

## Histopathological Prognostic Factors for Endometrial Carcinoma

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**ABSTRACT:** The purpose of our study was to determine the incidence and the relationship between prognostic factors (age at diagnosis, pTNM stage, histological grade, lymph vascular and myometrium invasion) in patients with endometrial carcinoma. We evaluated in terms of diagnosis 50 cases of endometrial carcinomas that were hospitalized during 2011-2014 in the Obstetrics, Gynecology and Surgery clinics of the Emergency County Hospital Craiova. The procedure consisted in fixation in 10% buffered formalin, followed by processing with usual technique of paraffin embedding and finally staining in hematoxylin and eosin. The histological analysis of the 50 endometrial carcinomas revealed well-differentiated carcinomas (G1) in 24 cases (48%), moderately differentiated carcinomas (G2) in 17 cases (34%) and poorly differentiated carcinomas (G3) in further 9 cases (18%). The myometrium invasion was present in the internal half of the myometrium in 12 internal cases (24%) and in the external half of myometrium in further 36 cases (72%). In 2 cases (4%) the myometrium invasion was absent. We achieved significant association between histological grade and invasion of myometrium, also between histological grade and lymphovascular invasion, as well as tumor stage and myometrium invasion. We are also able to report significant association between lymphovascular invasion and tumor stage or tumor stage and presence of lymph nodes. The results of this study emphasize the importance of pathological parameters as prognostic factors in endometrial carcinoma.

**KEYWORDS:** endometrial carcinoma, risk factors, prognostic

### Introduction

Endometrial cancer is responsible for approximately 4% of all cancers that affect women worldwide and it occurs prevalently after menopause [1].

Endometrial carcinoma is less frequent in patients under 40 years. In this age group, the disease can be hereditary or sporadic, associated with Lynch syndrome [2]. Most endometrial carcinomas that occur in this age group are associated with excess of estrogen. The endometrial carcinomas are usually endometrioid type with a high degree of differentiation and are usually associated with favorable clinical outcomes [2].

In 2008 over 288,000 women were diagnosed with endometrial cancer in the entire world with a mortality rate estimated at 1.7-2.4 per 100.000 women [3]. Studies performed in United States and in other developed countries incriminate cervical cancer as the most common cancer of the female genital tract, with reports of over 50.000 new cases each year that cause up to 8.600 deceases [4].

Romanian population studies indicate an incidence peak for endometrial cancer between 60-64 years in age, with estimates in 2013 of an average incidence value of around 8.06/100.000

women, with higher values in the age range with numerous risk factors. In recent years, Romania has experienced an increased incidence, with higher values recorded in urban areas compared to rural areas. Annually about 800 new cases are registered in our country. The diagnosis is often based on late appearing metrorrhagia, which is why 35% of endometrial cancers are diagnosed in advanced stages that are associated with poor prognosis [5].

The literature describes several risk factors incriminated in the occurrence and development of endometrial carcinoma such as: obesity, intake of oral contraceptives, hyperinsulinemia and metabolic syndrome, smoking, genetic or breeding factors such as nulliparity.

Meanwhile, the development of endometrial carcinoma and prognosis depend on numerous prognostic factors such as tumor stage, lymphovascular invasion, myometrium invasion and histological grade [6].

The objective of our study was to determine the incidence and the relationship between prognostic factors (age at diagnosis, pTNM stage, histological grade, lymph vascular and myometrium invasion) in patients with endometrial carcinoma.

## Material and methods

We evaluated in terms of diagnosis 50 cases of endometrial carcinomas that were hospitalized during 2011-2014 in the Obstetrics, Gynecology and Surgery clinics of the Emergency County Hospital Craiova.

The 50 cases of our study were represented by pieces of hysterectomy. The resection pieces were analyzed and diagnosed in the Pathology Clinic of the Emergency Hospital Craiova.

