

Accuracy of intra-operative frozen section in the diagnosis of female genital tract neoplasms

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Abstract

Objective: To evaluate the accuracy of intra-operative frozen section in the diagnosis of various pelvic neoplasms, including ovarian tumours.

Methods: The retrospective study was conducted at Shifa International Hospital and comprised records of all patients with lesions of female genital tract who underwent frozen section between January 2010 and December 2012. Comparison was made with the final diagnosis after histopathology was performed on examining permanent paraffin sections.

Results: The mean age of the 54 patients was 43.70±14.8 years (range: 19-75 years). The frozen section was accurate in 51(92.6%) cases. It had a moderately high sensitivity of 75%, high specificity of 97.6%, high positive predictive value of 90% and high negative predictive value of 93.2%. Lack of agreement was found in cases of ovarian tumours of the mucinous and borderline variety.

Conclusion: Frozen section showed a considerable level of accuracy when dealing with suspected pelvic neoplasms.

Keywords: Frozen section, Ovarian neoplasm, Paraffin, Diagnosis. (JPMA 66: 143; 2016)

Introduction

Differentiation of benign from malignant tumours during surgery, specially adnexal masses, is important for appropriate management of the patient. In addition, intra-operative consultation, or frozen section, not only categorises the tumour but can also give information about the nature of the mass e.g., lymphoma, sarcoma etc.¹⁻³

Common ovarian neoplasms are frequently of epithelial origin. Ovarian epithelial neoplasms are primarily categorised as benign, borderline and malignant. As is obvious by the nomenclature they have different biological features, principles of management and outcome. Tumours of 'borderline nature' are an important group bearing some microscopic features of malignancy (epithelial cell stratification, increased mitotic activity, nuclear atypia) but not exhibiting stromal invasion.

Benign and borderline tumours can be adequately treated with conservative surgery. Borderline tumours have an excellent prognosis. Therefore, in younger women the role of frozen section becomes even more important so that these tumours can be identified during surgery. Thus the accuracy of the technique becomes critical for fertility-conserving surgery.⁴⁻⁶

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When malignancy is reported on frozen section, the surgical field widens and staging is performed. The commonest malignant neoplasms are carcinomas. They require extensive surgery with removal of the uterus, bilateral tubes and ovaries. Pelvic and retro-peritoneal lymphadenectomy is also indicated as well as sampling from many peritoneal sites.

Preoperative imaging like ultrasound, computed tomography (CT) scan and magnetic resonance imaging (MRI) as well as tumour markers have only limited value in differentiating among benign, borderline and malignant tumour types.^{7,8} Frozen section has been reported by other workers also to have a good level of accuracy in diagnosing benign and malignant tumours, but a relatively lower accuracy in ovarian borderline tumours.⁹ This pitfall should be kept in mind by the surgeon.

The current study was planned to correlate the results of frozen section and the final diagnosis on paraffin sections in gynaecological neoplasms in order to document the efficacy of intra-operative frozen section.

Material and Methods

The retrospective study was conducted at Shifa International Hospital and comprised records of all patients with lesions of female genital tract who underwent frozen section between January 2010 and December 2012. Frozen section had been done as recommended A part of mass or the whole mass was

Table: Frozen and Paraffin sections in various ovarian neoplasms (n=30).

| Serial No. | Frozen section Reports | Total | Paraffin Section Diagnosis | | |
|------------|------------------------|-------|----------------------------|------------|-----------|
| | | | Benign | Borderline | Malignant |
| 1 | Benign | 20 | 17 | 01 | 02 |
| 2 | Borderline | 01 | -- | 01 | -- |
| 3 | Malignant | 06 | -- | -- | 06 |
| 4 | Deferred | 03 | -- | 01 | 02 |

immediately delivered to the laboratory in a fresh state with detailed clinical information. The specimens were examined macroscopically and sections were taken from the most representative areas by the consultant histopathologist. The smaller specimens (up to 2cm) were entirely submitted. The number of tissue blocks processed for frozen section ranged from 1 to 4; the exact number depending on the type and size of the specimen. A cryostat was used to cut 7-8µm thick sections and these were stained by routine haematoxylin and eosin (H&E) method. All the sections were examined by the consultant. The frozen section report was conveyed to consultant surgeons on telephone. The specimens were then allowed to fix in formalin overnight and processed for routine histopathology after detailed gross examination the next day. Further sections taken as well as the blocks submitted for frozen section were processed for paraffin sections.

