

Comparative Analysis of Borderline Ovarian Tumors: A 5-Year Tertiary Center Experience

Elif Ünlügedik Sayın^{1*}, Esra Keles¹, Meral Aban²

¹Kartal Dr Lütüfi Kırdar City Hospital, Department of Obstetrics And Gynecology

²Sancaktepe Şehit Prof. Dr. İlhan Varank Education and Research Hospital, Department of Gynecologic Oncology

ABSTRACT

To evaluate clinical, pathological, biochemical, and imaging differences among borderline ovarian tumors (BOTs) subtypes, serous, mucinous, and seromucinous, to improve preoperative diagnosis.

A retrospective analysis was conducted between January 2018 and October 2023, including 59 patients with histologically confirmed BOTs. Patients were classified into serous (n=36), mucinous (n=18), and seromucinous (n=5) subtypes. Demographic data, tumor markers, inflammatory indices, imaging characteristics, intraoperative frozen section results, and final histopathology were compared.

A total of 59 patients with BOTs were analyzed: 36 (61.0%) serous, 18 (30.5%) mucinous, and 5 (8.5%) seromucinous. The mean age was similar across groups: serous 44.1 ± 12.2 years, mucinous 47.5 ± 19.5 years, seromucinous 45.2 ± 4.3 years ($p=0.725$). Mucinous tumors were larger (14.0 ± 8.8 cm) than serous (6.9 ± 2.4 cm) and seromucinous (7.7 ± 4.5 cm) ($p=0.001$). CA-125 and CA19-9 levels differed significantly ($p=0.007$ and $p=0.017$), with the highest levels in seromucinous tumors. Solid components on ultrasound were more frequent in serous (50%) and seromucinous (60%) tumors compared to mucinous (16.7%) ($p=0.041$). MRI septation was most common in mucinous tumors (66.7%, $p=0.036$). No significant differences were observed for menopausal status, comorbidities, tumor laterality, or frozen section results. AARPTI values differed significantly ($p=0.001$), highest in mucinous tumors (0.66 ± 0.33).

This study revealed that mucinous BOTs are characterized by larger tumor size and higher AARPTI values, while seromucinous tumors exhibit elevated CA-125 and CA19-9 levels. Ultrasound and MRI findings also may aid in the differentiation among subtypes. These distinctions can enhance preoperative diagnosis and guide tailored surgical management.

Keywords: Borderline ovarian tumor, serous borderline tumor, mucinous borderline tumor, seromucinous borderline tumor, preoperative diagnosis, tumor markers, imaging features

Introduction

Gynecologic cancers, encompassing malignancies of the ovary, uterus, cervix, vulva, and vagina, remain a major contributor to cancer-related morbidity and mortality among women worldwide. Among these, ovarian cancer is particularly challenging due to its often asymptomatic early course, lack of effective population-based screening, and frequent diagnosis at advanced stages. Although advances in imaging techniques, tumor markers, and molecular pathology have improved diagnostic accuracy and individualized treatment strategies, distinguishing between benign, borderline, and malignant ovarian tumors continues to pose a significant clinical challenge, especially in the preoperative setting.

Borderline ovarian tumors (BOTs), also known as tumors of low malignant potential, constitute a distinct and intermediate disease entity. These tumors are characterized by atypical epithelial

proliferation without destructive stromal invasion, distinguishing them from both benign ovarian cysts and invasive carcinomas (1).

BOTs typically affect younger women, often in their reproductive years, with an average age of diagnosis around 45 years, which is approximately a decade earlier than the average age for invasive ovarian cancers (2). A significant proportion of BOTs are diagnosed at an early stage, with favorable prognosis. Despite a recent global decreasing trend in overall ovarian malignancies, the percentage of BOTs among ovarian malignancies has paradoxically increased (3). This shift is largely attributed to improved accuracy in the pathological diagnosis of BOTs and evolving understandings of their associated risk factors. This trend underscores the growing clinical relevance of precise BOT characterization and the need for continued research into this distinct disease entity.

