Journal of
Controversies in Obstetrics & Gynecology and Pediatrics

Original Article

DOI: 10.51271/JCOGP-0040

Prediction of preoperative and postoperative FIGO grade concordance in patients with endometrial cancer

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Cite this article: Öztürk UK, Akis S, Keleş E, et al. Prediction of preoperative and postoperative FIGO grade concordance in patients with endometrial cancer. *J Controv Obstetr Gynecol Ped.* 2025;3(1):9-13.

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Received: 19/09/2024 • **Accepted**: 17/10/2024 • **Published**: 09/01/2025

ABSTRACT

Aims: To determine the factors leading to upgrading in the final pathology result in cases with endometrial cancer.

Methods: We retrospectively analyzed the records of patients with endometrioid endometrial adenocarcinoma to evaluate the concordance between FIGO grade in preoperative endometrial sampling and postoperative final pathology grade. As a result of endometrial sampling, FIGO grade was reported as up-grading if it was lower than final pathology report, and as down-grading, if it was higher than final pathology report. The effects of tumor size, degree of myometrial invasion, lymphovascular invasion, FIGO stage, tumor localization, and additional uterine/endometrial pathologies on up-grading were evaluated.

Results: A total of 151 patients remained eligible for final analysis. The overall down-grading percentage was 8.6%, and the up-grading percentage was 25.2%. In preoperative endometrial sampling, the up-grading rates for FIGO grades 1 and 2 were analyzed as 30.5% and 20.0%. The concordance rates between preoperative endometrial sampling results and postoperative definitive pathology results were calculated as 69.5%, 55.6%, and 81.8% for FIGO grade 1,2,3, respectively.It was found that patients with more than 50% myometrial invasion (p=0.048), and those with advanced FIGO stages were more up-grading than those with earlier stages (p=0.005).

Conclusion: There is a substantial difference between the grade of preoperative endometrial sampling material and the postoperative final pathology grade in patients with endometrioid-type endometrial cancer.In the preoperative evaluation, assessment of additional markers in combination with magnetic resonance imaging may reduce misconceptions in the diagnosis, given that 25% of the patients were up-grading.

Keywords: Endometrial adenocarcinoma, endometrial sampling, FIGO grade, preoperative pathology, up-grading

INTRODUCTION

Endometrial cancer is the most prevalent malignancy of the reproductive system, accounting for 417.367 new cases and 97.370 deaths in 2020 in the World.[1] The most common histopathological type is endometrioid adenocarcinoma.[2] The management of this disease begins with the endometrial sampling result before the operation. Patients with early-stage endometrioid adenocarcinoma treated with total hysterectomy and bilateral salpingo-oophorectomy, while other patients undergo comprehensive surgical staging. Afterward, the stage of the disease is determined as a result of the histopathological evaluation of the surgical sample obtained, and the patients are evaluated in terms of the need for adjuvant treatment.[3]

The most common system used to grade endometrioid endometrial cancers is the International Federation of Gynecology and Obstetrics (FIGO) ternary grading system.[4] Ascending grade is associated with deep myometrial invasion and presence of lymph node metastasis. Furthermore, survival is lower in grade 3 tumors.[5]

Recent studies have shown that tumor grade in the preoperative endometrial sampling and tumor grade in the final histopathological result may differ.[6] Therefore, managing the operation based on the preoperative pathology may lead to incomplete surgery, as well as an increase in the morbidity of the patient with unnecessary lymphadenectomy.[7] The purpose

of the study to determine the factors leading to "up-grading" by comparing the tumor grade before and after the operation.

METHODS

This was a retrospective study conducted on 276 patients with pure endometrioid endometrial adenocarcinoma who were admitted to the gynecological oncology department at a tertiary healthcare center and evaluated for FIGO grade of preoperative endometrial sampling and postoperative final pathology grade between 2014 and 2020. This study was approved by the Research Ethics Committee of the Zeynep Kamil Women's and Children's Disease Training and Research Hospital (Date: 07.04.2021, Decision No: 87/2021). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The pathological tissues of all patients were obtained by dilatation and curettage (D&C) biopsy and examined by specialist gynecopathologists. FIGO grading was used to assess tumor grade. If the FIGO grade in the endometrial sampling report is lower than final histological report, it was recorded as up-grading; if the FIGO grade in the endometrial sampling report is higher than final histological report, it was recorded as down-grading. The possible effect of some factors on the up-grading was investigated including, maximum tumor diameter (MTD), degree of myometrial invasion (MI [≤1/2, >1/2]), lymphovascular invasion (LVSI), FIGO stage, tumor localization (fundus, corpus, lower segment, entire endometrium), and additional uterine/endometrial pathologies (endometrial polyp, adenomyosis, and leiomyomas). Lymph node dissection requirement was designed according to Mayo criteria. It was determined that tumor size ≤2 cm, myometrial invasion ≤1/2, and conditions that meet low-grade endometrioid endometrial cancer characteristics do not require lymph node dissection.[8] When staging was required, patients treated with adequate lymph node dissection were included, and lymph node dissection regarded as satisfactory when at least 15 pelvic and/or paraaortic lymph nodes removed.[9]One hundred twenty-four patients without FIGO grading on pre-operative endometrial sampling slides, and one patient with inadequate surgical staging were excluded. Flow diagram of the studyis shown in **Figure 1**.

