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Preoperative and postoperative histologic grade in endometrial cancer: correlation with myometrial invasion

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ABSTRACT

Aims: Preoperative tumor histologic evaluation plays a crucial role in determining the surgical and therapeutic approach for endometrial cancer. However, discrepancies between preoperative and postoperative histopathological findings are common, potentially affecting clinical management.

Methods: This retrospective study included 287 patients diagnosed with endometrial cancer at Bakırköy Maternity and Children Training and Research Hospital. All patients underwent preoperative fractional dilatation and curettage (D&C) followed by total abdominal hysterectomy with or without lymphadenectomy. Preoperative and postoperative pathology reports were compared to assess concordance in tumor grade and histological subtype. The correlation between grade agreement and myometrial invasion was also analyzed.

Results: The histologic type changed in 17.6% of cases between preoperative curettage and postoperative hysterectomy. The tumor grade was upgraded in 50.7% of grade 1 cases and 11.6% of grade 2 cases. The overall concordance between the preoperative and postoperative tumor grading was weak (kappa=0.292, p<0.001). The grade agreement was higher in cases with deep myometrial invasion (kappa=0.32) than in those with superficial invasion (kappa=0.24).

Conclusion: The substantial rate of discordance between preoperative and postoperative histologic findings highlights the limitations of D&C in accurately predicting tumor grade. Given the impact of tumor grading on surgical and adjuvant treatment decisions, multimodal preoperative assessment integrating imaging and molecular profiling may improve diagnostic accuracy and optimize treatment strategies for endometrial cancer.

Keywords: Endometrial cancer, tumor grading, histologic concordance, myometrial invasion, dilatation and curettage

INTRODUCTION

Endometrial cancer is the most common gynecologic malignancy in developed countries, with its incidence rising due to increasing life expectancy, obesity, and metabolic risk factors.[1] While it predominantly affects postmenopausal women, it can also occur in premenopausal patients with hereditary syndromes or hormone-related factors.[2] Effective management relies on preoperative histological assessment to guide treatment decisions and estimate prognosis.[3]

Preoperative evaluation, typically performed via endometrial biopsy or dilatation and curettage (D&C), helps differentiate endometrial carcinoma from benign conditions and identify aggressive histological subtypes. Endometrioid adenocarcinoma generally has a favorable prognosis, whereas non-endometrioid subtypes are associated with higher recurrence rates and poorer outcomes.[4]

Tumor grade, which reflects the differentiation status of cancer cells, is a key prognostic determinant of endometrial cancer.[5] High-grade tumors (grade 3) are more likely to exhibit deep myometrial invasion, lymphovascular space invasion, and metastasis, which necessitates aggressive surgical staging and adjuvant therapy. Accurate preoperative tumor grading is vital, as it guides decisions regarding the extent of surgery, including the necessity for lymphadenectomy and the choice between minimally invasive and open surgical techniques. In cases of high-grade disease, adjuvant chemotherapy and radiotherapy are frequently required even when other high-risk features are absent.[4,6]

This study systematically compares preoperative and postoperative tumor histology and grade in endometrial cancer patients. While previous research has suggested a correlation between tumor grade and myometrial invasion

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depth[8], the accuracy of preoperative grading in predicting myometrial invasion remains underexplored. By assessing the reliability of preoperative evaluations and identifying factors contributing to discrepancies, we aim to enhance diagnostic precision and optimize management strategies for endometrial cancer.

METHODS

This retrospective study was conducted as a graduation research project before 2020 in obstetrics and gynecology at Bakırköy Women and Children Training and Research Hospital (Thesis No: 10635735, Year: 2009). The study protocol was approved by the hospital's thesis approval committee and all research procedures were performed in accordance with the Declaration of Helsinki.

A total of 287 patients diagnosed with endometrial cancer through histopathological examination of hysterectomy specimens at the Gynecologic Oncology Clinic of Bakirköy Women and Children Training and Research Hospital were evaluated retrospectively. The study population included patients who had undergone preoperative fractional dilatation and curettage (D&C) for suspected endometrial pathology, received a confirmed postoperative diagnosis of endometrial cancer, and subsequently underwent hysterectomy with or without lymphadenectomy. Patients were excluded if they lacked a preoperative histopathological evaluation or had received preoperative chemotherapy or radiotherapy.

All patients underwent D&C as a diagnostic procedure before surgery. The surgical approach consisted of total abdominal hysterectomy (TAH) with or without bilateral salpingo-oophorectomy (BSO). When indicated, pelvic and/or para-aortic lymph node dissection was performed in accordance with the FIGO staging guidelines and based on the intraoperative findings. All surgeries were performed using an open surgical approach. At the time of this study, sentinel lymph node mapping had not yet been implemented as a standard procedure in our clinical practice for endometrial cancer management. Instead, systematic lymphadenectomy was performed based on preoperative and intraoperative risk assessments.

