



## Compatibility of the frozen section method in histopathological specimens for female pelvic masses with results for pathology and tumor markers

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### Abstract

**Background:** Detection of pelvic masses is of great value for scheduling a proper treatment process and is an important factor for detection. Frozen section is a diagnostic method for the evaluation of pelvic tumors during surgery. The purpose of this study was to measure the compatibility of the frozen section method for histopathological specimens of female pelvic masses with pathologic results of tumor markers.

**Methods:** This retrospective study was performed on 188 female pelvic mass specimens during 2014-2016. Medical files for all patients with injury of female genital system who had undergone frozen section surgery was compared with the results of pathology and tumor marker tests. SPSS version 19 was used for statistical analysis. The results were analyzed by Kappa test.

**Results:** Based on the final pathology of the 188 specimens, 150 (79.8%) were benign, 8 (4.2%) intermediate, and 30 (16%) malignant. Sensitivity, specificity, and validity of frozen section in benign tumors were calculated as follow: 96.7 Confidence Interval (CI95% : 92.6–98.9%), 97 (CI95%: 84.7–99.9%), and 96.8%; in intermediate tumors, the respective numbers were: 71.4 (CI95% :29–96.3%), 98.3 (CI95% :95, 2–99%, 7%), and 97.3%; and in the malignant tumors the numbers were: 96.3 (CI95% :81.9–99%), 97.4 (CI95% :93. 4–99.3%), and 97.2%. Positive and negative predictive values were calculated as follow: 99.3 (CI95% :96.3–99.9%) and 86.8% (CI95% :71.9–95.6%) in benign tumors; 62.5 (CI95% :24.5–91.5%) and 98.9% (CI95% :96–99.9%) in intermediate tumors; and 86.7 (CI95% :69.3–96.2%) and 99.3% (CI95% :96.3–99.9%) in malignant tumors.

**Conclusion:** The results of this study showed that the frozen section method has managed to keep its value and place among all diagnostic methods regarding pelvic masses to an acceptable extent. Except for the intermediate tumors, the frozen section method showed great accuracy in dealing with pelvic masses.

**Keywords:** Tumor, Frozen section, CA125

**Conflicts of Interest:** None declared

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### Introduction

Pelvic masses comprise a large portion of female surgeries. The origin and cause of these masses could be from the gynecological, urinary, or digestive systems (1). The most prevalent pelvic mass for all age groups was related to the ovaries. Pelvic masses are important in the

early diagnosis of malignant tumors of the ovaries (2). Ovarian cancer is the deadliest gynecological malignancy, the seventh malignant cancer, and the seventh prevalent cause of death due to cancer among females worldwide because the associated mortality is greater than the com-

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#### ↑What is “already known” in this topic:

Except for the intermediate tumors, the frozen section method has shown great accuracy in dealing with pelvic masses.

#### →What this article adds:

Higher precision in isolating specimens for frozen sections, especially in large masses, and cooperation of the surgeon and pathologist can enhance the value of this method. In addition, except for CA125, this method can prevent performing tumor marker tests, which are costly and are of low diagnostic value.

bined mortalities secondary to the cervix and endometrial cancers (3). Different kinds of benign and malignant pelvic masses with different percentages appear in various age groups; therefore, early diagnosis and choosing the correct method of surgery for these kinds of masses is of high importance (1).

Early diagnosis methods for pelvic masses comprise physical examinations, ultrasonography, computed tomography (CT) scans, magnetic resonance imaging scan (MRIs), tumor markers, and microscopic and frozen section diagnoses during surgery. Definite and final diagnoses are also recorded based on permanent histological specimens (4-6). In gynecological and obstetrical diseases, providing frozen sections has been the most helpful method in determining the type and method of treatment of suspicious pelvic masses (7). Many studies have been performed to determine the value of diagnostic precision of frozen section for masses of different body organs; however, each provided relatively different results depending on the organ and tissue under study. Taskiran et al (2008) concluded that frozen section has a high sensitivity and specificity in the diagnosis of adnexal masses (8).

