fortune Journals

Research Article

ARCHIVES OF
CLINICAL AND
BIOMEDICAL RESEARCH
ISSN: 2572-5017

Evaluation of Prognostic Factors in Early-Stage Endometrial Cancer

Afroza Khanom[1*], Shirin Akter Begum[2], Mehriban Amatullah[3], Tasfia Mahmud[4], Naznin Akter Zahan[5], Nasrin Akter[5]

Abstract

Background: Endometrial cancer (EC) is the most common malignancy of the female genital tract and the fourth most common gynecological cancer. Prognostic factors of endometrial carcinoma remain uncertain. This study aims to evaluate the prognostic factors in patients with early stage endometrial cancer.

Methods: This cohort study was conducted at the Department of Gynaecological Oncology, NICRH, from July 2016 to August 2017. A total 30 patients with endometrial cancer having history of total abdominal hysterectomy and bilateral salpingo-oophorectomy with lymphadenectomy were included in this study.

Results: Among 30 patients the highest 11(36.7%) each belonged to age group 41-50 and 51-60 years with a mean age of 47.75±6.13. BMI revealed that 25(83.3%) patients had BMI ≥25 and rest 5(16.7%) had BMI 18.5-24.9. The highest number of 28(93.3%) patients had tumor size <4cm whereas only 2(6.7%) patients had tumor size ≥4cm. The mean tumor size was 2.2±0.67 cm. 21(70%) had endometroid carcinoma and only 9(30%) had nonendometroid carcinoma. It was observed that 14(46.7%), 11(36.7%) and 5(16.7%) had Grade I, II and III endometrial carcinoma respectively. 20(66.7%) had myometrial invasion, 2(6.7%) had LVSI and 11(36.7%) had pelvic lymph node metastasis. 23(76.67%) and 7(23.33%) received EBRT and no EBRT respectively as adjuvant treatment. After treatment including surgery 27(90%) patients were survived with no locoregional recurrence and metastasis. Prognostic factors included Histology type, lymph node metastasis, LVSI and adjuvant radiotherapy (P = < 0.05).

Conclusion: Staging itself, lymph node metastasis, presence of LVSI are the most significant factors in case of endometrial carcinoma.

Keywords: Prognostic factors; Early stage; Lymphovascular space invasion

Introduction

The endometrium is the inner lining of the uterus, its main function being to receive the conceptus and to maintain a successful pregnancy. Under the control of ovarian hormones, monthly cyclic morphological and functional changes occur in this dynamic tissue replacing the top layer with a fresh one in order to accommodate the upcoming fertilized ovum. Postmenopausal endometrium responds to exogenous steroid hormones and has the ability to regain proliferative function. Endometrial cancer (EC) occurs predominantly after menopause. Molecular and hormonal aberrations play an important role in the neoplastic transformation of postmenopausal endometrium [1].

Affiliation:
[1]Associate Professor, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh
[2]Professor & Chairman, Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
[3]Assistant Professor, Department of Obstetrics and Gynecology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh
[4]Lecturer, Department of Pharmacology, Dr. Sirajul Islam Medical College, Dhaka, Bangladesh
[5]OSD, Directorate General of Health Services (DGHS), Dhaka, Bangladesh

***Corresponding author:**
Afroza Khanom, Associate Professor, Department of Gynecological Oncology, National Institute of Cancer Research & Hospital (NICRH), Dhaka, Bangladesh

Citation: Afroza Khanom, Shirin Akter Begum, Mehriban Amatullah, Tasfia Mahmud, Naznin Akter Zahan, Nasrin Akter. Evaluation of Prognostic Factors in Early-Stage Endometrial Cancer. Archives of Clinical and Biomedical Research. 8 (2024): 450-455.

Received: December 15, 2024
Accepted: December 22, 2024
Published: December 31, 2024

Khanom A, et al., Arch Clin Biomed Res 2024
DOI:10.26502/acbr.50170427

It is now the fourth most common gynecological cancer among women and the sixth worldwide cancer in Western countries. It is the most curable of the 10 most common cancers in women and the most frequent and curable of the gynecologic cancers [2]. The highest rates were reported in countries with a high Human Development Index, where nearly two-thirds of all cases occurred. Many Sub-Saharan African, Middle-Eastern, and South-Central Asian countries have low rates [3].

