ORIGINAL ARTICLE

# Investigation of the effect of ABO blood types on the prognosis of endometrioid-type endometrial cancer

## *Investigación del efecto de los grupos sanguíneos ABO en el pronóstico del cáncer de endometrio de tipo endometrioide*

*Havva H. Keser-Şahin[1]*, Fazıl Avcı[2], Mehmet Kulhan[2], Abdul Hamid-Güler[2], Mete Can-Ateş[2], Çetin Çelik[2], and Ahmet Bilgi[2]*

*[1]Department of Pathology, Hitit University Faculty of Medicine, Çorum; [2]Department of Obstetric and Gynecology, Selcuk University Faculty of Medicine, Konya. Turkey*

## Abstract

**Objective:** *The aim of this study was to examine how the ABO blood type affects endometrioid-type, EC prognosis.* **Method:** *A total of 522 patients diagnosed with EC between February 2010 and December 2021 were assessed, retrospectively. ABO blood types were used to divide the patients into four groups as A, B, O, and AB. Demographic data, menopause, prognostic variables, FIGO stage, and survival were evaluated. A in 217 patients, B in 84 patients, O in 181 patients, and AB blood type in 40 patients were analyzed.* **Results:** *Age, gravida, parity, body mass index, menopause, comorbidity, prognostic variables, FIGO stage, and survival according to the groups were similar (p > 0.012). Group A differed from other groups statistically in peritoneal fluid cytology (p = 0.004). B blood type had the best chance of cumulative overall survival, followed by AB, A, and O blood types, in that order (p = 0.170).* **Conclusion:** *In light of blood types sensitivity to endometrioid-type EC, O blood type has been identified as blood type with the highest risk of endometrioid EC.*

***Keywords:*** *ABO blood-type system. Endometrial cancer. Prognosis.*

## Resumen

**Objetivo:** *Examinar cómo los tipos de sangre ABO afectan el pronóstico del cáncer de endometrio de tipo endometrioide.* **Método:** *Se evaluaron retrospectivamente 522 pacientes diagnosticadas con CE entre 2010 y 2021. Se utilizaron los tipos de sangre ABO para dividir a las pacientes cuatro grupos: A, B, O, y AB. Se evaluaron la edad, la menopausia, las variables pronósticas, la etapa FIGO y la supervivencia. Se determinó el tipo de sangre A en 217 pacientes, el B en 84 pacientes, el O en 181 pacientes y el AB en 40 pacientes.* **Resultados:** *La edad, la menopausia, las variables pronósticas, la etapa FIGO y la supervivencia según grupos fueron similares (p > 0.012). El grupo A difirió estadísticamente de los otros grupos en la citología del líquido peritoneal (p = 0.004). El tipo de sangre B tuvo mejor probabilidad de una supervivencia global acumulativa, seguido por los tipos AB, A, y 0, en este orden (p = 0.170).* **Conclusión:** *A la luz de la sensibilidad de los tipos de sangre al cáncer de endometrio tipo endometrioide, el O ha sido identificado como el de mayor riesgo de cáncer endometrial tipo endometrioide.*

