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Diagnosis Accuracy with Frozen Section at Borderline Ovarian Tumors

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ABSTRACT

Objective: This study examined patients diagnosed with borderline ovarian tumors by frozen section. Some of these patients' final pathologies differed from the diagnosis of borderline ovarian tumors with frozen sections. The situations that cause this difference are the subject of this study.

Material and Methods: This research investigated 68 patients who had adnexal mass surgery at the Necmettin Erbakan University Meram Faculty of Medicine Hospital between 2010 and 2022 and whose frozen section diagnosis results were recorded as borderline ovarian tumors. The diagnostic accuracy of the frozen section approach was determined using univariate and multivariate analyses.

Results: Unlike the frozen diagnosis, the features of the patients diagnosed with malignancy through definitive pathology were investigated. In these instances, the preoperative cutoff value for carcinoembryonic antigen was 1.16 ng/ml and 43 years of age.

Results and conclusion: Unlike the frozen diagnosis, the features of the patients diagnosed with malignancy through definitive pathology were investigated. In these instances, the preoperative cutoff value for carcinoembryonic antigen was 1.16 ng/ml and 43 years of age.

Keywords: Frozen section, Borderline ovarian tumors, Malignant, Carcinoembryonic antigen, Age

ÖZET

Amaç: Bu çalışmada adneksiyal kitle nedeniyle opere edilen ve frozen section ile borderline over tümörü (BOT) tanısı konulan olguların son patolojileri ile arasındaki ilişki araştırıldı.

Gereç ve Yöntem: Bu araştırma, 2010-2022 yılları arasında Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Hastanesi'nde adneksiyal kitle cerrahisi geçiren ve frozen section tanısı BOT olarak kaydedilen 68 hasta incelendi. Frozen section yaklaşımının tanısal doğruluğu, tek değişkenli ve çok değişkenli analizler kullanılarak belirlendi.

Bulgular ve Sonuç: Frozen sectiondan farklı olarak kesin patoloji ile malign tanısı konulan hastaların özellikleri araştırıldı. Bu durumlarda ameliyat öncesi CEA eşik değerinin 1,16 ng/ml olduğu ve bu olguların 43 yaşından büyük olduğu belirlendi.

Anahtar kelimeler: Frozen section, Borderline over tümörü, Malignite, CEA, Yaş

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Introduction

Borderline ovarian tumors (BOTs) are a diverse group of lesions known as tumors with limited malignant potential. These lesions are histologically characterized by atypical epithelial proliferation that does not include stromal invasion (1). BOTs are noninvasive tumors that sometimes spread to the peritoneum (2). These neoplasms are midway between benign cystadenomas and invasive carcinomas. They are also known as borderline, atypical, and low-risk tumors. Most pathologists, gynecologists, and oncologists use the term "borderline neoplasm," endorsed by the World Health Organization WHO. (3). Approximately 14-15% of initial ovarian tumors are borderline (4). There are several histologies for borderline tumors, such as epithelial ovarian cancer (5, 6). Among these, serous or mucinous instances are the most common. However, endometrioid, clear-cell, and Brenner borderline cancers are rare. Approximately 15 to 20% of all ovarian serous neoplasms are borderline tumors. Approximately 65 to 70% of ovarian borderline tumors have histology classified as serous (6-8). Mucinous tumors make up 11% of borderline ovarian neoplasms (9). The incidence of these tumors varies from 1.8 to 5.5 per 100,000 women per year in the US, Denmark, and Sweden (4, 10, 11). One-third of borderline ovarian tumor patients are aged under 40 years (4, 6). This emphasizes ovarian function and fertility maintenance. BOTs have the same clinical appearance as other adnexal abnormalities. Some people present with no symptoms (12). BOTs are evaluated similarly to ovarian carcinomas, but serum cancer antigen-125 (CA 125) is not helpful. Borderline tumors may cause growth in the adnexa raising suspicions of ovarian cancer. This indication provides the basis for the decision to proceed with the surgical procedure. Intraoperative frozen section is a frequent procedure, and the information obtained helps determine the surgical treatment's scope. A meta-analysis of 18 studies on frozen section results of ovarian disease showed great sensitivity (65 to 100%) and excellent specificity (>99%) (13). Large neoplasms, mucinous tumors (which have greater histologic diversity), and borderline tumors all reduce the sensitivity of the frozen section malignancy detection method because they need more sections to remove a circumscribed zone of invasive illness.