The frozen section diagnosis was categorised as benign or malignant or deferred for paraffin sections. In case of ovarian tumours, a diagnosis of borderline tumour was also given on frozen section. This was compared with the final diagnosis made after thorough gross and detailed microscopic examination.

The sensitivity, specificity, positive predictive values (PPVs) and negative predictive values (NPVs) of frozen section diagnosis were calculated using the standard formulae.

Results

The mean age of the 54 patients was 43.70±14.8 years (range: 19-75 years). Of the total of 54 specimens received, 39(72%) were from the genital tract whereas 15(28%) belonged to the tissues around the genital tract obtained for clearance of margins or staging (Figure-1). In the first group, 30(77%) cases were from ovarian lesions (Table) and 06(15%) were myometrial lesions. There was 1(1.85%) case lesion from fallopian tube, endometrium and vulva/vagina. Pelvic fat was sampled in 8(15%) cases, urinary tract in 3(5.5%), round ligament in 2(3.7%), rectum and lymph node in 1(1.85%) case each.

The frozen section diagnosis concurred with the final

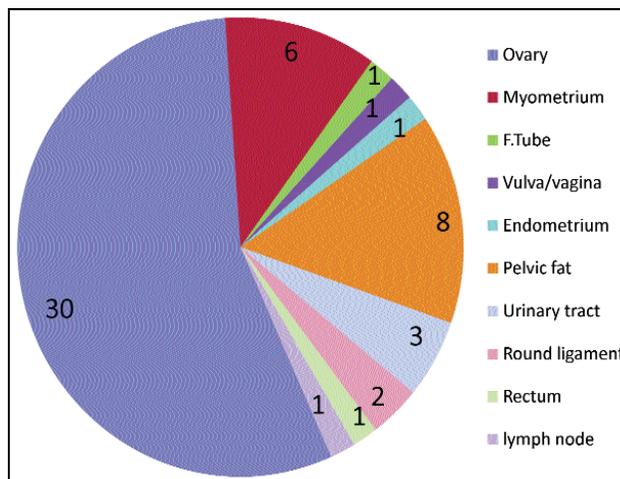


Figure: Site distribution of Frozen section n=54.

histopathology report as to the category of benign, borderline or malignant neoplasms in 47(92.6%) cases and disagreed in 3 (5.7%). In 3 (5.7%) cases, frozen section diagnosis was deferred for paraffin sections due to suspicion of malignancy in heterogenous, mucinous and borderline tumours, and in infarcted and necrotic lesions.

The diagnosis 'benign' used for frozen section included benign tumours and non-neoplastic conditions like luteal cysts 3(5.7%), endometriosis 2(3.7%), resection margins and other tissues taken for staging etc.

In the group of ovarian lesions 20 (66.6%) were reported as benign on frozen section .One of these proved to be a borderline tumour and 2 others were found to be malignant after paraffin sections. One case reported as borderline tumour by frozen section was confirmed as such. Out of 3 (10%) cases that were deferred for paraffin section, only 1 proved to be borderline and 2 others proved malignant on final diagnosis. All six tumours (20%) reported as malignant on frozen section were confirmed as such on final diagnosis. There were six myometrial lesions, all of which proved benign on frozen as well as final diagnosis.

The frozen section was accurate in 51(92.6%) cases, with a

moderately high sensitivity of 75%, high specificity of 97.6%, high PPV of 90% and high NPV of 93.2% for benign tumours/conditions and malignant tumours respectively.

The accuracy of the test in ovarian neoplasms exclusively was 86.6%, whereas it had a sensitivity of 72.7%, specificity 94.7%, PPV 88.8% and NPV 85.7% for benign tumours /conditions and malignant tumours.