The procedure consisted in fixation in 10% buffered formalin, followed by processing with usual technique of paraffin embedding and finally staining in hematoxylin and eosin. The case classification in terms of grade and stage of the tumor was performed in accordance with

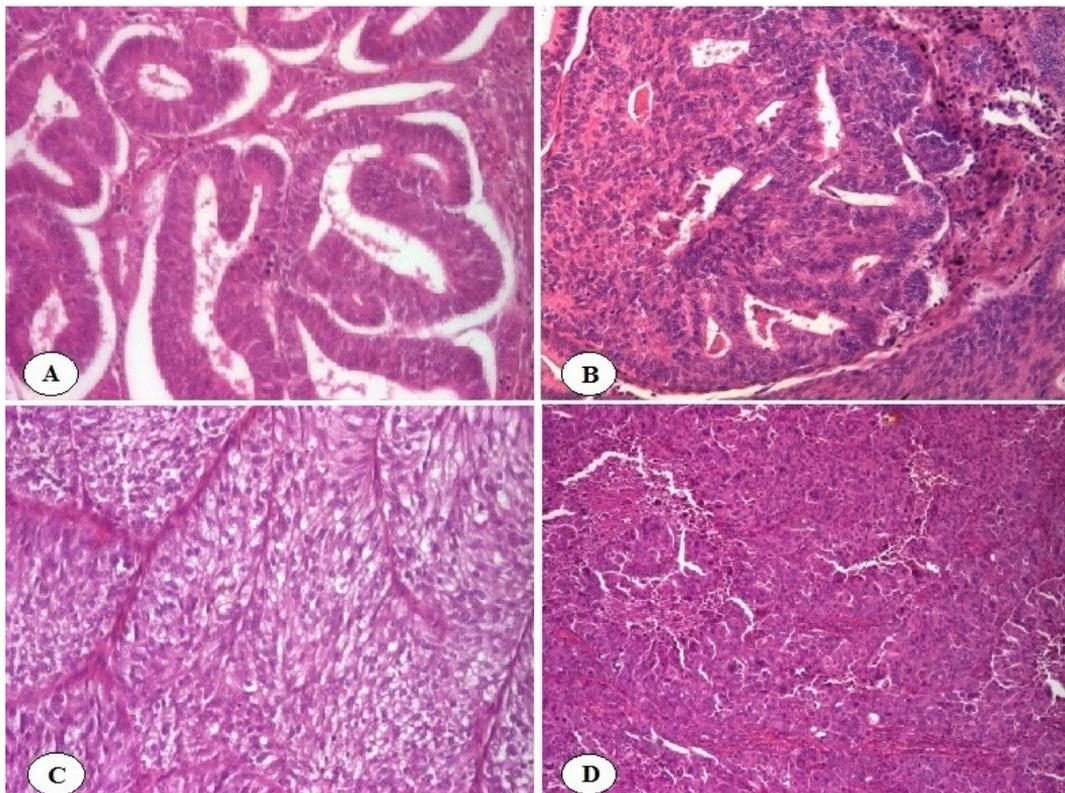
WHO recommendations (2015) [7]. We were interested in the histological grade, lympho-vascular and myometrium invasion, age at diagnosis and tumor stage by classifying pTNM system [8]. Statistical analysis of clinical and morphological parameters was performed using the chi-square, with values less than 0.05 being considered significant.

## Results

Our analysis included 50 cases of endometrial carcinoma hospitalized in a period between 2011-2014 (Table 1). Of the 50 cases analyzed, 47 (94%) were endometrial carcinomas type I (endometrioid carcinomas) and 3 cases (6%) were endometrial carcinomas type II (serous carcinomas).

**Table 1. Clinical and histological parameters of endometrial carcinomas**

Characteristics	Parametres	Number of cases	Percent %
types of endometrial carcinoma	serous adenocarcinoma	3	6
	endometrioid adenocarcinoma	47	94
age	< 60	17	34
	≥ 60	33	66
tumoral grade	G1	24	48
	G2	17	34
	G3	9	18
myometrium invasion	absent	2	4
	< ½ myometrium	12	24
	≥ ½ myometrium	36	72
lymphadenopathy (pN)	pNx	36	74
	pN0	12	22
	pN1	2	4
lymph vascular invasion	present	3	6
	absent	47	94
2015 FIGO classification [8]	IA	8	16
	IB	25	50
	II	12	24
	IIIA	2	4
	IIIB	1	2
	IIIC	2	4