This study aimed to explore the accuracy of frozen section BOT diagnosis and determine characteristics associated with an upgrade to a conclusive diagnosis of invasive cancer in patients with a frozen section BOT diagnosis.

Material and Methods

We analyzed the clinical, laboratory, and pathological data of patients who underwent surgery for adnexal masses in our hospital between 2010 and 2022 and were diagnosed with borderline ovarian tumors using the frozen section method. A review of electronic clinical and pathological files was performed to identify individuals diagnosed with BOTs based on a frozen section or a permanent histologic finding. In line with the purpose of the research, the computerized records of the patients were examined to obtain information on their ages, whether or not they had gone through menopause, the size of their tumors, serum tumor markers carcinoembryonic antigen (CEA) and CA-125, and permanent pathology reports.

SPSS version 22 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA) was used for all statistical calculations. Descriptive features (mean, median, and standard deviation) were evaluated with descriptive statistical tests. The normal distribution of the variables was analyzed according to Kolmogorov Smirnov and Shapiro–Wilk tests. Comparisons of categorical parameters were analyzed with the help of the chi-square test and Fisher's exact test. Since our data were not normally distributed, the nonparametric Kruskal Wallis test was used for multiple comparisons. The Mann Whitney U test was used to compare the two groups. In addition, the operating characteristic (ROC) curve was constructed to determine the optimal threshold value of CEA level and age for an elevation in permanent pathological diagnosis. A p-value of $p<0.05$ was considered significant.

All procedures performed in the current study were approved by the institutional review board (Reference number: 3822 and Year: 2022) following the 1964 Helsinki Declaration and its later amendments.

Results

We investigated 68 women aged 23 to 85, with a median of 50 years. Table 1 shows the patients' demographic information. It includes the patient's age, menopause status, preoperative CEA and CA-125 levels, maximum tumor sizes, tumor surface area, bilaterality, and permanent pathologies.

Among the 37 cases where the final pathology report was BOTs, seven were found to have microinvasion. Two were serous, two were mucinous, and one was an endometrioid-type BOT. All three types of BOTs showed a comparable microinvasion distribution.

Table 1 • Characteristics of 68 cases whose frozen section results were reported as borderline

Charecteristics	Median (min-max)
Age (year)	50 (23-85)
Menopause status	
Premenopause	32 (47.1%)
Postmenopause	36 (52.9%)
CEA (ng/ml)	1.09 (0.28-271)
CA-125 (u/ml)	28.5 (0.66-5196)
Largest diameter of the Tumor (mm)	100 (25-300)
Bilaterality	12 (17.6%)
Final pathology	
Benign	9 (13.2%)
Borderline	37 (54.4%)
Malignant	22 (32.4%)

[CEA: Carcinoembryonic antigen (0-5.2 ng/ml), CA-125: Cancer antigen 125 (0-35 U/ml)]

Table 2 compares age, number of children, CEA and CA-125 values, and largest tumor diameter of the patient groups with final pathology reports diagnosed as benign, malignant, or borderline.

We evaluated the variables associated with a diagnostic upgrade from borderline tumor to invasive carcinoma, as given in Table 3. In final reports, there was no statistically significant correlation between the tumor histologic type, maximum tumor diameter, or serum CA-125 levels and the transition from diagnosis of BOTs to invasive carcinoma. However, factors such as age, menopause status, and a higher blood CEA level were all substantially related to an upgraded invasive cancer diagnosis.

