International Journal of Research in Medical Sciences
Angadi V et al. Int J Res Med Sci. 2022 Sep;10(9):1925-1929
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20222266

Original Research Article

Clinicopathological features and prognostic factors in endometrial carcinoma: a retrospective analysis from a tertiary cancer centre

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Received: 10 August 2022
Accepted: 25 August 2022

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ABSTRACT

Background: Endometrial carcinoma (EC) is most common gynecological malignancy. The incidence of endometrial cancer is rising rapidly with only limited evidence on the clinicopathological features, survival data and prognostic factors. The study aimed to evaluate the clinicopathological features, treatment, recurrence pattern, survival and to assess the prognostic factors in patients with endometrial carcinoma.
Methods: After obtaining approval from institutional ethics committee, 94 patients who were diagnosed with EC were included in the study. The data were presented as proportions and survival curve analysis was done using the Kaplan Meir curve and significance using log rank tests.
Results: A total of 94 patients diagnosed with EC were included in the study with a mean age of 55.1 years. The Myometrial invasion was observed in 46.9% of the patients with 35.2% having lymphovascular involvement. Clinical characteristics of the patients showed grade 1 (35.1%) followed by grade III (17.02%). Survival analysis showed that elderly age, multi parity, advanced disease stage, more than 50% of myometrial invasion, grade II and grade III tumors, lymphovascular space invasion, adversely affected long-term survival when analyzed by log-rank test. The disease-free survival (DFS) at 5 years was found to be 77% and overall survival (OS) at 5 years was 79.7%.
Conclusions: Endometrial carcinoma is seen commonly in postmenopausal women wherein delaying the treatment significantly affects the long-term survival. Therefore, early diagnosis reduces the mortality and increases the disease-free survival in these patients.

Keywords: Endometrial carcinoma, Myometrial invasion, Postmenopausal

INTRODUCTION

Endometrial cancer is the most common gynecologic cancer in developed countries and it is the ninth most common cancer among Indian women, with an incidence of 2.3% in India.[1] Compared to other gynecological cancers, EC has a comparatively lower mortality rate. The incidence of EC increases with age, unopposed estrogen and also in patient's hormone replacement therapy (HRT).[2]

The standard treatment protocol for EC consists of surgery followed by adjuvant therapy based on pathological prognostic factors.[3] The true extent of endometrial cancer can be ascertained only after exploratory laparotomy and then various adjuvant therapies may be used based on the stage of the disease.

The majority of the tumors are surgically resectable on presentation. Hence, surgery remains the first-line of therapy with an abdominal hysterectomy and bi-lateral

salpingo-oophorectomy being the most performed surgeries.[2] Chemotherapy and adjuvant radiotherapy are used in case of adverse prognostic factors.

The most significant prognostic factor are tumor stage, histological grade and type, depth of myometrial invasion, lympho-vascular space or nodal involvement. The optimal adjuvant therapy in high and intermediate risk endometrial cancer is still controversial.[5] In patients with a postoperative incidental diagnosis of carcinoma endometrium, histopathological review, good clinical and radiological assessment can identify patients who will benefit from completion staging.[4]

Effective risk reduction interventions by capturing the mechanisms which drive endometrial carcinogenesis in patients with high risk for EC may help in early diagnosis and management of EC, thus reducing the disease related morbidity and mortality.

Thus, this study was undertaken to assess clinicopathological features, treatment, recurrence pattern, survival and prognostic factors in patients with endometrial carcinoma. This undertaking of the key risk factors and their role in tumorigenesis helps in developing preventive and early diagnostic strategies in the center.

Objectives

Objectives of the study were: to assess the clinicopathological features, treatment, recurrence pattern and survival in patients with endometrial carcinoma; and to assess the prognostic factors in patients with endometrial carcinoma.

METHODS

This retrospective study was conducted based on the data available on the endometrial carcinoma patients. All patients profile from January 2013 to December 2020 were included in the study. Data were obtained from the Registry of patients' profile from the department of medical oncology of Vydehi Institute of Medical Sciences and Research Centre, Bangalore. The study conducted after assessment and approval from the institutional ethics committee.