Discussion

Accurate frozen section is crucial in order for the technique to be of any use in patient management. The aim is to avoid under- as well as over-treatment of the patient. The results of the present study show that frozen section or intra-operative consultation, has a high overall accuracy for the diagnosis of female genital tract neoplasms (92.5%). Most studies have reported the accuracy to be from 90% to 97%.^{8,10-12} This figure would vary depending on the expertise of the pathologists. The overall inaccuracy should be consistently less than 10% for this procedure to be beneficial.

The test gave reasonable results for all 4 conventional indices (sensitivity, specificity, PPV and NPV, including benign conditions and malignant tumours. Frozen section should not and does not miss the diagnosis of benign and malignant ovarian tumours in the larger proportion of patients (high sensitivity). Histological diagnoses rendered on frozen section of ovarian tumours (benign and malignant) were also correct in most cases (high predictive values). In the current study, only in 3 patients out of the reported benign and borderline category was the diagnosis found to be malignant on paraffin sections. This implies that the patients may have been under-treated at initial surgery.

In only one patient out of the 10 diagnosed as malignant on frozen section was the final diagnosis different. It was finally reported as a borderline tumour. This carried the implication that this patient may have been over-treated at initial surgery. This is in concordance with studies carried out worldwide as diagnosis of borderline tumour on frozen section carries low sensitivity and specificity.¹⁰⁻¹²

Arikan et al. did a similar study involving 266 patients. The results of frozen sections were 235(88.3%) benign, 11(4.2%) borderline and 20(7.5%) malignant. The sensitivity was 100% for the benign tumours, 77.8% for the borderline tumours and 71.4% for the malignant tumours. The specificity of frozen section was 83.8%, 98.4% and 100% for the benign, borderline and malignant tumours.²

A meta-analysis of 18 studies comparing frozen section

diagnosis of ovarian lesions with the final histopathological showed that the sensitivity of frozen section for benign and malignant lesions varied from 65% to 97% and 71% to 100% respectively.¹⁰ The same study showed that the specificity varied from 97% to 100% and 98.3% to 100% for benign and malignant lesions respectively in different studies.

The situation is different in borderline ovarian tumours. The sensitivity and PPV of frozen section were 75% and 90% respectively in the current study. The reported sensitivity of frozen section in borderline tumours varies from 0-87% in various studies.¹⁰⁻¹⁵ Various reasons have been proposed for the relative inaccuracy of frozen section in the diagnosis of borderline tumours. In a large borderline tumour there may be only occasional foci of atypia amounting to borderline category. On the other hand, severe atypia and/or invasion may be focal but amounting to frank malignancy on final reporting. Final reporting may thus require a large number of sections to be processed, an option not usually available during frozen section as it is very labour-intensive and time-consuming. It has also been suggested that it may be more difficult to diagnose borderline mucinous tumours compared to borderline serous tumours because of their larger average size.^{5,12} In our study, inadequate clinical and operative information, and limited tissue sampling during frozen section for huge tumours were the reasons for the cases with benign frozen section report but borderline result on permanent sections and borderline frozen with malignant tumour reported on permanent section. In our study, out of two cases reported as borderline on frozen section only one proved correct on final diagnosis.

In our study two cases were incorrectly labelled as benign, but this did not have critical therapeutic implications since patients with benign tumours undergo conservative surgery. Radical surgery may be carried out later on. There was a greater therapeutic implication of the incorrect frozen section report of malignancy in one patient because extensive surgery is not required in borderline tumours, particularly in early stages.

Our results for ovarian tumours only showed sensitivity, specificity, PPV and NPV of 72.7%, 94.7%, 88.8% and 85.7% respectively. A review of 14 studies on the accuracy of frozen section in the diagnosis of ovarian tumours concluded that frozen section has high accuracy rates for the diagnosis of benign and malignant ovarian tumours, but the accuracy rates in borderline tumours are relatively low.^{4,11}

Conclusion

Frozen section proved to be a useful test in suspected

pelvic neoplasms. It had low false-positive and false-negative rates. However, studies including a larger number of cases are required to conclude if it can be safely used to guide the intra-operative management of pelvic masses regarding the type and extent of surgery. It was also seen that the accuracy of frozen section was low for borderline ovarian tumours.

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