Pathological assessments were conducted in the hospital's pathology laboratory, where D&C and hysterectomy specimens were examined to determine the tumor histology, grade, and staging. Endometrial cancers were staged according to the FIGO staging system[10], and key clinicopathological variables were recorded, including patient demographics (age, menopausal status, comorbidities such as hypertension and diabetes mellitus), histopathologic subtype and grade, depth of myometrial invasion, presence of lymphovascular space invasion (LVSI), and lymph node involvement in cases where lymphadenectomy was performed. The results of preoperative (D&C) and postoperative (hysterectomy) pathology evaluations were systematically compared to assess histologic concordance and grade agreement, and the relationship between grade concordance and myometrial invasion depth was analyzed to identify potential correlations.

Statistical Analysis

All statistical analyses were conducted using SPSS for Windows (version 15.0). Descriptive statistics were used to summarize the data, including means, standard deviations, and frequency distributions. Intergroup differences were assessed using one-way analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical data. The weighted kappa test was employed to evaluate the degree of agreement between the preoperative and postoperative tumor grades, while multivariate logistic regression was performed to identify independent predictors of grade discordance. Statistical significance was set at $p<0.05$ analyses.

RESULTS

This study included 287 patients diagnosed with endometrial cancer. The mean age was 56.4 years (range: 33–80 years), with 15 patients (5.3%) aged ≤40 years. Of the total cohort, 85 patients (29.6%) were of reproductive age and 202 patients (70.4%) were postmenopausal. The most frequently reported clinical complaint was postmenopausal vaginal bleeding, observed in 73.1% of the cases.

Obesity (BMI >30 kg/m^2) was noted in 152 patients (53%), while 8 patients (2.8%) had a first-degree relative with a history of endometrial cancer. Hypertension was present in 93 patients (32.4%), diabetes in 11 patients (3.8%), and both conditions were documented in 33 patients (11.5%). Two patients (0.7%) had a history of tamoxifen use for breast cancer. The mean gravida and parity were 4.14 (range: 0–14) and 3.32 (range: 0–11), respectively. The median interval between endometrial sampling and surgical intervention was 25.38 days (range: 5–189 days).

Preoperative histopathological analysis of D&C samples identified endometrioid adenocarcinoma as the most frequent diagnosis in 229 patients (79.9%). Other notable diagnoses included serous papillary carcinoma in 20 cases (7.0%), atypical complex hyperplasia in 10 cases (3.5%), and various rare histological subtypes (Table 1). In 262 cases (91.3%), the preoperative diagnosis was confirmed as endometrial cancer, although 12 pathology reports did not specify tumor grade.

Tablo 1. Distribution of preoperative histopathologic diagnoses based on curettage material in the study population

Histopathologic diagnosis	n	%
Endometrioid adenocancer	229	79.9
Serous papillary carcinoma	20	7.0
Atypical complex hyperplasia	10	3.5
Clear cell carcinoma	8	2.8
Mucinous carcinoma	5	1.7
Endocervical adenocarcinoma	4	1.4
Atypical glandular hyperplasia	3	1.0
Simple atypical hyperplasia	2	0.7
Malignant mixed Müllerian tumor	2	0.7
Insufficient material	2	0.7
Atrophic endometrium	1	0.3
Endometrial polyp	1	0.3

Regarding surgical procedures, 20 patients (7%) underwent TAH+BSO alone, 131 (45.6%) underwent TAH + BSO + pelvic lymph node dissection (PLND), and 136 (47.4%) underwent TAH+BSO+Pelvic and para-aortic lymph node dissection (PPALND). Intraoperative frozen sections were performed in 18 patients (6.3%). Patients with grade 3 tumors in the preoperative D&C material were significantly more likely to undergo TAH+BSO+PPALND than other patients (p<0.01) (Table 2).

Postoperative histopathological examination of hysterectomy specimens revealed endometrioid adenocarcinoma as the predominant tumor type in 257 cases (89.6%), followed by serous papillary carcinoma in 26 cases (9.1%), clear cell carcinoma in one case (0.3%), and mucinous carcinoma in three cases (1.0%). The diagnosis of atypical endometrial hyperplasia in 15 cases was revised to endometrioid adenocarcinoma on postoperative examination. In total, 46 cases (17.6%) showed discrepancies between the preoperative and postoperative histological diagnoses (Table 3).

