Survival Determinants in Endometrial Cancer Patients: 5-Years Experience

Abstract

Aim: The aim of the study was to explore five years survival in women with endometrial cancer.

Material and Methods: A retrospective review of 146 patients with endometrial cancer treated at Baskent University Hospital Gynecologic Oncology Clinic in Ankara, Turkey between 2010 and 2015 was performed. Demographic and clinic-pathological data were compared with survival.

Results: The median age of the patients was 61.4 y±5.3 years (36-82). The overall 5-years survival was 89%. Multivariate Cox regression model revealed that the FIGO stage, grade, age, histological type, myometrial invasion, and lymph node involvement were all predictive factors on survival (p<0.05). However, the menopausal status, age at menopause, parity, BMI, comorbidities, ECOG performance score, therapy modality, HR status, and family history were not associated with survival (p>0.05).

Conclusion: The results of our study, several clinic-pathological prognostic factors of EC have been identified on survival. These results provided significant evidence that early foresight of EC survival. Further prospective randomized studies are necessary to clarify the role of these factors.
1. The Patient Information Form; This form includes 15 questions to define individual and medical characteristics of the women with EC such as age, body mass index (BMI), menopause status, menopause age, hormone receptor (HR) status, parity, subtype, stage, grade, type of therapy, lymph node involvement and myometrial invasion. Histology was classified based on the International Classification of Diseases for Oncology (ICD-O) as endometrioid and non-endometrioid. Stage categories were based on the International Federation of Gynecology and Obstetrics (FIGO) stages I, II, III and IV [13]. Survival time was calculated from date of diagnosis until death. BMI values of patients were classified as underweight (BMI <18.5 kg/m²), normal (BMI 18.5–24.9 kg/m²), overweight (BMI 25–29.9 kg/m²), and obese (BMI ≥30 kg/m²) according to World Health Organization (WHO) criteria [14].

2. The Charlson Comorbidity Index (CCI); Comorbidity was measured for each patient using the CCI, categorized as 0, 1, or ≥2, with a higher score indicating a larger number or greater severity of comorbidities. The CCI, ranging from 0 to 29, consists of a weighted sum of 17 major illnesses (e.g., myocardial infarction, stroke, diabetes, liver disease, dementia, renal disease) [15].

3. European Cooperative Oncology Group (ECOG) Performance Scale; This scale was developed by the Eastern Cooperative Oncology Group (ECOG) in 1982 to classify a patient according to their functional impairment, compare the effectiveness of therapies, and assess the prognosis of a patient (from 0 to 5, with 0 denoting perfect health and 5 death) [16].

The statistical program SPSS version 18 (SPSS, Inc, Chicago, IL) was used to process the results. Data were given as percent or mean ± standard deviation (SD). Statistical analysis was performed Chi-square, Fisher’s exact tests, Multivariate Cox regression, Kaplan–Meier survival analysis. The level of significance was established at p<0.05.

Results

Detailed characteristics of the patient set are shown in Table 1. Totally, 146 women with EC who met the inclusion criteria were included in the study. The median age of the patients was 61.4 y ±5.3 years (min:36, max:82), 54.1 % patients were younger than 60 years and average age of menopause was 50±5.24 years (min:41–max:56). The mean parity was 3.21±4.5, ranging from 0 to 14 and 58.2% were overweight + obese.

According to the 1988 FIGO criteria, 116 (79.4%) patients had stage I–II and 30 (20.6%) had stage III–IV disease. Grades of the disease were grade I in 90 (61.6%) and grade ≥II in 56 (38.4%) patients. EC was classified as endometrioid (n=124) and non-endometrioid type (n=22). Lymph node involvement was found in 26 patients (17.8%), the depth of myometrial invasion was smaller than 50% in 94 patients (64.3%), and HR status was positive in 112 patients (76.7%). Among patients with EC, 31.5% had CCI- 0, and 68.5% had CCI- ≥1. ECOG performance status was “0-1” (67.1%), “≥2” (32.9%) in patients’ last hospitalizations (Table 1). The most common symptom at presentation for patients was postmenopausal bleeding (88.9%). Twenty-five percent of women had cancer stories in their families. All patients underwent primary surgery (a hysterectomy with bilateral salpingo-oophorectomy). Lymphadenectomy was performed on forty-five patients with/without omentectomy and bowel surgery. Postoperative external-beam pelvic radiotherapy (EBRT) and/or brachytherapy (BT) were administered to the majority of the patients (82.2%).