***Palabras clave:*** *Sistema de tipo sanguíneo ABO. Cáncer endometrial. Pronóstico.*

***Correspondence:**
Havva Hande Keser-Şahin
E-mail: hndksr@hotmail.com

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# Introduction

In developed countries, endometrial cancer (EC) is the fourth most common cancer in females and the most common gynecological cancer[1]. EC has 1.1% lifetime rate, 0.4% fatality rate, and good prognosis with early diagnosis[2]. Post-menopausal women account for more than 80% of patients with EC[3]. Type 1 and type 2 ECs are the categories of EC. Grade 1 and 2 endometrioid tumors associated with persistent estrogen stimulation are included in type 1 EC. They have typically a good prognosis because of early diagnosis. Type 2 EC encompasses grade 3 endometrioid and non-endometrioid tumors that develop from the atrophic endometrium and have a worse prognosis[4]. The most typical kind of EC is endometrioid-type EC[5]. Therefore, early detection of EC ensures an excellent survival rate[6] and this is associated with a reduction in cancer-related mortality. The ABO blood type has an important role in human blood systems. The ABO gene localization is on chromosome 9q34 and contains two specific glycosyltransferase alleles, A and B[6]. First, Landsteiner defined ABO antigens as surface components of erythrocytes[7]. The relationship between blood types and cancers has been investigated for a long time. Since the association between gastric cancer and A blood type was reported in 1953[8], many reports about other types of cancer have been published[9-12]. In addition, the relationship between gynecological cancers and the ABO blood type system was also investigated. Studies by Tryggvadottir et al. and Ravn et al. reported high levels of estradiol in association with the presence of A-B transferase proteins in human endometrial cells[12,13]. However, A and AB blood types were reported more frequently in recurrent miscarriages[14]. Some studies showed a positive relationship between the ABO blood type and the risk of EC[13] or other types of cancer[6,15]. The exact mechanisms underlying the effect of ABO blood types on cancer pathogenesis are unknown. However, a number of theories have been proposed. It is likely that specific blood type antigens help cancer cells to behave biologically more aggressively[16]. It was demonstrated, in particular, that the presence of the A antigen can increase cellular motility and gradually accelerate cell-to-cell contact between malignant cells[17]. In addition, it was suggested that ABO blood type antigens may contribute to the immune system generally and confer aggressive resistance to programmed cell death (apoptosis) specifically[18]. In addition, Wolpin et al. discovered relationships between the ABO blood types and various concentrations of chemicals related to cell adhesion, immunological defense, inflammation, and cellular signaling[10]. At present, studies showing that there is a relationship between ABO blood types and EC were carried out[19-22]. In addition, studies researching the effect of ABO blood types on the prognosis of EC were carried out[17,23-25].

The aim of the present study was to examine how the ABO blood type affects endometrioid-type, EC prognosis.

## Materials and methods

Approval for this study was obtained from the Selçuk University Faculty of Medicine Ethics Committee with decision 2022/306 in accordance with the principles of the Declaration of Helsinki. In this retrospective study, a total of 522 patients were included from the Selçuk University Faculty of Medicine, Department of Gynecological Oncology between February 2010 and December 2021. The inclusion criteria were endometrioid-type EC diagnosed and followed up in the present clinic. Cases diagnosed with non-endometrioid type EC, cases diagnosed with concomitant cancer, and cases that were not operated on in the present clinic and could not be followed up were accepted as exclusion criteria. The patients were analyzed according to blood type (A, B, AB, and 0), age, menopause status (pre-menopause and post-menopause), prognostic factors (tumor size, myometrial invasion, grade degree, cervical involvement, lymphovascular invasion, and lymph node involvement), FIGO stage, overall survival (OS), and disease-free survival (DFS). Tumors were divided into three categories according to their grade: grade 1 or weak, grade 2 or moderate, and grade 3 or severe, and were named according to the FIGO grading system[26]. The blood types of the patients were recorded. FIGO stages 1 and 2 were called early stages, and 3 and 4 were named advanced stages[21].

### *Statistical analysis*

SPSS version 21.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA) was used for all statistical calculations. Descriptive features (mean, median, minimum, maximum, and standard deviation) in the study were evaluated with the help of descriptive statistical tests. The normal distribution of the variables was analyzed with the Kolmogorov–Smirnov test. Comparisons for categorical parameters were analyzed with the aid

**Table 1. Comparison of demographic data of patients diagnosed with endometrioid type endometrial cancer according to blood groups**

| Variables | A (n = 217) | B (n = 84) | O (n = 181) | AB (n = 40) | p-value |
|---|---|---|---|---|---|
| Age, year | 64.1 ± 10.4 | 64.0 ± 8.5 | 64.5 ± 9.9 | 62.1 ± 11.2 | 0.566 |
| Gravida, n | 4 (1-9) | 4 (1-12) | 4 (1-11) | 4 (2-7) | 0.208 |
| Parity, n | 3 (0-8) | 3 (0-11) | 3 (0-8) | 3 (1-6) | 0.464 |
| Body mass index (kg/m$^2$) | 32.8 ± 2.8 | 32.4 ± 2.4 | 32.1 ± 2.8 | 32.2 ± 2.0 | 0.073 |
| Menopause, n | | | | | 0.236 |
| Premenopause | 21 (9.7) | 3 (3.6) | 11 (6.1) | 4 (10.0) | |
| Post-menopause | 196 (90.3) | 81 (96.4) | 170 (93.9) | 36 (90.0) | |
| Co-morbidity, n | | | | | 0.983 |
| None | 122 (56.2) | 53 (63.1) | 108 (59.7) | 24 (60.0) | |
| DM | 8 (3.7) | 3 (3.5) | 7 (3.9) | 1 (2.5) | |
| Hypertension | 26 (12.0) | 10 (12.0) | 20 (11.0) | 6 (15.0) | |
| Other | 61 (28.1) | 18 (21.4) | 46 (25.4) | 9 (22.5) | |

n: number of patients; DM: diabetes mellitus.