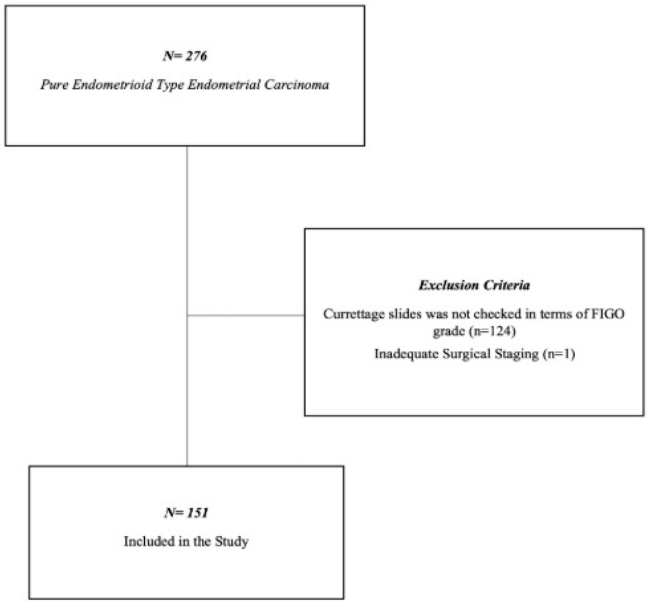

Figure 1. Flowchart of the study

RESULTS

A total of 151 patients were included in the study. The mean age of patients was 57.3 ± 0.8 years. The distribution ratio of FIGO grade 1 in preoperative endometrial sampling (62.9%) and final pathology (51.0%) was higher than FIGO grades 2 and 3. All detailed pathology-related data are given in **Table 1**.

Table 1. Pathology-related characteristics (n=151)

	n (%)
Preoperative endometrial sampling FIGO grade	
1	95 (62.9)
2	45 (29.8)
3	11 (7.3)
Final FIGO grade	
1	77 (51.0)
2	55 (36.4)
3	19 (12.6)
MI	
≤½	103 (68.2)
>½	48 (31.8)
LVSI	
No	98 (64.9)
Yes	53 (35.1)
FIGO stage	
1	125 (82.8)
2	4 (2.7)
3	16 (10.6)
4	6 (3.9)
Tumor localization	
Fundus	32 (21.2)
Corpus	78 (51.7)
Lower segment	9 (5.9)
Entire endemetrium	32 (21.2)
Additional uterine pathology	
None	93 (61.6)
Polyp	11 (7.3)
Adenomyozis	20 (13.2)
Myoma uteri	27 (17.9)

n: Number, %: Percent, PC: Probe curettage, MI: Myometrial invasion, LVSI: Lymphovascular space invasion

The overall down-grading percentage was 8.6%, and the up-grading percentage was 25.2%. According to the results of preoperative endometrial sampling, the up-grading rates for FIGO grades 1 and 2 were analyzed as 30.5% and 20.0%, respectively. The concordance rates between preoperative endometrial sampling results and postoperative definitive pathology results were calculated as 69.5%, 55.6%, and 81.8% for FIGO grade 1,2,3, respectively (**Figure 2**). There was no statistical difference between these rates (p=0.140). All detailed down/up-grading and concordance percentages are given in **Table 2**.