Table 1: Clinical characteristics of the women with EC and survival analysis.

| Variables            | N   | %   | 5-y survival Median: 89% | x²/p  |
|----------------------|-----|-----|--------------------------|-------|
| Age (Mean: 61.4 y ±5.3) |     |     |                          |       |
| ≤60                  | 79  | 54.1| 88.4                     | 5.394 | 0.002 |
| >60                  | 67  | 45.9| 71.5                     |       |       |
| Menopausal status    |     |     |                          |       |
| Premenopausal        | 20  | 13.7| 94.4                     | 0.026 | 0.761 |
| Postmenopausal       | 126 | 86.3| 81.5                     |       |       |
| Age at menopause (Mean: 50.6±5.24) |     |     |                          |       |
| ≤50                  | 63  | 43.2| 80.3                     | 0.493 | 0.164 |
| >50                  | 83  | 56.8| 85.4                     |       |       |
| BMI                  |     |     |                          |       |
| Normal (18.5-24.9 kg/m²) | 61  | 41.8| 84.5                     | 1.254 | 0.232 |
| Overweight + Obese ≥25 kg/m²) | 83  | 58.2| 81.9                     |       |       |
| Parity (Mean: 3.21±4.5) |     |     |                          |       |
| Yes                  | 129 | 85.4| 81.9                     | 1.022 | 0.056 |
| No                   | 17  | 14.6| 80.0                     |       |       |
| Grade                |     |     |                          |       |
| I                    | 90  | 61.6| 88.1                     | 7.942 | 0.014 |
| II-III               | 56  | 38.4| 64.4                     |       |       |
| Stage                |     |     |                          |       |
| I-II                 | 116 | 79.4| 91.7                     | 6.561 | 0.020 |
| III-IV               | 30  | 20.6| 56.2                     |       |       |
| Subtype              |     |     |                          |       |
| Endometrioid         | 124 | 84.9| 93.4                     | 11.670| <0.001 |
| Non-endometrioid     | 22  | 15.1| 71.5                     |       |       |
| Lymph node involvement|     |     |                          |       |
| Positive             | 26  | 17.8| 69.4                     | 10.230| <0.001 |
| Negative             | 120 | 82.2| 88.7                     |       |       |
| Myometrial invasion  |     |     |                          |       |
| ≤50 %                | 104 | 74.3| 92.6                     | 9.781 | <0.001 |
| >50 %                | 42  | 25.7| 66.0                     |       |       |
| CCI                  |     |     |                          |       |
| 0                    | 46  | 31.5| 88.4                     | 0.452 | 0.462 |
| ≥1                   | 100 | 68.5| 79.2                     |       |       |
| ECOG                 |     |     |                          |       |
| 0-1                  | 98  | 67.1| 83.5                     | 0.309 | 0.135 |
| 2-3                  | 48  | 32.9| 80.0                     |       |       |
| HR status            |     |     |                          |       |
| Positive             | 112 | 76.7| 89.0                     | 1.200 | 0.356 |
| Negative             | 34  | 23.3| 78.4                     |       |       |

HR: Hormone receptor, BMI: Body Mass Index, CCI: The Charlson Comorbidity Index, ECOG: European Cooperative Oncology Group.
Survival analysis was performed in the evaluation of 146 patients. The median of survival was 89%. HR status, BMI, CCI, menopause status, age at menopause, family history, ECOG performance status and treatment type were not significant for the survival of the EC (p>0.05). Lower stage and grade of disease, endometrioid subtype, lymph node involvement, and depth of myometrial invasion ≤ 50% were prognostic factors for better survival (p<0.05). Increased age was associated with decreased survival (p<0.05) (Table 1).

Similarly, on multivariate analysis; advanced age was significantly associated with worse OS (HR, 1.4 [95% CI, 1.3–1.4]) than younger women. Non-endometrioid was associated with worse OS than endometrioid cancers (HR, 1.3 [95% CI, 1.2–1.5]). Higher grade (HR, 1.1 [95% CI, 1.1–1.3]), stage (HR, 2.0 [95% CI, 1.1–2.8]), myometrial invasion (HR, 1.3 [95% CI, 1.1–1.6]), and lymph node involvement (HR, 1.2 [95% CI, 1.0–1.3]) had significantly poorer OS rates (Table 2).

### Discussion

EC is most common amongst postmenopausal women and the main symptom is irregular or postmenopausal bleeding so the prognosis is generally favorable [5]. In our study, postmenopausal bleeding was seen in 88.9% of patients. In accordance with our study, Keskin et al. also reported postmenopausal vaginal bleeding as the most common complaint [7]. Over the past few decades, several studies have demonstrated the prognostic importance of different parameters [6–12]. In this study, 5-year survival of patients was 89%. The previous study confirmed that in these data on survival. Gottwald et al. [12], found that the 5-year survival for EC was 87%. Ayhan et al. [17], reported that the 5-year overall survival rate of entire group was 86% [17]. Karateke et al. [9], documented that 5-year survival of patients with EC was 76.9%. In a study by Craighead et al. [10], a 5-year survival rate of 65% was identified. By contrast, Jhingran et al. [18], reported a 4-year survival rate of only 42%.