*Corresponding Author: Elif Ünlügedik Sayın, Kartal Dr Lütüfi Kırdar City Hospital, Department of Obstetrics And Gynecology

ORCID ID: Elif Ünlügedik Sayın: 0000-0002-6238-0446, Esra Keles: 0000-0001-8099-8883, Meral Aban: 0000-0002-0612-961X

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Borderline ovarian tumors are histologically diverse, with serous and mucinous types accounting for over 96% of all cases. Other less common subtypes include seromucinous, endometrioid, clear cell, and Brenner tumors (4). The geographical distribution of these subtypes can vary, with serous types being more prevalent in Western countries and mucinous types more common in Asian populations (5). Importantly, these histological subtypes exhibit differing clinical behaviors, recurrence risks, and prognostic implications, necessitating a nuanced approach to their diagnosis and management (6).

Preoperative diagnosis of BOTs remains challenging due to inconsistencies in tumor marker expression and the limitations of imaging modalities in definitively distinguishing them from benign or malignant lesions (7). Intraoperative frozen section diagnosis, while crucial for guiding immediate surgical decisions, exhibits a lower accuracy for BOTs compared to benign or malignant tumors, often leading to misdiagnosis (8). This diagnostic ambiguity poses a significant dilemma for intraoperative surgical staging. The inherent complexity of BOTs, particularly their histological heterogeneity and multilocularity, contributes to sampling and interpretation errors during rapid frozen section analysis (9). This highlights why comprehensive clinicopathologic evaluations, which correlate various parameters with final histology, are vital for improving preoperative suspicion and intraoperative guidance, thereby mitigating the challenges posed by frozen section limitations.

Given the distinct clinical implications of BOT subtypes, a detailed understanding of their baseline characteristics, laboratory profiles, and imaging features is paramount for improving preoperative differential diagnosis and optimizing surgical planning. This study aims to contribute to this understanding by providing a comprehensive clinicopathologic evaluation of BOT subtypes from a tertiary center, focusing on identifying distinguishing features that can aid in diagnosis and management.

Material and Methods

Study design and setting: This retrospective study was conducted between January 2018 and October 2023. Following the requisite approval from the institutional ethics committee (Approval No. 2023/514/260/13, October 30, 2023) and in accordance with the Declaration of Helsinki, patients with histopathologically confirmed

borderline ovarian tumors were identified from final pathology records and included in the analysis. The BOTs were stratified into three histological subtypes based on their final pathology reports: serous (n=36), mucinous (n=18), and seromucinous (n=5). Patients with invasive ovarian cancer, benign ovarian tumors, or incomplete clinical or pathological data were excluded from the analysis.

Data Collection: Comprehensive clinical and pathological data were retrospectively collected from electronic medical records, pathology archives and imaging reports. The collected parameters included baseline demographic and clinical characteristics, pathological features, preoperative serum levels of tumor markers, hematological and biochemical parameters, detailed ultrasonographic features, magnetic resonance imaging (MRI) findings, were also recorded. In addition, the intraoperative frozen section diagnosis were noted.

Inflammatory indices such as Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR), Systemic Immune-Inflammation Index (SII), and Systemic Inflammatory Response Index (SIRI) were also computed. Changes in hematocrit (Δ HCT, %) and hemoglobin (Δ HB, g/dL) were also calculated. AARPTI (Acute-Phase Reactants and Preoperative Tumor Indicators) and APRI (Aspartate Aminotransferase to Platelet Ratio Index) are valuable in gynecologic oncology for improving preoperative tumor assessment and prognostic accuracy. In this study, AARPTI was calculated as (AST/ALT) divided by platelet count, while APRI was determined as the ratio of AST to platelet count, reflecting systemic inflammatory status related to tumor behavior.

Statistical Analysis: All statistical analyses were performed using Statistical Package for Social Sciences (SPSS v.25, IBM). Descriptive statistics were used to summarize patient characteristics. Continuous variables were presented as mean \pm standard deviation (SD). Categorical variables were presented as counts and percentages. Comparisons of continuous variables across the three histological subtypes (serous, mucinous, seromucinous) were performed using Analysis of Variance (ANOVA) for normally distributed data. For non-normally distributed continuous variables, the Kruskal-Wallis H-test was employed. Comparisons of categorical variables were performed using the Chi-squared (χ^2) test or Fisher's exact test, as appropriate, particularly when expected cell counts were less than five. A

p-value of <0.05 was considered statistically significant.