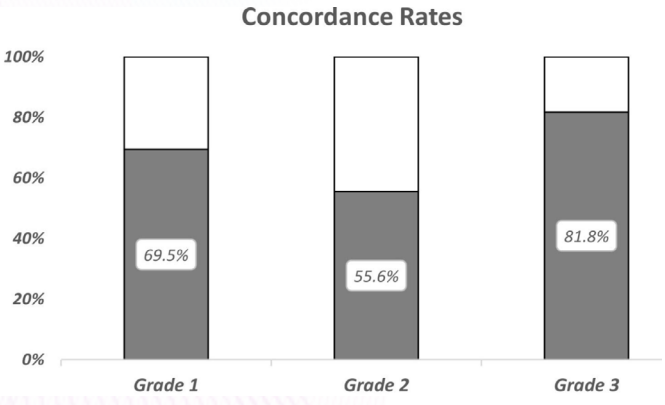

Figure 2. Concordance rates between preoperative endometrial sampling results and postoperative definitive pathology resultsfor FIGO grades

Table 2. Detailed up-staging and concordance analysis according to probe curettage and final pathology FIGO grade data (n= 151)

		Final FIGO grade			Down-grading (%)	Up-grading (%)	Concordance (%) (p= 0.140)*	Total
		1	2	3				
Pre Op E.S FIGO grade	1	**66**	28	1	-	30.5	69.5	95
	2	11	**25**	9	24.4	20.0	55.6	45
	3	-	2	**9**	18.2	-	81.8	11
Total		77	55	19	**8.6**	**25.2**	**66.2**	151

Pre Op E.S: Preoperative endometrial sampling
-Down-grading was defined as FIGO grade on probe curettage more than FIGO grade on final pathology.
-Up-grading was defined as FIGO grade on probe curettage less than FIGO grade on final pathology.
* Statistical analysis of concordance rates for preoperative FIGO grade 1,2,3.

When possible factors that might have an effect on up-grading were analyzed; 35.4% of patients with more than 50% myometrial invasion (p=0.048) and patients with advanced FIGO stage had more up-grading than those with earlier stages (p=0.005). Analysis of factors associated with up-grading are presented in **Table 3**.

DISCUSSION

Management of endometrial canceris usually made according to the results of the preoperative endometrial sampling. However, the question of how compatible these endometrial sampling results are with the final pathology is controversial.[10] Therefore, the present study aimed to evaluate the concordance between preoperative and final histological pathologies in patients with endometrial cancer.

Francis et al.[10] reported that the concordance rates of preoperative endometrial sampling with final pathology were 73%, 52%, and 53% for grades 1, 2, and 3, respectively. Petersen et al.[8] foundthese rates as 60%, 71%, and 84% for grade 1, grade 2, and grade 3, respectively.Wang et al.[9] showed in their study that with 52 women, concordancy rates were 20%,61.5%, and 77.8% for grade 1, 2, and 3, respectively. In our study, similar to the studies of Francis et al.[10] the concordance rate was 69.5% in grade 1 tumors and 55.6% in grade 2 tumors. The percentage of concordancy in grade 3 tumors was 81.8%, similar to the studies of Petersen[8] and Wang.[9]

There are publications in the literature recommending surgical staging for all endometrial cancer patients, including those diagnosed with preoperative grade 1 endometrial cancer.[11,12] Although it is known that extra-uterine spread is low in grade 1 disease, Francis et al.[10] drew attention to the importance of the upgrading percentage, which they found as 27% in grade 1 patients. They stated that it is controversial to make a surgical decision based on this solely in patients with preoperative grade 1. In our study, an upgrading rate of 30.5% in preoperative grade 1 patients supports this view.

The study by Eltabbakh et al.[13] indicated that approximately 30% of the patients with grade 1 endometrial adenocarcinoma as a result of preoperative endometrial sampling were found to be grade 2 or grade 3 in the hysterectomy specimen, and advanced surgical stage (stage III or IV) was found in 12.6%. Similarly, in our study, 30.5% up-grading was found in grade 1 tumors and 20% in grade 2 tumors. Considering that our total up-grading rate is 25.2%, the grade elevation

Table 3. Analysis of the factors in terms of up-grading (n= 151)

