Diagnostic Accuracy of Intraoperative Frozen Section in Ovarian Neoplasms: Experience in a Tertiary Oncology Centre

Bajracharya Shakya A,[1] Jain V,[2] Sekhon R,[2] Rawal S,[3] Mehta A[4]

Department of Gynae-Oncology

Nepal Cancer Hospital and Research Centre

Harisidhhi, Lalitpur.

[2]Department of Gynae-Oncology

[3]Department of Uro-gyneoncology

[4]Department of Patholgy

Rajiv Cancer Hospital and Research Centre,

Delhi.

Corresponding Author

Anu Bajracharya Shakya

Department of Gynae-Oncology

Nepal Cancer Hospital and Research Centre

Harisidhhi, Lalitpur.

E-mail: dr.anubajracharya42@gmail.com

ABSTRACT

Background

Ovarian cancer is the second most common type of female genital tract malignancy. Treatment planning differs for benign, borderline and malignant subtypes of surface epithelial tumours and depends on accurate histopathological diagnosis. A pre-operative diagnosis of the nature of ovarian tumors is not always reliable. Frozen section is a valuable diagnostic tool in rapid intraoperative categorization of ovarian masses and thereby helps in planning the surgical management. Adequate management and treatment of ovarian carcinoma requires a complete surgical staging supported by frozen-section examination. To achieve this goal it is necessary to have a high level of accuracy.

Objective

To assess the accuracy of intra-operative frozen section in the diagnosis of various categories of ovarian neoplasm conducted in Rajiv Gandhi Cancer Institute and Research Centre.

Method

Intra-operative frozen sections for suspected ovarian neoplasm that underwent surgery as primary line of therapy at this institution were analyzed retrospectively from Jan. 2014 - Dec. 2015. The results of frozen section were compared with the final histopathology diagnosis on paraffin sections and the overall accuracy, sensitivity, specificity, positive and negative predictive values were determined.

Result

The study included 159 cases and the mean age of patients was 44.72±14.28 years (Range 19-75 years). The mean size of tumor was 12.5±5.9 cm. Sensitivity of frozen section for benign, borderline and malignant tumors was 98.53%, 73.33% and 94.74% respectively and the related specificities were 95.60%, 96.53% and 100% respectively. There were 150 concordant cases and 9 discordant cases. Overall diagnostic accuracy of frozen section was 94.33%.

Conclusion

Intra-operative frozen section diagnosis appeared to be an accurate and comparable technique for the histopathology diagnosis of ovarian tumors.

KEY WORDS

Accuracy, Frozen section, Ovarian neoplasm, Sensitivity

INTRODUCTION

Ovarian malignancy accounts for 25% of gynecological cancers and 50% of all deaths from cancers of the female genital tract.[1] The three main categories of ovarian neoplasm are benign, borderline and malignant which differ with respect to their biologic characteristics, management and prognosis. Preoperative imaging and tumor markers have only limited value in differentiating between these tumor categories.[2,3] The diagnosis of malignancy is usually straightforward, but in some cases it may be difficult to distinguish whether the malignant tumor is of ovarian origin or represents metastases from other sites.[4] Rapid intra-operative diagnosis of the nature of ovarian tumors is challenging for effective planning of the surgical management of these tumors, particularly in a young woman as it can avoid unnecessary removal of contra lateral ovary and helps preserve fertility.[5] The use of intra-operative diagnosis with frozen section (FS) is important as it guides the surgeons to determine the extent of surgery and staging to give the patient maximum benefit of a single surgical exercise. This study was conducted to evaluate the accuracy of intra-operative frozen section in the diagnosis of ovarian neoplasm at Rajiv Gandhi Cancer Institute and Research Centre (RGCI and RC).

METHODS

This retrospective study was conducted in the Department of Gynecologic Oncology and Pathology at RGCI and RC after being approved by the research committee. In this study, we analyzed 159 cases of ovarian neoplasms that underwent surgery and in which intra-operative frozen section examination was done from January 2014 to December 2015.

Inclusion criteria:

1. Patients with unilateral or bilateral ovarian masses in whom frozen section examination was performed intra-operatively.

