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Comparison of prognostic factors in patients diagnosed with endometrial cancer before and after COVID 19 pandemic: a retrospective study

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ABSTRACT

Aim: We aimed to compare prognostic factors in patients diagnosed with endometrial cancer before and after COVID 19 (Coronavirus Disease 19) pandemic.

Material and Method: This study was conducted in the Department of Gynecologic Oncology at Selçuk University Faculty of Medicine. After the World Health Organization (WHO) announced the COVID 19 pandemic on March 11, 2020, the Ministry of Health of the Republic of Turkey made an urgent decision on health services. The surgical cases diagnosed with endometrial cancer were divided into two groups based on the date when the pandemic was announced on March 11, 2020 and described group 1: 19 months before the pandemic, group 2: 19 months after the pandemic. Demographics, prognostic variables (stage, histologic type, grade, myometrial invasion, lymphovascular invasion, stromal involvement, and tumor size), endometrial cancer histological types, and treatment phases were all statistically assessed (early stage, advanced stage).

Results: A total of 194 cases were included, 96 cases in the first group and 98 cases in the second group. The mean age of the first group was 60.9±9.8 (40-86) years, the second group was 60.9±9.4 (36-82) years. There was statistically significant difference in clinicopathologic of endometrial cancer between group 1 and group 2, histologic type and grade (p=0.02; p=0.009 and p=0.018, respectively). There was no statistical difference between the two groups in age, stage, lymphatic and vascular space infiltration, muscular layer infiltration, interstitial infiltration and tumor size.

Conclusion: In the post-COVID 19 pandemic, more detection of type 2 of endometrial cancer, poor histological type and high grade, which have bad prognostic factors are found to be which may be due to the early admission of extra genital complaints. More randomized multicenter studies are needed on this subject.

Keywords: COVID 19 pandemic, endometrial cancer, prognostic factors

INTRODUCTION

As of the end of December 2019, the COVID 19 (Coronavirus Disease 19) infection has affected the World. During the pandemic, people's mental state has been affected by anxiety and depression (1). This situation has caused public health problems in Turkey and worldwide (2, 3). During the pandemic, the hospitalization rate, the number of patients requiring intensive care, and the COVID 19 infection rate have continued to increase (4, 5). Most hospital beds in most countries are crowded with COVID 19 patients. All specialist doctors are assigned to help COVID 19 patients, and elective surgeries were limited. Under these circumstances, the management of cancer patients has remained controversial. According to reports, cancer patients were found more susceptible to COVID 19 (6). However, during the COVID 19 epidemic numerous organizations such as the Gynecological Oncology Society (SGO), the European Gynecological Oncology Society (ESGO), and the Turkish Gynecological Oncology Society (TRSGO) gave their advice on how to treat patients with gynecological cancer (7, 8). In the study, titled "Cancer patients with SARS-CoV-2 infection: A nationwide analysis in China," patients diagnosed with cancer had a higher risk of being infected with COVID 19 than those without cancer, and cancer patients diagnosed with COVID 19 had worsening clinical outcomes (9). While surgical treatment for gynecological cancer is

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curable, it has been shown that postponing treatment can result in poor outcomes (10).

Endometrial cancer is the most common type of gynecological cancer in developing countries. It is the second most common type of cancer after cervical cancer in the female population.(11). The average age of women diagnosed with endometrial cancer is 63, and more than 90% of endometrial cancer is diagnosed after the age of 50 (12). More aggressive histology and high grade malignancies have been documented in older women with poor prognosis associated with increased age (13, 14). In high-risk patients, treatment for endometrial cancer includes hysterectomy, bilateral salpingoooforectomy, and lymphadenectomy (12). While type 1 endometrial cancer accounts for around 80% of endometrial cancer, type 2 endometrial cancer accounts for the remaining 20% (15).

In this study, we aimed to compare of prognostic factors in patients diagnosed with endometrial cancer before and after COVID 19 pandemic periods.