**Fig.1. Histopathological aspects of endometrial carcinomas. A. Well differentiated endometrioid adenocarcinoma (G1), HE-ob.10x; B. Moderately differentiated endometrioid adenocarcinoma (G2), HE-ob.10x; C. Poorly differentiated endometrioid adenocarcinoma (G3), HE-ob.10x; D. Serous adenocarcinoma HE-ob.10x**

The analysis of patients' age indicated that the age varied from 36 to 92 years, of whom most (66%) belonged to the age group 60-79 years and above 80 years (32 and respectively 1 case). Also a significant proportion of the endometrial carcinoma (14 cases = 28 %) was found in relatively young patients, belonging to the age group 50-59 years. A small number of 3 (6%) endometrial cancer cases occurred in women under 50 years (2 cases aged between 40-49 years and 1 case between the ages of 30-39 years).

The histological analysis of the 50 endometrial carcinomas revealed well-differentiated carcinomas (G1) in 24 cases (48%), moderately differentiated carcinomas (G2) in 17 cases (34%) and poorly differentiated carcinomas (G3) in further 9 cases (18%).

The myometrium invasion was present in the internal half of the myometrium in 12 internal cases (24%) and in the external half of myometrium in further 36 cases (72%). In 2 cases (4%) the myometrium invasion was absent.

The lymphovascular invasion was present in 3 cases (6%).

According to the pTNM classification we assessed the lymph node invasion and we were able to report that there were 2 cases (4%) with lymph node invasion, 12 cases (22%) with no lymph node invasion and 36 cases (74%) that could not assess lymph invasion.

Significant statistical associations between analyzed parameters are shown in Table 2.

**Table 2. Statistical associations between the analysed parameters.**

Analysed parameters	Histological grade	Tumoral stage
Myometrium invasion	p=0,039	p=0,035
Lymph vascular invasion	p=0,045	p=0,0001
Lymphadenopathy (pN)	p=0,569	p=0,0006

We achieved significant association between histological grade and invasion of myometrium, also between histological grade and lymphovascular invasion, as well as tumor stage and myometrium invasion. We are also able to report significant association between lymphovascular invasion and tumor stage or tumor stage and presence of lymph nodes. (Fig. 2,3).