The inclusion criteria in the study were those who were diagnosed histologically as malignant and who had completed the treatment. The exclusion criteria were those whose cancer was not proven histologically as primary endometrial cancer and those who did not complete the cancer directed treatment. Patient demographics, clinical and drug data, details of the surgery, chemotherapy, radiotherapy, the onset of disease, medications, outcome, procedures conducted, the pattern of disease and survival data were noted in the proforma. Factors affecting the prognostic factors were analyzed. Confidentiality of data was maintained.

Assessment tools

Disease free survival

The DFS was defined as the period from primary surgery until relapse.

Overall survival

Overall survival (OS) was defined as the period from primary surgery until death or until completion of a 5-year follow-up.[5]

The staging was defined according to the international federation of gynecology and obstetrics (FIGO) guidelines for the staging of EC.[6]

Statistical analysis

Data were entered and analyzed by statistical package for the social sciences (SPSS) version 25. Variables such as age, parity co-morbidities and clinical characteristics were expressed as frequencies and percentages. Survival data were analyzed using Kaplan-Meier estimates, and compared using the log-rank test.

RESULTS

A total of 125 were taken from the electronic hospital records from 2013 to 2020 for the study, but 29 patients were excluded as they did not meet the inclusion criteria. The results of the present study are based on the 94 study patients. The detailed demographic characteristics of the patients are mentioned in Table 1. The mean age of the study patients was 55.1±9.21. The majority of the patients were between the age groups 51-69 years (63.83%).

The majority of the patients were multiparous (86.1%). Comorbidities like type 2 diabetes mellitus (T2DM) was present in 23.4% and hypothyroidism was seen in only 7.45% of the patients. 26.5 % of the patients were pre-menopausal and 52.3% were post-menopausal. Myometrial invasion was more than 50% in 46.9% of the population and lymph-node involvement was seen in 35.2% of the patients. Clinical characteristics of the patients were also evaluated and majority of the patients were grade 1 (35.1%) followed by grade III (17.02%).

Risk assessment of endometrial carcinoma patients with the available data showed the majority of the patients were low risk category (12.77%). The staging was done and the majority of the patients belonged to stage III (40.4%). The treatment given was also evaluated with the available data and was taken by 79.7% of the patients and adjuvant chemo was given to 26.6% of patients and radiotherapy to 14.8% of patients. Adjuvant radiotherapy was given as pelvic external beam radiotherapy (EBRT) or vaginal brachytherapy (VBT) either singly or in combination as per risk factors present. EBRT and VBT was present in 18.09% and VBT was present in 14.89% of the patients.

Table 1: Demographic characteristics of patients with endometrial carcinoma (n=94).

Demographic characteristics	N=94	Percentage
Age (years)		
<50	27	28.72
51-69	60	63.83
>70	7	7.45
Parity		
Nulliparous	13	13.8
Multiparous	81	86.1
Diabetes mellitus		
Absent	64	68.09
Present	22	23.40
Unknown	10	10.64
Hypothyroidism		
Absent	76	80.85
Present	7	7.45
Unknown	11	11.70
Pre-menopausal		
Absent	69	73.4
Present	25	26.5
Post-menopausal		
Absent	39	41.49
Present	49	52.13
Unknown	6	6.38
Abdominal pain		
Absent	64	68.09
Present	26	27.66
Unknown	4	4.26
Water density volume		
Absent	77	81.91
Present	13	13.83
Unknown	4	4.26
Myometrial involvement		
<50	50	53.1
>50	44	46.9
Lymphovascular invasion		
Absent	61	64.8
Present	33	35.2

During the follow-up period, many patients had disease recurrence. The mean observation time was 7 years. The tumour recurrence rate was 11.7% (11 patients) and the mortality rate was 24.46% (6 patients); 75.6% (n=71) of patients were alive at the closure of the study and they continued with follow-up. The DFS at 5 years was 77% and OS at 5 years was 79.7% (Figure 1 and 2). The mean DFS (in months) was 36.98±10.65. The mean OS (in months) was 40.09±10.41. We evaluated various clinicopathological features as potential prognostic factors for survival. We observed that elderly age, multi parity, advanced disease stage, more than 50% of myometrial invasion, grade II and grade III tumors and lymphovascular space invasion adversely affected long-term survival when analyzed by log-rank test.