Type I EC is hormone dependent, about 80% is characterized by well to moderately differentiated tumors that present at diagnosis and therefore the overall prognosis is optimistic [2].

Type II is non-hormone dependent, with around 23% of cases characterized by more aggressive tumors that are not associated with unopposed estrogens or hyperplasia, and has a high mortality rate and a poor prognosis.

In endometrial carcinoma, at least 12 prognostic variables are described. Some of them can also predict treatment outcomes and tumor recurrence [5]. Eight of these parameters (age, FIGO stage, histology, FIGO grade, nuclear grade, DNA ploidy, myometrial infiltration, and p53 expression) were examined for their impact on the risk of tumor recurrence, including both total rate and locoregional and distant recurrence [5].

Over the past two decades, several pathological features that clearly separate two or more groups of these patients with different outcomes (ie, disease-free survival or recurrence) have been described and confirmed [4]. Several studies done by the Gynecologic Oncology Group have demonstrated that the prognostic parameters for endometrial carcinoma can be separated into uterine and extrauterine factors. Uterine factors include (1) histological type, (2) histological grade, (3) depth of myometrial invasion, (4) vascular invasion, (5) presence of atypical endometrial hyperplasia, (6) cervical involvement, (7) DNA ploidy and S-phase fraction, and (8) hormone receptor status. Extrauterine factors include (1) positive peritoneal cytology, (2) adnexal involvement, (3) pelvic and para-aortic lymph node metastasis, and (4) peritoneal metastasis. (8) Patients with extrauterine disease, cervical involvement, and vascular invasion constitute a high-risk group (with an approximate 65% frequency of recurrence) [6]. Alternatively, patients with tumors confined to the corpus uteri (without cervical involvement) and with no evidence of vascular invasion have a lower overall risk of recurrence. However, their prognosis varies significantly, depending on 3 main pathological parameters: (1) histological type, (2) histological grade, and (3) depth of myometrial invasion [6].

Although not perfect, FIGO stage is the single strongest prognostic parameter for women with endometrial carcinoma. The 1971 FIGO clinical staging system (based on sounding of the uterus, fractional curettage, and pelvic examination) proved to be less accurate than histological evaluation of the hysterectomy specimen [4]. The new staging system requires hysterectomy as well as assessment of pelvic and para-aortic lymph nodes, adnexa, and peritoneal fluid cytology. Pathological evaluation includes histological grade, depth of myometrial invasion, and determination of cervical involvement [4].

In clinical stage I carcinomas, the frequency of lymph node metastasis is related to the depth of myometrial invasion. Endometrial carcinomas associated with pelvic and/or paraaortic lymph node metastasis are classified as stage IIIC tumors [4]. Almost 33% of patients with positive pelvic lymph nodes have positive para-aortic nodes as well. The prognosis with positive pelvic lymph nodes seems more favorable than that with positive para-aortic lymph nodes [6]. In fact, in a Gynecologic Oncology Group study, only 36% of patients with positive aortic nodes were free of tumor at 5 years, compared with 85% of those with negative aortic nodes; yet these 2 findings are both considered stage IIIC in the FIGO staging system [6].

Objective

To evaluate the prognostic factors in patients with early stage endometrial cancer. To determine the impact of clinical stage on the disease outcome.

Methodology and Materials

This cohort study was conducted at the Department of Gynaecological Oncology, National Institute of Cancer Research and Hospital from July 2016 to August 2017. A total 30 patients with endometrial cancer having history of total abdominal hysterectomy and bilateral salpingo-oophorectomy with lymphadenectomy (in high risk group) were included in this study.

Inclusion Criteria: Are diagnosed as a case of early-stage (stage I) Endometrial cancer

1. Have history of total abdominal hysterectomy and bilateral salpingo-oophorectomy with lymphadenectomy (in high-risk group)
2. Are treated with or without adjuvant radiotherapy

Exclusion Criteria:

1. Patients with advanced-stage endometrial cancer

Data collection: All the patients diagnosed as a case of endometrial cancer during 2016 and 2017 were enrolled in this study. The patients were diagnosed after fractional curettage of the endometrium. After proper preoperative evaluation surgery was done.