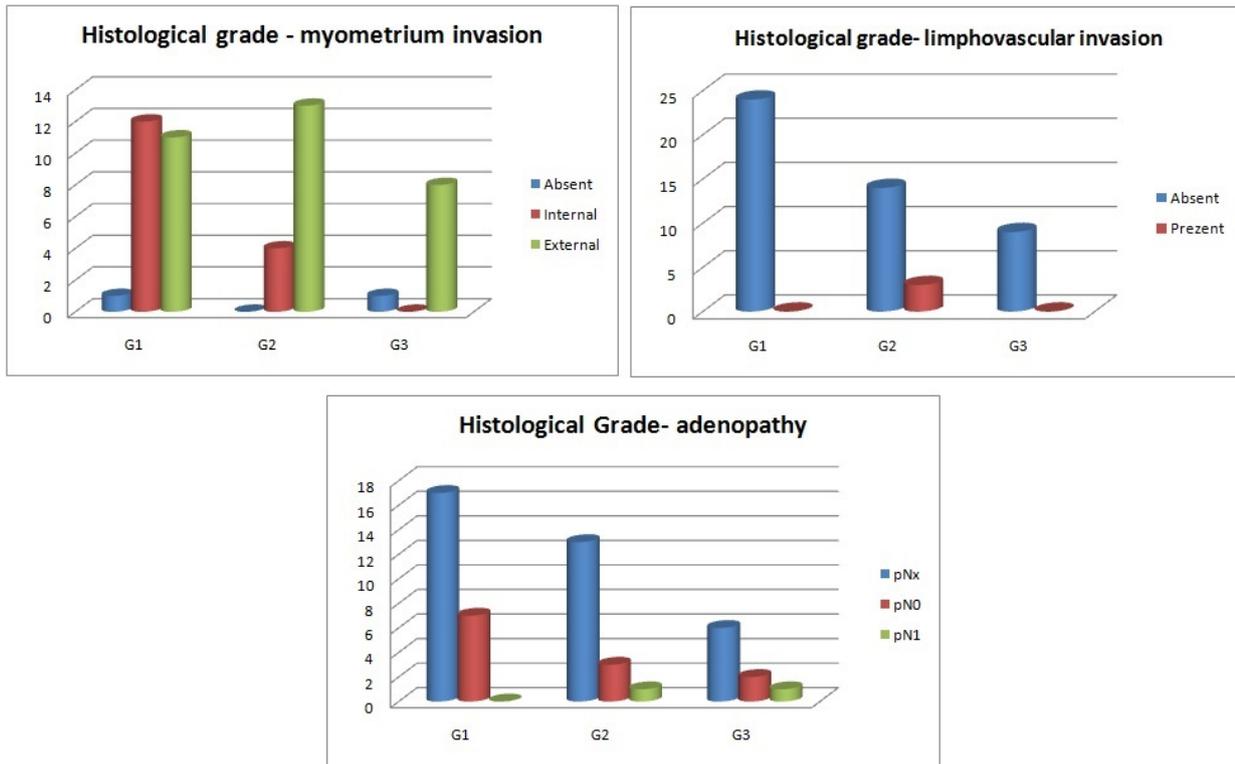


Fig.2. Associations between the analysed parameters

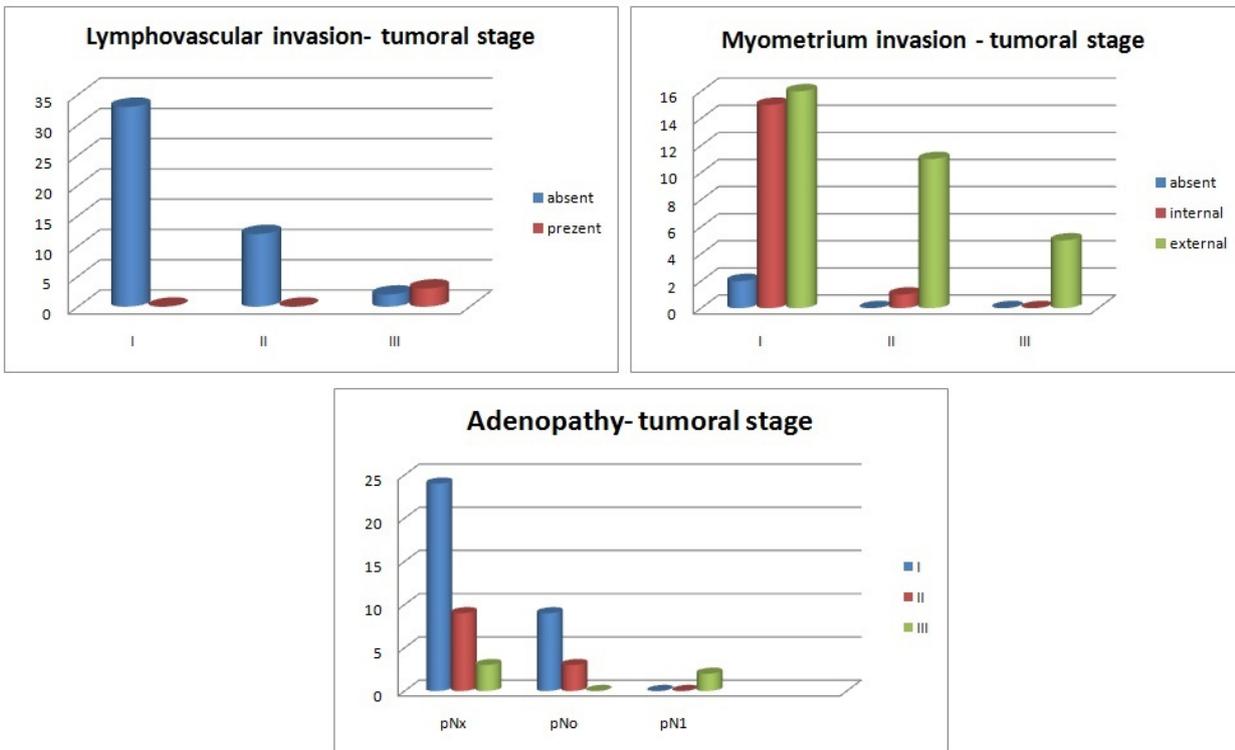


Fig.3. Associations between the analysed parameters

According to the histological grade, the more it is higher (G2 or G3), the invasion of the myometrium is extended to the external half of the myometrium ( $p = 0.039 < 0.05$ , chi square test).