Table 2: Clinical characteristics of patients with endometrial carcinoma (n=94).

Clinical characteristics	N=94	Percentage
Grade		
I	33	35.11
II	12	12.77
III	16	17.02
Unknown	33	35.11
Risk		
LR	12	12.77
LIR	7	7.45
HIR	5	5.32
HR	11	11.70
Unknown	59	62.77
Stage		
IA	27	28.72
IB	15	15.96
II	12	12.77
III	38	40.43
IV	2	2.13
Post op HPE		
Endometrial adeno carcinoma	76	80.85
Papillary Ca	2	2.13
Sarcoma	6	6.38
Serous	1	1.06
Unknown	9	9.57

Table 3: Treatment history of patients diagnosed with endometrial carcinoma (n=94).

Treatment	N=94	Percentage
Adjuvant chemo		
Absent	58	61.70
Present	25	26.60
Unknown	11	11.70
RT EBRT		
Absent	69	73.40
Present	14	14.89
Unknown	11	11.70
EBRT+ VBT		
Absent	66	70.21
Present	17	18.09
Unknown	11	11.70
VBT only		
Absent	68	72.34
Present	14	14.89
Unknown	12	12.77
Treatment taken		
Absent	19	20.21
Present	75	79.71
Mortality		
Dead	23	24.46
Alive	71	75.53

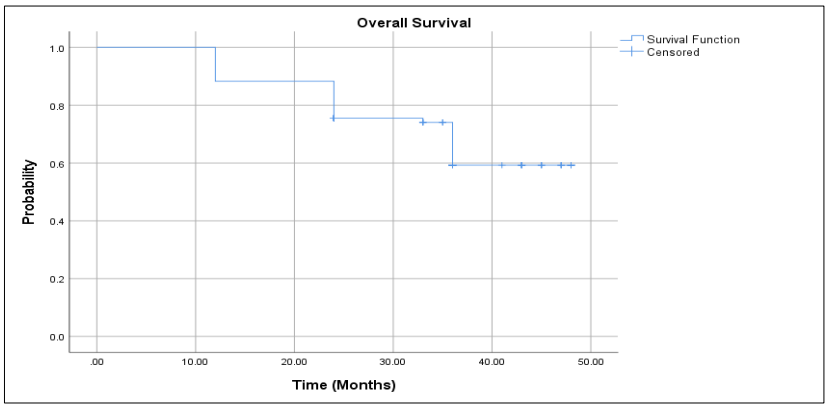

Figure 1: Kaplan Meier curve showing overall survival over a period of 5 years.

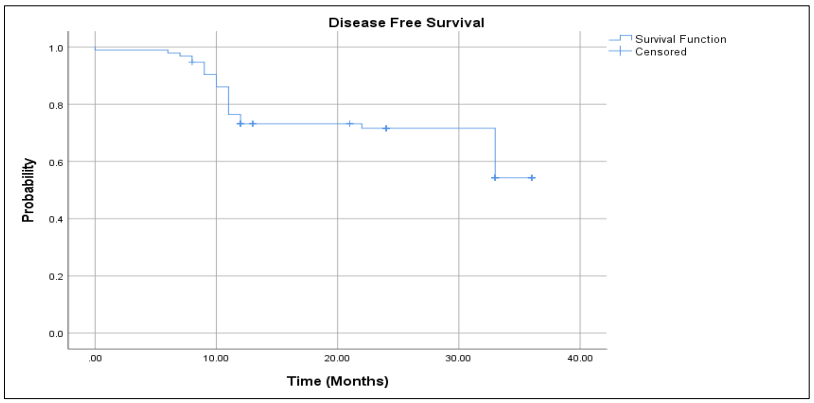

Figure 2: Kaplan Meier curve showing disease free survival over a period of 5 years.

Table 4: Survival analysis of various prognostic factors.