Statistical analyses were performed using IBM SPSS Statistics for Windows (Version XX.X; IBM Corp., Armonk, NY, USA). Normally distributed continuous variables were expressed as mean \pm standard deviation and compared using one-way analysis of variance (ANOVA). Non-normally distributed variables were presented as median (interquartile range) and compared using the Kruskal–Wallis test.

For post-hoc analyses, Tukey's honestly significant difference (HSD) test was applied following ANOVA, while Dunn–Bonferroni correction was used following Kruskal–Wallis tests to identify pairwise group differences. Categorical variables were expressed as frequencies and percentages. Comparisons between categorical variables were performed using the chi-square test when expected cell counts were ≥ 5 , and Fisher's exact test was used when expected cell counts were <5.

A p-value <0.05 was considered statistically significant. Exact p-values were reported to three decimal places. Given the retrospective nature of the study and inclusion of all eligible patients diagnosed within the study period, a priori sample size calculation or power analysis was not performed.

Results

A total of 59 patients diagnosed with BOTs were included in the analysis. The study group was stratified into three histological subtypes: serous (n=36), mucinous (n=18), and seromucinous (n=5). The mean age of the patients was comparable among the subgroups: 44.1 \pm 12.2 years for serous, 47.5 \pm 19.5 years for mucinous, and 45.2 \pm 4.3 years for seromucinous tumors (p=0.725). Parity (p=0.486), gravidity (p=0.329), and history of abortion (p=0.984) did not differ significantly across groups (Table 1).

Tumor size demonstrated a statistically significant difference among BOTs subtypes (p=0.001), with mucinous tumors exhibiting the largest mean diameter (14.0 \pm 8.8 cm), compared to serous (6.9 \pm 2.4 cm) and seromucinous tumors (7.7 \pm 4.5 cm). Serum CA-125 levels were also significantly different (p=0.007), being highest in the seromucinous group (543.6 \pm 1001.6 U/mL), followed by serous (92.9 \pm 153.3 U/mL), and mucinous tumors (36.5 \pm 42.6 U/mL). CA19-9 levels varied markedly across groups (p=0.017),

with the seromucinous subgroup showing the highest values (319.9 \pm 533.8 U/mL).

Preoperative hematological parameters showed significant differences in hematocrit (p=0.018) and hemoglobin (p=0.027) levels, with higher values observed in the seromucinous group. ALT levels differed significantly between groups (p=0.016), with seromucinous tumors associated with elevated ALT (25.4 \pm 19.3 U/L). Monocyte counts also showed intergroup variation (p=0.035), being highest in the serous group (0.54 \pm 0.16 $\times 10^9$ /L).

Among the systemic inflammatory indices evaluated, no statistically significant differences were observed in APRI values across the three histological subtypes of BOTs (p = 0.097). AARPTI values differed significantly among subtypes (p = 0.001). Mucinous BOTs exhibited the highest mean AARPTI (0.66 \pm 0.33), followed by serous (0.47 \pm 0.20) and seromucinous BOTs (0.37 \pm 0.09).

Hospitalization duration varied significantly by histologic subtype (p=0.011), with patients in the seromucinous group having the longest mean length of stay (4.8 \pm 0.7 days), compared to mucinous (3.9 \pm 0.4 days) and serous (3.1 \pm 0.2 days) tumors.

Ultrasonographic findings revealed significant differences in the presence of solid components (p=0.041), which were most frequently observed in serous (50%) and seromucinous (60%) tumors, compared to mucinous tumors (16.7%) (Table II). MRI findings showed a statistically significant difference in septation (p=0.036), being most prevalent in mucinous tumors (66.7%). While contrast enhancement on MRI was more frequent in seromucinous tumors (66.7%) compared to serous (43.8%) and mucinous tumors (8.3%), this difference did not reach statistical significance (p=0.057).

The mode of presentation at diagnosis did not significantly differ among groups (p=0.560), although incidental findings were more common in the serous subtype (28%) and seromucinous subtype (40%). Mode of delivery was not significantly associated with histologic subtype (p=0.408). Similarly, no significant differences were observed in menopausal status (p=0.972), presence of chronic disease (asthma p=0.732, diabetes mellitus p=0.137, hypertension p=0.580), or history of previous surgery (p=0.484).

