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Clinicopathologic Features and Surgical Management of Mucinous Tumors Involving the Ovary: A Retrospective Study of Benign, Borderline, Primary Ovarian, and Metastatic Tumors

Overi Tutan Müsinöz Tümörlerin Klinikopatolojik Özellikleri ve Cerrahi Yönetimi: Benign, Borderline, Primer Over Karsinomu ve Metastatik Tümörlerin Retrospektif Analizi

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ABSTRACT

Objective: To compare the clinicopathologic features and surgical management of benign, borderline, and malignant mucinous tumors involving the ovary and to characterize primary ovarian and extraovarian origins among malignant cases.

Methods: We retrospectively reviewed 67 patients who underwent surgery between May 2015 and February 2021 and classified their tumors as benign, borderline, or malignant. Clinicopathologic, surgical, treatment, and follow-up data were recorded. Continuous variables are presented as medians (minimum-maximum) and categorical variables as numbers and percentages. Groups were compared using the Kruskal-Wallis, chi-square, or Fisher's exact test, as appropriate.

Results: Of the 67 patients, 33 had benign tumors, 19 had borderline tumors, and 15 had malignant tumors; the malignant group included 10 primary mucinous ovarian carcinomas and five metastases from extraovarian primary tumors. The median age was 43 years (range, 16-86), and the median tumor diameter was 13 cm (range, 5-50); six tumors (9.0%) were bilateral. Median age was higher in the malignant group than in the benign and borderline groups [56 (31-71), 38 (21-86), and 42 (16-69) years, respectively; $p=0.004$]. Tumor diameter also differed among the groups [10 (5-25), 16 (5-50), and 13 (5-40) cm, respectively; $p=0.043$]. All benign and borderline tumors were unilateral, whereas 40.0% of malignant tumors were bilateral ($p<0.001$). Appendectomy rates were 53.3% in the malignant group, 47.4% in the borderline group, and 6.1% in the benign group ($p<0.001$). Among 19 appendectomy specimens, two showed metastatic involvement by primary mucinous ovarian carcinoma, one represented a primary appendiceal carcinoma with ovarian metastasis, and one contained a serrated adenoma. Five malignant tumors (33.3%) arose from extraovarian primary sites: three colorectal, one gastric, and one appendiceal; all colorectal metastases were bilateral. Six of 10 primary ovarian carcinomas were stage I.

Conclusion: Older age and bilateral involvement were associated with malignant mucinous tumors, whereas tumor diameter did not increase linearly across the benign-borderline-malignant spectrum. Because one-third of malignant tumors originated from extraovarian sites, integrated clinicopathologic assessment is essential. Surgical extent and appendectomy should be individualized according to macroscopic findings, fertility goals, and the distinction between primary and metastatic disease.

Keywords: mucinous ovarian tumor; borderline ovarian tumor; mucinous ovarian carcinoma; ovarian metastasis; appendectomy; surgical staging

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INTRODUCTION

Mucinous epithelial tumors of the ovary encompass a broad morphologic spectrum that includes benign mucinous tumors, mucinous borderline tumors, and mucinous carcinoma. The World Health Organization classifies these lesions as distinct diagnostic categories; accurate classification requires adequate sampling to assess both the presence and pattern of invasion and the heterogeneous architecture of the tumor (1). The coexistence of benign, borderline, and invasive areas within the same tumor may complicate both intraoperative assessment and final histopathologic diagnosis (2).

Primary mucinous ovarian carcinoma is rare and differs from other epithelial ovarian carcinoma histotypes in its clinical and pathologic features and response to treatment (3). In addition, mucinous adenocarcinomas arising in the colon, appendix, stomach, and other gastrointestinal sites may metastasize to the ovary and mimic a primary ovarian tumor. Therefore, the central initial question in a malignant mucinous tumor involving the ovary is whether the tumor is primary or metastatic.