of Spearman $X^2$ and Fisher's exact test. Tests for parametric values used the one-way analysis of variance test, and Tukey test as *post hoc* test. Non-parametric values were analyzed with the Kruskal–Wallis test and differences between groups were examined with Bonferroni correction and Mann–Whitney U test. DFS was the time from the end of cure to the presence of local recurrence or metastasis. OS was the time from the end of cure to the date of death or last follow-up. Outcome data were investigated with the Kaplan–Meier analysis and survival curves were evaluated using the log-rank test. Cox regression analysis was used for the outcome data. A $p < 0.05$ was considered significant.

## Results

Of the 522 patients included in this study, A blood type was present in 217 patients, B blood type in 84 patients, 0 type in 181 patients, and AB blood type in 40 patients. The mean ages of the patients were similar in terms of the A, B, 0, and, AB blood types ($p = 0.566$). While there was no significance in terms of parity, gravida, body mass index, menopausal status, co-morbidity, grade of tumor, degree of myometrial invasion, tumor size, presence of LVIS, cervical involvement, type of surgery, pelvic and paraaortic lymph node positivity, presence of recurrence, and surgical stage, there was statistical significance in terms of peritoneal fluid among the blood types ($p = 0.004$). In the peritoneal fluid pathology, group A was statistically significant compared to the other groups ($p = 0.004$), and in the surgical stage, only O blood type was found to be significant ($p = 0.006$) (Tables 1 and 2). Group B had the best prognosis for cumulative DFS and OS, followed by AB, A, and O blood types, respectively (Figs. 1 and 2). In Cox regression analysis between blood types, – 2 log-likelihood (222.298) was calculated as $p = 0.171$.

## Discussion

In this study in which endometrioid type EC cases were evaluated according to blood groups, when demographic and prognostic factors were compared between the cases, only peritoneal mayi positivity was found to be significantly different in blood group A. The best prognosis was found in blood group B, whereas the most risky blood group was found in blood group 0.

It was shown that blood types can affect different neoplastic and non-neoplastic processes in the body. Neoplastic cells can cause biologically aggressive behavior in specific blood types of antigens[26]. There are a number of studies that investigated the relationship between ABO blood type and EC[16,20,22,23,27]. In this study, blood type A (40.3%) was the most commonly detected blood type[23,24] and this was consistent with other studies about ECs in Iran[23], Siberia[16], China[20], and Italy[22,28]. In addition, contrary to this study, O blood type was most common among EC patients in Georgia and Saudi Arabia, whereas AB blood type was more common in an Armenian study and Le Pendu et al. detected that B blood type was the most common[17,21,29]. The distribution of blood types may differ between societies due to ethnic and regional differences.