Pathologic evaluation revealed no significant differences in tumor laterality among BOT

Table 1: Baseline Demographic, Clinical, and Laboratory Characteristics of Patients By Histological Subtype of Borderline Ovarian Tumors

Characteristic	Serous (n=36)	Mucinous (n=18)	Seromucinous (n=5)	p-value
Age (years),	44.14 ± 12.21	47.50 ± 19.45	45.20 ± 4.32	0.725
Gravidity,	3.42 ± 2.47	4.13 ± 2.42	2.00 ± 0.00	0.329
Parity,	2.72 ± 2.13	3.19 ± 2.17	1.67 ± 0.58	0.486
Live births,	2.64 ± 2.03	2.94 ± 1.53	1.67 ± 0.58	0.549
Abortions,	0.42 ± 0.97	0.44 ± 0.81	0.33 ± 0.58	0.984
Ectopic pregnancies,	0.03 ± 0.17	0.00 ± 0.00	0.00 ± 0.00	0.775
Curettage history,	0.17 ± 0.45	0.38 ± 0.81	0.00 ± 0.00	0.382
Tumor size (cm),	6.95 ± 2.44	14.04 ± 8.79	7.67 ± 4.51	0.001
CA-125 (U/mL),	92.95 ± 153.32	36.45 ± 42.58	543.55 ± 1001.64	0.007
CA 15-3 (U/mL),	15.24 ± 9.00	10.04 ± 4.85	10.95 ± 3.79	0.073
CA 19-9 (U/mL),	12.82 ± 8.90	111.12 ± 272.83	319.88 ± 533.78	0.017
CEA (ng/mL),	2.51 ± 4.47	7.13 ± 14.42	11.44 ± 14.55	0.100
AFP (ng/mL),	4.32 ± 12.72	2.51 ± 1.05	3.91 ± 1.75	0.856
Preoperative hemoglobin (g/dL),	12.27 ± 1.10	12.46 ± 1.84	14.18 ± 1.80	0.027
Postoperative hemoglobin (g/dL),	10.77 ± 1.18	11.43 ± 1.86	12.08 ± 1.24	0.119
ALT (U/L),	15.37 ± 7.76	12.65 ± 4.17	25.40 ± 19.27	0.016
AST (U/L),	18.12 ± 6.50	20.47 ± 9.66	24.60 ± 12.38	0.213
Lymphocytes (×10 ⁹ /L),	2.15 ± 0.69	1.68 ± 0.52	1.90 ± 0.86	0.058
Neutrophils (×10 ⁹ /L),	5.47 ± 2.03	5.63 ± 4.36	7.13 ± 3.77	0.524
Monocytes (×10 ⁹ /L),	0.54 ± 0.16	0.42 ± 0.11	0.43 ± 0.20	0.035
Eosinophils (×10 ⁹ /L),	0.17 ± 0.16	0.11 ± 0.06	0.12 ± 0.09	0.383
Basophils (×10 ⁹ /L),	0.04 ± 0.03	0.03 ± 0.02	0.02 ± 0.02	0.451
PIV,	548.29 ± 637.57	704.79 ± 1593.06	438.12 ± 195.61	0.831
SII,	951.46 ± 883.54	1337.18 ± 2225.02	1820.07 ± 2369.93	0.450
NLR,	3.10 ± 2.62	4.38 ± 5.99	5.95 ± 7.19	0.302
PLR,	166.51 ± 117.17	183.84 ± 90.51	203.36 ± 147.53	0.742
MLR,	0.30 ± 0.26	0.29 ± 0.17	0.23 ± 0.10	0.801
d-NLR,	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.990
SIRI,	1.76 ± 1.85	2.21 ± 4.34	1.55 ± 0.93	0.830
APRI,	0.16±0.07	0.19±0.09	0.21±0.10	0.097
AARPTI,	0.47±0.20	0.66±0.33	0.37±0.09	0.001
ΔHCT (%),	4.52 ± 2.29	4.42 ± 3.22	6.94 ± 2.83	0.158
ΔHB (g/dL),	1.45 ± 0.70	1.40 ± 1.04	2.10 ± 0.72	0.233
Length of hospital stay (days),	3.06 ± 0.20	3.94 ± 0.41	4.80 ± 0.74	0.011

Clinical and demographic characteristics of patients with borderline ovarian tumors according to histological subtype.