Khanom A, et al., Arch Clin Biomed Res 2024
DOI:10.26502/acbr.50170427

Operative procedure: Abdomen was opened by midline incision. After taking the peritoneal washing with normal saline, exploration of abdominal organs were done. Total abdominal Hysterectomy and bilateral salpingo-ophorectomy was done routinely in every case. In case of endometroid variety high risk group (evidenced by myometrial invasion > half of myometrium or grade III or endometrial growth > 2 cm) and in the nonendomeroid variety (eg serous or clear cell), pelvic lymphadenectomy was done. Pelvic lymph node sampling was done in rest of the cases. After getting the histopathology report, adjuvant radiotherapy was planned.

A group of patients with endometrial cancer characterized by non-endometroid variety in histology or endometroid variety but> half myometrial invasion, or LVSI positive or involved lymph node or extension of growth in cervix—Adjuvant Radiotherapy was given. In rest of the cases no adjuvant treatment was given.

After completion of treatment by surgery with or without Radiotherapy, patients were followed up till 2019. The patient will attend the outdoor at 3 monthly for two years and 6 monthly there after according to the schedule. In each follow-up, detailed history is taken along with clinical examination. Ultrasonograms of whole abdomen and Ca 125 were done. CT scan of abdomen, Chest X-ray was done in clinically suspicious cases. A data collection form was filled up daily in every visit of the patient.

Ethical consideration: In accordance with the 1964 Helsinki Declaration for Medical Research Involving Human Subjects, the study subjects' parents were informed about the study design, purpose, and right to withdraw from the project at any time, for any reason. The study sample included the parents of study subjects who provided informed consent to participate in the investigation.

Statistical analysis of data: In survival analysis, overall survival time was defined as time from diagnosis until death; the follow-up of patients still alive was censored at their latest date of follow-up. Survival curves were made using the Kaplan-Meier method and compared using the log-rank test. Statistical analyses were performed using SPSS software v25.0. A p-value of less than or equal to 0.05 was considered as statistically significant.

Results

Table 1 shows that among 30 patients the highest 11(36.7%) each belonged to age group 41-50 years and 51-60 years. Besides, 7(23.3%) and 1(3.3%) belonged to age group >60 years and ≤40 years. The mean age of the respondents was 47.75±6.13 years (age range: 36-68) years. BMI revealed that 25(83.3%) patients had BMI ≥25 and rest 5(16.7%) had BMI 18.5-24.9.

Table 2 classified tumor grading where <5% nonsquamous or nonmorular solid growth in **Grade I**, 6–50% in **Grade II,** and >50% with pleomorphic nuclei and frequent mitoses in **Grade III**.

Table 1: Baseline Characteristics of the respondent.

Variables		Frequency	Percentage(%)
Age (in years)	≤40	1	3.3
	41 – 50	11	36.7
	51 – 60	11	36.7
	>60	7	23.3
	Mean age±SD (in years)	47.75±6.13	
	Age range (in years)	36 – 68	
BMI	18.5 – 24.9	5	16.7
	≥25	25	83.3
Family history	Present	0	0
	Absent	30	100
Occupation	Housewife	30	100

Table 2: Classification of FIGO grading system for endometrial cancer.

Grade	Architectural	Nuclear
Grade I	Less than 5% nonsquamous, or nonmorular solid growth pattern	Oval/elongated nuclei, fine chromatin, small nucleoli, few mitoses
Grade II	6% to 50% nonsquamous, or nonmorular solid growth pattern.	Features between grades 1 and 3
Grade III	More than 50% nonsquamous, or nonmorular solid growth pattern.	Enlarged/pleomorphic nuclei, coarse chromatin, prominent nucleoli, many mitoses

Table 3 shows that out of 30 patients, the highest 28(93.3%) patients had tumor size <4cm whereas only 2(6.7%) patients had tumor size ≥4cm. The mean size of the tumor is 2.2±0.67 cm and range is 1-4cm. The highest 21(70%) had endometroid

Khanom A, et al., Arch Clin Biomed Res 2024
DOI:10.26502/acbr.50170427

carcinoma and only 9(30%) had non endometrioid carcinoma. Regarding grade, it was observed that 14(46.7%), 11(36.7%) and 5(16.7%) had Grade I, II and III endometrial carcinomas respectively. Had myometrial invasion, 2(6.7%) had LVSI and 11(36.7%) had pelvic lymph node metastasis.