The surgical approach varies according to the patient's age and fertility goals, intraoperative findings, frozen section assessment, disease extent, and the likelihood that the tumor is primary or metastatic. Sampling error may reduce the accuracy of frozen section diagnosis, particularly in large, heterogeneous mucinous tumors, thereby creating a risk of either undertreatment or overtreatment (4,5). The appropriate roles of appendectomy and lymph node assessment also remain controversial in mucinous tumors.

This study aimed to compare the clinicopathologic characteristics and surgical management of benign, borderline, and

malignant mucinous ovarian tumors treated surgically at a single center and to describe the distribution and clinical features of primary ovarian carcinomas and tumors metastatic to the ovary from extraovarian primary sites within the malignant group.

MATERIALS AND METHODS

This retrospective, single-center observational study included patients who underwent surgery between May 2015 and February 2021 and whose final histopathologic diagnosis was a mucinous tumor involving the ovary. Benign mucinous tumors, mucinous borderline tumors, and malignant mucinous tumors were included. Ovarian tumors with nonmucinous histology were excluded. Patients aged 16–86 years were included.

The study was approved by the Antalya Training and Research Hospital Clinical Research Ethics Committee at its 15th meeting held on September 3, 2026 (decision no. 15/28). Individual informed consent was not obtained because of the retrospective medical record review design of the study. Patient data were anonymized before analysis, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

The malignant group comprised two components: primary mucinous ovarian carcinoma and mucinous carcinoma metastatic to the ovary from a primary tumor in another organ. For comparisons among the benign, borderline, and malignant groups, these two components were analyzed together under the malignant category; primary ovarian and metastatic tumors were also described separately. Because these components represent biologically distinct entities, comparisons involving the combined malignant group were interpreted as descriptive and exploratory.

Data were obtained from pathology reports, electronic and paper medical records, and operative records. Age, final pathologic subgroup, largest tumor diameter, laterality, surgical procedure, appendectomy, lymph node dissection, primary tumor site, FIGO stage, adjuvant chemotherapy, follow-up duration, and last known clinical status were recorded. Tumor diameter was defined as the largest dimension reported in the pathology record. Fertility-sparing surgery was defined as preservation of the uterus and all or part of at least one ovary.

Histopathologic diagnoses were reported according to the World Health Organization criteria applicable during the study period (1). Primary invasive ovarian carcinomas were staged using the 2014 FIGO staging system (6). No retrospective central pathology review was performed. All diagnoses were based on final histopathologic examination. The distinction between primary ovarian and metastatic disease was based on the final pathology findings together with the clinical history and imaging findings. Ultrasonographic evaluation was available for all patients, whereas computed tomography and/or magnetic resonance imaging findings were available for selected patients. Immunohistochemical findings were also considered when available; however, no uniform diagnostic algorithm or standardized immunohistochemical panel was applied retrospectively.

The extent of surgery was individualized according to age, fertility goals, preoperative assessment, intraoperative findings, and frozen section results; subsequent management was guided by the final diagnosis. Recorded procedures included cystectomy, unilateral salpingo-oophorectomy (USO), total abdominal hysterectomy with bilateral salpingo-

oophorectomy (TAH+BSO), and procedures that included lymph node dissection (LND). For Table 1, these were recorded as mutually exclusive principal surgical categories; procedures involving LND were classified in the LND category rather than additionally in the TAH+BSO category. When staging surgery was indicated, peritoneal washings for cytologic examination, infracolic omentectomy, and resection of visible suspicious lesions were performed. Pelvic and/or para-aortic lymph node dissection was performed in selected patients according to the intraoperative and postoperative assessment of malignancy.

A fertility-sparing approach was preferred for premenopausal patients desiring fertility when considered oncologically appropriate. In patients with benign tumors, the extent of surgery was determined according to age, symptoms, tumor size, and fertility goals. Rather than following a routine protocol, appendectomy was performed at the surgeon's discretion on the basis of intraoperative appearance, suspicion of malignancy, and evaluation for a possible primary site.