Data are presented as mean ± standard deviation or n (%).

p-values were obtained using one-way ANOVA or Kruskal–Wallis test for continuous variables, and chi-square or Fisher’s exact test for categorical variables, as appropriate.

Table 2: Ultrasonographic, Clinical, and Pathological Characteristics of Patients By Histological Subtype. A p Value of <0.05 Indicates A Significant Difference

Feature	Serous (n=36)	Mucinous (n=18)	Seromucinous (n=5)	p-value
Presentation at diagnosis, n (%)				0.560
Pain	9 (25.0)	6 (33.3)	1 (20.0)	
Abnormal uterine bleeding	0 (0.0)	1 (5.6)	0 (0.0)	
Follow-up for cyst	2 (5.6)	2 (11.1)	1 (20.0)	
Postmenopausal complaint	1 (2.8)	0 (0.0)	0 (0.0)	
Referral from another center	14 (38.9)	8 (44.4)	1 (20.0)	
Incidental finding	10 (27.8)	1 (5.6)	2 (40.0)	
Mode of delivery, n (%)				0.408
Nulliparous	4 (11.1)	3 (16.7)	2 (40.0)	
Vaginal delivery	14 (38.9)	10 (55.6)	2 (40.0)	
Cesarean section	11 (30.6)	2 (11.1)	1 (20.0)	
Vaginal + Cesarean	7 (19.4)	3 (16.7)	0 (0.0)	
Menopausal status, n (%)				0.972
Yes	7 (19.4)	4 (22.2)	1 (20.0)	
No	29 (80.6)	14 (77.8)	4 (80.0)	
Comorbidity, n (%)				
Asthma	3 (8.3)	2 (11.1)	0 (0.0)	0.732
Diabetes mellitus	3 (8.3)	3 (16.7)	2 (40.0)	0.137
Hypertension	4 (11.1)	3 (16.7)	0 (0.0)	0.580
Previous surgery, n (%)				0.484
Yes	16 (44.4)	6 (33.3)	1 (20.0)	
No	20 (55.6)	12 (66.7)	4 (80.0)	
Ultrasonographic features, n (%)				
Septation	13 (36.1)	6 (33.6)	0 (0.0)	0.267
Papillary projection	8 (22.2)	2 (11.1)	0 (0.0)	0.338
Solid area	18 (50.0)	3 (16.7)	3 (60.0)	0.041
MRI findings, n (%)				
Septation	3 (18.8)	8 (66.7)	1 (33.3)	0.036
Solid area	7 (43.8)	1 (8.3)	2 (66.7)	0.057
Contrast enhancement	7 (43.8)	5 (41.7)	2 (66.7)	0.729
Pathological laterality, n (%)				0.157
Right	15 (41.7)	11 (61.1)	1 (20.0)	
Left	10 (27.8)	6 (33.3)	3 (60.0)	
Bilateral	11 (30.5)	1 (5.6)	1 (20.0)	
Frozen section diagnosis, n (%)				0.121
Benign	4 (11.8)	6 (42.9)	1 (25.0)	
Malignant	2 (5.9)	1 (7.1)	0 (0.0)	
Indeterminate	1 (2.9)	1 (7.1)	1 (25.0)	
Borderline	27 (79.4)	6 (42.9)	2 (50.0)	

Data are presented as mean \pm standard deviation or median (interquartile range)
p-values were calculated using one-way ANOVA or Kruskal–Wallis test for continuous variables. Post-hoc analyses were performed using Tukey HSD or Dunn–Bonferroni correction, as appropriate

subtypes, and the accuracy of frozen section (FS) categorization also showed no statistically significant difference ($p = 0.121$).

