

Survival Analysis and Prognostic Factors of Endometrial Cancer- Regional Cancer Centre Experience

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Abstract:

Background: Endometrial cancer (EC) is the most common gynecological malignancy in developed countries, with rising incidence globally, especially in Asia. Prognosis depends on multiple clinicopathological factors, but their relative impact on survival remains to be fully clarified.

Aim: To analyze survival outcomes and identify independent prognostic factors affecting overall survival in patients with endometrial cancer treated at our institute (Regional Cancer Center).

Methodology: This retrospective observational study included 166 patients treated at the Department of Gynecologic Oncology, Kidwai Memorial Institute of oncology and research institute, Bangalore, between 2014 and 2019. Clinical, pathological, treatment, and follow-up data were analyzed. Survival was estimated using Kaplan-Meier methods, and prognostic factors were assessed by Cox regression analysis.

Results: The majority (86.1%) had endometrioid histology with significantly better mean overall survival (83.98 months) compared to non-endometrioid tumors (50.21 months, $p=0.000$). Higher tumor grade and presence of lymphovascular space invasion (LVSI) were associated with poorer survival ($p=0.000$). LVSI showed a more than fourfold increased risk of mortality (HR 4.736, $p=0.002$). Older age (≥ 70 years) also predicted worse outcomes (HR 2.593, $p=0.037$). Advanced stage correlated with decreased survival ($p=0.000$). Myometrial invasion and lymph node involvement were not independent predictors in multivariate analysis.

Conclusion: Histological subtype, tumor grade, LVSI status, age, and stage significantly influence survival in EC patients. LVSI and age are strong independent prognostic markers and should be integral to risk stratification and personalized treatment planning to improve outcomes.

Keywords: Endometrial Cancer, Lymphovascular, Space Invasion, Prognostic Factors, Survival Analysis, Tumor Grade.

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Introduction

Endometrial cancer (EC) is the most prevalent gynecologic cancer in high-income countries, with more than 40,000 new cases reported worldwide in the year 2020 [1]. The incidence and prevalence of EC in the United States is approximately 25.7 cases per 100,000 women, per year, and the incidence, particularly in many Asian countries including Japan and Singapore is certainly increasing [2]. Taiwan is particularly alarming, as the incidence increased from 1.69 per 100,000 women in 1980 to 11.36 per 100,000 women in 2010, a striking increase in just thirty years [3].

Many different contributors have been associated with this increase. One significant contributor is the decrease in fertility rates, probably as a result of continuous socioeconomic change factors of delayed childbearing, urbanization, and more nuclear families. These factors of change are likely associated with risk for EC because of the extended duration of unopposed estrogen exposure with fewer pregnancies and breastfeeding [4]. Lifestyle changes in the little kids and young adults of the Western Hemisphere and emerging developing economies with regards to lifestyle behaviours of

sedentary behaviour, inactivity, and obesity trends that greatly increase risk for EC [5]. These modifiable risk factors are accompanied by life expectancy, better diagnosing techniques that have contributed long term to the EC burden. As such, that epidemiologic trends and causes are important in approaching prevention and public health responses for the developed as well as developing countries.

Endometrial cancer (EC) most often reveals itself as postmenopausal vaginal bleeding in approximately 90% of patients, which serves as one of the few gynecologic cancers with early and apparent symptoms which leads to timely consultation with a healthcare provider for them to be referred for a diagnosis [6]. Due to this vast percentage of early detection of EC, this explains the rapid turnaround for the patient to be treated and access medical care for the best prognosis. The gold-standard treatment for EC is surgical treatment consisting of a total hysterectomy with bilateral salpingo-oophorectomy and pelvic lymphadenectomy. With the development of minimally invasive techniques, laparoscopic/Robotic surgery has become standard technique with benefits of less postoperative pain, shorter hospital stay, early resumption of daily activity without compromising the oncologic outcome [7]. For patients diagnosed with advanced stage or have high-risk features i.e - deep myometrial invasion, lymphovascular space invasion, or high-grade tumor - postoperative adjuvant treatment is recommended which includes pelvic external beam radiation therapy (EBRT), vaginal brachytherapy, systemic chemotherapy, or combination for the purpose of mitigating recurrence and improving distant survival [8].