For patients with malignant tumors, follow-up was scheduled every 3 months during the first 2 years, every 6 months until the fifth year, and annually thereafter. Follow-up visits included medical history and physical and pelvic examinations, with ultrasonography and laboratory testing when indicated and cross-sectional imaging when clinically warranted. Follow-up duration was calculated from the date of surgery to the date of the last visit or death. Patients lost to follow-up were described according to their last available record.

Statistical analyses were performed using SPSS for Windows, version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables are

presented as medians (minimum-maximum), whereas categorical variables are presented as numbers and percentages. Age and tumor diameter were compared among the benign, borderline, and malignant groups using the Kruskal–Wallis test. Post-hoc pairwise comparisons were not performed because of the limited and unequal subgroup sizes; therefore, the Kruskal–Wallis results were interpreted as overall group differences. Categorical variables were compared using the chi-square test or Fisher’s exact test when expected cell counts were insufficient. A two-sided p value <0.05 was considered statistically significant.

RESULTS

A total of 67 patients were evaluated during the study period. Final pathology showed a

benign mucinous tumor in 33 patients (49.3%), a mucinous borderline tumor in 19 (28.4%), and a malignant mucinous tumor in 15 (22.4%). In the entire cohort, the median age was 43 years (range, 16-86), and the median tumor diameter was 13 cm (range, 5-50). Six patients (9.0%) had bilateral ovarian involvement.

TAH+BSO was the most frequently recorded principal surgical category (29/67, 43.3%). Cystectomy was performed in 13 patients (19.4%), USO in 18 (26.9%), and surgery including LND in seven (10.4%). Each patient was assigned to one mutually exclusive principal category; thus, procedures that included LND were counted only in the LND category. The distribution of surgical procedures by pathologic subgroup is presented in Table 1.

Table 1. Distribution of principal surgical procedures by pathologic subgroup

N, %	Cystectomy	USO	TAH+BSO	LND	Total
Benign	12 (36.4)	12 (36.4)	9 (27.3)	0 (0)	33 (100)
BOT	1 (5.3)	6 (31.6)	9 (47.4)	3 (15.8)	19 (100)
Malignant	0 (0)	0 (0)	11 (73.3)	4 (26.7)	15 (100)

USO, unilateral salpingo-oophorectomy; TAH+BSO, total abdominal hysterectomy with bilateral salpingo-oophorectomy; LND, lymph node dissection. The categories are mutually exclusive. The LND column represents comprehensive procedures that included lymph node dissection, including procedures that also involved TAH+BSO; these patients were not counted again in the TAH+BSO

Age differed significantly among the groups ($p=0.004$). Median age was 38 years (range, 21-86) in the benign group, 42 years (range, 16-69) in the borderline group, and 56 years (range, 31-71) in the malignant group. Tumor diameter also differed among the groups ($p=0.043$); median diameter was 10 cm (range, 5-25) in the benign group, 16 cm (range, 5-50) in the borderline group, and 13 cm (range, 5-40) in the malignant group.

All benign and borderline tumors were unilateral. In the malignant group, nine tumors (60.0%) were unilateral and six (40.0%) were

bilateral; the distribution of laterality differed significantly among the groups ($p<0.001$). Appendectomy was performed in 19 patients (28.4%). The appendectomy rate was 6.1% in the benign group, 47.4% in the borderline group, and 53.3% in the malignant group ($p<0.001$) (Table 2). Invasion pattern was specified in three patients with primary mucinous ovarian carcinoma: two had an expansile pattern and one had an infiltrative pattern. Procedures including LND were performed in seven patients: three with borderline tumors and four with malignant tumors. Lymph node metastasis was reported in four patients, all in the malignant group.

