RESEARCH COMMUNICATION

Accuracy of Intra-operative Frozen Sections in the Diagnosis of Ovarian Masses

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Abstract

The accuracy of frozen section diagnosis in the intraoperative evaluation of ovarian masses is very important with regard to surgeon selection of appropriated operating procedures. For evaluation in our institute, the records of 127 patients with ovarian masses submitted for intraoperative frozen sections between January 2001 and December 2005 were reviewed. After exclusion of 4 completely infarcted masses and 11 cases with deferred frozen section diagnoses, 112 were analyzed for diagnostic accuracy by comparing with the final histologic results. We found sensitivity in the diagnosis of benign, borderline and malignant tumors to be 100%, 84%, and 92 %, respectively, with specificities of 92.7%, 97.9%, and 100%, respectively. The overall accuracy with frozen sections was 94 %. Among 18 patients with deferred or discordant diagnoses, mucinous tumors accounted for 72 % of cases. No over-diagnosis of malignancy or misdiagnosis of metastatic lesions as primary ovarian cancer by frozen sections was observed. In conclusion, the accuracy of intraoperative frozen section for the diagnosis of ovarian masses is high. Frozen sections also help in the evaluation of metastatic tumors to the ovary. Mucinous tumors constitute an important group causing diagnostic discrepancies.

Key Words: Ovarian tumours - diagnostic accuracy - frozen sections

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Introduction

Clinically detected ovarian masses have a heterogenous nature, including neoplasms and benign non-neoplastic lesions or cysts. Primary ovarian neoplasms form a complex group of tumors with various histogenetic origins such as epithelial, sex cord-stromal, and germ cell (Scully,1999). Furthermore, patients with ovarian metastasis from non-genital cancers may have a presentation similar to primary ovarian cancer which contributes to confusion in the diagnosis and inappropriate management (Seidman et al., 2003).

For management purposes, primary ovarian neoplasms are categorized as benign, malignant, and an intermediate group of epithelial neoplasms (borderline tumors). The extent of surgical management is based on the histologic diagnosis and the category of tumors. In benign and borderline ovarian tumor, fertility conserving surgery is a preferred approach, whereas, in malignant tumors, complete surgical staging that involves total hysterectomy, bilateral salpingo-oophorectomy, partial omentectomy and retroperitoneal lymph node sampling should be done(Berek, 2002). For borderline tumors, surgical staging should be performed but with a conservative approach and lymph node sampling may be omitted if the node is not grossly abnormal. Preoperative assessment in the patients with ovarian masses includes the evaluation of the clinical history, physical examination, radiologic imaging studies, and serologic tumor markers (Andolf et al., 1990). The intra-operative findings including gross examination of tumors by the surgeons are frequently helpful in reaching a preliminary impression that guides the surgical management. However, these assessments have a limitation in predicting the diagnosis of ovarian tumors. Intra-operative pathology consultation or frozen sections can help clinicians in making an appropriate decision on the surgical management of ovarian neoplasms (Van Nagell et al., 2003). As the accuracy of frozen section diagnosis in ovarian tumors is very important, we conducted this retrospective study to evaluate the performance of frozen sections of ovarian neoplasms in our setting.

Materials and Methods

This study was approved by the research ethics committee. The records of ovarian masses submitted for intraoperative frozen section in the department of Pathology, Chiang Mai University Hospital between January 2001 and December 2005 were retrieved. The request for intra-operative frozen sections was based on the decision of the attending gynecologic surgeons. Intra-

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operatively, fresh specimens of ovarian masses submitted to the laboratory were examined for the gross appearance and were sampled for frozen sections. The number of frozen section(s) in each case depended on the decision of the attending pathologists. The frozen section diagnosis was usually reported a specific histologic diagnosis whenever possible. The frozen section diagnosis was deferred when there were some suspicious pathologic features of borderline or malignant tumor which were considered not definitely diagnostic. After the frozen section diagnosis was reported, the ovarian specimens were fixed in 10 % formalin overnight and sampled for routine histologic sections. Almost all cases in the group of mucinous neoplasms and tumors with malignant potential (borderline and malignant) had adequate tissue sampling with at least 1 section per 1 cm maximal tumor diameter. The histologic diagnosis of ovarian lesions was based on the WHO Classification.1

Basic clinical data of each patients were collected form the medical records. The frozen section diagnoses were compared to the final histologic diagnoses in each case, which were considered as the gold standard. The diagnoses were categorized as benign, borderline and malignant groups. Agreement of both frozen and final diagnoses was considered when both diagnoses were identical or were within the same subgroup of malignancy (i.e. epithelial, sex cord-stromal, germ cell, and metastatic).