Wootipoon et al (2006), after studying 229 ovarian specimens, found that frozen section seems to be a useful method for the diagnosis of ovarian masses (9). The present study measures the compatibility of the frozen section method in histological specimens of female pelvic masses with the results of pathology and tumor markers.

## Methods

This retrospective study was performed on 188 specimens of female pelvic masses. Samples were collected from women's ward of Beesat hospital in Sanandaj, Iran, during 2014-2016. First, file numbers for patients with pelvic masses who had undergone surgery by gynecology and obstetrics specialists were extracted. Then, a designed questionnaire was filled out based on patient data, results

Table 1. Cross table for calculation of diagnostic test

Results of frozen section	Result of pathology	
	+	-
+	a	b
-	c	d

of pathology testing, results of tumor markers, and results of frozen section. After the data collection, SPSS version 19 was used to describe the frequency and means. The results were analyzed using Kappa test and important indices were calculated using the following formula: sensitivity:  $a/(a+c)$ , specificity:  $d/(b+d)$ , positive predictive value:  $a/(a+b)$ , and negative predictive value:  $d/(c+d)$  (Table 1).

## Results

In this study, the mean age for the group with non-neoplastic masses was  $41.8 \pm 13$  and was  $57.2 \pm 12.9$  for the group with neoplastic masses. Among 188 patients, based on the final pathology, 150 (79.8%) cases were benign, 8 (4.2%) intermediate, and 30 (16%) malignant. The most prevalent benign ovarian tumor was Serous Cystadenoma (32 cases, 17%), followed by Dermoid Cyst (19 cases, 10%), Mucinous Cystadenoma (18 cases, 9.5%), Endometriotic Cyst (16 cases, 8.5%), physiologic cysts, including follicular and corpus luteum cysts (15 cases, 8%), and sex cord-stromal tumors (11 cases, 8.5%). Among the intermediate specimens, 7 cases were Serous and one was Mucinous (Table 2).

Serous Carcinoma was the most prevalent malignant ovarian neoplasm (6 cases, 3.2%), followed by Granulosa cell tumors (4 cases, 2.1%). The most common benign uterine lesions were Leiomyoma (40 cases, 21.3%), followed by Uterine Adenomyosis (3 cases, 1.6%). Also, the most prevalent malignant uterine masses were Adenocarcinoma (10 cases, 5.3%), followed by Uterine Leiomyosarcoma (2 cases, 1.1%) (Table 2). The sensitivity, specificity, and validity of frozen section in benign tumors (Table 3, 4)

Table 2. The frequency of different pelvic masses based on reports of frozen section method and final pathology

Origin of Mass		Pelvic Masses	Frequency	
			Frozen section	Final pathology
	Germ cell	Dermoid cyst	19(10.1%)	19(10.1%)
		Fibroma	1(0.5%)	1(0.5%)
	Sex cord-stromal	Fibrothecoma	6(3.2%)	5(2.7%)
		Thecoma	0(0%)	10.5%)
Ovary		Granulosa cell tumor	42.1%)	4(2.1%)
		Endometriotic cyst	16(8.5%)	16(8.5%)
		Serous cystadenoma	31(16.5%)	32(17%)
		Mucinous cystadenoma	18(9.6%)	18(9.6%)
		Serous tumor	7(3.7%)	6(3.2%)
		Mucinous tumor	0(0%)	0(0%)
		Endometrioid tumor	2(1.1%)	2(1.1%)
Epithelial		Physiologic cyst	19(10.1%)	15(8%)
		Borderline tumor	7(3.7%)	8(4.3%)
		Papillary cell carcinoma	1(0.5%)	1(0.5%)
Metastatic tumor			2(1.1%)	3(1.6%)
Uterus	Uterine	Adenocarcinoma	10(5.3%)	10(5.3%)
		Endometrial polyp	1(0.5%)	1(0.5%)
		Leiomyosarcoma	2(1.1%)	2(1.1%)
		Endometrial stromal sarcoma	0(0%)	0(0%)
		Leiomyoma	39(20.7%)	40(21.3%)
		Adenomyosis	3(1.6%)	3(1.6%)
		Endometriosis	0(0%)	1(0.5%)
Total			188(100%)	188(100%)