There have been many studies that have identified a number of prognostic variables of EC. Multiple histopathological findings, which include depth of myometrial invasion, cervical involvement, serosal involvement of the uterus, and lymph-vascular space invasion (LVSI), have long been established as important prognostic factors in EC as have other pathological staging factors in addition to clinical factors such as race, body mass index (BMI), age, and medical conditions such as diabetes mellitus (DM) [9].

The disease is highly treatable in early stages with a 5 year overall survival of as high as 80% but can be as low as 20% 5 year overall survival in patients with late-stage endometrial cancer [10]. The mean time to recurrence is generally 22.5 months, with age, International Federation of Gynecology and Obstetrics (FIGO) stage, and initial treatment being independent risk factors for recurrence [11]. Thus, we need to investigate the important prognostic factors affecting EC survival of patients and the most effective treatment. Previous studies have looked at the prognostic factors and their relationships with survival and prognosis of patients. However, survival and prognosis remain multifactorial for patients with EC. For these reasons, we want to study Survival

Analysis and Prognostic Factors of Endometrial Cancer- the experience from a Regional Cancer Centre.

Methodology

Study Design: This study is a retrospective observational analysis conducted to evaluate survival outcomes and prognostic factors among patients with endometrial cancer.

Study Area: The study was carried out in the Department of Gynecologic Oncology, Kidwai Memorial Institute of Oncology and Research Institute, Bangalore, a recognized regional cancer center in South India.

Study Duration: The study period spanned six years, from January 2014 to December 2019.

Sample Size: A total of 166 patients who fulfilled the inclusion criteria were included in the final analysis.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Patients with histopathologically confirmed diagnosis of carcinoma endometrium.
- Patients who underwent definitive treatment (surgery ± adjuvant therapy/chemotherapy) at the institute.
- Availability of complete clinical, pathological, and follow-up data.

Exclusion Criteria

- Patients with a history of any other malignancy diagnosed within the last five years.
- Patients lost to follow-up after primary treatment.
- Incomplete medical or treatment records.

Procedure: Patient records were retrieved from the institutional medical records department and reviewed retrospectively. Demographic data, clinical presentation, histopathological reports, treatment modalities, follow-up details, recurrence, and survival outcomes were collected. The staging was based on FIGO classification, and risk stratification followed ESGO guidelines. Treatment included surgical intervention (total abdominal hysterectomy with bilateral salpingo-oophorectomy and lymphadenectomy where indicated), adjuvant radiotherapy, chemotherapy, or a combination thereof, as clinically appropriate. Survival time was calculated from the date of histopathological diagnosis to either the date of last follow-up or death. All ethical protocols for retrospective data usage were observed as per institutional guidelines.

Statistical Analysis: All statistical analyses were performed using SPSS software version 11. Kaplan-Meier survival estimates were used to calculate overall survival (OS) and disease-free survival

(DFS). Differences in survival among groups were compared using the log-rank test. Multivariate analysis was performed using the Cox proportional hazards regression model to identify independent prognostic factors, with Wald statistics employed to assess the significance of each variable in the final model. A p-value <0.05 was considered statistically significant.

Result

Table 1 presents the overall survival (OS) outcomes based on the histological type of endometrial cancer.

Histological Type	N (%)	Os (Months)	P Value
EEC	86.10%	OS=83.98	P =0.000
Non Endometroid	13.90%	OS= 50.21	

The data indicate that patients with endometrioid endometrial carcinoma (EEC), comprising 86.10% of the cohort, had a significantly higher mean overall survival of 83.98 months. In contrast, patients with non-endometrioid histology, accounting for 13.90% of cases, exhibited a notably lower mean OS of 50.21 months. The observed difference in survival outcomes between the two histological subtypes was statistically significant, with a p-value of 0.000, highlighting histological type as a critical prognostic factor in endometrial cancer.

Table 2 illustrates the distribution of tumor grades among patients and their corresponding overall survival (OS) in months. Grade 1 tumors constituted the majority (50.60%) and were associated with a mean OS of 77.61 months. Grade 2 and Grade 3 tumors each accounted for 24.70% of cases, with Grade 2

showing the highest OS of 81.74 months, while Grade 3 had the lowest OS of 56.68 months. The p-value of 0.000 indicates a statistically significant association between tumor grade and overall survival, suggesting that higher-grade tumors are linked with reduced survival outcomes.