Exclusion criteria:

1. Pre-operatively proven malignancy cases.

2. Advanced ovarian tumors on chemotherapy

Each specimen collected from the operation site was transferred to the pathology department in a fresh state with detailed clinical information. The specimens were examined macroscopically and sections were taken from the most representative areas by the pathologist. One to four sections depending on the size and heterogeneity of the tumor were processed in a cryostat and sections were stained by hematoxylin-eosin. Then the slides were evaluated and the pathologist reported the frozen section diagnosis to the surgeon within 20 minutes.

The frozen section diagnosis was categorized as benign, borderline and malignant. The results of frozen section were compared with the final histopathology diagnosis on paraffin sections. The neoplastic lesions included epithelial tumors, germ cell tumors, sex cord stromal tumors and metastatic tumors. Also, the following parameters were noted: age of the patient, size of the tumor and its laterality. Overall accuracy was defined as the percentage of concordance between frozen and final diagnosis i.e., total number of cases in which there is concordance between frozen section diagnosis and final tissue diagnosis divided by the total number of patients with ovarian masses expressed as percentage. Statistical analyses were carried out by SPSS 21 and sensitivity, specificity, positive predictive values and negative predictive values of each group were determined.

RESULTS

The study included 159 cases where the patients had undergone frozen section for ovarian masses. The age group ranged from 19-75 years and the mean age was 44.72 years. The mean size of tumor was 12.5 cm (range 2.5 to 29 cm). There were 37 cases with bilateral ovaries involvement. The results of definitive histopathological diagnosis of all tumors are presented in Table 1. Histologically, the commonest tumor type was epithelial. Five tumors were metastatic to the ovary: appendix (n=2), small intestine (n=1), metastatic Renal Cell Carcinoma (n=1) and metastatic adenocarcinoma in a known case of carcinoma breast (n=1).

Table 1. Distribution of various ovarian lesions according to paraffin permanent section.

Histopathological diagnosis	Total Number (N=159)
Non-neoplastic lesion	37 (23.27%)
Epithelial tumors	97 (61%)
Sex cord stromal tumors	9 (5.66%)
Germ cell tumors	11 (6.91%)
Metastatic	5 (3.14%)

Among the frozen section results, 71 were benign, 16 borderline and 72 were malignant. However, in paraffin diagnosis, 68 were benign, 15 borderline and 72 were malignant. There were four cases with benign in frozen but borderline in paraffin results; four had borderline in frozen section but malignant in paraffin block results and one case borderline in frozen and benign in paraffin block results (Table 2).

Among 159 cases, 150 cases were concordant and 9 were discordant in the final paraffin result. The overall diagnostic accuracy of frozen section was 94.33%. Sensitivity of frozen section for benign, borderline and malignant tumors was 98.53%, 73.33% and 94.74% respectively and the related specificities were 95.60%, 96.53% and 100% respectively. The positive predictive value (PPV) and negative predictive

Table 2. Comparison between frozen section and paraffin sections report. (N=159)

Frozen Diagnosis	Paraffin Diagnosis			
	Benign	Borderline	Malignant	Total (FS Diagnosis)
Benign	67	4	0	71
Borderline	1	11	4	16
Malignant	0	0	72	72
Total (Permanent paraffin Diagnosis)	68	15	76	159

value (NPV) for benign, borderline and malignant tumors were 94.37%, 68.75%, 100% and 98.86%, 97.2% and 95.4% respectively. The false positive rate for malignant tumors was 0% and false negative rate was 5.26% (Table 3).

Table 3. Statistical value of benign, borderline and malignant ovarian tumors.