were calculated as follow: 96.7 (CI<sub>95%</sub>: 92.6–98.9%), 97 (CI<sub>95%</sub>: 84.7–99.9%), and 96.8%. The sensitivity, specificity, and validity of frozen section in intermediate tumors were 71.4 (CI<sub>95%</sub>: 29–96.3%), 98.3 (CI<sub>95%</sub>: 95.2–99.7%), 97.3%; and in malignant tumors: 96.3 (CI<sub>95%</sub>: 81.9–99.9%), 97.4 (CI<sub>95%</sub>: 93.4–99.3%), and 97.2%. Positive and negative predictive values were calculated as follow: 99.3 (CI<sub>95%</sub>: 96.3–99.9%) and 86.8% (CI<sub>95%</sub>: 71.9–95.6%) in benign tumors; 62.5 (CI<sub>95%</sub>: 24.5–91.5%) and 98.9% (CI<sub>95%</sub>: 96–99.9%) in intermediate tumors; and 86.7 (CI<sub>95%</sub>: 69.3–96.2%) and 99.3% (CI<sub>95%</sub>: 96.3–99.9%) in malignant tumors. The results of this study showed that frozen section method has sensitivity of 96.3% (CI<sub>95%</sub>: 81.9–99.9%), specificity of 97.5% (CI<sub>95%</sub>: 93.8–99.3%), positive predictive value of 86.7% (CI<sub>95%</sub>: 69.3–96.2%), negative predictive value of 99.4% (CI<sub>95%</sub>: 96.5–99.9%), accuracy of 97.3%, and Kappa of 0.868 (Table 5).

The significant association of positive tumor markers with reports of final pathology was seen in CA125 ( $p < 0.001$ ) (Table 6).

## Discussion

In gynecological and obstetrical diseases, providing frozen sections has been the most helpful method in determining the type and method of treatment of suspicious pelvic masses (7). Many studies have been performed to determine the value of diagnostic precision for frozen sections in masses of different body organs; however, each

have provided relatively different results depending on the organ and tissue under study. Ilvas et al (2005), in a retrospective study on 1494 ovarian specimens, out of which 617 had gone under frozen section during 1995–2003, calculated the total value of frozen section to be 97%. That 21 cases were incorrectly diagnosed by frozen section. The primary reason for these errors was determined to be Mucinous and Borderline tumors. Finally, they reached the conclusion that frozen section is a reliable method in the diagnosis of ovarian masses (10). Allameh et al (2005) studied 45 tissue samples from patients during ovarian mass surgery and found that the sensitivity and specificity of diagnosis by frozen section in malignant ovarian masses were 100% and 88.5%, respectively; however, for benign masses, they were 88.5% and 77%, respectively. Finally, they concluded that frozen section is a reliable method for diagnosing the type of histology and ovarian masses (11). Taskiran et al (2008) conducted a study on 207 patients, which according to preliminary calculations that considered borderline histology as malignant, the diagnostic sensitivity and specificity of frozen section was 97% and 92%, respectively. In the secondary analysis, in which borderline cases were considered benign, diagnostic sensitivity and specificity of this method was 100% and 98%, respectively. They concluded that frozen section have high sensitivity and specificity; however, other diagnostic markers are required to enhance the diagnostic value, especially in patients with large lesions, borderline

Table 3. Agreement between the results of pathology test and reports of frozen section

Compatibility between the report of frozen section and final pathology	Frequency	Percent
Compatibility (both positive and both negative)	175	93.1
Not compatibility	13	6.9
Total	188	100.0

Table 4. Comparison of frozen section and final pathology in the diagnosis of different kinds of pelvic masses

Results of Frozen Section	Final Pathology			Total
	Neoplastic	Non neoplastic	Border line	
Neoplastic	26(13.8%)	0(0%)	1(0.5%)	27(14.4%)
Non neoplastic	3(1.6%)	149(79.3%)	2(1.1%)	154(81.9%)
Borderline	1(0.5%)	1(0.5%)	5(2.7%)	7(3.7%)
Total	30(16%)	150(79.8%)	8(4.2%)	188(100%)

Table 5. Estimations of sensitivity, specificity, positive and negative predictive values, false positive and negative cases, and validity of frozen section in the diagnosis of pelvic masses