**Table 2. Clinicopathological features of endometrioid endometrial cancer cases according to blood types**

| Variables | A (n = 217%) | B (n = 84%) | O (n = 181%) | AB (n = 40%) | p-value |
|---|---|---|---|---|---|
| Surgery method, n | | | | | 0.233 |
| Laparoscopic | 23 (10.6) | 12 (14.3) | 30 (16.6) | 8 (20.0) | |
| Laparatomic | 194 (89.4) | 72 (85.7) | 151 (83.4) | 32 (80.0) | |
| Surgery stage, n | | | | | 0.063 |
| Early | 192 (88.5) | 71 (84.5) | 150 (82.9) | 32 (80.0) | |
| Advanced | 25 (11.5) | 13 (15.5) | 31 (17.1) | 8 (20.0) | |
| Peritoneal fluid | | | | | 0.004* |
| Benign | 214 (98.6) | 78 (93.0) | 167 (92.3) | 35 (87.5) | |
| Malign | 3 (1.4) | 6 (7.0) | 14 (7.7) | 5 (12.5) | |
| Grade | | | | | 0.660 |
| 1 | 152 (70.1) | 55 (65.5) | 120 (66.2) | 30 (75.0) | |
| 2 | 48 (22.1) | 26 (31.0) | 45 (25.0) | 8 (20.0) | |
| 3 | 17 (7.8) | 3 (3.5) | 16 (8.8) | 2 (5.0) | |
| Degree of myometrial invasion, n | | | | | 0.192 |
| < 50% | 183 (84.3) | 64 (76.2) | 151 (83.4 ) | 28 (70.0) | |
| > 50% | 34 (15.7) | 20 (23.8) | 30 (16.6) | 12 (30.0) | |
| Tumor size, cm | 3.8 ± 2.2 | 4.5 ± 2.2 | 4.1 ± 2.4 | 3.9 ± 2.2 | 0.138 |
| Lymphovascular invasion | | | | | 0.493 |
| Yes | 20 (9.2) | 12 (14.3) | 24 (13.3) | 4 (10.0) | |
| No | 197 (90.8) | 72 (85.7) | 157 (86.7) | 36 (90.0) | |
| Cervical involvement | | | | | 0.436 |
| Yes | 26 (12.0) | 16 (19.0) | 28 (15.5) | 5 (12.5) | |
| No | 191 (88.0) | 68 (81.0) | 153 (84.5) | 35 (87.5) | |
| Pelvic lymph node metastasis, n | | | | | 0.399 |
| Yes | 16 (7.9) | 9 (11.2) | 20 (12.3) | 6 (15.8) | |
| No | 187 (92.1) | 71 (88.8) | 143 (87.7) | 32 (84.2) | |
| Paraaortic lymph node metastasis, n | | | | | 0.270 |
| Yes | 9 (4.4) | 5 (6.3) | 15 (9.3) | 4 (10.5) | |
| No | 194 (95.6) | 75 (93.7) | 147 (90.7) | 34 (89.5) | |
| Recurrence, n | | | | | 0.997 |
| Yes | 15 (6.9) | 6 (7.1) | 12 (6.6) | 3 (7.5) | |
| No | 202 (93.1) | 78 (92.9) | 169 (93.4) | 37 (92.5) | |
| Ex status, n | | | | | 0.175 |
| Yes | 8 | 1 | 12 | 1 | |
| No | 209 | 83 | 169 | 39 | |
| OS, month | 137.3 ± 7.0 | 149.6 ± 5.2 | 205.5 ± 16.0 | 141.2 ± 4.7 | 0.170 |
| DFS, month | 137.2 ± 7.0 | 151.4 ± 3.6 | 203.1 ± 16.5 | 141.2 ± 4.7 | 0.149 |

n: number of patient; OS: overall survival; DFS: disease-free survival.
*p-value is significant statistically.

EC is usually seen at advanced age and endometrioid-type is often detected in the early stage. Therefore, it has a good prognosis. However, Type 2 EC is estrogen-independent and has a poor prognosis. In the studies by Gitas et al.[24], and Mandato et al.[22], there were no significant associations between blood types according to age and death. Similarly, there was no difference between blood types in this study. In terms of menopause status, no difference was found in the studies by Gitas et al.[24], Xu et al.[20], and Abu-Zaid et al.[21] in accordance with this study. In addition, Mohammadian et al.[23] and Mandato et al.[22] also found a low risk of Grade 3 EC occurring in patients with A blood type. Consistent with these studies, the risk of developing Grade 3 EC was found to be less in the A blood type. Contrarily, there was no difference in terms of grade in the studies by Abu-Zaid et al.[21], and Gitas et al[24].

