The Accuracy of Intraoperative Frozen Sections in the Diagnosis of Ovarian Tumors

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Objective: *To determine whether frozen section evaluation of ovarian tumors can be used to establish a histopathologic diagnosis and guide the surgeon to perform the appropriate surgical procedure.*
Material and Method: *Between January 2002 and December 2006, 376 ovarian specimens were submitted for frozen section examination and received for permanent section evaluation. The accuracy, sensitivity, specificity, and positive and negative predictive values of the frozen sections were studied.*
Results: *The overall accuracy was 87.8% while the inaccuracy was 12.2%. The sensitivity for malignant tumors was 79.6%, the sensitivity for borderline tumors was 61.8%, and the sensitivity for benign tumors was 98.2%. The specificity for the benign tumors was 88.6%, 93.8% for borderline tumors, and 97.1% for malignancy. The positive predictive value was 92.2% for benign tumors, 63% for borderline tumors, and 91.1% for malignant tumors.*
Conclusion: *The present study confirms that frozen section diagnosis is a reliable method for the surgical management of patients with ovarian masses.*

Keywords: *Ovarian tumor, Frozen section, Permanent section*

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Frozen sections have been used intra-operatively for ovarian tumors in gynecology to ensure that proper surgical staging is carried out and to ascertain microscopic diagnosis prior to performing definitive surgery to prevent over-treatment or under-treatment of patients with ovarian masses. In many cases, fertility is preserved, especially in young women, whereas tumors of borderline malignancy in premenopausal patients may be treated with unilateral adnexectomy and a benign diagnosis may require only cystectomy. This retrospective study attempts to determine the accuracy of frozen sections in the diagnosis of ovarian tumors in our institution.

Material and Method

A retrospective study was performed at the Department of Obstetrics and Gynecology, Rajavithi Hospital, Bangkok to compare the results of 376 consecutive frozen sections during January 1, 2002 to December 31, 2006 wherein permanent sections of whole specimens were conducted. Each specimen was examined by both frozen and permanent section by five pathologists at the Department of Pathology, Rajavithi Hospital, Bangkok. The tissue mass can be examined by frozen section for one or two slides in each case. To facilitate comparison, both the frozen section diagnosis and permanent section diagnosis were categorized as benign, borderline malignancy, or malignancy, and the result of the permanent section was used as a gold standard.

The present study protocol was approved by the Ethical Clearance Committee on Human Rights Related to Research Involving Human Subjects, Rajavithi Hospital, Bangkok. The comparison is shown in a 3 x 3 table wherein the sensitivity, specificity, and positive and negative predictive values of the frozen section diagnosis of the ovarian tumors was computed.

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Results

Three hundred seventy six cases of ovarian tumors underwent surgery where frozen and permanent sections were performed intraoperatively in our Department between January 1, 2002 and December 31, 2006. The final histopathologic diagnoses were benign in 218 cases (57.98%), borderline in 55 cases (14.63%), and malignant in 103 cases (27.39%), shown in Table 1.

The agreement between the frozen and permanent section diagnoses are listed in Table 2. By overall, the cases with comparable diagnoses between frozen section and permanent section comprised 87.8% whereas cases with diagnostic discrepancy of 12.2%.

Table 1. The diagnoses of permanent section

Permanent section	Number of cases
Mucinous cystadenoma	65
Serous cystadenoma	57
Hemorrhagic cyst	12
Endometriotic cyst	31
Dermoid cyst	31
Fibrothecoma	5
Follicular cyst	15
Abscess	1
CA Ovary Ia	72
CA Ovary Ib	5
CA Ovary IIa	6
CA Ovary IIb	1
CA Ovary IIIa	3
CA Ovary IIIb	4
CA Ovary IIIc	8
Krukenberg's tumor	3
Brenner tumor	1
Mixed mullerian tumor	1
BL- Mucinous cystadenoma	46
BL-Serous cystadenoma	9
Total	376

BL = borderline

Table 2. Comparision of frozen section diagnosis and permanent diagnosis

Frozen section diagnosis	Permanent section			
	Benign	Borderline	Malignant	Total
Benign	214	15	3	232
Borderline	2	34	18	54
Malignant	2	6	82	90
Total	218	55	103	376

There were disagreements between the diagnoses on frozen sections and the diagnoses on permanent sections in 46 cases (Table 3). Forteen mucinous cystadenoma on frozen sections were found to be borderline malignancies of mucinous cystadenoma in the final diagnosis. Four cases of benign tumors on frozen sections turned out to be serous cystadenoma of borderline malignancy, papillary mucinous cystadenocarcinoma, immature teratoma, mixed mucinous adenocarcinoma, and clear cell carcinoma. Another 20 cases of borderline malignancy on frozen sections had a final diagnosis of benign in two cases and malignancy in 18 cases. Eight cases of malignancy on frozen sections were diagnosed as one serous cystadenoma, one endometriotic cyst, and six borderline malignancies in the permanent section. The variation of pathologists in two persons was 8.7%, and each three was 10.87%, 30.43%, and 41.30%.