Frozen Section	Benign Percent (CI <sub>95%</sub> )	Borderline Percent (CI <sub>95%</sub> )	Malignant Percent (CI <sub>95%</sub> )
Sensitivity	99.3% (96.3–99.9%)	62.5% (24.5–91.5%)	86.7% (69.3–96.2%)
Specificity	86.8% (71.9–95.6%)	98.9% (96–99.9%)	99.4% (96.5–99.9%)
Positive predictive value	96.7% (92.6–98.9%)	71.4% (29–96.3%)	96.3% (81–99.9%)
Negative predictive value	97% (84.7–99.9%)	98.3% (95.2–99.7%)	97.5% (93.8–99.3%)
False positive	13.2% (4.4–28.1)	1.1% (0.13–3.9)	0.63% (0.02–3.5%)
False negative	0.67% (0.02–3.7%)	37.5% (8.5–75.5%)	13.3% (3.7–30.7%)
Accuracy	96.8% (93.2–98.8%)	97.3% (93.9–99.1%)	97.3% (93.9–99.1%)
Kappa	89.7 (81.6–97.8)	65.3 (36.9–93.7)	89.7 (80.7–98.6)

CI<sub>95%</sub>: 95% Confidence interval

Table 6. The association of positive tumor markers with reports of final pathology

Positive Tumor marker	Report of final pathology		p
	Not Neoplastic	Neoplastic	
LDH	11(7%)	5(16.7%)	0.081
CA125	21(13.3%)	12(40%)	< 0.001
CEA	3(1.9%)	3(10%)	0.053
AFP	8 (5.1%)	1 (3.3%)	1
BHCG	2 (1.3%)	0 (0%)	1

tumors, and Mucinous (8). Also, Maghami et al (2010) studied 31 patients with a preliminary diagnosis of endometrial carcinoma to compare the value of diagnostic accuracy of the frozen section with final reports of their pathology. It was found that pathologic invasion to myometrium was correctly reported for 90% of patients. Finally, frozen sections were considered valuable in the detection of the early stages of low-grade tumors (12). Ah et al (2016) performed a retrospective study at Shafa International Hospital to determine the value of frozen section during surgery in the detection of different pelvic neoplasms, including ovarian tumors. The mentioned study was performed on all the patients with injury to the female genital system who had undergone frozen section surgery between January 2010 and December 2012. They concluded that frozen section had considerable value in dealing with pelvic masses with suspicious malignancy (13). Other studies have also pointed out the role of frozen sections in dealing with pelvic masses (14-18).

In the present study, out of 188 studied patients, there were 4 errors in the detection of benignity, malignancy, or borderline regarding the masses. Moreover, 2 of these cases were related to borderline tumors and the other 2 were mistakenly reported as benign instead of malignant due to inadequate frozen section specimens. Because of a conservative treatment approach in these 2 cases, no errors were made. In 175 cases (93.1%), the type of reported mass was completely compatible with frozen sections and final pathology, but they were incompatible in 13 cases (6.9%). The most prevalent reason for incompatibility in the 4 cases was related to borderline tumors. In another 4 cases, the inadequacy of frozen section specimens and in 2 cases, incompatibility was related to Granulosa cell tumors. Contrary to other similar studies that had pointed out Mucinous tumors as a reason for error, in this study, there were only 2 erroneous cases when distinguishing between benign Mucinous cysts and Serous. Studying the results of tumor marker tests also showed that among CEA, CA125, BHCG, and LDH, there was a significant relationship only between CA125 and the report of final pathology. Therefore, to reduce the costs of the treatment for patients, only the CA125 tumor marker can be evaluated.

### Conclusion

The results of this study showed that frozen section method has managed to keep its value and place among all diagnostic methods regarding pelvic masses to an acceptable extent. Higher precision in isolating specimens for frozen sections, especially in large masses, and cooperation of the surgeon and pathologist can enhance the value of this method. In addition, except for CA125, this method can prevent performing tumor marker tests, which are costly and are of low diagnostic value.

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### Conflict of Interests

The authors declare that they have no competing interests.

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