Tumour Grade	N%	Os (Months)	P Value
1	50.60%	OS= 77.61	P=0.000
2	24.70%	OS= 81.74	
3	24.70%	OS= 56.68	

Table 3 illustrates the relationship between the depth of myometrial involvement and overall survival (OS) in patients with endometrial cancer. Patients with less than 50% myometrial involvement constituted 60.80% of the study population and demonstrated a higher mean OS of 90.20 months. In

contrast, those with 50% or greater myometrial invasion, comprising 39.20% of cases, had a lower mean OS of 74.50 months. However, the observed difference in survival between the two groups was not statistically significant, as indicated by a p-value of 0.338.

Myometrial Involvement	N%	Os (Months)	P Value
<50%	60.80%	OS=90.20	P=0.338
≥50%	39.20%	OS=74.50	

Table 4 illustrates the association between Lymphovascular Space Invasion (LVSI) status and Overall Survival (OS) rates. Patients with focal or negative LVSI, comprising 86.10% of the study group, demonstrated a significantly higher overall survival rate of 91.12%. In contrast, those with substantial or

positive LVSI, representing 13.90% of the patients, had a markedly lower overall survival rate of 47.18%. This data suggests that the presence of substantial LVSI is strongly associated with poorer survival outcomes.

LVSI	N%	Os (Months)	P Value
Focal/Negative	86.10%	OS=91.12	0
Substantial/Positive	13.90%	OS=47.18	

Table 5 presents the age-wise distribution of patients along with their corresponding overall survival (OS) percentages. The majority of patients (75.9%) were

between 50 and less than 70 years old, showing an OS of 89.30%. Patients younger than 50 years constituted 21.7% of the group with an OS of 87.31%,

while those aged 70 years and above made up only 2.4% but had a notably lower OS of 61.60%. The p-value of 0.544 indicates that the differences in

overall survival across these age groups are not statistically significant.

Age	N%	Os (Months)	P Value
<50YRS	21.70%	OS=87.31	P=0.544
50-< 70YRS	75.90%	OS=89.30	
>/= 70 YRS	2.40%	OS=61.60	

Table 6 presents the stage-wise survival rates of endometrial cancer patients, showing a clear decline in survival as the disease progresses. Patients diagnosed at Stage IA have the highest survival rates, with 50.40% surviving at 0 years and 83.69% surviving over the observed period. Survival rates decrease notably in Stage IB, with 26.50% at 0 years and 71.41% overall survival. In Stage II, the survival at 0 years drops sharply to 6%, but the overall

survival remains relatively high at 75.62%. More advanced stages show significantly poorer outcomes: Stage III patients have 13.30% survival at 0 years and 47.76% overall survival, while Stage IV patients exhibit the lowest survival rates of 3% at 0 years and 22.76% overall. The p-value of 0.000 indicates that these differences in survival rates across stages are statistically significant.

Stage	Survival(0s)	Survival(Overall)	P Value
IA	50.40%	83.69%	P =0.000
IB	26.50%	71.41%	
II	6%	75.62%	
III	13.30%	47.76%	
IV	3%	22.76%	