Statistical result (%)	Benign%	Borderline%	Malignant%
Sensitivity	98.53	73.33	94.74
Specificity	95.60	96.53	100
Positive predictive value	94.37	68.75	100
Negative predictive value	98.86	97.20	95.40
False Positive	4.40	3.47	0.00
False Negative	1.47	26.67	5.26

DISCUSSION

Accuracy of frozen section in this era is important to tailor the extent of surgery. This is especially important for young women who have not completed child bearing and conservative surgery has been recommended for Stage IA Grade I epithelial ovarian tumors.[6] Over diagnosis during frozen section examination can lead to unnecessary widening of surgical field thereby increasing morbidity and mortality, whereas under diagnosis can lead to second surgery and possible tumor spread.[7,8] Hence, the accuracy of frozen section examination should therefore be evaluated in order to consider this diagnostic tool to

Table 4. Sensitivity and Overall Accuracy of FS in Ovarian Tumor as seen in different studies

Author	Sample	Benign %	Borderline %	Malignant %	Overall %
Subbian[9]	135	90.4	31.1	91.5	84.2
Sukumaran[10]	233	99.2	88.95	82.95	91.85
Ilker[11]	266	100	77.8	71.4	96.2
Wootipoom[12]	213	98.2	57.1	86.1	89.7
Gorisek[13]	131	100	76.1	89	84.7
Rajanbabu[14]	178	99	72.7	89	92.7
Rakhshan[15]	282	99	60	92	95.7
Pinto[16]	243	98	61	93	87.5
Present Study	159	98.53	73.33	94.74	94.33

be dependable. In our study, the overall accuracy rate was 94.33% which is comparable with different studies quoted by different authors (Table 4).

Geomini et al. had done a meta-analysis of 18 studies and found that the sensitivity of frozen section diagnosing ovarian lesions ranged from 65 to 97% for benign and from 71 to 100% for malignant lesions.[17] They also found specificity ranged from 97 to 100% for benign and from 98.3 to 100% for malignant tumors. In the current study the sensitivity in diagnosing benign lesions was 98.53% and that for malignant lesions was 94.74%. The specificity was 95.60% and 100% in diagnosing benign and malignant lesions respectively.

In our study, 9 cases were discordant in the final paraffin result. Of these; 8 cases were under diagnosed ie, four cases were borderline which was classified as benign and the other 4 cases were diagnosed as mucinous borderline in frozen section that turned out to be mucinous carcinoma on final paraffin result. The overall false negative rate of malignancy in our study was 5.26% and the false positive rate was 0%. In the literatures, the false-positive rate is lower than the false-negative rate; reported false-positives rates range from 2.2 to 10.7% and false-negative rates; from 5.4 to 29.3%.[18,19] In a study done by Subbian et al. the overall false negative rate was 13.6% and false positive rate was 0.3% which was consistent with other studies but was high in comparision to the present study.[20]

Borderline ovarian tumors were a major cause of diagnostic discrepancy in this study. Of the 9 incorrectly diagnosed cases, 8 were mucinous tumors and only 1 was serous tumor. Mucinous borderline tumors are notorious for diagnostic discrepancy because of large size of the tumors and because of the heterogeneous histology with benign, borderline and malignant areas present in the same lesion.[21] Nigrisoli et al. also found that adequate sampling may be difficult in mucinous tumors due to their larger average size compared to serous tumors.[22] Sampling error has often been mentioned as one of the limitations of frozen section diagnosis. In the present study, the mean diameter of mucinous tumors in the disagreement group was significantly larger than the mean diameter of the mucinous tumor in the agreement group.

Tempfer et al. reviewed three large studies investigating the accuracy of frozen section examination in diagnosing borderline ovarian tumors and found an overall sensitivity of 71.1% and positive predictive value of 84.3%.[23] In the present study the sensitivity and positive predictive value of frozen section analysis in diagnosing borderline tumors was 73.33% and 68.75% respectively. With the exception of borderline tumors, the sensitivity, specificity and diagnostic accuracy of frozen section is high for benign and malignant ovarian tumors.

CONCLUSION

This study showed that intra-operative frozen section is highly sensitive and specific method for the rapid histopathological diagnosis of ovarian tumors. It is a valuable tool to guide the surgeons to avoid under treatment and overtreatment in the management of patients. However, it has some limitations especially in cases of borderline tumors. This modality is most effective when the pathologist and surgeon are aware of the advantages and limitations. Regular re-evaluation regarding the disagreement between frozen section diagnosis and final paraffin section diagnosis should be conducted as a part of quality assurance of any institute.

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