Table 2 • Comparison of the variables according to permanent pathologies

Age (year)	50.22±20.71	55.68±11.69	43.81±16.43	0.027
Number of children	3.0±1.3	2.9±1.3	2.9±1.5	0.966
CEA (ng/ml)	0.92±0.58	3.43±5.17	1.5±2.57	0.018
CA-125 (u/ml)	38.14±56.89	144.19±209.37	252.97±901.44	0.172
Largest diameter of Tumor (mm)	82.23±60.8	131.3±72.03	135.2±85.2	0.082

Kruskal Wallis test, [CEA: Carcinoembryonic antigen (0-5.2 ng/ml), CA-125: Cancer antigen 125 (0-35 U/ml)].

Table 3 • Variables that cause invasive cancers to be diagnosed as BOTs in frozen section.

	Permanent pathology report		
Characteristics	**Borderline tumor (*n* = 37)**	**Carcinoma (*n* = 22)**	***p*-value**
Age, median (min-max)	40 (23-79)	54.50 (31-74)	**0.006**
Menopause, number (percentage)	15 (40.5%)	16 (72.7%)	**0.017**
The largest diameter of the tumor (cm)			
Median (min-max)	11 (2.5-30)	11.25 (3-30)	0.784
Serum tumor markers			
CEA, median (min-max)	0.95 (0.44-16.20)	1.27 (0.42-20.50)	0.013
CA125, median (min-max)	26.40 (5.42-5196)	62.11 (7.01-750)	0.221 0.319
Histologic cell types (number, percentage)			
Mucinous	17 (45.9%)	11 (50%)	
Serous	19 (51.4%)	8 (36.4%)	
Endometrioid	1 (2.7%)	2 (9.1%)	
Clear cell	0	1 (4.5%)	

In the ROC curve analysis, the cutoff threshold for CEA was determined to be 1.16 ng/mL using the Youden index (Figure 1). This value was 43 for the age variable.

Discussion

In this particular study, we concluded that frozen section biopsy failed to correctly identify invasive carcinomas as BOTs in 32.24% of all patients. In comparable research, this percentage was 27% (14). In a similar study, the final pathology of 6, 13.6% of 44 patients examined with the frozen section procedure was reported as malignant (15). This rate is much lower than the value we found in our study. In another study examining 41 patients diagnosed with BOTs with frozen sections, the final pathology of 13 patients was reported as malignant. The rate here is 31.7% (16). This result is compatible with our study.

The risk factors for a change in the final diagnosis from frozen sections include the largest diameter of the tumor size, the presence of solid components, and a multilocular appearance (17). Because intraoperative frozen sections are performed without the assistance of immunohistochemical staining and molecular studies, the accuracy of the diagnosis is largely dependent on the patient's clinical history, as well as the gross examination and microscopic interpretation of the morphologic findings (18). Misdiagnosis by frozen section biopsy has been attributed to sampling and interpretation errors.

Brun et al. determined the elements that influenced the accuracy of the diagnosis of ovarian cancers using frozen section analysis. They discovered that the expertise of pathologists might predict the incorrect diagnosis of borderline tumors (19).

According to the statistical analysis, the preoperative CEA values were significantly different between cases with benign and malignant final pathology reports. Similar to this finding, we found that this distinction was observed between the borderline and malignant subgroups. However, our investigation revealed that this distinction was not observed between the benign and BOT groups. In a similar study, preoperative CEA values did not differ between the final pathology report groups, while CA-125 values were significantly different (14). According to the permanent pathology reports, our analysis did not find a significant difference in CA-125 levels between the borderline and malignant groups.

Among the cases whose final pathologies were reported as carcinoma, endometrioid and clear cell types were at a similar rate, while the incidence of mucinous and serous types was different from these two and showed similarity to each other. The histological type of the tumor effectively upgraded the final pathology report as carcinoma in a similar study (14). Our study did not find such an effect on the histological type of the tumor.

The present study has several shortcomings due to its restrictions. It was a retrospective study performed at a single center with BOT patients. Another limitation was that different pathologists evaluated the frozen and permanent pathologies. The lack of clearly defined criteria for using the frozen section approach was another limitation of the study.

