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Evaluation of Prognostic Factors in Patients with Endometrial Cancer

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Abstract

Background: Endometrial cancer (EC) is a leading gynecological malignancy worldwide, with rising incidence in developing countries. Prognostic factors play a critical role in guiding management, especially in resource-limited settings where molecular testing is not routinely available. ***Aim of the study:*** To evaluate clinicopathological prognostic factors influencing recurrence in patients with endometrial cancer treated at a tertiary care hospital in Bangladesh. ***Methods:*** A retrospective observational study was conducted on 45 histologically confirmed EC patients who underwent hysterectomy-based surgery. Demographic, clinical, pathological, and treatment-related data were analyzed using SPSS version 26.0. Univariate analysis was performed with Chi-square or Fisher's exact test, and multivariate Cox regression was used to determine independent predictors of recurrence. Hazard ratios (HR) with 95% confidence intervals (CI) were reported, and a p-value <0.05 was considered statistically significant. ***Result:*** The mean age was 54.9±12.4 years; 55.6% were postmenopausal. Most patients presented with stage I disease (77.8%). Significant independent predictors of recurrence included tumor grade 3 (HR 2.75; p=0.039), myometrial invasion ≥50% (HR 3.80; p=0.023), LVSI presence (HR 4.25; p=0.007), advanced FIGO stage III–IV (HR 5.67; p=0.004), and lymph node positivity (HR 3.92; p=0.032). Surgical approach and adjuvant therapy were not significantly associated with recurrence. ***Conclusion:*** Advanced stage, high tumor grade, deep myometrial invasion, LVSI, and lymph node involvement are key prognostic factors for recurrence in EC. In low-resource settings, reliance on these clinicopathological predictors is essential for risk stratification and optimizing treatment strategies.

Keywords: Endometrial cancer, Prognostic factors, Recurrence, FIGO stage, Lymphovascular space invasion, Bangladesh.

INTRODUCTION

Endometrial cancer (EC) is defined as a malignant neoplasm arising from the endometrium, the inner lining of the uterus, and represents the most common gynecological malignancy in developed countries [1]. Globally, endometrial cancer ranks as the sixth most frequently diagnosed cancer among women, with an estimated 417,000 new cases and 97,000 deaths reported in 2020, according to the Global Cancer Observatory (GLOBOCAN) [2]. In Bangladesh, while nationwide cancer surveillance is still developing, institutional reports and hospital-based registries indicate that endometrial cancer is the second most common female genital tract malignancy [3], accounting for approximately 15% of all gynecological cancers, with a rising trend in incidence observed over the past decade [4]. The global burden of endometrial cancer has been increasing steadily, largely due to the rising prevalence of risk factors such as obesity, metabolic syndrome, diabetes mellitus, hypertension, prolonged exposure to unopposed estrogen, late menopause, early menarche, infertility, nulliparity, and genetic predisposition including Lynch syndrome [5]. Among these, obesity is a particularly potent modifiable risk factor, as excess adipose tissue increases peripheral

aromatization of androgens to estrogens, leading to continuous endometrial stimulation and hyperplasia [6]. Additionally, the global shift toward sedentary lifestyles and urban dietary patterns has further escalated these risks, particularly in low- and middle-income countries [7]. Although most cases of EC are diagnosed in postmenopausal women at an early stage when prognosis is generally favorable and five-year survival rates exceed 80% a significant proportion of patients in resource-limited settings present at more advanced stages [8]. This is often due to limited awareness, lack of effective screening, socio-cultural barriers, and inadequate access to specialized oncology services. Furthermore, endometrial cancer encompasses a heterogeneous group of tumors, both histologically and molecularly, with varied clinical behaviors and treatment responses [9]. Traditionally, prognostic assessment in EC has relied on clinicopathologic parameters such as FIGO stage, histological subtype, tumor grade, depth of myometrial invasion, lymphovascular space invasion (LVSI), cervical stromal involvement, and lymph node metastasis [10]. These factors are well-established in risk stratification models and play a central role in guiding treatment decisions, including the need for adjuvant therapy. More recently, molecular classification—based on The Cancer Genome Atlas (TCGA) has identified four biologically distinct subgroups that offer improved prognostic stratification and have significant therapeutic implications [11]. However, in countries like Bangladesh, routine molecular testing is not widely available, and most clinical decisions are still based on histopathological evaluation alone [12]. As such, identifying and validating clinically accessible and cost-effective prognostic factors remain crucial for improving outcomes and optimizing resource allocation in such contexts [13]. This study aims to evaluate the key clinicopathological prognostic factors influencing outcomes in endometrial cancer patients treated at a tertiary care center, thereby contributing to evidence-based risk stratification and improved clinical management in resource-constrained settings.