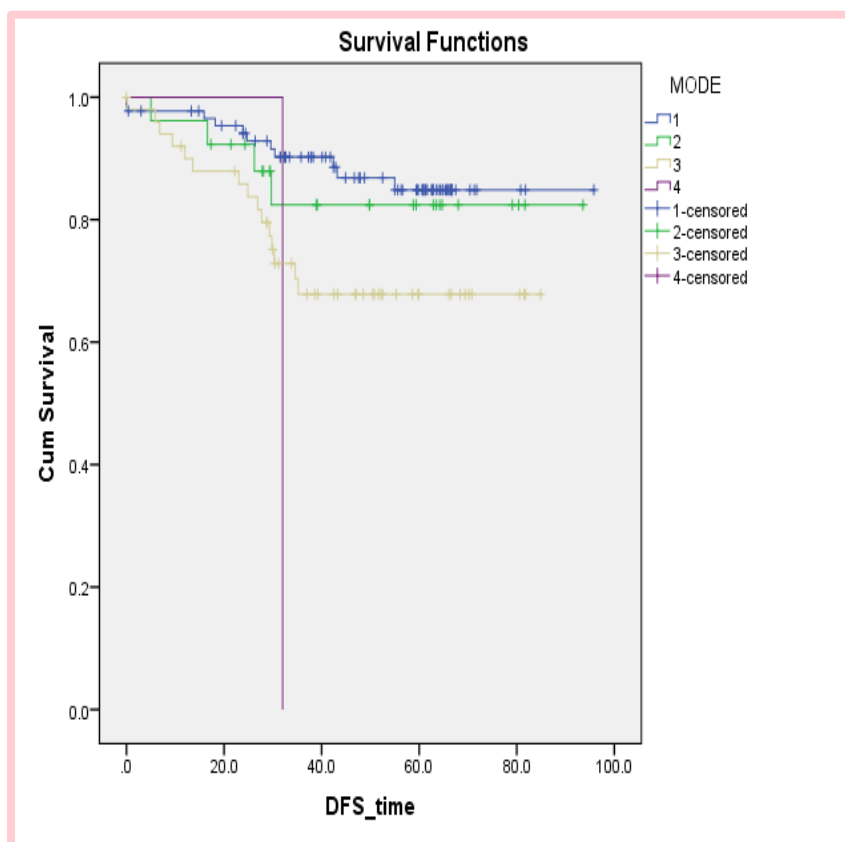


Figure 1: Survival Function

Table 7 presents a regression analysis of various prognostic factors along with their hazard ratios (Exp(B)) and statistical significance (Sig.). Among

these factors, lymphovascular space invasion (LVSI) shows a strong and significant association with prognosis (Hazard Ratio 4.736, p = 0.002),

indicating that its presence considerably increases risk. Age also emerges as a significant factor (HR 2.593, $p = 0.037$), suggesting higher age correlates with worse outcomes. Other variables such as tumor diameter (T_DIA) and mode of treatment (MODE) show a trend toward significance ($p = 0.068$ and $p = 0.094$ respectively) but do not reach conventional

significance levels. Factors like residual disease (RD), histology, grade, myometrial invasion (MY_INV), pelvic lymph node involvement (PELVIC_LN), and stage did not show statistically significant effects on prognosis in this model. Overall, LVSI and age appear to be the most critical independent prognostic factors in this analysis.

Table 7: Regression Analysis of Prognostic Factors with Hazard Ratios and Significance

	B	SE	Wald	df	Sig.	Exp(B)	95.0% CI for Exp(B)	
							Lower	Upper
RD	-0.714	1.111	0.412	1	0.521	0.49	0.055	4.325
MODE	0.773	0.462	2.797	1	0.094	2.166	0.876	5.359
ADJ_RT	-0.034	0.4	0.007	1	0.931	0.966	0.441	2.114
ADJ_CT	-0.131	0.805	0.027	1	0.871	0.877	0.181	4.249
HISTOLOGY	0.205	0.178	1.334	1	0.248	1.228	0.867	1.739
GRADE	0.31	0.298	1.082	1	0.298	1.364	0.76	2.448
MY_INV	-0.437	0.581	0.567	1	0.451	0.646	0.207	2.015
LVSI	1.555	0.501	9.638	1	0.002	4.736	1.774	12.644
PELVIC_LN	0.728	0.671	1.177	1	0.278	2.072	0.556	7.724
PA_LN_DIS	-0.104	0.587	0.031	1	0.859	0.901	0.285	2.847
T_DIA	1.907	1.046	3.324	1	0.068	6.733	0.867	52.31
STAGE	0.008	0.382	0	1	0.984	1.008	0.476	2.133
AGE	0.953	0.456	4.363	1	0.037	2.593	1.06	6.339

Discussion

The present study highlights several key prognostic factors influencing overall survival (OS) in patients with endometrial cancer, consistent with findings reported in the literature. The histological subtype emerged as a crucial determinant of patient outcomes. Patients with endometrioid endometrial carcinoma (EEC) demonstrated significantly better survival compared to those with non-endometrioid histology. This finding aligns with existing evidence that EEC, generally considered a less aggressive subtype, is associated with a more favorable prognosis, whereas non-endometrioid carcinomas often represent high-grade tumors with aggressive clinical behavior and poorer outcomes.