Disease free survival (DFS) and overall survival (OS) at 5 years	DFS		OS (%)
	Percen -tage	P value	
Age (years)			
<50	59.5	Ref	61.5
51-69	62.3	0.001	65.3
>70	8.2	0.0002	9.2
Parity			
Nulliparous	65.7	Ref	68.7
Multiparous	54.3	0.037	69.2
Stage			
I	68.1	Ref	71.1
II-IV	38.2	<0.001	39.3
Grade			
I	65.1	Ref	62.2
II	58.1	0.032	59.8
III	34.2	<0.001	34.2
MI			
<50	66.1	Ref	69.2
>50	53.4	<0.001	55.4
LVI			
Absent	67.1	Ref	71.1
Present	44.3	0.001	46.3

DISCUSSION

Endometrial cancer is the cause of increasing morbidity among women, but the disease has been underdiagnosed and its management has been considered more casual than its virulency expects.[7] Incidental diagnosis of endometrial cancer following hysterectomy poses a clinical dilemma to the gynaecologic oncologist.

Underdiagnosed patients have an increased risk of developing end-stage disease where the management imposes the mortality threat in such patients. Hence the present study was undertaken conducted to the prognostic factors which influences the disease pattern in EC, so that early diagnosis strategies can be framed for improving survival.

Total of 94 patients were included in the study. The mean age of the patients was 51.1 years as reported by Elissawy et al and Signorelli et al in previous studies.[7,8] EC is a disease of post-menopausal women and in the present study 52.3% of the patients were post-menopausal.[6]

Treatment for EC is mainly surgery. In this study, out of 94 patients, 89 underwent a standard primary surgical procedure (TAH with BSO + pelvic/para-aortic LND) and only 5 patients underwent simple hysterectomy. Post-

Surgical management was done by adjuvant chemotherapy, RT EBRT, EBRT+VBT and only VBT.[10]

Mainstream post operative histopathological examination (HPE) showed endometrial adenocarcinoma (80.85%), which is on par with the study conducted by Singh et al.[3] The prognostic factors that adversely affects the long-term survival of EC are attributed to age at diagnosis, multi parity, advanced disease stage, more than 50% of myometrial invasion, grade II and grade III tumors and lympho-vascular space invasion.

The majority of the patients were multiparous but the nulliparous women have higher DFS. As nulliparity is not the independent risk factor the DFS could be attributed to the high number of anovulatory menstrual cycles in infertile and sub-fertile women.[9]

Generally known factors that affect the survival is the clinical stage of the disease.[5] In the present study, after complete surgical staging, most of our patients had the late-stage disease (stage II and stage III) and patients with stage I disease had higher DFS. This highlights the importance of early complete surgical staging in the adequate and appropriate management of endometrial cancer, especially in early-stage endometrial cancer for better outcomes for such patients.

In the present study in patients with <50% myometrial involvement and with no lympho-vascular invasion have shown a higher DFS. A study conducted by Sartori et al showed that, that the site of relapse as the most important factor affecting the disease-free interval.[7]

In our study DFS and OS over the period of 5 years showed similar data as published by Gottawald et al, were 81.7% and 83.1% respectively.[8]

Limitations

Study's limitations were the retrospective nature of the study. Large trials with a high sample size are required to assess its therapeutic benefit. As the study was conducted in a single centre there could be possible bias in the patient profile and thus generalisability to a larger population is not possible.

CONCLUSION

The present study provides comprehensive data on the patients with endometrial carcinoma. Majority of the patients were elderly, post-menopausal, nulliparous women with EC. It is important to note that in patients with advanced age, multiparity, advanced disease, stage II to III, more than 50% of myometrial invasion, grade II and grade III tumors and lymphovascular space invasion are the strong predictors of poor prognosis. Considering these findings seriously while treating patients with EC, enhances clinical suspicion which leads to early diagnosis. Thus, reduces the mortality along with increase in disease free survival in these patients.

ACKNOWLEDGEMENTS

Authors would like to thank all the faculty members of the department of medical oncology, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, for their support in conducting the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Angadi V, Praisy E, Tatineni T, Karpurmath SV, Nandennavar MI. Clinicopathological features and prognostic factors in endometrial carcinoma: a retrospective analysis from a tertiary cancer centre. Int J Res Med Sci 2022;10:1925-9.