For the calculation of diagnostic accuracy of frozen sections, the cases with deferred diagnoses or with non-diagnostic specimens due to complete infarction were excluded. Diagnostic parameters including accuracy, sensitivity, specificity, predictive values of frozen section for the diagnosis were calculated. T-test statistic was used to compare the mean value. All analysis was performed by using SPSS for Windows version13. The cases with discordant diagnosis between frozen section and final histology or the cases with deferred diagnosis were reviewed in detail.

Results

A total of 127 patients were identified. The mean age was 49 ± 16 years (range 15-83). The majority of the patients (74%) were over 40 years old and 48 % of them were postmenopausal. In 4 patients, the ovarian masses were cystic lesion with complete hemorrhagic infarction, the definite nature of which could not be identified by either frozen section or final histology. The frozen section diagnoses were deferred in 11 cases (8.7 %). In the remaining 112 patients, the frozen section diagnoses were benign in 48 (42.9 %), borderline in 18 (16.1 %), and malignant in 46 (41.1 %), whereas the final diagnoses were benign in 43 (38.4 %), borderline in 19 (17.0 %), and malignant in 50 (44.7 %). Of 50 malignant neoplasms, 27 were epithelial carcinoma, 6 were sex cord-stromal tumors, 4 were germ cell tumors, and 13 were metastatic tumors to the ovary, most of which originated from the digestive tract.

The comparison between frozen section diagnoses and final diagnoses is shown in Table 1. The overall accuracy of intra-operative frozen section diagnosis was 93.8 %. The sensitivity for frozen section diagnosis was 100 % for benign, 84.2 % for borderline and 92.0 % for malignant category, whereas the specificity was 92.8 %, 97.8 %, and 100.0 %, respectively. The positive predictive value was 89.6 % for benign, 88.9 % for borderline, and 100.0 % for malignant group, and the negative predictive value was 100.0 %, 96.8 %, and 94.0 %, respectively (Table 2)

Table 1. Comparison between Frozen Section and Final Histologic Diagnoses of Ovarian Masses (n = 112)

Frozen Diagnosis	Final Histologic Diagnosis		
	Malignant	Borderline	Benign
Malignant	46	0	0
Borderline	2	16	0
Benign	2	3	43
Total	50*	19**	43

*including 27 epithelial carcinomas, 6 sex cord-stromal , 4 germ cell and 13 metastatic tumours, ** including 3 serous, 15 mucinous, and 1 endometrioid borderline tumour

Table 2. Diagnostic Value of Frozen Sections for Benign, Borderline and Malignant Lesions (n = 112)

	Benign*	Borderline*	Malignant*
Accuracy (%)	95.5 (91.7-99.3)	95.5 (91.7-99.3)	96.4 (94.4-98.4)
Sensitivity (%)	100.0 (89.8-100)	84.2 (59.5-95.8)	92.0 (79.4-97.4)
Specificity (%)	92.8 (83.2-97.3)	97.8 (91.9-99.6)	100.0 (92.7-100)
Positive predictive value (%)	89.6 (76.6-96.1)	88.9 (63.9-98.1)	100.0 (90.4-100)
Negative predictive value (%)	100.0 (92.9-100)	96.8 (90.3-99.2)	94.0 (84.4-98.0)

*Value (95 % CI)

There were 7 cases with discordance between the frozen section diagnoses and the final diagnoses, all of which were under-diagnosed by frozen sections. Five of seven were mucinous tumors and the other two were uncommon sex cord-stromal tumors. The mean of tumor greatest dimension of the masses in the discordant or deferred cases (N= 18) was significantly greater than that of the agreement group (N= 109) (19.13 + 8.53 cm versus 14.14 + 6.79 cm, p value = 0.02). The mean number of frozen sections was 1.57 (range 1 to 4) in the agreement group and 1.94 (range 1 to 4) for discordant or deferred cases.

In 11 cases in which the frozen section diagnoses were deferred, the final diagnoses included borderline mucinous tumor in 6, mucinous cystadenoma in 2, mature teratoma in 2, and immature teratoma grade 1 in one case. The intra-operative communications for deferred diagnosis was “benign versus borderline tumor” in 8 cases, “mature versus immature teratoma” in 2, and “atypical squamous epithelium in postmenopausal mature teratoma” in 1.