METHODOLOGY & MATERIALS

This retrospective observational study was conducted at the Department of Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh to evaluate the clinicopathological and surgical prognostic factors associated with recurrence in patients diagnosed with endometrial cancer. The study was carried out from for one year from July 2023 to June 2024. A total of 45 patients with histologically confirmed endometrial cancer who underwent primary surgical treatment were included.

Inclusion criteria:

- Histologically confirmed endometrial cancer,
- Patients who underwent hysterectomy-based surgery,
- Complete clinical, pathological, and follow-up data available.

Exclusion criteria:

- Non-surgical management,
- Synchronous malignancies,
- Prior history of gynecologic malignancy.

Ethical Considerations

The study protocol was approved by the institutional ethics committee. All patient data were anonymized and handled confidentially. Written consent was taken from each patient.

Data Collection

Clinical, histopathological, surgical, and follow-up data were collected retrospectively from patient medical records using a standardized data abstraction form. The demographic and clinical variables included age at diagnosis, menopausal status, body mass index (BMI), presence of comorbidities such as diabetes mellitus and hypertension, family history of cancer, and pregnancy history. Tumor-related pathological characteristics comprised histologic subtype, tumor grade, depth of myometrial invasion, presence of lymphovascular space invasion (LVSI), and FIGO stage at diagnosis. Surgical and treatment-related information included the route of surgery (open vs. laparoscopic), lymph node involvement, and details of any adjuvant therapy administered, including radiotherapy, chemotherapy, or hormone therapy. The primary outcome assessed was disease recurrence during the follow-up period. Recurrence was defined as the reappearance of disease either locally or at distant sites, confirmed radiologically or histologically during follow-up.

Statistical Analysis

All statistical analyses were performed using SPSS version 26.0. Descriptive statistics were used to summarize baseline characteristics. Categorical variables were expressed as frequencies and percentages, and continuous variables were summarized using means and standard deviations (SD). Univariate analysis was conducted using Chi-square or Fisher's exact test to identify variables associated with disease recurrence. Multivariate analysis was performed using a Cox proportional hazards regression model to determine independent prognostic factors, with hazard ratios (HR) and 95% confidence intervals (CI) reported. A p-value of <0.05 was considered statistically significant.

RESULT

Table 1 presented the baseline characteristics of the study population (n=45). The mean age of participants was 54.87±12.43 years, with the majority being postmenopausal (55.56%), followed by perimenopausal women (40.00%), and a small proportion premenopausal (4.44%). The mean BMI was

27.38±4.76. Among comorbidities, hypertension was the most prevalent (31.11%), followed by diabetes mellitus (15.56%). A family history of cancer was observed in 17.78% of cases, and 82.22% of women had a history of pregnancy. Endometrioid carcinoma was the predominant histologic type (86.67%), with smaller proportions of mixed cell carcinoma (4.44%), endometrioid with squamous differentiation (4.44%), clear cell carcinoma (2.22%), and serous carcinoma (2.22%). Among endometrioid cases, most tumors were grade 1 (44.44%), followed by grade 2 (37.78%) and grade 3 (17.78%). Myometrial infiltration was confined to the endometrium in 53.33% of cases, ≤50% in 22.22%, and ≥50% in 6.67%, while 17.78% had unknown infiltration status. Lymphovascular space invasion (LVSI) was present in 26.67% of patients (Table 2). Table 3 showed surgical and staging characteristics. The majority of patients were diagnosed at FIGO stage I (77.78%), with fewer at stage II (4.44%), stage III (15.56%), and stage IV (2.22%). Lymph node metastasis was identified in 13.33% of cases. Laparoscopic surgery was the primary approach (77.78%), with 22.22% undergoing open surgery. Regarding adjuvant treatment, radiotherapy was administered in 35.56% of patients, chemotherapy in 17.78%, and hormone therapy in 2.22%. Higher recurrence rates were observed among patients with grade 3 tumors (37.5%, p=0.048), myometrial invasion ≥50% (66.7%, p=0.006), LVSI presence (50.0%, p=0.002), advanced FIGO stage III–IV (57.1%, p=0.001), and lymph node positivity (50.0%, p=0.005). Other variables, including age, BMI, comorbidities, surgical approach, and adjuvant therapy, did not show significant associations with recurrence (Table 4). Table 5 demonstrated the multivariate Cox regression analysis. Independent predictors of poor outcome included tumor grade 3 (HR: 2.75; 95% CI: 1.05–7.22; p=0.039), myometrial invasion ≥50% (HR: 3.80; 95% CI: 1.20–11.95; p=0.023), LVSI presence (HR: 4.25; 95% CI: 1.48–12.20; p=0.007), advanced FIGO stage III–IV (HR: 5.67; 95% CI: 1.70–18.85; p=0.004), and lymph node positivity (HR: 3.92; 95% CI: 1.12–13.70; p=0.032).

