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# High-Grade Endometrial Cancer: 28 Cases

**G Bassir*, K Fadil, Y Bencherifi, M Benhassou, M Ennachit and M El Kerroumi**

Center Mohammed 6 of cancer treatment Casablanca, Morocco

***Corresponding author:**

G Bassir,
Center Mohammed 6 of cancer treatment
Casablanca, Morocco

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## 1. Abstract

High-grade endometrial cancer, although rare, is formidable due to its aggressiveness and poor prognosis. This retrospective study conducted at the Ibn Roch University Hospital in Casablanca between 2017 and 2020 analyzed 28 cases to better understand its clinical and histopathological characteristics as well as the therapeutic challenges it poses.The median age of the patients was 66.75 years, and postmenopausal metrorrhagia was the main warning sign (89.28%). The diagnosis was confirmed in 82.14% of cases by biopsy curettage, revealing a predominance of papillary serous adenocarcinoma (35.72%), followed by endometrioid adenocarcinomas and carcinosarcomas. More than 78% of patients presented with deep myometrial infiltration, and vascular emboli were detected in 64.28% of cases, highlighting the aggressiveness of these tumours.While surgery remains the cornerstone of treatment, it was followed by multimodality (radiotherapy, chemotherapy, and/or brachytherapy) in 85.71% of patients. Despite these therapeutic efforts, the rate of locoregional and metastatic recurrence reached 57.14%. Two patients died, while 42.85% enjoyed event-free survival.This work highlights the complexity of high-grade endometrial cancer and the need for more targetedmanagement. A better understanding of prognostic factors and the integration of advances in molecular typing could pave the way for more effective and personalized therapeutic strategies.

### 1. 2. Introduction

High-grade endometrial cancer, though rare, is notorious for its aggressiveness and poor prognosis. This retrospective study, conducted at CHU Ibn Roch inCasablanca between 2017 and 2020, Analyses 28 cases to better understand its clinical and histopathological characteristics as well as the therapeutic challenges it presents.

The median age at diagnosis was 66.75 years, with postmenopausal bleeding being the primary warning sign (89.28%). Diagnosis was confirmed in 82.14% of cases through endometrial biopsy, revealing a predominance of serous papillary adenocarcinoma (35.72%), followed by endometrioid adenocarcinomas and carcinosarcomas. More than 78% of patients had deep myometrial infiltration, and vascular emboli were detected in 64.28% of cases, highlighting the aggressive nature of these tumours.While surgery remains the cornerstone of treatment, it was followed by multimodal therapy (radiotherapy, chemotherapy, and/or brachytherapy) in 85.71% of cases. Despite these therapeutic efforts, the rate of locoregional recurrences and distant metastases reached 57.14%. Two patients died, while 42.85% achieved disease-free survival.This study underscores the complexity of high-grade endometrial cancer and the need for a more targeted approach. A better understanding of prognostic factors and the integration of molecular profiling advances could pave the way for more effective and personalized therapeutic strategies.

## 2. Introduction

Endometrial cancer is the most common gynaecological cancer in developed countries, and the fourth in incidence after breast, colorectal and lung cancers [1]. Its incidence increases with age, and generally occurs after menopause in more than 75% of cases, while it is much rarer before the age of 40, with approximately 3% of cases [2]. High-grade endometrial cancer is less common; however, it is more aggressive with a poorer prognosis and accounts for the majority of relapses and deaths

related to endometrial cancer. High-grade endometrial cancers include grade 3 endometrioid carcinomas and tumours with non-endometrioid histology: papillary serous carcinomas, clear cell carcinomas, undifferentiated carcinomas, and carcinosarcomas [3-6]. Risk factors for this cancer include mainly hypoestrogenism for endometrioid forms, obesity, diabetes, high blood pressure, and treatment with tamoxifen [2]. Some forms have a genetic character and fall within the framework of Lynch syndrome [7]. The most common presenting symptoms are postmenopausal metrorrhagia, which may be associated with other signs of local or distant invasion [8]. Definitive diagnosis is based on endometrial biopsy or curettage biopsy with histological examination [8].

### 2.1. Objectives

The aim of this study is to review our experience with high-grade endometrial cancers, analyze their clinical and histopathological characteristics, discuss the diagnostic and therapeutic difficulties associated with them, assess their prognoses, and compare our series with data from the literature.

### 2.2. Materials and Methods

This is a retrospective study spanning a four-year period, from January 1, 2017, to December 31, 2020. It included 28 cases of high-grade endometrial cancer collected from the registry of the Onco-Gynaecology Department (CM6) at the Ibn Roch University Hospital in Casablanca, and from the computerized medical records of patients hospitalized in the department.