Discussion

Intraoperative histological assessment of ovarian tumors help clinicians to select an appropriate surgical procedure for the patients, avoiding both under- and overtreament. The overall accuracy of frozen section diagnosis of ovarian masses in our study, was high (93.8 %) and was within the range of the previous reports (90-97%) (Twaalfhoven et al.,1991; Wang et al.,1998; Gol et

al.,2003; Boriboonhirunsarn et al.,2004; Tangjitgamol et al., 2004; Ilvan et al. 2005; Maheshwari et al., 2006; Stewart et al., 2006; Wootipoom et al., 2006). Frozen section had high sensitivity, specificity and predictive values in the prediction of benign lesions and malignant neoplasms of the ovary. The accuracy of "malignant" frozen section diagnosis was very high, with no benign or borderline tumors being misdiagnosed as malignancy. Furthermore, frozen sections helped confirm the diagnosis of metastatic tumors which resulted in different surgical management from primary ovarian cancers. Metastatic tumors were relatively frequent in this study, accounting for 26 % of malignant ovarian lesions submitted for intraoperative consultation.

All 7 cases with diagnostic disagreement in this study had under-diagnosis by frozen section. Five of these cases had "benign" frozen section diagnosis (Table 3) which could result in the alteration of the surgical management due to the omission of staging procedure for borderline or malignant ovarian tumors. This was of a major concern in 2 cases of uncommon types malignant sex cord-stromal tumors.

Several factors can affect the accuracy of frozen section diagnosis, including sampling error, quality of frozen section (technical factor), and experience of pathologists (Stewart et al., 2006). Sampling error was considered to be the main reason for the diagnostic discrepancy in most studies (Tangjitgamol et al., 2004). This is particularly true in some groups of tumors, in which there was remarkable heterogeneity of tumor from areas to areas within the same ovarian mass, such as mucinous tumors and teratomas. Frozen section may fail to sample the most severe lesion or frankly malignant area in a limited number of sections intraoperatively (Tangjitgamol et al., 2004). Another factor that causes difficulty in frozen section diagnosis is the quality of sections prepared by this technique that limits the evaluation of cellular detail. This technical factor is rather underemphasized in most clinical studies on frozen section diagnosis (Stewart et al., 2006). Although the section quality was not the reason of deferred or discordant diagnoses in our study, it caused difficulty in some cases of primary epithelial carcinoma and malignant sex cord-stromal tumors in the agreement group, when pathologists tried to predict the further specific histologic subtypes. However, such limitation did not result in the alteration of the intra-operative surgical management in our cases.

In this study, mucinous borderline tumor was the diagnosis most commonly involved in the deferred and discordant categories. Difficulty in the frozen section diagnosis of mucinous tumors and borderline tumors has been well addressed in the recent reports (Houck et al., 2000; Tangjitgamol et al., 2004; Stewart et al., 2006; Tempfer et al.,2007). It has also been suggested that, among the common types of borderline tumors, the diagnostic difficulty is greater in the mucinous type compared to the serous counterpart (Houck et al., 2000; Tempfer et al.,2007). Large tumor size and tumor heterogeneity of mucinous tumors were the main contributing factors of the diagnostic difficulty. In the present study, the mean maximal diameter of the disagreement and deferred cases was significantly larger than the agreement group. Wang et al (1998) recommended that multiple frozen section samples may help increase the accuracy in the diagnosis and taking one frozen section per each 10 cm diameter of the mass was suggested. However, multiple frozen sections may not be able to eliminate the deferred or discordant cases as seen in some of our deferred or discordant cases in which up to 4 frozen sections were taken. In addition, performing many frozen sections in each case is time-consuming and is usually not practical in the intra-operative settings.

The deferred diagnostic category reflects an uncertainty in the diagnosis based on limited tissue sampling. An adequate sampling is usually required for a definite diagnosis of such examples as the diagnostic areas may be focal in nature. In our study, mucinous tumor and teratoma accounted for the majority of cases with deferred frozen section diagnosis. Five of 11 deferred cases also had maximal tumor dimension greater than 20 cm. The final diagnoses other than benign lesions in these cases were borderline tumors with low-grade epithelial proliferation or low-grade immature teratoma, both of which could be managed by conservative surgery without serious necessity for repeated exploratory laparotomy for surgical staging. In a meta-analysis by Geomini et al, (2005) it was recommended that the decision to perform a radical surgery should be suspended until a malignant diagnosis is reported by the final histologic examination. The rate of deferred frozen section diagnosis in our study was comparable to several other previous reports (Twaalfhoven et al.,1991; Tangjitgamol et al., 2004; Wootipoom et al., 2006).

Frozen section diagnosis represents a method of intraoperative pathology consultation which is based on the evaluation of the clinical information, the pathologic examination in a limited time, and the communication between clinicians and pathologists. It is important that both clinician and pathologist involved in this process should have a good communication of clinical findings and pathologic features and that both should understand the limitation of frozen section diagnosis. In conclusion, the frozen section is an accurate and useful test in the intra-operative evaluation of patients with ovarian masses.

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