Three hundred seventy six cases were analyzed statistically (Table 4). In 218 instances, benign lesions diagnosed by frozen sections were subsequently confirmed by permanent sections in 214 cases. These 214 cases, therefore, were regarded as true negatives. Of the 103 malignant lesions confirmed by final diagnoses, frozen section examination was able to identify 82 cases, and these were regarded as true positives. As for the remainder, 21 cases were represented as false negatives and four cases were false positives.

The sensitivity of frozen section diagnosis, which represents the probability that a frozen section result will be positive in a patient with malignancy, was 79.6% while the specificity of frozen sections, which represents the probability that the test will yield a negative result in a patient who does not have a malignancy, was 88.6%. The positive predictive value of a positive (or malignancy) frozen section was 91.1% and negative predictive value of a negative (or benign) frozen section was 97.2%. Among the 103 patients with malignant tumors, the sensitivity of frozen section diagnosis was 79.6% while the specificity for malignant tumors was 97.1%. For malignant tumors, intraoperative frozen sections had a positive predictive value of 91.1% and a negative predictive value of 92.7%.

Overall, the sensitivity for borderline tumors was 61.8% and the specificity was 93.8%. The positive and negative values of frozen sections for ovarian tumors of borderline malignancy were 63% and 93.5%, respectively.

The sensitivity for benign tumors was 98.2% and the specificity was 88.6%. For benign ovarian

Table 3. Cases with disagreement between frozen sections and permanent sections (n = 46)

Number of cases	Frozen section diagnosis	Permanent section diagnosis
14	Mucinous cystadenoma	BL-mucinous cystadenoma
1	Benign	BL-Serous cystadenoma
1	Benign	Papillary mucinous cystadenocarcinoma
1	Benign	Immature teratoma
1	Benign	Mixed mucinous adenocarcinoma and clear cell carcinoma
1	Borderline	Serous cystadenoma
1	Borderline	Papillary serous cystadenoma
1	Borderline	Endometrioid adenocarcinoma,well differentiated with capsular invasion
5	Borderline	Mucinous cystadenocarcinoma
3	Borderline	Well differentiated cystadenocarcinoma
1	Borderline	Poorly differentiated endometrioid carcinoma
1	Borderline	Mixed mucinous and serous cystadenocarcinoma
1	Borderline	Granulosa cell tumor
1	Borderline	Clear cell carcinoma
1	Borderline	Papillary endometrioid carcinoma
1	Borderline	Endometrioid adenocarcinoma
1	Borderline	Endometrioid carcinoma
2	Borderline	Well differentiated adenocarcinoma
1	Malignant	Papillary Serous cystadenoma
1	Malignant	Endometriotic cyst
2	Malignant	BL-Papillary serous tumor
4	Malignant	BL-Mucinous cystadenoma

BL = borderline

Table 4. Diagnostic values of frozen sections for ovarian tumors of various histological types (n = 376)

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Benign	98.2	88.6	92.2	97.2
Borderline	61.8	93.8	63.0	93.5
Malignant	79.6	97.1	91.1	92.7

Table 5. The sensitivity of frozen sections in the diagnosis of ovarian tumors

Author	No.	Benign (%)	Malignant (%)	Borderline (%)
Twaalfhoven, 1991[1]	176	92.8	88.5	44.4
Obiakor I, 1991[2]	303	100	93.2	ND
Rose PG, 1994[3]	383	98.7	92.5	44.8
Yeo EL, 1998[5]	316	99.6	87	60
Pinto PB, 2001[6]	243	98	93	61
Current study	376	98.2	79.6	61.8

ND = not determined in the series

tumors, frozen sections had a positive predictive value of 92.2% and a negative predictive value of 97.2%.

Discussion

The value of frozen sections in the diagnoses of ovarian neoplasia was not extensively examined in the literature reviewed. The goal of frozen sections of ovarian tumors is to identify malignant ovarian tumors because the diagnosis affects the operative procedure.

In one study of 243 ovarian tumors published in 2001, Pinto PB found that frozen section was accurate in 94% of the cases and inaccurate in 6%[6] of the cases. The present study of 376 cases revealed similar results, with frozen section diagnosis being accurate in 87.8% of the cases, and inaccurate in 12.2% of the cases.

The sensitivity of frozen section diagnosis in the present study was 79.6%, which indicates the probability that a frozen section result will be positive in patients with a malignancy. This is similar to the findings by some previous studies as shown in Table 5.

The specificity of frozen sections, which indicates the probability that the test will yield negative results in patients who do not have malignancy, was

88.6% in the present study. The positive predictive value of a positive frozen section was 91.1% and the negative predictive value was 92.7% for malignancy. It can be concluded, therefore, that frozen section diagnosis is extremely accurate. Also of great importance is the fact that there were false positives in 8.9% of the specimens. Therefore, the surgeons were misled into performing extensive warranted surgical procedures based on false positive results.