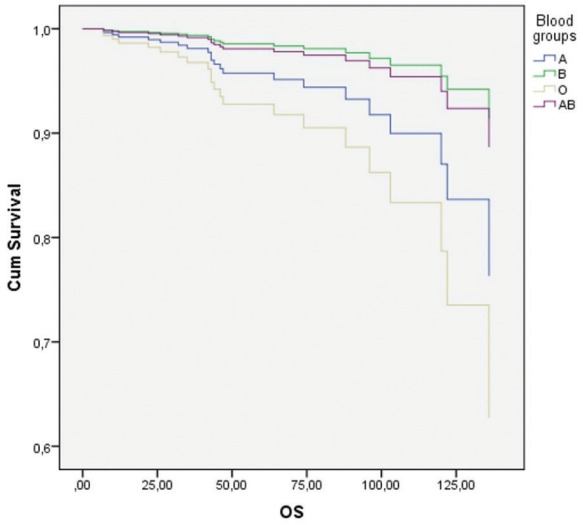


**Figure 1.** *Cox regression analysis of the relationship between the ABO blood types and overall survival.*

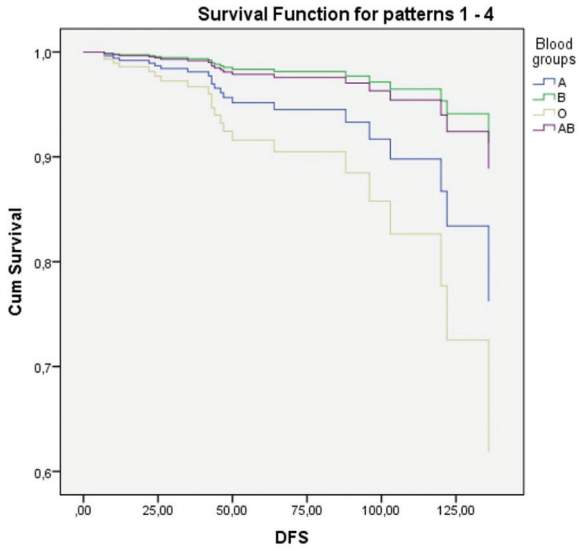


**Figure 2.** *Cox regression analysis of the relationship between the ABO blood types and disease-free survival.*

The presence or degree of myometrial invasion is one of the most important risk factors in EC. According to Mohammadian et al.[23], no significant difference was found in terms of myometrial invasion, which is one of the prognostic factors for EC. Mohammadian et al.[23] showed that there was no significant relationship between ABO blood type and cervical involvement. Similar to this study, no significant difference was found in terms of findings in this study either. In the studies by Mandato et al.[22], Abu-Zaid et al.[21], Gitas et al.[24], and Mohammadian et al.[23], there was no correlation between surgical stage and blood type. It was reported that there was no relationship[21,22]. In this study, there was no statistical significance in terms of blood types and surgical stage. Gitas et al.[24], Mandato et al.[22], and Mohammadian et al.[23] did not find any difference in terms of lymph node metastasis. Similarly, there was no difference in this study.

EC follow-ups frequently involve check-ups every 3-4 months for the first 2 years. Recurrences are usually detected within the first 2 years. No difference was found in terms of recurrence in the studies by Gitas et al.[24], Mandato et al.[22], and Abu Zaid et al.[21] Consistent with these studies, no difference was found in this study. Likewise, Mandato et al. reported that there was no significant association between ABO blood types, OS, and DFS times in patients diagnosed with EC[22]. Consistent with these studies, no difference was found in this study in terms of lymphovascular space invasion and OS. In terms of histological type, this study only included endometrioid-type. Contrary to these studies, a statistically significant difference was found between blood types in terms of peritoneal fluid (p = 0.004). There was no significant association among patients according to parity, tumor size, and surgical mode of operation (laparoscopy and laparotomy). No significant difference was found in the Cox regression analysis for DFS and OS by blood type. However, the cumulative survival time was maximum for B blood types followed by AB, A, and O blood types with decreasing frequency.

### *Limitations of the study*

While the limitations of this study were that it was a single-center and retrospective study, the strengths of the study were that only endometrioid-type EC patients were included in the study, the high number of patients, and the evaluation of prognostic factors.

## Conclusion

Blood types can be evaluated as an easily accessible and useful indicator in terms of sensitivity to endometrioid-type EC. O blood type is the riskiest blood type for endometrioid-type EC.

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## Conflicts of interest

The authors declare no conflicts of interest.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the approval of the Ethics Committee for the analysis and publication of clinical data obtained routinely. The informed consent of the patients was not required because it was a retrospective observational study.

**Use of artificial intelligence for generating text.** The authors declare that they have not used any type of generative artificial intelligence for the writing of this manuscript nor for the creation of images, graphics, tables, or their corresponding captions.

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