng/ml

Table 3 shows the mean and SD of the tumor markers of our study patients. The mean of CA125 was

295.35±588.24 with a normal value of 0-35 U/ml. The mean of LDH was 262.44±489.17 with a normal value of 140-280 U/l.

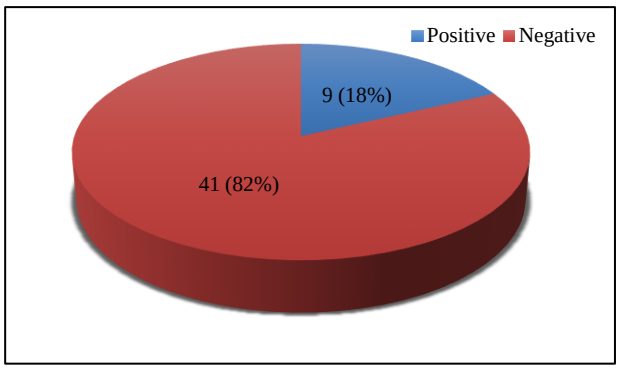

Figure 2: Distribution of patients based on frozen section biopsy report (N=50).

The pie chart shows the frozen section biopsy reports of the ovarian masses. On frozen section forty-one patients (82%) were diagnosed as negative while nine patients (18%) were identified as positive.

Table 4 shows the distribution of ovarian masses evaluated by histopathology. According to histopathology findings total 18 (36%) patients were diagnosed as benign non-neoplastic lesions. Twenty (40%) patients had surface epithelial tumours. Of them six were diagnosed as malignant by HPR. Among 11 germ cell tumours five were malignant.

Table 5 shows the distribution of ovarian tumour by frozen section and histopathological findings. In frozen section biopsy out of 50 cases 41 (82%) were diagnosed as benign cases while nine (18%) were reported as malignant cases. In histopathological examination, 12 patients (24%) were found to be malignant cases without any metastasis.

Table 4: Distribution of ovarian masses evaluated by histopathology (n=50).

Types of lesions	HPR	
	Benign (%) (Total =38)	Malignant (%) (Total =12)
Benign non-neoplastic lesions		
Endometroiotic cyst	7 (14)	-
Corpus luteal cyst	7 (14)	-
Follicular cyst	3 (6)	-
Chronic granulomatus inflammation	1 (2)	-
Surface epithelial tumor		
Serous	10 (20)	4 (8)
Mucinous	4 (8)	2 (4)
Germ cell tumor		
Dysgerminoma	-	2 (4)
Yolk sac tumor	-	2 (4)
Mixed germ cell tumor	-	1 (2)
Mature cystic teratoma (dermoid)	6 (12)	-
Sex cord stroma tumor		
Adult granulosa cell tumor	-	1 (2)

Table 5: Distribution of ovarian tumor by frozen section and histopathological findings.

Type of section	Benign	Borderline	Malignant
Frozen section biopsy (n, %)	41 (82)	0 (0.0)	9 (18)
HPR (n, %)	38 (76)	0 (0.0)	12 (24)

Table 6: Diagnostic values of frozen section biopsy and histopathology for ovarian masses.

Frozen section	Histopathology		Sn[a] (%)	Sp[b] (%)	PPV[c] (%)	NPV[d] (%)	DA[e] (%)
	Malignant	Benign					
Malignant	9	0	75.0	100.0	100.0	92.6	94.0
Benign	3	38					

[a] Sn=Sensitivity; [b] Sp=Specificity; [c] PPV= Positive predictive value; [d] NPV= Negative predictive value; [e] DA = Diagnostic accuracy

Table 6 shows that there were 9 true positive cases, 38 cases were true negative, false positive was 0, and 3 cases were false negative. The effectiveness of frozen section biopsy (FSB) of ovarian mass was assessed against the

gold standard of histopathology. It was found that FSB was 75% sensitive to diagnose the ovarian mass correctly while it showed 100% specificity to rule out the condition. The positive predictive value, the negative predictive value and diagnostic accuracy of FSB were found as 100%, 92.6% and 94% respectively.