Table 2. Clinicopathologic characteristics by pathologic subgroup

	Laterality n, (%)		Total n, (%)	Appendectomy n, (%)		Total n, (%)	Age Median (range)	Tumor dia- meter Median (range)
	Unilate- ral	Bilate- ral		No	Yes			
Benign	33 (100)	0 (0)	33 (100)	31 (93.9)	2 (6.1)	33 (100)	38 (21-86)	10 (5-25)
BOT	19 (100)	0 (0)	19 (100)	10 (52.6)	9 (47.4)	19 (100)	42 (16-69)	16 (5-50)
Malignant	9 (60)	6 (40)	15 (100)	7 (46.7)	8 (53.3)	15 (100)	56 (31-71)	13 (5-40)
p-value			<0.001			<0.001	0.004	0.043

Continuous variables are presented as medians (minimum-maximum). p values were obtained using the chi-square or Fisher's exact test for laterality and appendectomy and the Kruskal-Wallis test for age and tumor diameter.

Among the 19 patients who underwent appendectomy, two had appendiceal metastases from primary mucinous ovarian carcinoma. These two patients had FIGO stage IVB and IIIC primary mucinous ovarian carcinoma, respectively. One patient had a primary appendiceal carcinoma with ovarian metastasis. A serrated adenoma of the appendix was identified in one patient with benign ovarian pathology. No malignancy or mucinous neoplasm was identified in the remaining appendectomy specimens.

Of the 15 malignant tumors, 10 (66.7%) were

primary mucinous ovarian carcinomas and five (33.3%) were metastases to the ovary from extraovarian primary tumors. Among the primary ovarian carcinomas, seven (70.0%) were unilateral and three (30.0%) were bilateral; among the metastatic tumors, two (40.0%) were unilateral and three (60.0%) were bilateral. Of the metastatic tumors, three were colorectal, one was gastric, and one was a primary appendiceal carcinoma with ovarian metastasis. Ovarian involvement was bilateral in all three patients with colorectal primaries and unilateral in those with gastric and appendiceal primaries (Table 3).

Table 3. Clinical characteristics of patients with ovarian metastases from extraovarian primary tumors

Krukenberg	Primary site	Age	Laterality	Tumor diameter (cm)	Surgery
1	Colon	80	Bilateral	10-10	TAH+BSO
2	Appendix	67	Unilateral	8	TAH+BSO
3	Colon	74	Bilateral	20-30	TAH+BSO
4	Stomach	53	Unilateral	40	TAH+BSO+LND
5	Colon	37	Bilateral	10-15	TAH+BSO

TAH+BSO, total abdominal hysterectomy with bilateral salpingo-oophorectomy; LND, lymph node dissection. For bilateral tumors, diameters are reported separately for each ovary.

Among the 10 patients with primary mucinous ovarian carcinoma, three had stage IA disease, three had stage IC2 disease, and one each had stage IIB, IIIB, IIIC, and IVB disease. Thus, six patients (60.0%) had stage I disease and four (40.0%) had stage II-IV disease. Eleven of the 15 patients (73.3%) in the malignant group received chemotherapy. Of the four patients who did not receive chemotherapy, three had stage IA disease; one patient died early because of a postoperative fistula.

The median follow-up duration in the malignant group was 48 months (range, 1-125). Four patients initially diagnosed with malignant tumors were lost to follow-up. The patient with a gastric primary experienced postoperative disease progression and died of COVID-19 at month 10. One patient with a borderline tumor died of infection and acute kidney injury at month 58. The patient with stage IVB primary mucinous ovarian carcinoma died in the first postoperative month because of a surgical fistula, and the patient with stage IIIC disease died at month 6 because of massive pulmonary embolism.

The patient with an appendiceal primary and peritoneal carcinomatosis experienced recurrence at month 69 and underwent secondary cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. At month 125, the patient was alive with disease and receiving treatment. Of the two patients with colonic primaries, one developed lung metastasis at month 3 and the other at month 24; both were subsequently lost to follow-up. One patient who initially underwent cystectomy for a benign mucinous cyst developed a mucinous borderline tumor at month 71 and subsequently underwent TAH+BSO.