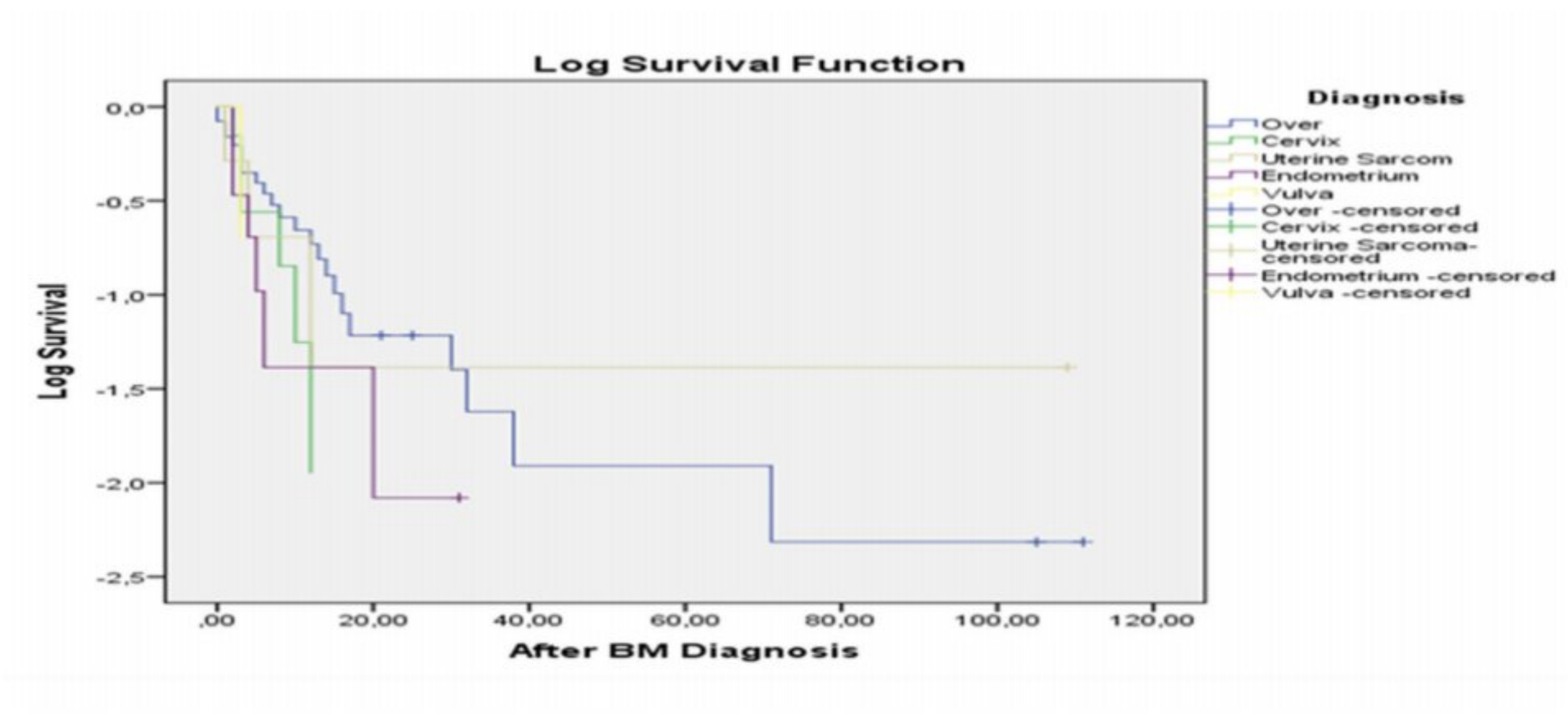

Figure 1: Upgrade to the final pathology report based on a receiver operating characteristic curve with varying CEA level and age cutoff values.

Conclusion

BOTs discovered by frozen section had an increased likelihood of being permanently diagnosed as invasive carcinoma in cases where the patient was older than 43 years and exhibited elevated levels of the tumor marker CEA (>1.16 ng/mL) in their blood. These results can be helpful inpatient counseling and surgical decision-making.

Conflict Of Interest

The authors declare no conflicts of interest.

Funding

None.

Data Availability Statement

Upon a reasonable request, the corresponding author can provide access to the data supporting the conclusions of this research.

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