Tumor grade assessment showed an increase in grade in 69 patients (50.7%) initially diagnosed with grade 1 endometrial cancer and in 10 patients (11.6%) diagnosed with grade 2 endometrial cancer. The preoperative and postoperative tumor grade concordance rates were 49.3%, 69.8% for grade 2, and 50.0% for grade 1, 2, and 3 tumors, respectively. The overall agreement between the D&C and hysterectomy grades was weak but statistically significant (kappa=0.292, p=0.000) (Table 4).

Table 4. Comparison of tumor grade in curettage material with hysterectomy material

	Hysterectomy					
	Grade 1		Grade 2		Grade 3	
D&C	n	%	n	%	n	%
Grade 1	67	49.3	63	46.3	6	4.4
Grade 2	16	18.6	60	69.8	10	11.6
Grade 3	2	7.1	12	42.9	14	50.0

D&C: Dilatation curettage

Regarding myometrial invasion, 169 cases (58.9%) exhibited less than half myometrial invasion, 89 cases (31.0%) exhibited more than half invasion, and 29 cases (10.1%) showed no invasion.

Analysis of tumor grade concordance in relation to myometrial invasion demonstrated a weak but significant correlation in cases with less than half myometrial invasion (kappa=0.24, p=0.000). In cases with more than half myometrial invasion, the grade concordance was slightly improved (kappa=0.32). However, in cases without myometrial invasion, no significant correlation between the preoperative and postoperative tumor grades was observed (kappa=0.176, p=0.293) (Table 5).

DISCUSSION

This study aimed to evaluate the concordance between preoperative and postoperative tumor histology and grade in patients with endometrial cancer as well as its correlation with myometrial invasion. Our findings revealed a notable

Table 2. Operation performed according to the grade of the tumor in the curettage material

	Grade 1		Grade 2		Grade 3			
Surgical procedure	**n=136**	**%**	**n=86**	**%**	**n=28**	**%**	**Chi-square**	**p**
TAH+BSO	5	3.7	4	4.7	2	7.1		
TAH+BSO+PLND	79	58.1	31	36.0	7	25,0		
TAH+BSO+PPALN	52	38.2	51	59.3	19	67.9	16.187	.003

TAH+ BSO : Total abdominal hysterectomy and bilateral salpingo-oophorectomy, TAH+BSO+PLND: Total abdominal hysterectomy and bilateral salpingo-oophorectomy+pelvic lymph node dissection, TAH+BSO+PPALN: Total abdominal hysterectomy and bilateral salpingo-oophorectomy+ pelvic and paraaortic lymph node dissection

Table 3. Comparison of preoperative and postoperative histopathologic diagnosis

		Postoperative histopathologic diagnosis			
		Endometrioid adenocancer	**Serous papillary carcinoma**	**Clear cell carcinoma**	**Mucinous carcinoma**
Preoperative histopathologic diagnosis	Endometrioid adenocancer	210	15	1	3
	Serous papillary carcinoma	14	6	0	0
	Clear cell carcinoma	7	1	0	0
	Mucinous carcinoma	5	0	0	0
	Endocervical adenocarcinoma	2	2	0	0
	Simple atypical hyperplasia	2	0	0	0
	Atypical glandular hyperplasia	3	0	0	0
	Atypical complex hyperplasia	10	0	0	0
	Malignant mixed Müllerian tumor	1	1	0	0
	Insufficient material	1	1	0	0
	Endometrial polyp	1	0	0	0
	Atrophic endometrium	1	0	0	0

Table 5. A comparison of tumor grade in curettage material with hysterectomy material according to myometrial invasion

Myometrial invasion	D&C grade	Hysterectomy grade	n	%	Kappa	p-value
Less than half (<50%)	Grade 1	Grade 1	41	49.4	0.24	0.000
	Grade 1	Grade 2	38	45.8	0.24	0.000
	Grade 1	Grade 3	4	4.8	0.24	0.000
	Grade 2	Grade 1	12	21.4	0.24	0.000
	Grade 2	Grade 2	37	66.1	0.24	0.000
	Grade 2	Grade 3	7	12.5	0.24	0.000
	Grade 3	Grade 1	2	15.4	0.24	0.000
	Grade 3	Grade 2	6	46.2	0.24	0.000
	Grade 3	Grade 3	5	38.5	0.24	0.000
More than half (>50%)	Grade 1	Grade 1	9	28.1	0.32	0.000
	Grade 1	Grade 2	21	65.6	0.32	0.000
	Grade 1	Grade 3	2	6.3	0.32	0.000
	Grade 2	Grade 1	0	0	0.32	0.000
	Grade 2	Grade 2	22	88.0	0.32	0.000
	Grade 2	Grade 3	3	12.0	0.32	0.000
No invasion	Grade 1	Grade 1	17	81.0	0.176	0.293
	Grade 1	Grade 2	4	19.0	0.176	0.293
	Grade 1	Grade 3	0	0	0.176	0.293
	Grade 2	Grade 1	4	80.0	0.176	0.293
	Grade 2	Grade 2	1	20.0	0.176	0.293
	Grade 2	Grade 3	0	0	0.176	0.293
	Grade 3	Grade 1	0	0	0.176	0.293
	Grade 3	Grade 2	0	0	0.176	0.293
	Grade 3	Grade 3	1	1	0.176	0.293