DISCUSSION

In this series, patients with malignant mucinous tumors were older than those in the benign and borderline groups, and bilateral involvement was observed only in the malignant group. In contrast, the borderline group had the largest median tumor diameter, and tumor size did not increase linearly across the benign-borderline-malignant spectrum. The finding that one-third of malignant tumors arose from extraovarian primary sites highlights the central role of distinguishing primary from metastatic disease. All three colorectal metastases in this small series were bilateral; however, this observation is based on only three cases and should not be generalized.

Tumor size and laterality provide useful clues in distinguishing primary from metastatic disease: large unilateral tumors favor an ovarian primary, whereas bilateral or smaller tumors favor a metastatic origin. However, these features are not absolute and are not independently diagnostic (7-10). Macroscopic appearance, surface involvement, nodular growth, pattern of invasion, associated borderline areas, and clinical-radiologic evaluation for a possible extraovarian primary should be considered together. In particular, an appropriate immunohistochemical panel, including CK7 and SATB2, may complement morphologic assessment when distinguishing primary ovarian tumors from colorectal and appendiceal metastases (11).

Although primary mucinous ovarian tumors are often large and unilateral, metastatic tumors may also be large and unilateral. Algorithms based on tumor size and laterality have generally been useful across several series; however, the risk of misclassification persists, particularly for unilateral metastases larger than 10 cm

(7-10). In our limited metastatic subgroup, all three colorectal metastases were bilateral, whereas the gastric and appendiceal metastases were unilateral. Given the small numbers, these distributions are descriptive and do not establish site-specific laterality patterns. A CK7/SATB2-based panel has been shown to facilitate the distinction of colorectal and appendiceal metastases in cases with discordant morphology or clinical suspicion (11).

Fertility preservation is an important clinical objective in patients with borderline and invasive tumors. Current guidelines recommend unilateral salpingo-oophorectomy rather than cystectomy and avoidance of routine hysterectomy and lymphadenectomy in patients with early-stage mucinous borderline tumors who desire fertility (12). Although long-term outcomes of fertility-sparing surgery appear acceptable in selected patients with early-stage invasive epithelial ovarian cancer, most evidence is derived from retrospective series (13,14). In our series, 36.9% of patients in the borderline group underwent cystectomy or USO, and 15.8% underwent surgery that included LND.

Appendectomy was performed more frequently in the borderline and malignant groups in our series. Of 19 appendectomy specimens, two showed metastases from primary ovarian carcinoma, one represented a primary appendiceal carcinoma with ovarian metastasis, one contained a serrated adenoma, and the remaining specimens were benign. Retrospective series and systematic reviews have reported that the probability of detecting a primary or metastatic mucinous malignancy in a macroscopically normal appendix is very low, leaving the benefit of routine appendectomy uncertain (15-17). In contrast, a larger pathology series suggested that findings such as an abnormal-appearing

appendix, peritoneal disease, or bilaterality may be associated with appendiceal pathology (18). Only 19 patients underwent appendectomy, and the indications were neither standardized nor prospectively recorded. Accordingly, selection bias is likely, and the appendiceal findings cannot be used to estimate the diagnostic yield of routine appendectomy. Although our findings support careful intraoperative evaluation of the appendix, the retrospective data do not permit causal inference either for or against routine appendectomy.

Procedures including LND were performed in seven patients: three with borderline tumors and four with malignant tumors. Lymph node metastasis was reported in four patients, all in the malignant group. However, because LND was performed selectively and the malignant group comprised both primary ovarian carcinomas and extraovarian metastases, this observation should not be interpreted as a nodal metastasis rate for the entire cohort. Isolated nodal metastasis has been reported to be uncommon in primary mucinous ovarian carcinoma, particularly when disease appears macroscopically confined to the ovary. Schmeler et al. found no nodal metastases among 51 patients with apparently ovary-confined primary mucinous carcinoma (19). In a systematic review and meta-analysis, the rate of nodal upstaging was 0.8% among patients with presumed clinical stage I-II disease (20). Nevertheless, risk features such as infiltrative invasion, suspicious lymph nodes, or extraovarian disease may alter individualized surgical decision-making.