Discussion

This study provides a comprehensive comparative analysis of clinicopathologic characteristics, laboratory findings, and radiological features across serous, mucinous, and seromucinous BOTs, offering valuable insights into their distinct characteristics. In line with the diagnostic challenges, this study adopts an integrative approach by simultaneously evaluating conventional tumor markers, systemic inflammatory indices, and detailed imaging features across BOT subtypes. In particular, the inclusion of seromucinous BOTs as a distinct analytical group and the assessment of inflammatory indices such as AARPTI represent important innovations, as data on these parameters in BOT subtypes—especially seromucinous tumors—remain limited in the literature. The findings underscore the importance of recognizing subtype-specific clinicopathologic and biomarker profiles for optimized patient management and improved preoperative risk stratification.

According to our study, the mean age of patients with BOTs 44.71 ± 14.16 years is consistent with existing literature, which frequently reports that BOTs typically occur in younger women, approximately 45 years of age, representing about a decade earlier than the average age of diagnosis for invasive ovarian cancers (2, 10-15). On the other hand, some previous studies have reported age variations, such as BOTs occurring at an older age (16, 17) or, conversely, being significantly younger than in other cohorts (18, 19). It can be argued that these observed differences are due to different geographical locations or the effects of unmeasured factors.

Serous and mucinous subtypes account for the majority of BOTs, while endometrioid, clear cell, seromucinous, and transitional cell (Brenner) subtypes are encountered less frequently (5). In our study, the distribution of histological subtypes was broadly consistent with existing literature, with serous BOTs comprising 61%, mucinous 30.5%, and seromucinous 8.5% of cases. Previous studies have reported similar proportions, with serous tumors accounting for 55–65% and mucinous tumors for 34–45% of cases (20). In addition, we observed bilateral tumours in 21.9%

of cases, similar to the reported incidence of 10–40% (21).

The finding that mucinous tumors are significantly larger (mean 14.0 cm) than serous (6.9 cm) and seromucinous (7.7 cm) tumors is consistent with established literature. Mucinous BOTs are well-known for their propensity to grow to substantial sizes and often present as multilocular cystic masses (22). Ultrasonographic analysis in this study revealed solid components more frequently in serous (50%) and seromucinous (60%) tumors, while MRI demonstrated septation to be most prevalent in mucinous BOTs (66.7%). These distinct imaging characteristics align with established patterns in which serous BOTs often present with papillary projections and solid areas, and mucinous tumors are characterized by multiple septations (22, 23). The distinct imaging features reinforce the utility of advanced imaging modalities, including ultrasound and MRI in preoperative differential diagnosis (24).

Interestingly, this study identified markedly elevated serum CA-125 and CA 19-9 levels in patients with seromucinous BOTs compared to those with serous or mucinous subtypes. Notably, the mean CA-125 and CA 19-9 levels in the seromucinous group reached 543.6 U/mL and 319.9 U/mL, respectively, despite the limited sample size ($n=5$). This elevation may be primarily driven by one patient whose CA 19-9 level exceeded 1,000 U/mL. That patient, a 40-year-old nulligravid, morbidly obese premenopausal woman with a history of pulmonary valve surgery and chronic warfarin use, presented with abdominal pain and a 20 cm right adnexal cystic mass on ultrasound. Tumor markers were markedly elevated, with CA-125 at 2046 U/mL and CA 19-9 at 1120 U/mL. Final histopathology revealed seromucinous BOTs with focal (<10%) transition to a clear cell borderline component. CA 19-9, widely recognized as a tumor marker for mucinous neoplasms of the pancreas and biliary tract, can also be elevated in gynecologic conditions such as mucinous ovarian tumors, endometriosis, and teratomas, as well as in various benign and inflammatory disorders (25). Its elevation in seromucinous BOTs has received only limited attention in prior studies. The elevation of CA 19-9 in seromucinous BOTs may be attributable to the inflammatory tumor microenvironment, specifically, the characteristic neutrophilic infiltration within the stroma and epithelium, which may promote overexpression of glycoproteins detected by CA 19-9 assays. Furthermore, the frequent coexistence of

endometriosis in seromucinous BOTs, as supported by previous studies, may contribute to both CA 125 and CA 19-9 elevation through mechanisms involving chronic inflammation and metaplastic epithelial activation (26). In addition, Nakagawa et al. have shown that CA 19-9 levels are significantly elevated in patients with endocervical-type borderline mucinous tumors — the histological category now subsumed under the seromucinous subtype, further supporting the observed biomarker profile in our cohort (27). Thus, the distinct histopathological and inflammatory features of seromucinous BOTs likely underpin the disproportionately high CA 125 and CA 19-9 levels observed in this study.