In this study, older women were found to have a poorer prognosis, survival declined with increased age (p<0.05). Analysis of 165 women of EC indicated that old age was associated with poor survival [11]. Bristow et al. [8] and Ferlay et al. [19], demonstrated that EC survival decreases in older patients. However, Karateke et al. [9], Gottwald et al. [12], and Bajracharya and Juan [6], found age at diagnosis was not significant predictor of survival for EC.

When diagnosed at a local or regional stage, the 5-year survival rate is 96% and 67% respectively, while distant stage survival decreases to 16%. [20]. Bajracharya and Juan [6], found that stage was among the most important prognostic factors in EC. In a large study conducted by Karateke et al. [9], five years survival rates in patients with stage I-IV disease were 83.3%, 80%, 62.5% in stage III and 33.3%, respectively. Craighead et al. [10], demonstrate that disease stage was the most important prognostic factor affecting survival. Our findings match well with previous studies, these rates in patients with stage I-II and II-IV disease were 91.7%, and 56.2%, respectively. Consequently, staging became one of the most important prognostic factors (p<0.05) and this was similar to the results of previous studies.

In the literature, tumor grade is also known to affect survival [5,6,9]. In this study showed there was a significant correlation between histological grades (88.1% for grade I and 64.4% for grade II–III) as prognostic factors (p<0.05). In the other study, 5 years survival rates of grade 1-3 EC were 71–88% for grade I, 60–79% for grade 2 and 32–65% for grade 3 [20]. In the present study, five years survival rates were 93.3% for grade I, 77.3% for grade II and 60% for grade III, and these rates were consist with literature. Consequently, the overall survival analyzes showed a statistically significant difference among grade I–III (p<0.05).

In general, patients with tumors of non-endometrioid subtypes have a worse prognosis than those with tumors of endometrioid subtypes [12,20]. In this study, patients with non–endometrioid subtype (71.5%) were lived shorter than those with endometrioid type (93.4%) (p<0.05). According to Karateke et al. [9] and Bajracharya and Juan [6], non-endometrioid type of endometrial carcinoma tends to have lower survival rates as compared to endometrioid type. In contrast to this, Craighead et al. [10], documented that subtypes of EC on endometrial carcinoma prognosis was not remarkable (p>0.05).

Previous studies showed that the depth of myometrial invasion ≤ 50% were independent prognostic factors for better survival [6,9,12,21]. In a large study, five years survival rates of patients with or without deep myometrial invasion were found as 60% and 80%, respectively [20]. In our study, myometrial invasion had a significant impact on survival. Five years survival rates were differed between patients with tumor confined to inner 1/2 of myometrium and those had beyond this level (92.6%, 66.0%, respectively, p<0.05). The results do not match well with those of Lim et al. [11] and Ayhan et al. [22], deeper myometrial invasion was not associated with prognosis for women with EC.

Based on the available scientific evidence, lymph node involvement is also known to affect survival in EC [11]. In this study, significant difference by means of five years survival was found between patients with lymph node involvement and those with no involvement (69.4% and 88.7%, respectively, p<0.05). Fader et al. [5] and Ayhan et al. [22], reported that the most important prognostic factor in EC is nodal involvement.

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**Table 2: Multivariate Cox regression model of OS (5-year).**

| Variables | HR | 95% CI   | P       |
|-----------|----|----------|---------|
| Age at diagnosis (≥60y vs >60y) | 1.43 | 1.31-1.49 | 0.002   |
| Stage (III-IV vs I-II) | 2.01 | 1.13-2.80 | 0.020   |
| Subtype (endometrioid vs others) | 1.34 | 1.23-1.53 | 0.001   |
| Grade (1 vs ≥2-3) | 1.15 | 1.11-1.34 | 0.003   |
| Lymph node involvement (+/-) | 1.23 | 1.06-1.36 | 0.031   |
| Myometrial invasion (≤ 50% vs >50%) | 1.32 | 1.18-1.67 | 0.015   |

HR: hazard ratio, CI: Confidence Interval.

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Conclusion

In the result of this study, the median 5-year survival for OC was 89%. Age at diagnosis, histological subtype, stage, grade, depth of myometrial invasion and lymph node involvement have been identified as predictors of survival. The results of our work may contribute to better understand its clinical behavior. Further multicenter randomized studies are necessary on large number of patients to prove the role of these factors, which leads to improve the survival.