Table 4 shows that after receiving treatment including surgery and adjuvant radiotherapy 27(90%) patients were alive and rest 3(10%) patients died. There was no locoregional recurrence and metastasis was observed.

Table 3: Distribution of patients according to size of growth, histopathology in clinical status.

Variables		Frequency	Percentage (%)
Size of growth (in cm)	<4	28	93.3
	≥4	2	6.7
Mean size ± SD (in cm)		2.2±0.67	
Range (in cm)		1 – 4	
Histopathology status	Nonendometroid carcinoma	9	30
	Endometroid carcinoma	21	70
Grade	Grade I	14	46.7
	Grade II	11	36.7
	Grade III	5	16.7
Myometrial invasion	Yes	20	66.7
	No	10	33.3
LVSI	Yes	2	6.7
	No	28	93.3
Lymph node metastasis	Pelvic	11	36.7
	No metastasis	19	63.3

Table 4: Distribution of patients according to outcome (n=30).

Outcome		Frequency(n)	Percentage (%)
Status of patients	Alive	27	90
	Dead	3	10
Locoregional recurrence	Present	0	0
	Absent	30	100
Metastasis	Present	0	0
	Absent	30	100

Table 5 shows that in our aspect histology type lymph node metastasis, LVSI and adjuvant radiotherapy are significant prognostic indicators for overall survival (P=<0.05).

Table 5: Survival outcome and multiple high risk factors in early stage endometrial cancer (n=30).

Outcome		Overall survival		
		1 yr (%)	HR (5% CI)	P-value
Age (yr)	≤50	61.7	Reference	0.79
	>50	62.3	1.03 (0.59-1.86)	
Histology type	Endometrioid carcinoma	79.6		
	Nonendometroid carcinoma	95.7		
Stage	Grade I	75.79	Reference	<0.001
	Grade II	68.29	1.09(0.57-2.75)	
	Grade III	38.23		
Adjuvant radiotherapy	EBRT	63.7	Reference	0.05
	Vault radiation	77.8	0.57 (0.32-1.02)	
Lymph node	No metastasis	67.39	Reference	<0.0001
	Metastasis		01.39(0.56-3.79)	
LVSI	Absent	78.37	Reference	0.03
	Present	68.23	1.97(0.99-3.67)	

Citation: Afroza Khanom, Shirin Akter Begum, Mehriban Amatullah, Tasfia Mahmud, Naznin Akter Zahan, Nasrin Akter. Evaluation of Prognostic Factors in Early-Stage Endometrial Cancer. Archives of Clinical and Biomedical Research. 8 (2024): 450-455.

Khanom A, et al., Arch Clin Biomed Res 2024
DOI:10.26502/acbr.50170427

Figure 1 shows that 14 months survival was recorded and in this regard initially staging denotes one risk factor. Secondly staging and lymph node metastasis showed 2 risk factors and finally, staging lymph node metastasis and presence of LVSI showed 3 risk factors.

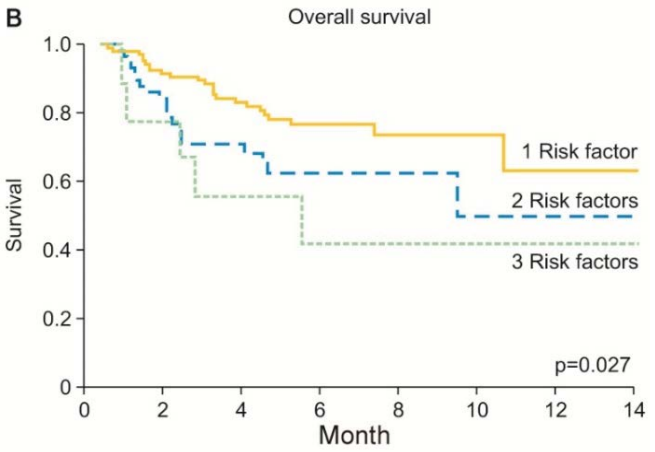

Figure 1: Kepler mirror to show the overall survival analysis (n=30).