### 2.3. Results

In our study, the median age at diagnosis was 66.75 years (range, 38-83 years). The median time to consultation was 6 months (range, 1-18 months). The main complaint presented by patients was postmenopausal metrorrhagia, representing 89.28% of the patients. Endometrial curettagebiopsy was performed in all our patients and resulted in a definitive diagnosis of high-grade endometrial cancer in 82.14% of cases, with a predominance of papillary serous adenocarcinoma (35.72%). Preoperative FIGO staging was performed using pelvic MRI, performed in only 23 patients (82.14%), demonstrating: stage I in five cases (17.85%), stage II in two cases (8.7%), stage III in 12 cases (52.17%), and stage IV in four cases (17.39%). FIGO staging underestimated FIGO stage in 8.7% of cases (n = 2) and overestimated FIGO stage in 34.78% of cases (n = 8). There was aconcordance in 56.52% of cases (n = 13). An ESMO prognostic classification wasperformed and demonstrated a high risk in all patients except one who had anintermediate risk. The pathological analysis of the hysterectomy specimen with pelvic and/or lumbar-aortic lymphadenectomies showed that four patients had stage IA endometrial cancer (14.29% of FIGO 2018), eight (28.57%) had stage IB cancer, three (10.71%) had stage II cancer, one patient had stage IIIA cancer (3.57%), four had stage IIIB cancer (14.29%), four had stage IIIC1 cancer (14.29%), one patient had stage IIIC2 cancer (3.57%), and three had stage IVB cancer (10.71%). The most frequently found histological type was papillary serous adenocarcinoma in 10 patients (35.72%), followed by endometrioid adenocarcinoma in 7 patients (25%), carcinosarcoma in 6 patients (21.43%), undifferentiated carcinoma in 3 cases (10.71%), mixed adenocarcinoma in one case (3.57%), and clear cell adenocarcinoma in one case (3.57%). They were all high-grade. Myometrial infiltration was more than 50% in 22 patients (78.57%), and less than 50% in 6 patients (21.43%). Cervical invasion was found in 11 patients, or 39.28%. Vascular emboli were present in 64.28% of cases. Peritoneal cytology was performed in 10 patients in our series, or 35.71%, and was positive in one patient. Omentectomy was performed in 12 patients, or 42.85%, and tumour recurrence in two patients. Right ovarian invasion was present in three patients in our series, or 10.71%. Fallopian tube invasion was found in one patient, or 3.57%. Metastatic lymph nodes were identified on pelvic and/or lumbar-aortic dissection. It was positive in eight patients, or 28.57%. In our experience, 24 patients, or 85.71%, were referred after surgeryfor further treatment in the oncology department (P40): Six patients,or 21.42%, received treatment combining external beam radiotherapy,chemotherapy, and vaginal brachytherapy. Five patients, or 17.85%, were treatedwith external beam radiotherapy and vaginal brachytherapy. Six patients, or 21.42%, were treatedwith external beam radiotherapy and chemotherapy. Three patients, or 10.71%, were treatedwith exclusive chemotherapy. Exclusive vaginal brachytherapy was received by one patient and exclusive radiotherapy was received by another. At the time of our data analysis, postoperative complications were found in six patients (21.42%), including deglobulisation, suppuration of the wall, urinary tract infection, and frank left ureter hydronephrosis. In our series, 12 patients (42.85%) had an uneventful survival. However, 16 patients (57.14%) had locoregional recurrences and distant metastases. Overall survival was 92.86% (26 cases); two patients died.

## 3. Discussion

Lax and Kurman were the first to propose a classification of endometrial tumours into two types based on their histological and biomolecular characteristics. Type 1 tumours include endometrioid carcinomas of all grades, characterized by abnormalities in mitotic signal transduction pathways, with rare p53 alteration and estrogen dependence. In contrast, type 2 tumours (serous carcinomas, clear cell carcinomas, carcinosarcomas) exhibit early p53 involvement and are estrogenic independent. However, clear cell carcinomas exhibit mixed characteristics between the two types.Our study confirms the poor prognosis of high-grade endometrial cancers, characterized by a high rate of locoregional recurrence and distant metastases, often diagnosed at advanced stages. We observed that patients with type 2 cancer were older and had a lower BMI than those with type 1 cancer (mean age: 69.5 years vs. 63.1 years; mean BMI: 28.3 vs. 31.4). Our results also suggest that grade 3 endometrioid

carcinomas may benefit from similar staging as type 2 tumours, in accordance with recent INCa recommendations. Among the most aggressive forms are carcinosarcomas and serous carcinomas, while clear cell carcinomas appear to have an intermediate prognosis, similar to that of grade 3 endometriosis.Treatment of endometrial carcinomas is based on key histopathological criteria, recently updated by the WHO 2020 classification. Furthermore, molecular typing is now a central element of management, directly influencing prognosis and therapeutic strategies. TP53-mutated/serous-like and hypermutated/dimmer subtypes can be identified by immunohistochemistry, while the identification of ultra mutated/POLE-mutated tumours requires genetic sequencing. Better integration of these advances into clinical practice could improve the management and prognosis of patients with high-grade endometrial cancer.

## 4. Conclusion

Based on this work and the literature review, we concluded that high-grade endometrial cancer is a less common entity but carries a poor prognosis, with a high frequency of locoregional recurrences and distant metastases, often diagnosed at advanced stages. Better identification of its clinical and histopathological characteristics is needed to better guide the therapeutic strategy.

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