Invasion pattern was specified in only three patients with primary mucinous ovarian carcinoma: two had an expansile pattern and one had an infiltrative pattern. Expansile and infiltrative patterns of invasion may exhibit

different clinical behavior. The infiltrative pattern is more frequently associated with advanced stage, nodal metastasis, and recurrence, whereas the expansile pattern is usually associated with stage I disease and a more favorable prognosis (21,22). This distinction is clinically relevant in contemporary pathologic reporting. Because invasion pattern was not reassessed through central pathology review and was available for only three patients, primary carcinomas could not be compared according to this criterion.

The finding that 60.0% of primary mucinous ovarian carcinomas were stage I is consistent with the tendency of this histotype to be diagnosed at an early stage (3). In contrast, evidence regarding systemic treatment for advanced-stage disease remains limited. Hess et al. showed that response to platinum-based chemotherapy and survival may be lower in advanced mucinous ovarian carcinoma than in other epithelial histotypes (23). Gynecologic Oncology Group data and matched comparisons have likewise shown lower survival and chemosensitivity in advanced mucinous histology (24,25). The mEOC/GOG-0241 trial was terminated early after enrolling 50 patients because of slow accrual; on central pathology review, only 45% of evaluable tumors were confirmed as primary mucinous ovarian carcinoma (26). Contemporary reviews therefore recommend that surgical and systemic treatment decisions be guided by histotype-specific evidence, disease stage, and central pathology assessment (27). Although 73.3% of patients in our malignant group received chemotherapy, treatment outcomes could not be compared across regimens because of the small sample size, inclusion of metastatic tumors in the same group, and absence of chemotherapy regimen details in the source data.

A strength of this study is that it presents benign, borderline, primary malignant, and

metastatic malignant mucinous tumors within the same clinical series and evaluates surgical management, laterality, and appendiceal findings together. However, the study is retrospective and single-center, and the sample size is small. Central pathology review could not be performed, and data on invasion pattern, immunohistochemical panels, concordance between frozen and final pathology, tumor markers, and chemotherapy regimens were not systematically available. Follow-up data were incomplete, and several patients were lost to follow-up. Moreover, because the malignant group included both primary ovarian carcinomas and extraovarian metastases, group comparisons reflect a biologically heterogeneous malignant category. The observation that all colorectal metastases were bilateral was based on only three patients. In addition, appendectomy was performed in a limited and selected subset without standardized indications, restricting interpretation of the appendiceal findings. For these reasons, survival analysis was not performed, and the findings were interpreted as descriptive and exploratory.

CONCLUSION

Among mucinous tumors involving the ovary, the malignant group was associated with older age and a higher rate of bilateral involvement, whereas tumor diameter alone did not distinguish malignancy in a linear manner. The finding that one-third of malignant tumors originated from extraovarian primary sites underscores the need to investigate a gastrointestinal primary, particularly in bilateral tumors, and to integrate clinical and pathologic findings. Fertility-sparing surgery, appendectomy, and lymph node assessment should be individualized according to patient goals, macroscopic findings, and the distinction between primary and metastatic disease. Multicenter studies incorporating

central pathology review and standardized long-term follow-up are needed to provide more robust evidence.

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Author Contributions

GES: Conception and design, data acquisition, data analysis and interpretation, writing the manuscript; TT: Conception and design, data acquisition, data analysis and interpretation, critical revision of the manuscript; GS, HRT, YS, ET, MA, MG: Data acquisition; HAT: Pathological evaluation. All authors read and approved the final manuscript.

Conflict of Interests

The authors declare that they have no conflict of interest.

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Ethics Committee Approval

Ethics committee approval was not obtained for this retrospective study

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