Table 1: Baseline characteristics of the study population (n=45)

Age (years)	**Frequency (n)**	**Patients (%)**
Premenopausal (<45)	2	4.44
Perimenopausal (45-55)	18	40.00
Postmenopausal (>55)	25	55.56
Age (years), (Mean±SD)	54.87±12.43	
BMI (Mean±SD)	27.38±4.76	
Comorbidities		
DM	7	15.56
HTN	14	31.11
Family History of Cancer	8	17.78
Pregnancy History	37	82.22

Table 2: Histopathological features of the study population (n=45)

Variables	**Frequency (n)**	**Patients (%)**
Histology		
Clear cell carcinoma	1	2.22
Mixed cell carcinoma	2	4.44
Endometrioid	39	86.67
Serous carcinoma	1	2.22
Endometrioid with squamous	2	4.44
Endometrioid Grade		
Grade 1	20	44.44
Grade 2	17	37.78
Grade 3	8	17.78
Status of myometrial infiltration		
Endometrium alone	24	53.33
≤50%	10	22.22
≥50%	3	6.67
Unknown	8	17.78
Lymphovascular Space Invasion (LVSI)		
Present	12	26.67
Absent	33	73.33

Table 3: Surgical and staging characteristics among participants (n=45)

Variables	Frequency (n)	Patients (%)
FIGO stage		
Stage 1	35	77.78
Stage 2	2	4.44
Stage 3	7	15.56
Stage 4	1	2.22
Lymph Node Involvement		
Positive	6	13.33
Negative	39	86.67
OP route		
Open	10	22.22
Laparoscopy	35	77.78
Adjuvant therapy		
Radiotherapy	16	35.56
Chemotherapy	8	17.78
Hormone therapy	1	2.22

Table 4: Univariate analysis of prognostic factors associated with poor outcome (recurrence)

Variable	Recurrence Rate (%)	P-value
Age Group		
≤55	14.3	0.43
>55	24	
BMI		
<30	15.4	0.51
≥30	25	
Comorbidities		
Present	28.6	0.38
Absent	17.6	
Histologic Type		
Endometrioid	15.4	0.18
Non-endometrioid	33.3	
Tumor Grade		
Grade 1–2	13.9	0.048
Grade 3	37.5	
Myometrial Invasion		
≤50%	13.6	0.006
≥50%	66.7	
LVSI		
Present	50	0.002
Absent	9.1	
FIGO Stage		
Stage I–II	9.1	0.001
Stage III–IV	57.1	
Lymph Node Involvement		
Positive	50	0.005
Negative	10.3	
Surgical Approach		
Open	30	0.15
Laparoscopy	11.4	
Adjuvant Therapy		
Yes	20	0.64
No	15.4	

Table 5: Multivariate cox regression analysis of independent prognostic factors

Variable	Adjusted HR (95% CI)	P-value
Tumor Grade (G3)	2.75 (1.05–7.22)	0.039

Myometrial Invasion ≥50%	3.80 (1.20–11.95)	0.023
LVSI Present	4.25 (1.48–12.20)	0.007
FIGO Stage III–IV	5.67 (1.70–18.85)	0.004
Lymph Node Positive	3.92 (1.12–13.70)	0.032