Among the systemic inflammatory indices evaluated, only AARPTI showed a significant difference across BOT subtypes, with elevated values in mucinous BOTs, suggesting its potential utility in predicting tumor behavior. Consistent with prior evidence indicating the utility of inflammatory indices such as NLR in mucinous BOTs (28), our results suggest that AARPTI may represent an additional, easily accessible inflammatory marker with potential discriminatory value. Integrating AARPTI with established models such as IOTA logistic regression and GI-RADS may enhance preoperative malignancy risk assessment in adnexal masses (29).

In our analysis, the diagnostic accuracy of intraoperative FS for BOTs was 67.3%. FS identified 63.2% of cases as borderline, 22.8% as benign, 8.8% as malignant, and 5.3% as inconclusive. These findings align with previously reported FS accuracy rates for BOTs, which range from 55.5% to 79%, markedly lower than the diagnostic accuracy typically observed for benign and malignant ovarian neoplasms (94% and 98%, respectively) (1). Notably, mucinous BOTs in our study were frequently underdiagnosed as benign, underscoring the diagnostic challenges posed by their considerable size and histologic heterogeneity. Sampling error, morphologic overlap, and intraoperative interpretive challenges likely account for the observed diagnostic discordance. Consistent with prior literature, 20–30% of FS-diagnosed BOTs may be subsequently upgraded to carcinoma on final pathology, while up to 30% of histologically confirmed BOTs may be initially misclassified as either benign or malignant (8). Although conducted in a different gynecologic malignancy, prior studies evaluating diagnostic agreement between sampling techniques highlight the inherent limitations of partial tissue assessment, a challenge that is also

evident in frozen section diagnosis of BOTs (30). These limitations necessitate a cautious interpretation of FS findings, with final histopathologic evaluation serving as the definitive basis for clinical decision-making, particularly in scenarios involving fertility-sparing surgical approaches.

Strengths and Limitations: This study offers several key strengths that enhance our understanding of borderline ovarian tumors. The study conducted a thorough analysis by collecting a wide array of data, including baseline demographics, detailed clinical presentations, a broad panel of tumor markers, extensive hematological parameters, and both ultrasonographic and MRI features, alongside intraoperative frozen section and final pathological findings. This comprehensive approach allows for a multifaceted comparison across different BOT subtypes. However, this study has several notable limitations. This study's retrospective nature and single-center design with limited sample size curtails the external validity of our findings and introduces a risk of selection bias. As a clinicopathologic evaluation, this study did not include long-term follow-up data, which are critical outcomes for BOTs. In addition, we were unable to evaluate the impact of key sociodemographic and lifestyle variables, including socioeconomic status, education level, or oral contraceptive use. Finally, the study did not include molecular profiling, which could provide additional insights into the biological behavior and prognostic indicators of BOTs and their subtypes. Future large-scale, multicenter studies with long-term follow up and integrated molecular analyses are crucial to further elucidate the biological underpinnings of these differences and refine clinical guidelines.

This study provides a comprehensive clinicopathologic comparison of serous, mucinous, and seromucinous borderline ovarian tumors (BOTs), highlighting distinct demographic, radiologic, and biomarker characteristics. While serous BOTs were the most prevalent, mucinous tumors were significantly larger, and seromucinous BOTs exhibited markedly elevated CA-125 and CA 19-9 levels. Among systemic inflammatory and routine hematologic markers, only AARPTI demonstrated potential utility in preoperative differentiation by showing elevated levels in mucinous borderline ovarian tumors. The diagnostic accuracy of intraoperative FS was 67.3%, with mucinous tumors frequently underdiagnosed. These findings underscore the

diagnostic challenges associated with BOTs. Moreover, advanced imaging modalities such as ultrasound and MRI remain valuable in supporting the preoperative assessment and differential diagnosis of BOT subtypes.

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