D&C: Dilatation curettage

discrepancy between preoperative curettage and final hysterectomy pathology, particularly in cases of tumor grade and histologic subtype. These results align with those of previous studies that emphasized the limitations of preoperative sampling in accurately predicting the final tumor characteristics.[10,11]

Our study found that in 17.6% of cases, the histologic type changed between preoperative curettage and postoperative hysterectomy, indicating moderate inconsistency. This is in line with the prior literature, which reported discordance rates ranging from 10% to 30%.[7] Similarly, tumor grade upgrading was observed in 50.7% of grade 1 cases and 11.6% of grade 2 cases, reinforcing previous reports of grade misclassification due to the limited sampling area for curettage.[11]

A considerable proportion of tumors were found to have a higher grade on final pathology than that initially indicated by curettage specimens. The limitations of preoperative biopsy in capturing high-grade tumor foci have been previously highlighted by Vrede et al.[12], who found that increasing the amount of preoperative endometrial tissue sampled did not significantly improve concordance with the final tumor classification. This finding underscores the inherent challenges in accurately assessing tumor grade preoperatively, and suggests that factors beyond tissue volume, such as sampling bias and tumor heterogeneity, contribute to discordance.

Our weighted kappa value (0.292, p<0.001) suggests a weak agreement between the preoperative and postoperative grading, which is consistent with prior studies.[10]

The depth of myometrial invasion emerged as a crucial factor influencing grade concordance, with a higher concordance observed in tumors with deep myometrial invasion (kappa=0.32) than in those with superficial invasion (kappa=0.24). These findings underscore the importance of incorporating imaging modalities, such as magnetic resonance imaging (MRI), into preoperative assessments to improve accuracy in predicting tumor behavior.[11]

An important clinical implication of our findings is the potential for both overtreatment and undertreatment based on preoperative pathology alone. In our study, grade 3 tumors identified in curettage material were significantly associated with more extensive surgical interventions (p<0.01), aligning with the standard practice of performing pelvic and para-aortic lymphadenectomy in high-grade disease. However, in some cases where tumors were upgraded postoperatively, the initial surgical approach may have been insufficient, reinforcing the necessity of comprehensive preoperative assessment to optimize surgical planning.[11]

Compared with previous reports, our study supports the idea that D&C, despite being a widely used diagnostic tool, has inherent limitations in grading accuracy.[10]

Alternative approaches, such as hysteroscopic-guided biopsy and molecular profiling, may offer greater precision in predicting the final tumor characteristics and should be explored in future research.[11]

Previous studies have explored various factors influencing grading discrepancies, including tumor heterogeneity, sampling limitations, and interobserver variabilit. Recent research has also suggested that obesity-related factors, including body-mass index (BMI), may play a role in tumor grading variability. A higher BMI has been associated with differences in the tumor microenvironment and sampling limitations due to increased endometrial thickness, potentially contributing to grading discordance.[13] However our study did not include BMI as a variable and instead focused on histologic subtype and depth of myometrial invasion as key determinants of grading discrepancies.

Limitations

Our study has several strengths, including a large sample size (n=287) and systematic comparison of preoperative and postoperative histologic findings. However, this study has some limitations. First, its retrospective design introduced a potential selection bias. Second, the lack of routine use of advanced imaging techniques (such as MRI) may have influenced the assessment of myometrial invasion. Finally, interobserver variability in histological grading remains an inherent challenge in pathology.

CONCLUSION

Our findings highlight the substantial rate of discordance between preoperative and postoperative tumor histology and grade, reinforcing the need for cautious interpretation of preoperative biopsy results. Given the implications of tumor grade on surgical decision-making and adjuvant therapy selection, multimodal preoperative assessment—including advanced imaging and molecular profiling—should be considered to improve diagnostic precision. Future prospective studies integrating novel biomarkers and imaging modalities could enhance preoperative risk stratification and lead to more tailored treatment approaches in endometrial cancer.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study protocol was approved by the thesis approval committee of Bakırköy Women and Children Training and Research Hospital (Thesis No: 10635735, Year: 2009).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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