Discussion

The prognostically most important variables in endometrial cancer are FIGO stage, histological subtype and differentiation grade; no single other (clinical or molecular) biomarker has shown to have more independent prognostic value to date [7].

The causes of endometrial cancer are multifaceted. Overall, increased BMI and obesity are well-established risk factors for endometrial cancer in both premenopausal and postmenopausal women [8]. Before menopause, oestrogen is largely obtained from the ovaries. However, during menopause, fat tissue becomes the primary source of oestrogen. The level of aromatase enzyme rises as people age and gain weight. Aromatase is responsible for the peripheral aromatisation of rostenedione to oestrone and oestradiol. Overweight/obese reduces the level of sex hormone-binding globulin (SHBG), which binds oestrogens [8].

This biological concept is particularly prominent in postmenopausal women. The total outcome is an increase in unopposed estrogens, which promote endometrial proliferation, a precondition for endometrial cancer. Other menarche symptoms include late menopause, the use of tamoxifen or exogenous estrogens without progestins, physical inactivity, diabetes, hypertension, and Lynch syndrome. Grading determines the level of tumor aggressiveness [9]. Histotype, grade, and stage are important pathogenic characteristics that are integrated into various risk prediction clinical models used to guide treatment. Preoperative grade and histologic subtype are two factors used to determine lymphadenectomy during a hysterectomy. However, tumor grade after hysterectomy frequently differs from initial endometrial biopsy.

Visser et al. [10] found a 67% agreement between preoperative tumor grading and final diagnosis in a meta-analysis of 16 prior studies published between 1997 and 2016 that evaluated the accuracy of endometrial sample in endometrial cancer [10]. Several prior studies have demonstrated that the rate of concordance increases with tumor grade, with the greatest divergence occurring in grade 1 tumors. Wang et al. [11] evaluated the histological grades of curettage and hysterectomy specimens and found a 50% increase in grade 1 tumors [11].

In this study, the highest 11(36.7%) each out of 30 patients belonged to age group 41-50 years and 51-60 years. Besides, we have observed 17(56.67%) out of 30 patients were from ≥50 years of age. The mean age of the respondents was 47.75±6.13 (age range: 36-68) years. Our these findings were very nearer to the findings of a previous study [12].

Simultaneously, the histological findings like endometroid carcinoma and non-endometroid carcinoma were diagnosed in case of 9(30%) and 21(70%) patients respectively out of 30 patients. These are agreed by a previous study [12]. Nine of our patients had positive family history which was consistent with the findings of a previous study [13].

Among 30 cases, though all were enrolled as early endometrial carcinoma, only 5(16.7%) were diagnosed as Grade III endometrial cancer according to histopathology which unfortunately presented clinically as early cancer. Besides 14(46.7%) and 11(36.7%) were diagnosed as Grade I and Grade II carcinoma respectively. These findings were in line to a previous study [13].

Among 30 patients with endometrial carcinoma 20(66.7%) had myometrial invasion, 2(6.7%) had LVSI, 11(36.7%) had paraortic lymph node metastasis. Besides, among them 23(76.67%) and 7(23.33%) received vault radiation and EBRT respectively. Our these findings were very nearer to that of a previous study [14].

Regarding outcome, it was observed that after receiving treatment 3(10%) out of 30 patients expired. Locoregional recurrence and metastasis were not observed in a single patient. These findings were also supported by a previous study [15].

The attributable significant prognostic factors were proved in this study were histology type, adjuvant radiotherapy, lymph node metastasis and LVSI in our study which were partially supported by a previous study [13].