Intraoperative frozen section diagnosis depends upon careful gross evaluation of the tumor for selection of tissue for frozen section analysis. Furthermore, this decision ought to be made within minutes, otherwise, the purpose of the rapid diagnosis procedure will be defeated. The final pathologic diagnosis has the advantage of extensive sampling of entire specimens, which increases the chances of identifying microscopic foci of epithelial malignant changes in a predominantly benign mass.

The reasons for disagreements between frozen section diagnoses and permanent section diagnoses were considered to be mainly due to sampling errors in 46 cases. The details of which are shown in Table 3.

Previous studies have demonstrated a low sensitivity in the diagnosis of borderline ovarian tumors[1-13]. Furthermore, due to the fact that lesions may be very focal, it is recommended that one histologic section for each centimeter of the greatest tumor diameter is taken to improve sensitivity[3]. This procedure, however, is nearly impossible for the capability of laboratories performing routine frozen section studies that require swiftness and, therefore, are limited in terms of the extent of sampling. It has also been suggested that, due to their greater average size, borderline mucinous tumors are more difficult to be diagnosed intraoperatively than borderline serous tumors[1].

Some clinicians may not consider an intraoperative diagnosis of a tumor of borderline malignancy to be important because the prognosis is favorable and the role of surgical staging and adjuvant therapy has not been established. However, the greatest significance of the intraoperative diagnosis of a tumor of borderline malignancy is that the lesion may be potentially invasive and should be managed as such.

Conclusion

Frozen section evaluation of ovarian tumors can be used to establish a histopathologic diagnosis and guide the surgeon to perform the appropriate surgical procedure.

Between January 1, 2002 and December 31, 2006, 376 ovarian tumor specimens were removed for frozen section and permanent section assessment wherein frozen and permanent section diagnoses were divided into three categories (benign, borderline, and malignant) in which the sensitivity, specificity, and predictive values of each category were determined. The ovarian tumors were correctly diagnosed on frozen section as either benign or malignant in 330 cases (accuracy 87.8%), and the positive predictive value of the positive frozen sections was 91.1%, while the negative predictive value of the negative frozen sections was 97.2%. There were false positives at the rate of 8.9%.

The authors concluded from the present study that, with the exception of borderline tumors, the sensitivity and specificity of frozen section diagnosis of ovarian tumors is high. Intraoperative frozen sections for diagnosis of ovarian tumors are of value in preventing the under-treatment and over-treatment of patients when the surgeons and pathologists are aware of limitations. Finally, to reduce the number of false negatives, more extensive frozen section sampling should be performed for clinically suspicious cases in which the speed of diagnosis can be compromised.

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ความแม่นยำในการตรวจวินิจฉัยด้วยวิธีการตัดชิ้นเนื้อแช่แข็งแบบชั่วคราวในการผ่าตัดเนื้องอกรังไข่

พรสวรรค์ วาสิงหนท์, ชีพสุมน สุทธิพินทะวงศ์, สุเพ็ชร ทุ้ยแป

วัตถุประสงค์: *เป็นการศึกษาถึงความแม่นยำการใช้วิธีการตัดชิ้นเนื้อแช่แข็ง แบบชั่วคราวในการผ่าตัดเนื้องอกรังไข่เพื่อความเหมาะสมในการวินิจฉัย*

วัสดุและวิธีการ: *ศึกษาทบทวนระหว่าง มกราคม พ.ศ. 2545 ถึง ธันวาคม พ.ศ. 2549 ในผู้ที่ได้รับการผ่าตัดเนื้องอกรังไข่และได้รับการวินิจฉัยทั้งการตัดชิ้นเนื้อแช่แข็งชั่วคราว และการตัดชิ้นเนื้อแช่แข็งอย่างถาวรทั้งหมด 376 คน ที่ส่งตรวจที่กลุ่มงานพยาธิวิทยา โรงพยาบาลราชวิถี*

ผลการศึกษา: *พบว่ามีความแม่นยำรวมเท่ากับร้อยละ 87.8 โดยความไวในการวินิจฉัยมะเร็งเท่ากับร้อยละ 79.6 ความไวในการวินิจฉัยเนื้องอกชนิด borderline เท่ากับร้อยละ 61.8 ส่วนความไวในการวินิจฉัยเนื้องอกเท่ากับร้อยละ 98.2 ความจำเพาะในการวินิจฉัยเท่ากับร้อยละ 97.1, ร้อยละ93.8, ร้อยละ88.6 ตามลำดับ โดยค่าความถูกต้องในการวินิจฉัยว่าเป็นโรคเท่ากับร้อยละ 91.1, ร้อยละ63, ร้อยละ92.2 ตามลำดับ*

สรุป: *การวินิจฉัยโดยใช้ชิ้นเนื้อแช่แข็งอย่างรวดเร็วมีความแม่นยำและช่วยบอกแนวทางการรักษาในระหว่างการผ่าตัด จำเป็นต้องตระหนักถึงข้อจำกัดของการตรวจวินิจฉัยเพื่อช่วยควบคุมคุณภาพ และให้การรักษาที่เหมาะสม ในระหว่างการผ่าตัด*