MATERIAL AND METHOD

This study was approved by Selçuk University Local Ethics Committee (Date: 26.10.2021, Decision No: 2021/478). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was conducted by the gynecological oncology department at Selcuk University, Faculty of Medicine. The Ministry of Health of the Republic of Turkey took immediate decisions for health services after the World Health Organization (WHO) declared the COVID 19 illness as a pandemic impacting the entire World on March 11, 2020. According to the date of the pandemic declaration in March 2020, the cases operated for endometrial cancer were separated into two groups: 19 months before the COVID 19 pandemic and 19 months after the COVID 19 pandemic. The study comprised 194 patients, with group 1 (n=96) before the COVID 19 pandemic and group 2 (n=98) after the COVID 19 pandemic. The FIGO (The International Federation of Gynecology and Obstetrics) 2009 staging and grading standards were used to stage all of the patients (16). Demographic factors, prognostic markers (stage, histomorphological type, grade, myometrial invasion, lymphovascular invasion, stromal involvement, and tumor size), endometrial cancer types (type 1 and type 2), and surgical types (early stage, advanced stage) were all analyzed statistically.

Statistical Analysis

Statistical evaluation was performed using the SPSS 20 (Statistical Package for Social Sciences) for Windows (IBM SPSS Inc., Chicago, IL) program. For homogeneity, the Kolmogorov-Smirnov test was applied. The categorical variables between groups were tested using the Chi-square test and Fisher's Exact test. Parametric variables were tested using the Student T test and the Mann-Whitney test, which is a non-parametric test. The p value of less than 0.05 was considered significant.

RESULTS

Group 1 had a mean age of 60.9±9.8 (40-86) while group 2 had a mean age of 60.9±9.4 (36-82) and mean age differences between the groups were not statistically significant. In terms of endometrial cancer clinicopathologic type, histomorphological type, and grade, there was a statistically significant difference between groups 1 and 2 (p=0.02, p=0.009, and p=0.018 respectively). Group 2 had a higher rate of type 2 endometrial cancer and grade 3 than group 1. There was no significant difference between the grade 1 and 2 groups. In terms of stage, type of stage, lymphovascular space invasion, myometrial invasion, stromal invasion, and tumor size, there was no statistically significant difference between the two groups. Data of patients diagnosed with endometrial cancer were presented in **Table 1**.

Table. Datas of patients diagnosed with endometrial cancer

	Before COVID 19 n=96	%	After COVID 19 n=98	%	P
Age (year)	60.9±9.8 (40-86)		60.9±9.4 (36-82)		0.640
Clinicopathologic types					0.02
Type 1	82	85.4	71	72.4	
Type 2	14	14.6	27	27.5	
Histology					0.02
Endometrioid	90	88.7	76	77.5	
Serous	6	11.3	16	16.3	
Mucinous	0	0	3	3.06	
Clear cell	0	0	2	2.04	
Neuroendocrine	0	0	1	1.02	
Grade					0.083
1	55	57.3	46	46.9	0.097
2	27	28.1	25	25.5	0.402
3	14	14.6	27	27.5	0.02
Stage					0.487
Stage 1	73	76.0	74	75.5	0.220
Stage 2	0	0	4	4.1	
Stage 3	17	17.7	16	16.3	
Stage 4	6	6.2	4	4.1	
Stage type					0.336
Early	73	76.04	78	79.6	
Advanced	23	23.9	20	20.4	
LVSI					0.398
Yes	17	17.3	15	15.3	
No	79	82.2	83	84.7	
Myometrial invasion					0.281
Yes	26		22	22.4	
No	70	72.9	76	77.5	
Stromal invasion					0.176
Yes	12	12.5	18	18.4	
No	84	87.5	80	81.6	
Tumor size (cm)	4.3±2.1 (3.9-4.77)		4.6±2.6 (4.0-5.1)		0.304

DISCUSSION

In today's COVID 19 pandemic, the care and safety of cancer cases is critical, and most cancer centers must develop an emergency plan because of the immunosuppressive state created by both anticancer medications and surgery, cancer patients are more susceptible to infections (17-19). At the same time, the COVID 19 pandemic has had a negative impact on people's mental health. Clinicians should be aware of posttraumatic stress disorder (PTSD), weakness, exhaustion, and anxiety (1). As a result, most cancer patients might be unconcerned about their complaints, paid little attention to them, and either did not go to the doctor or went late, resulting in the disease progressing to an advanced stage.