DISCUSSION

Endometrial cancer is one of the most common gynecologic malignancies worldwide, with rising incidence in developing countries. Prognostic factors such as age, tumor grade, stage, histological type, and comorbidities significantly influence patient outcomes and treatment strategies. The study focused on identifying key determinants that influence disease progression and patient outcomes in endometrial cancer. The mean age of patients was 54.87 ± 12.43 years, with the majority being postmenopausal (55.56%) in our study. Similar finding regarding the age group was reported by Rai *et al* [14]. Patients older than 55 years had a higher recurrence rate (24%) compared to those ≤55 years (14.3%), though this difference was not statistically significant (P=0.43). Numerous studies have reported older age as a poor prognostic factor, with age-related declines in immune function and comorbidity burden potentially contributing to worse outcomes [15]. In this study, the mean BMI was 27.38 ± 4.76, indicating that a significant portion of patients were overweight, reflecting established links between obesity and EC risk. Comorbidities were common, with hypertension (31.11%) and diabetes (15.56%) being the most prevalent. Recurrence rates were higher in patients with BMI ≥30 (25%) compared to BMI <30 (15.4%), but the difference did not reach statistical significance (P=0.51). Obesity is widely recognized as a risk factor for development of endometrial cancer and has been variably associated with prognosis [16]. Obesity and diabetes are strong risk factor for endometrial cancer—meta-analyses show BMI ≥ 30 kg/m² roughly doubles risk compared to BMI < 25 kg/m² and diabetes raises endometrial cancer risk by ~1.5–2.0 times when adjusted for BMI [17]. Hypertension confers modest increased risk, particularly among obese women [18]. Patients with comorbidities (diabetes, hypertension) had a higher recurrence rate (28.6%) compared to those without (17.6%), but this difference was not statistically significant (P=0.38). Comorbidities can influence cancer prognosis by affecting treatment tolerance and overall health status [19]. In our cohort, the vast majority (86.7%) had endometrioid carcinoma, with rare cases of clear cell (2.2%), serous (2.2%), mixed cell (4.4%), or endometrioid with squamous differentiation (4.4%). Study reported that endometrioid type comprises 80–90% of all sporadic endometrial cancers [20]. According to our study, most endometrioid cancers are diagnosed as low or intermediate grade, with about 10–20% classified as Grade 3. High tumor grade (Grade 3) was significantly associated with poorer outcomes (HR 2.75, p 0.039). This aligns with other studies where Grade 3 tumors were linked to higher recurrence and lower overall survival in endometrioid endometrial carcinoma [21,22]. Over half of patients (53.3%) had disease confined to the endometrium alone, 22.2% had ≤50% myometrial invasion, 6.7% had ≥50% invasion, and depth was unknown in 17.8%. Patients with ≥ 50% myometrial invasion had a markedly elevated risk of recurrence (HR 3.80, p 0.023). This is consistent with previously established prognostic importance of deep invasion, which has long been recognized as a key risk factor for both recurrence and nodal metastasis [22,23]. LVSI was present in 26.7% of your patients, similar to reported rates of other study in unselected endometrial cancer cohorts [24]. In our cohort, LVSI presence conferred an adjusted HR of 4.25 (p 0.007). LVSI as a strong, independent predictor of recurrence and nodal disease—even in early-stage, low-risk patients. A study found LVSI in early-stage low-risk disease was associated with significantly worse recurrence-free survival [25]. We found that the majority had early- FIGO stage disease: Stage I was most common (77.8%), followed by Stage II (4.4%), Stage III (15.6%), and Stage IV (2.2%). This mirrors global trends where early-stage diagnosis remains common due to symptomatic abnormal uterine bleeding [26]. Patients with advanced FIGO stage (III–IV) had a substantially higher recurrence rate (57.1%) compared to early stages (I–II) at 9.1% (P=0.001). Advanced stage disease was associated with the highest hazard ratio in our analysis (HR 5.67; 95% CI: 1.70–18.85; P = 0.004). This finding is consistent with multiple international series where FIGO stage is considered the most important determinant of survival [27]. Only 13.33% had nodal metastasis, reflecting the predominance of low-stage disease. The majority underwent laparoscopic surgery (77.78%), reflecting a global shift toward minimally invasive approaches that have been shown to yield equivalent oncologic outcomes with fewer perioperative complications [28]. Positive lymph node status correlated with a 50% recurrence rate compared to 10.3% in node-negative patients (P=0.005). This is consistent with the recognized importance of lymph node metastasis in predicting disease relapse [29]. Lymph node involvement increased recurrence risk nearly fourfold (HR 3.92; P = 0.032). This aligns with previous analyses showing nodal metastasis as a key predictor of both recurrence and mortality [30]. Adjuvant radiotherapy (35.6%) and chemotherapy (17.8%) were administered selectively, in accordance with individual risk profiles, consistent with international practice patterns [31,32]. No statistically significant differences in recurrence rates were observed between open versus laparoscopic surgery (30% vs 11.4%, P=0.15) or between patients who did and did not receive adjuvant therapy (20% vs 15.4%, P=0.64). While minimally invasive surgery has been shown to have equivalent oncologic outcomes in large trials, the lack of association with recurrence in our cohort may be due to small sample

size. Similarly, the non-significant effect of adjuvant therapy may reflect heterogeneous indications and limited power [33].

Limitations of the study:

The present study was limited by its retrospective design and relatively small sample size, which may reduce the statistical power and generalizability of the findings. Data collection was dependent on medical records, potentially leading to incomplete documentation. Follow-up duration was not long enough to fully assess long-term survival outcomes. Moreover, the absence of molecular profiling restricted evaluation to traditional clinicopathological parameters, which may not capture the full spectrum of prognostic determinants in endometrial cancer.

CONCLUSION

This study demonstrates that advanced FIGO stage, high tumor grade, deep myometrial invasion, lymphovascular space invasion, and lymph node metastasis are significant independent prognostic factors for recurrence in endometrial cancer. Although most patients presented with early-stage disease and underwent laparoscopic surgery, adverse pathological features were strongly associated with poorer outcomes regardless of surgical approach or adjuvant therapy. These findings emphasize the need for careful pathological evaluation and risk-based stratification to guide postoperative management. In resource-limited settings such as Bangladesh, where molecular profiling is not widely available, reliance on these readily accessible clinicopathological predictors is crucial for optimizing treatment decisions and improving patient survival.

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Ethical approval: The study was approved by the Institutional Ethics Committee.

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