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, et al. (2008) Cancer statistics. CA Cancer J Clin 58: 71-96. Link: https://goo.gl/95izm4
2. Sankaranarayanan R, Ferlay J (2006) Worldwide burden of gynecological cancer: the size of the problem. Best Pract Res Clin Obstet Gynaecol 20: 207-25. Link: https://goo.gl/aadpLU
3. Republic of Turkey Ministry of Health (2009) Department of Cancer Control National Cancer Program, Ministry Publication No: 760. Link: https://goo.gl/ffQw18
4. Kim JW, Kim SH, Kim YT, Kim DK (2002) Clinicopathologic and biological parameters predicting the prognosis in endometrial carcinoma. Yonsei Med J 43: 769-78. Link: https://goo.gl/A1mJ33
5. Fader AN, Arriba LN, Frasure HE, Vivian EG (2009) Endometrial cancer and obesity: epidemiology, biomarkers, prevention and survival. Gynecol Oncol 114: 121-127. Link: https://goo.gl/aGBPCO
6. Bajracharya SR, Juan FY (2013) Prognostic factors in endometrial cancer. Cancer J Clin 58: 71-96. Link: https://goo.gl/95izm4
7. Keskin N, Buyru F, Frasure HE, Vivian EG (2009) Endometrial cancer: the role of cytoreductive surgery and determinants of survival. Gynecol Oncol 78: 85-91. Link: https://goo.gl/tyWpv1
8. Bajracharya SR, Juan FY (2013) Prognostic factors in endometrial cancer. Journal of Institute of Medicine 35: 9-17. Link: https://goo.gl/5IWpv1
9. Keskin N, Buyru F, Bengisu E, Sihhaçılı Y, Berkman S (1996) Factors influencing the prognosis of endometrial carcinoma. T Klin J Gynecol Obstet 6: 254-8.
10. Bristow RE, Zerbe MJ, Rosenshein NB, Francis CG, FJ Montz (2000) Stage IVB endometrial carcinoma: the role of cytoreductive surgery and determinants of survival. Gynecol Oncol 78: 85-91. Link: https://goo.gl/v4DYWn
11. Karateke A, Selcuk S, Asoglu MR, Tug N, Cam C, et al. (2012) Prognostic Factors Affecting Survival In Endometrial Carcinoma. J Turk Soc Obstet Gynecol 9: 42-6. Link: https://goo.gl/E3hK0
12. Craighead PS, Sait K, Stuart GC, Arthur K, Nation J, et al. (2000) Management of aggressive histologic variants of endometrial carcinoma at the Tom Baker Cancer Centre between 1984 and 1994. Gynecol Oncol 77: 248-253. Link: https://goo.gl/1wQFlPL
13. FIGO (International Federation of Gynecology and Obstetrics) (1989) FIGO stages, 1988 revision. Gynecol Oncol 35: 125-7.
14. WHO (World Health Organization) (2000) Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organization technical report series 894: 1-253. Link: https://goo.gl/65ZGQ9
15. Keskin N, Buyru F, Bengisu E, Sihhaçılı Y, Berkman S (1996) Factors influencing the prognosis of endometrial carcinoma. T Klin J Gynecol Obstet 6: 254-8.
16. Bristow RE, Zerbe MJ, Rosenshein NB, Francis CG, FJ Montz (2000) Stage IVB endometrial carcinoma: the role of cytoreductive surgery and determinants of survival. Gynecol Oncol 78: 85-91. Link: https://goo.gl/1wQFlPL
17. Ayhan A, Taskiran C, Celik C, Yüce K (2004) The long-term survival of women with surgical stage II endometrioid type endometrial cancer. Gynecol Oncol 93: 9-13. Link: https://goo.gl/pbl2fbg
18. Jhingran A, Burke TW, Eifel PJ (2003) Definitive radiotherapy for patients with isolated vaginal recurrence of endometrial carcinoma after hysterectomy. Int J Radiat Oncol Biol Phys 56: 1366-1372. Link: https://goo.gl/pbCRoC
19. Farley JH, Nycum LR, Birrer MJ, Park RC, Taylor RR (2000) Age specific survival of women with endometrial adenocarcinoma of the uterus. Gynecol Oncol 79: 86-9. Link: https://goo.gl/vzhbDZ
20. Pessini SA, Zettler CG, Wender MC, Silveria GP (2007) Survival and prognostic factors of patients treated for Stage I to Stage III endometrial carcinoma in a reference cancer center in Southern Brazil. Eur J Gynaecol Oncol 28: 48-50. Link: https://goo.gl/OOr4vU
21. Sorbe B, Juresta C, Ahlin C (2014) Natural history of recurrences in endometrial cancer. Oncol Lett 8: 1800-6. Link: https://goo.gl/Z6q0ES
22. Ayhan A, Taskiran C, Celik C, Inci G, Kunter Y, et al. (2002) Is there a survival benefit to adjuvant radiotherapy in high-risk surgical stage I endometrial cancer? Gynecol Oncol 86: 259-63. Link: https://goo.gl/46a2bc