The endometrioid type of endometrial cancer is the most prevalent histological type. The endometrioid type of endometrial cancer that has good prognosis, causes abnormal uterine bleeding in the early stage. As a result, when patients arrive at the clinic, up to 70% of cases are diagnosed at stage 1 (20). Types of endometrial cancer include those that are estrogen-dependent (type 1) and those that are estrogen-independent (type 2) (21). Serous and clear cell tumors, which are histological forms of endometrial cancer with poor prognosis, have a higher incidence of myometrial invasion, vascular invasion, and peritoneal carcinomatosis (22). Endometrial tumors that are not estrogen-dependent have a low incidence but a high malignancy and a poor prognosis (23, 24). Besides, serous and clear cell histologic types have had high rates of extragenital spread and recurrence (25). Regardless of grade or stage, metastatic endometrial cancer has a bad prognosis, and the overall survival rate is dramatically reduced (26). There is a 5-year overall survival rate of 80-90 % in stage 1, 70-80% in stage 2, and 20-60% in stage 3-4 in the prognosis that correlates with the stage and grade of cancer (16).

In patients who came to our clinic before and after COVID 19 pandemic, there was no statistically significant difference between the two groups in terms of age, stage, type of stage (early stage and advanced stage), lymphovascular space invasion, myometrial invasion, stromal invasion, and tumor size. However, between the two groups, there was an increased frequency of type 2 endometrial cancer, poor histological types (serous, clear cell, neuroendocrine), and a high grade (grade 3), which is an indicator of poor prognosis.

Alemderoglu et al. (27) showed a significant difference between two groups (>70 age and 70 age) in terms of non-endometrioid histology, high-grade malignancies, and >50 myometrial invasions. However, FIGO stages of both groups were similar. Type 1 endometrial cancer was observed at a rate of 78.9% in our study, while type 2 endometrial cancer was observed at a rate of 21.1% in this study. This rate is smilar to with previous research. However, type 2 endometrial cancer was found at a statistically significant rate of 14.6 percent in group 1 and 27.5 percent in group 2 (p=0,02) As a difference from Alemderoglu study, this study consist on similar age group and COVID 19 pandemic. Besides, there is no study about this topic.

Dolyy et al. (27) showed that a protracted delay between diagnosis and treatment period resulted in an important decrease in survival in a single-center 7-year retrospective study of 889 endometrial cancer diagnoses. Cortilla et al. (10) reported that focusing health resources on COVID 19 and delaying normal oncological treatments during the pandemic period can result in poor outcomes in cancer cases. Furthermore, it has been stressed that postponing surgical operations will cause progression of cancer and be inoperable of malignancy from being curable.

The limitation of this study is that the status of COVID 19 cases is not known retrospectively and the study is in a single center. In this study, while we expect the cases to be in advanced stages due to be delayed and be neglected of complaint of abnormal uterine bleeding, which is the most common complaint in endometrial cancer, due to stress of COVID 19 in women, the situation we encounter in the clinic is at the same stage in the pre-COVID 19 and post-COVID 19 periods, but factors such as type 2 endometrial cancer, poor histologic types (serious, clear cell and neuroendocrine), and high grade (grade 3) are all frequently found in the post-COVID 19 period, which is surprising. We think that this may be due to the early admission of patients with poor prognostic types to the clinic.

CONCLUSION

As a result, while endometrial cancer is the most common cancer in developed countries, the most common reason for admission is abnormal uterine bleeding. During COVID 19, gynecological surgery can be performed under suitable conditions. Early detection of endometrial prognostic factors will improve the early diagnosis of endometial cancer and increase the survival rate of cases. In the post-COVID 19 period in endometrial cancer, more detection of type 2 endometrial cancer, poor histologic types, and high grade (grade 3) may be due to early admission because of extra genital complaints. The early detection of endometrial cancer in the two groups and the fact that the stages of the two groups are the same support this study. More randomised control trials are needed on this topic.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by Selçuk University Local Ethics Committee (Date: 26.10.2021, Decision No: 2021/478).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

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Author Contributions: The author declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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