*Sergiusz Demczuk, Wojciech Wierzchowski, Wojciech Szczepański, Grzegorz Dyduch,
Jacek Czopek, Jerzy Stachura*

# The Comparison of the Agreement in Determining the Histological Grade of Uterine Endometrial Endometrioid Carcinoma, Using the Three-Grade FIGO Classification and the Two-Grade System

Department of Clinical and Experimental Pathomorphology, Collegium Medicum, Jagiellonian University, Kraków

**The objective of the investigation was to compare the degree of interobserver agreement in determining the histological grade of uterine endometrial endometrioid adenocarcinoma using the criteria proposed by the three-grade FIGO classification (1988) and the new, two-grade system proposed by Lax et al. (2000). In the FIGO system, the assessment is focused on the amount of solid, non-squamous growth pattern and the additional feature is the presence of the so-called "notable nuclear atypia" (nuclear grade), with the latter criterion not having been precisely defined. In the two-grade system, the evaluation concentrates on the amount of the solid component, regardless of its character, type of neoplastic growth pattern (expansive or diffusely infiltrating) and the presence of necrosis within the tumor mass. A total of 133 cases of uterine endometrial carcinoma were evaluated, determining the stage according to the FIGO classification and assessing the histological grade based on the criteria presented by the above two systems. All the cases were separately examined by 5 pathologists with varying degrees of experience in gynecological pathology. A higher degree of interobserver agreement was demonstrated when the two-grade system was employed as compared to the FIGO system, regardless whether the material was evaluated by experienced pathologists (FIGO k - 0.64 - 0.71, binary - 0.91 - 0.92), or by individuals with little experience in gynecological pathology (FIGO k - 0.23 - 0.48, binary - 0.21 - 0.57). The data point to the superior character of the two-grade system as to the agreement of the histological grade assessment, but also suggest a considerable effect of experience on the precision of the evaluation.**

## Introduction

Endometrial carcinoma belongs to the most common malignancies in women. In the majority of cases, the neoplasm is histologically diagnosed as the endometrioid type and its stage at the time of diagnosis is determined as I. Some histological properties of endometrial carcinoma have a prognostic value, as they are associated with the risk of metastases, recurrence and the length of survival. Such prognostic factors include the histological type, grade, depth of myometrium infiltration and lymph-vascular space involvement (LVSI) [2].

At present the most commonly used classification system for grading endometrial carcinoma is that proposed by the International Federation of Gynecology and Obstetrics (FIGO) [1]. The system is based on the assessment of the percentage of the tumor mass that is occupied by a solid, other than squamous component. In addition, the presence of "notable nuclear atypia inappropriate for the architectural grade" results in classifying the neoplasm one grade higher. The failure to achieve a high reproducibility of results when employing the above system, as well as the lack of precisely defined criteria for determining the nuclear grade necessitate a search for a new method for defining endometrial carcinoma grade that would eliminate the drawbacks of the presently employed classifications.

Taylor et al. suggested the reduction of the FIGO system to a two-grade classification through eliminating the intermediate grade, but using similar criteria in the evaluation. The proposed discriminating criterion was the presence of a solid, other than squamous component occupying 20% of the tumor mass [6]. Other authors attempted to improve the FIGO system through a more precise definition of the criteria used in assessing the nuclear grade [4, 5, 7]. In some reports attempts were made at evaluating the interobserver agreement in assessing the histological grade of endometrial carcinoma. The resultant kappa value equaled 0.61 [4], 0.526 - 0.648 [6] or 0.55 [3]. Investigators who evaluated the agreement in assessing the nuclear grade arrived at kappa values ranging from 0.22 [3] to 0.56 [4].

As if follows from the above quoted results, the degree of interobserver agreement among pathologists using the FIGO system in assessing the grade of endometrial adeno-

carcinoma was relatively low; the agreement was very low when nuclear grade was assessed.

## Material and Methods

A total of 133 cases of endometrial carcinoma were selected from the surgical material of the Department of Gynecology and Oncology, Collegium Medicum, Jagiellonian University, Kraków, in the years 1994 - 2000. Serous papillary and clear cell endometrial carcinomas were excluded from the investigation.

The assessment of histological grade was performed by five pathologists (three experienced and two with little experience in gynecological pathology). While evaluating the cases, the investigators were not supplied with information on clinical data and stage of the disease. The assessment of histological grade was based on the FIGO classification and the two-grade system. Representative slides were selected (2.3 slides per case, on the average) and evaluated basing on the following criteria.

The FIGO classification includes three grades:

G I     the percentage of solid growth (other than squamous) in the tumor mass up to 5%;

G II    the percentage of solid growth accounts for 5% to 50%;

G III   the percentage of solid growth above 50%.

In addition, the presence of "notable nuclear atypia" results in classifying the tumor to a higher grade [1].

To evaluate the nuclear atypia (nuclear grade) the authors adopted the criteria developed by Zaino et al.:

Grade 1:  identical nuclei, round or oval, with evenly dispersed chromatin and inconspicious nucleoli;

Grade 2:  oval nuclei with irregular outlines, clumping chromatin and medium-sized nucleoli;

Grade 3:  large, pleomorphic nuclei with coarse, clumped chromatin and prominent nucleoli.

Grade 3 was accepted as "notable nuclear atypia" that resulted in grade modification [7].