Also, the invasion of the myometrium was significantly associated with tumor stage ( $p = 0.035 < 0.05$ , chi square test).

Lymphovascular invasion was present in only 3 cases, with myometrium invasion in the external half, showing a significant statistical association with the histological grade ( $p = 0.045$ ) and with tumor stage ( $p = 0.0001 < 0.05$  chi square test).

The presence of adenopathies was not significantly associated with histological grade ( $p = 0.569$ ), but was significantly associated with tumor stage ( $p = 0.0006 < 0.05$ , chi square test).

## Discussion

Endometrial cancer is the most common malignant injury to the female genital tract, especially in postmenopausal women [9]. The literature already recognizes several factors involved in the development of endometrial cancer such as obesity, hyperinsulinemia, metabolic syndrome, intake of oral contraceptives, smoking, alcohol consumption, nulliparity, or infertility [6].

The prognostic factors involved in the development of endometrial cancer which were followed in our study are age, myometrium invasion, lymphovascular invasion and the presence of lymph nodes.

Regarding the age of the studied group we have shown that most cases (66%) belonged to the age group 60-79 years. At the same time a significant proportion belonged to the age groups 50-59 years old (14 cases = 28%). The data described in literature states that women of European descent are prone to type I endometrial cancer with an average age at diagnosis between 59.6 and 67.7 years [10]. The data is also supported by Zursterezeel et al. who claimed in a study published in 2008 that age over 60 years is an important prognostic factor and may be associated with an increased proportion of recurrence ( $p < 0.05$ ) [11]. Endometrial cancer can be also diagnosed at younger ages, in which a more important role seems to be attributed to nulliparity or obesity [12].

In matters of age and histological analysis we noticed an increased incidence of endometrial carcinoma in patients aged 60-79 and

endometrioid type carcinoma (94%) with moderately differentiated histological grade G2 (42%).

Histological grade was significantly associated in our study with myometrium invasion because myometrium invasion is more extensive in the external half of myometrium in higher histological grade of tumor differentiation (G2 or G3). Reported studies state similar results such as the study published in 2008 by Nofech-Mozes, who alongside his collaborators evaluated 827 cases with endometrioid endometrial cancer type and analyzed the histological grade, myometrium and lymphovascular invasion. The study confirmed a statistically significant association between tumor grade and invasion of myometrium and between tumor grade and lymphovascular invasion [13]. The results of our study are also consistent to this study, since the evaluation of lymphovascular invasion was observed in cases that presented invasion in the external half of myometrium, indicating a significant association in statistical terms.

Regarding the presence of lymph nodes, a study published in 2009 that analyzed a sample of 834 patients with endometrial cancer certified that the risk of metastatic lymph node is correlated with increased tumor invasion and degree of tumor differentiation [14]. Our study notes, however, the absence of association between the two parameters.

Many studies claim that lymphadenopathy is frequently present in tumors, endometrial high grade and in the late stages of the disease [15, 16]. Our study also indicates that lymphadenopathies were present in endometrial carcinoma type endometrioid stage III, showing a significant statistical association between these two parameters.

Also numerous studies claim that lymphovascular invasion is a significant prognostic factor, being most often associated with the invasion deep myometrium, as well as G3 differentiated tumours and late stages of the disease [17, 18, 19, 20]. In this matter, the results of our study are consistent because lymphovascular invasion was present in 3 cases of stage III endometrial carcinoma, endometrioid type with vast myometrium invasion in external half, which shows a significant statistical association.

## Conclusion

The results of this study emphasize the importance of pathological parameters as prognostic factors in endometrial carcinoma.

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