Tumor grade also significantly impacted survival. Interestingly, Grade 2 tumors showed the highest OS in this cohort, even surpassing Grade 1 tumors, which may reflect variations in biological behavior or treatment responsiveness in this specific population. However, Grade 3 tumors were clearly associated with worse survival, consistent with their higher malignancy potential and propensity for invasion and metastasis. Moreover, Verrier et al. [12] stated that clear cell was the second most common histological type with an incidence of 22%. Our case had a different finding, the second most common was serous-papillary tumor (10%), which is similar to the ASTEC study findings [13]. They also found differences in grade of differentiation. In the ASTEC study G1 was the most frequent (51%) followed by G3 (34%). In our case G2 was the most

common (42%) followed closely by G1 (40.2%). When we compared the FGIO stages to the ASTEC study, we saw similar percentages in their early stages; we had stage I at 81% versus 78-81% in the ASTEC study. Myometrial invasion, while clinically considered an important risk factor, did not show a statistically significant difference in survival between patients with less than 50% versus 50% or greater invasion in this study. Although a trend toward lower survival with deeper invasion was observed, the lack of statistical significance could be due to sample size limitations or other confounding factors.

Lymphovascular space invasion (LVSI) status strongly correlated with survival outcomes. Patients with substantial or positive LVSI had markedly reduced OS, underscoring the role of LVSI as a marker of tumor aggressiveness and a predictor of metastatic potential. Regression analysis further confirmed LVSI as an independent prognostic factor, with a hazard ratio indicating a more than fourfold increased risk of mortality. Tejerizo-García et al. indicated that tumor grade was an independent prognostic factor for OS in patients with EC [14]. Also, the endometrioid subtype, LVSI, and LN invasion were important variables related to survival. In a retrospective cohort study conducted to study the impact of LVSI on survival among patients with EC overall also concluded that patients with positive LVSI initially had worse overall survival than those with negative LVSI [15]. A similar finding was reported in the study conducted by Oliver-Perez et al.,

with patients with EC with positive LVSI had a lower disease-free survival [16].

Age was another significant independent prognostic factor. Older patients (≥ 70 years) had lower survival rates, which may reflect comorbidities, decreased physiological reserve, or differences in treatment tolerance and aggressiveness.

Stage-wise survival analysis demonstrated the expected pattern of declining survival with advancing disease stage. Early-stage (IA) patients had the highest OS, whereas patients with stage III and IV disease had significantly worse outcomes, consistent with the natural history of endometrial cancer and the impact of disease dissemination on prognosis. The most significant predictor of OS in our multivariate analysis was consistently greater than 60 years old at diagnosis. Also, we observed that OS is highly dependent on stage at diagnosis, with advanced stage (III to IV) patients having lower OS. Of note, it is shown that OS deteriorates the more undifferentiated the tumor, with serous-papillary having a lower probability of survival than endometrioid. Our data disagree with other previous studies, such as Matsubara et al. [17], who in their multivariate analysis, found stage at diagnosis to be the independent clinical variable with the most influence on OS.

Interestingly, factors such as histology, tumor grade, myometrial invasion, pelvic lymph node involvement, and stage did not independently predict prognosis in the regression model, possibly due to the interplay of multiple variables and the strong influence of LVSI and age. These findings highlight the critical importance of LVSI assessment and patient age in prognostic evaluation and risk stratification of endometrial cancer. The data also reinforce the need for individualized treatment planning, considering these factors to optimize outcomes.

Conclusion

The study demonstrates that there are multiple factors that affect prognosis in endometrial cancer with histological subtype, tumor grade, lymphovascular space invasion (LVSI), age, and disease stage known to play the most important roles. Endometrioid endometrial carcinoma has a markedly better survival than a non-endometrioid tumor. Tumor grade had an impact on outcomes; however, higher grades had worse survival outcomes. LVSI appeared to be a strong independent prognostic factor with patients with LVSI having over fourfold increase in mortality risk making it a marker of aggressive disease. Age was also shown to be of importance because of the effects of comorbidities and tolerability of treatment; older patients did much worse as compared to younger patients. Advanced stage did correspond to lower survival rates, while other known prognostic factors such as the extent of myometrial invasion, and lymph node metastasis had no

independent effect size in the multivariate analysis possibly due to intertwining relationships of variables. These findings demonstrate the importance of LVSI and age in risk stratification, and molecular typing in the personalization of treatment decisions in order to improve survival in patients with endometrial cancer.

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