The two-grade system differentiates between two grades of malignancy - low and high. In the system, three parameters are evaluated:

a. the presence of a solid growth, which occupies more than 50% of the tumor structure (without distinction between squamous and non-squamous differentiation);

b. the presence of necrosis within the tumor;

c. the presence of diffusely infiltrating pattern of tumor growth (as opposed to expansive type).

A tumor is classified as high-grade when at least two of the above-specified features are present. In carcinomas con-fined to the endometrium, the two initial criteria must be jointly fulfilled. If only one of the above criteria is met, the tumor is classified as low-grade [3].

Both classifications are applicable only in cases of uterine endometrial endometrioid adenocarcinoma. Other histological carcinoma subtypes (serous papillary or clear cell carcinoma) are a *priori* classified as high-grade.

The statistical analysis was performed using the Statistica 5.5 PL software (StatSoft).

## Results

Using the FIGO classification while the carcinoma grade was assessed by pathologists experienced in gynecological pathology, the kappa value equaled 0.64 - 0.71 (Table 1), but in comparison to individuals without such experience, the relevant kappa value was only 0.23 - 0.48 (Table 2). Employing the two-grade system, the kappa value amounted to 0.91 - 0.92 in the group of experienced pathologists (Table 3), but when the assessment of the experienced vs. inexperienced individuals was compared, the value of kappa reached 0.21 - 0.57 (Table 4).

## Discussion

The histological grade of 133 cases of endometrial endometrioid carcinoma of various clinical stages was evaluated based on the criteria presented in the new, two-grade classification proposed by Lax et al. and the three-grade FIGO system. The analysis showed a markedly higher degree of interobserver agreement in the assessment of histological grade in the group of pathologists experienced in gynecological pathology when using the two-grade scale. In the group characterized by little experience, interobserver agreement was slightly improved. In addition, the authors demonstrated that inexperienced pathologists manifested individual characteristic tendencies towards erroneous assessment (overestimation or underestimation of the grade) regardless of the classification system they employed (results not reported in the present article). Moreover, in the case of the two-grade system, significant associations were demonstrated between the histological grade and the stage of adenocarcinoma. The same association was also shown for the FIGO system and it was non-significant in the case of one of the less experienced pathologists (results not reported in the present article).

The results suggest the superior character of the two-grade system with respect to interobserver agreement; nevertheless, the lack of data on survival does not allow for assessing its prognostic value, but points to a necessity of further studies in this area.

**TABLE 1**

Comparison of histological grade according to FIGO; experienced pathologists

|         | *D1*   |        | *D2*   |        | D3*    |        | D1 |
|---------|--------|--------|--------|--------|--------|--------|----|
| Grade 1 | 67     |        | 65     |        | 80     |        | 67 |
| Grade 2 | 48     |        | 49     |        | 34     |        | 48 |
| Grade 3 | 18     |        | 19     |        | 18     |        | 18 |
| **kappa** |      | 0.6625 |        | 0.7051 |        | 0.6372 |    |

**TABLE 2**

Comparison of histological grade according to FIGO; experienced vs. inexperienced pathologists

|         | *D4* |        | D1 |        | D5 |        | D2 |        | D4 |        | *D3*\* |        | D5 |       | D4 |
|---------|------|--------|----|--------|----|--------|----|--------|----|--------|--------|--------|----|-------|----|
| Grade 1 | 92   |        | 67 |        | 53 |        | 65 |        | 92 |        | 80     |        | 53 |       | 92 |
| Grade 2 | 29   |        | 48 |        | 75 |        | 49 |        | 29 |        | 34     |        | 75 |       | 29 |
| Grade 3 | 12   |        | 18 |        | 5  |        | 19 |        | 12 |        | 18     |        | 5  |       | 12 |
| **kappa** |    | 0.3965 |    | 0.2999 |    | 0.3396 |    | 0.4844 |    | 0.4833 |        | 0.2669 |    | 0.233 |    |

**TABLE 3**

Comparison of histological grade in the two-grade system; experienced pathologists

|            | *D1*  |        | *D2*  |        | D3*   |        | D1 |
|------------|-------|--------|-------|--------|-------|--------|----|
| Low-grade  | 95    |        | 98    |        | 97    |        | 95 |
| High-grade | 38    |        | 35    |        | 35    |        | 38 |
| **kappa**  |       | 0.9057 |       | 0.9222 |       | 0.9054 |    |

**TABLE 4**

Comparison of histological grade in the two-grade system; experienced vs. inexperienced pathologists

|            | *D4* |        | D1 |        | D5 |        | D2 |        | D4 |        | *D3*\* |        | D5 |        | D4 |
|------------|------|--------|----|--------|----|--------|----|--------|----|--------|--------|--------|----|--------|----|
| Low-grade  | 98   |        | 95 |        | 62 |        | 98 |        | 98 |        | 97     |        | 62 |        | 98 |
| High-grade | 35   |        | 38 |        | 71 |        | 35 |        | 35 |        | 35     |        | 71 |        | 35 |
| **kappa**  |      | 0.5660 |    | 0.3424 |    | 0.3006 |    | 0.5735 |    | 0.5723 |        | 0.2977 |    | 0.2132 |    |

*Pathologist D3 evaluated 132 cases

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**Address for correspondence and reprint requests to:**
S. Demczuk
Department of Pathomorphology
Grzegórzecka 16, 31-561 Kraków