Early-stage cervical cancer patients with multiple high-risk factors had similar survival outcomes when compared

to advanced-stage disease. When tumors expressed 2 and 3 high-risk factors, 1-year DFS of the patients were 50.3% and 30%, respectively, which are comparable to that of reported 5-year DFS of FIGO stage III cervical cancer, 30% to 50% [16].

Limitations of the Study

Data was availed from a single center, thus, presented data on a small sample. So, the results may not represent the whole community.

Conclusion and Recommendations

Staging itself, lymph node metastasis, presence of LVSI are the most significant factors in case of endometrial carcinoma. A multicentered study in the divisional/ tertiary hospitals of whole Bangladesh. The study period should be long. Multi-disciplinary approach of research work can make a study more precise and authentic in this regard.

Financial support and sponsorship

No funding sources.

Conflicts of interest

There are no conflicts of interest.

Ethical approval

The study was approved by the Institutional Ethics Committee.

References

1. Hapangama D. Androgen receptors are acquired by healthy postmenopausal endometrial epithelium and their subsequent loss in endometrial cancer is associated with poor survival. British Journal of Cancer 114 (2016): 688-96.
2. Bajracharya SR, Juan FY. Prognostic factors in endometrial cancer. J Inst Med 35 (2013): 9-17.
3. Lortet-Tieulent J, Ferlay J, Bray F, et al. International Patterns and Trends in Endometrial Cancer Incidence 1978–2013. J Natl Cancer Inst 110 (2018): 354-361.
4. Prat J. Prognostic parameters of endometrial carcinoma. Hum Pathol 35 (2004): 649-62.
5. Sorbe B. Predictive and Prognostic Factors in Definition of Risk Groups in Endometrial Carcinoma. ISRN Obstet Gynecol 2012 (2012): 1-8.
6. Morrow CP, Bundy BN, Kurman RJ, et al. Relationship between surgical-pathological risk factors and outcome in clinical stage I and II carcinoma of the endometrium: a Gynecologic Oncology Group study. Gynecol Oncol 40 (1991): 55-65.
7. Salvesen HB, Haldorsen IS, Trovik J. Markers for individualized therapy in endometrial carcinoma. Lancet Oncol 13 (2012): e353-61.
8. Schmandt RE, Iglesias DA, Co NN, et al. Understanding obesity and endometrial cancer risk: opportunities for prevention. American Journal of Obstetrics and Gynecology 205 (2011): 518-25.
9. Cakiroglu Y, Doger E, Yildirim Kopuk S, et al. Prediction of tumor grade and stage in endometrial carcinoma by preoperative assessment of sonographic endometrial thickness: Is it possible? Turkish Journal of Obstetrics and Gynecology 11 (2014): 211-14.
10. Visser NCM, Reijnen C, Massuger L, et al. Accuracy of Endometrial Sampling in Endometrial Carcinoma: A Systematic Review and Meta-analysis. Obstetrics and Gynecology 130 (2017): 803-13.
11. Wang X, Zhang H, Di W, et al. Clinical factors affecting the diagnostic accuracy of assessing dilation and curettage vs frozen section specimens for histologic grade and depth of myometrial invasion in endometrial carcinoma. American Journal of Obstetrics and Gynecology 201 (2009): 194.e1-e10.
12. Zhou QC, Singh SK, Li Y, et al. Preoperative Histopathological Grading and Clinical Staging versus Surgico-Pathological Grading and Surgical Staging in Endometrial Carcinoma Patients: A Single Centre Retrospective Study. Global Journal of Medical Research 18 (2018): 19-28.
13. Matsuo K, Mabuchi S, Okazawa M, et al. Clinical implication of surgically treated early-stage cervical cancer with multiple high-risk factors. J Gynecol Oncol (2014): 3-11.
14. Onsrud M. Long-term outcomes after pelvic radiation for early-stage endometrial cancer. J Clin Oncol 31 (2013): 3951-56.
15. Soliman PT. Limited public knowledge of obesity and endometrial cancer risk: what women know. Obstet Gynecol 112 (2008): 835-42.
16. Jiang X, Tang H, Chen T. Epidemiology of gynecologic cancers in China. J Gynecol Oncol 29 (2018): e7.