DISCUSSION

Frozen Section service for immediate intraoperative reporting is desirable for the gynecology surgeon. It allows for a single optimal operative staging procedure to be indicated and for a non-staging procedure if not required.[8]

In the study, the mean age of the patients was 31.68 years with SD±11.04 years and their age ranged from 17 to 65 years. Prakash et al reported the mean age of presentation was 42.69±14.55 years.[9] Pal et al showed that patients ranged in age from 1.5 to 69 years with a mean age of 33.84 years.[10] Bandyopadhyay et al also reported that the age range varied from 2 to 65 years, with the mean age being 42 years.[11]

The current study showed that a clinical lump was found in 44 (88%) cases. From these 44 cases, 22 patients had fixed lumps, where FSB reports were negative for malignancy in 15 cases and positive for malignancy in 7 cases, but the HPR report showed negative for malignancy in 14 cases and positive for malignancy in 8 cases. In the Prakash et al study 65.4% of cases were presented with lump in the abdomen.[9] The study by Pal et al reported that the most common symptom was an abdominal lump (71.43%).[10] Mehdi et al reported that the most common presenting feature was an abdominal mass (90.5%), Ray et al reported that abdominal mass in (68.83%) cases.[12,13]

Our study showed that in the majority cases of palpable masses were unilateral in 40 (90.09%) and bilateral in 4 (9.09%) cases. In the Rajavigneshwari et al study, most of the cases were found to have unilateral involvement 96% as compared to bilateral involvement which was seen in only 4% of tumors.[14] In the Pal et al study, 52 cases (74.28%) were unilateral and 18 cases (25.72%) had bilateral ovarian involvement.[10] Patel et al found ovarian tumors were unilateral in 89.5% of cases and bilateral in 10.5% of cases which is correlated with studies by Thakkar and Shah.[15,16]

Our result regarding the mass morphology we observed, the majority of ovarian masses were cystic 22 (50%), where 19 (43.2%) were solid and 3 (6.8%) cases were mixed. Patel et al reported majority of the ovarian tumors were grossly cystic in 68.5% of cases followed by mixed tumors in 25.3% and 6.1% of cases were solid tumors.[15] Another study by Sawant and Mahajan found on gross examination that 44.78% of cases were cystic, 22.39% were solid and 32.83% of cases were partly cystic and partly solid.[17]

The present study showed an overall accuracy of 94% which is very reliable and within the limit of the accuracy range from the literature. The overall accuracy of the frozen section diagnosis for ovarian tumors reported by most studies ranges from 73.8% to 98.7%.[2,8,18-20]

There were no false-positive cases in the current study giving rise to 100% specificity. It was observed that out of three false-negatives, two were mucinous adenocarcinoma and one was papillary serous cyst adenocarcinoma giving a false-negative result of 25% which was higher than the false-negative rates of other studies that ranged from 2% to 13.6%.[2,18-20]

The current study showed a sensitivity of 75% on the frozen section. A published meta-analysis of 18 studies comparing frozen section diagnosis of ovarian pathology with the final histopathology showed the sensitivity of frozen section varied from 65% to 97%.[21]

Any frozen section service must be of clinical use. Both the clinician and pathologist involved in this process must understand the limitations of FS diagnosis. At the same time, patients have to be fully informed of this before consenting to operations with the knowledge that further extensive procedures may be required.

There are some limitations of the study. Our study was a single-center study. We took a small sample size due to our short study period. After evaluating those patients, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

CONCLUSION

This study showed a diagnostic accuracy of 94%, which is an eye-opener for gynecological oncologists regarding the usefulness of frozen section biopsy as an important diagnostic tool. Our research demonstrated that frozen section diagnoses can be extremely helpful in the clinical management of ovarian cancers, as shown by the association between frozen section analyses and histological results in the evaluation of ovarian tumors in our hospital. Thorough gross examination, representative area sampling, and effective communication between the pathologist and surgeon can help to prevent the restrictions and provide the fast and accurate diagnosis that's needed to avoid recurrent surgeries.

So further study with a prospective and longitudinal study design including a larger sample size needs to be done to validate the findings of our study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee of Dhaka Medical College Hospital

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Cite this article as: Jolly RS, Chowdhury M, Amin R, Elora AL, Afrose T, Kader M. Role of frozen section biopsy in the diagnosis of ovarian masses. Int J Reprod Contracept Obstet Gynecol 2024;13:3466-71.