	FIGO grade*		
	No-upgrading (n=113)	Up-grading (n=38)	p value
Age	57.8±0.9	56.1±1.7	0.346[a]
Tumor size	38.2±2.5	44.5±4.2	0.203[a]
MI			**0.048**[b]
≤ ½	82 (79.6)	21 (20.4)	
> ½	31 (64.6)	17 (35.4)	
LVSI			0.067[b]
No	78 (79.6)	20 (20.4)	
Yes	35 (66.0)	18 (34.0)	
FIGO stage			**0.005**[c]
1	99 (79.2)	26 (20.8)	
2	4 (100.0)	0 (0.0)	
3	8 (50.0)	8 (50.0)	
4	2 (33.3)	4 (66.7)	
Tumor localization			0.300[b]
Fundus	22 (68.8)	10 (31.3)	
Corpus	58 (74.4)	20 (25.6)	
Lower segment	9 (100.0)	0 (0.0)	
Entire endometrium	24 (75.0)	8 (25.0)	
Additional uterine pathology			0.868[b]
None	68 (73.3)	25 (26.7)	
Endometrial polyp	9 (81.8)	2 (18.2)	
Adenomyozis	16 (80.0)	4 (20.0)	
Myoma uteri	20 (74.1)	7 (25.9)	

MI: Myometrial invasion, LVSI: Lymphovascular space invasion, * Upgrading was defined as FIGO grade on probe curettage less than FIGO grade on final pathology. a Statistical analysis were based on the independent sample T Test. b Statistical analysis were based on the Pearson Chi-Square test. c Statistical analysis were based on the Fisher Exact test

seen in one out of every four patients suggests that only preoperative endometrial sampling may not be sufficient for the operation management in patients planned for endometrial cancer surgery. Additionally, the advanced surgical stage (Stage III or IV) draws attention in 31.5% of our up-grading patients. This finding shows that patients with preoperative endometrial sampling results of grade 1 and 2 may have an advanced stage after surgical staging, and the need for adjuvant treatment may arise.

There are publications in the literature showing that increasing grade in endometrial cancers is associated with increased myometrial invasion, positive lymph node count, and extra-uterine disease spread.[14] Prior studies showed that deep myometrial invasion was associated with an increased risk of recurrence of disease.[15] In our study, the fact that patients with more than 50% myometrial invasion and those with advanced FIGO stage showed higher up-grading compared to the early stages, showing the importance of the role of grade in preoperative pathology in determining the final pathology. Because the patients' need for adjuvant treatment is carried out according to the final pathology.

There are publications stating that other factors besides preoperative pathology are important for the surgical staging decision in endometrial cancer. Recently, new methods have been proposed to determine tumor grade in the preoperative period using magnetic resonance imaging.[16] Preoperative magnetic resonance imaging has a sensitivity of approximately 84% in detecting deep myometrial invasion.[17] There are publications showing that high preoperative CA125 levels can predict lymph node metastases with high accuracy.[18] In addition, a prediction model using serum CA125 has recently been published.[19] Intraoperative frozen applications provide information in the confidence interval of 67% to 91% for myometrial invasion, and in the confidence interval of 40% to 100% in determining the final pathology.[20,21] Considering these rates, it is controversial how much to trust the intraoperative frozen result. Moreover, frozen applications cannot be performed in every center. Considering these situations, the importance of a strong preoperative evaluation emerges.

Limitations

A limitation of this study was that it was a retrospective, single-centerstudy. The information on whether the pathologists evaluating the hysterectomy material knew the preoperative endometrial sampling results were not included in our study. On the other hand, the main strengths are the high number of patients, and evaluation of the cases by expert gynecological oncologistsand pathologists.

CONCLUSION

There is a substantial difference between the grade of the preoperative endometrial sampling material and the postoperative final pathology grade in patients with endometrioid-type endometrial cancer. Considering that 25% of the patients are upgrading, it is aimed to reduce the misconceptions in the diagnosis with the combined evaluation of other markers and magnetic resonance imaging results in the preoperative evaluation. There is a need for prospective randomized controlled studies in which many preoperative markers are evaluated together in this regard.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Research Ethics Committee of the Zeynep Kamil Women's and Children's Disease Training and Research Hospital (Date: 07.04.2021, Decision No: 87/2021).

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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Associate Professor Ugur Kemal Öztürk is a distinguished expert in gynecologic oncology, particularly in the molecular profiling of endometrial cancer. He earned his medical degree from Ankara University Faculty of Medicine and completed his PhD at Zeynep Kamil Women's and Children Training and Research Hospital. His research focuses on the molecular mechanisms underlying endometrial cancer, aiming to identify biomarkers for early detection and targeted therapies. Dr. Öztürk has published extensively in peer-reviewed journals, contributing valuable insights into the genetic and epigenetic alterations associated with endometrial malignancies. He is actively involved in clinical practice, translating his research findings into improved patient management strategies. As a dedicated educator, he mentors future medical professionals, promoting a thorough understanding of both the clinical and research aspects of gynecologic oncology. His contributions have solidified his reputation as a leading figure in the field.