Factors Affecting Survival in COVID-19 Patients with Genitourinary Cancer

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Abstract

Background: COVID-19 emerged at the end of 2019 and is still one of the most important health problems today. In cancer patients, COVID-19 disease is more severe and fatal. Increased immune system response in COVID-19 leads to increased disease severity and mortality. This study aimed to evaluate the prognostic factors and inflammatory indices in patients with COVID-19 and genitourinary cancer.

Methods: This retrospective study included 40 patients diagnosed with genitourinary cancer treated for COVID-19 between April 2020 and July 2021. A total of 27 potential prognostic variables were examined for univariate and multivariate analyzes for survival.

Results: A total of 27 variables were analyzed univariable. 3 out of 27 parameters were found to be statistically significant in the univariate analysis: mechanical ventilation requirement ($p=0.05$), serum fibrinogen level ($p=0.046$), receiving radiotherapy in the last 28 days ($p=0.000$). In the multivariate logistic regression analysis; mechanical ventilation requirement independent risk factors for severe COVID-19 in genitourinary cancer ($P=0.042$).

Discussion: In conclusion, mechanical ventilator requirement may be an independent risk factor for prognosis in COVID-19 patients with genitourinary cancer. The increase in fibrinogen due to hypercoagulopathy may be a prognostic independent predictor of survival in patients with genitourinary cancer with COVID-19. Larger, prospective studies are needed.

Introduction

COVID-19 emerged at the end of 2019 and is still one of the most important health problems today. In cancer patients, COVID-19 disease is more severe and fatal. The presence of active cancer, hematological malignancies and co-morbidity have been found to be associated with increased mortality and morbidity [1–3]. The results of studies showing that recent anti-cancer treatment increases the severity of COVID-19 are contradictory [4–6].

Increased immune system response in COVID-19 leads to increased disease severity and mortality. The hyperinflammatory response is associated with an increase in interleukin-6, interleukin 10, and interleukin 2. The hyper inflammation associated with COVID-19 in cancer patients elicits a damaging response. Previous studies; showed that neutrophilia, c-reactive protein increase, hypoalbuminemia and lymphopenia are poor prognostic factors in patients with COVID-19 [7, 8].

This study aimed to evaluate the prognostic factors and inflammatory indices in patients with COVID-19 and genitourinary cancer.

Materials And Methods

Patient Population

This study was conducted in Mersin City Hospital as a single-center, retrospective study. Between April 2020 and July 2021, Mersin City Hospital's electronic information system was scanned and the ICD-10 code was cancer and COVID-19 among 256 patients diagnosed with cancer and COVID-19. 40 patients diagnosed with genitourinary cancer out of 251 cancer patients were included in the study. The distribution of cancer in 40 patients included in the study is as follows: 13 bladder cancers, 13 renal cell carcinomas, 6 ovarian cancers, 3 endometrial cancers, 2 testicular cancers.

Demographic characteristics, cancer diagnoses, hemogram and biochemistry results of the patients included in the study were obtained from the electronic information system. Prior to the study, ethics committee approval was obtained from Mersin University Ethics Committee, dated 22.09.2021 and numbered 633.

For thorax CT findings in our study; COVID-RADS grade 3 patients in the reference study were considered severe involvement [9].

Inflammatory indexes [Neutrophil: lymphocyte ratio (NLR), Platelet: lymphocyte ratio (PLR), Prognostic Index (PI), modified Glasgow Prognostic Score (mGPS)] were calculated accordingly in each patient. A previous study was referenced in calculating inflammatory indices [10].

Statistical Analysis

All data statistical software program package (SPSS) version 26.0. loaded into the system.

All analyzes were performed using statistical software program package (SPSS) version 26.0.

Continuous variables were expressed as the median and interquartile range (IQR), while categorical variables were expressed as frequencies and percentages. Univariate and multivariate regression analyses were performed to detect the association of the different parameters assessed with the COVID-19 and genitourinary cancers. Overall survival (OS) was calculated with the log-rank test. The Kaplan–Meier method was used survival curves. The Cox proportional hazards regression model was used to determine statistically significant variables related to survival. At a 95% confidence interval $P < 0.05$ was considered statistically significant.

Results

This retrospective study included 24 male and 16 female patients with colon genitourinary cancer who had COVID-19. The distribution of cancer in 40 patients included in the study is as follows: 13 bladder cancers, 13 renal cell carcinomas, 6 ovarian cancers, 3 endometrial cancers, 2 testicular cancers. The median age of patients was 67 years (range 26–93). The patient's baseline characteristics and laboratory parameters are shown in Table 1.

Table 1
General Characteristics and Laboratory Parameters of the Patients

Characteristic	n (%)
Age (years)	67 (26–93)
Age $\geq$ 65 years/ Age < 65 years	24 (60)/ 16 (40)
Sex (Male/ Female)	24 (60)/ 16 (40)
Tumor stage	21 (52,5)/ 19 (47,5)
Non-metastatic / Metastatic	
Anticancer treatment history	6 (15)/ 34 (85)
Chemotherapy in the past 28 days: Yes/ No	1 (2.5)/ 39 (97.5)
Radiotherapy in the past 28 days: Yes/ No	
Comorbidities	25 (62,5)
Hypertension	16 (40)
Diabetes mellitus	20 (50)
Cardiovascular disease	
Number of comorbidities	23 (57,5)/ 17 (42.5)
≤ 2 / > 2	
Hospitalization in the intensive care unit	20 (44.4)/ 25 (55.6)
Yes/ No	
Additional treatments	19 (47.5)
Mask oxygen	21 (52.5)
Non-invasive / invasive mechanical ventilation	
COVID 19 corticosteroid treatment doses	14 (35)/ 26 (65)
≤ 1 mg/kg/ > 1 mg/kg	
Hospitalization result	24 (60)
Survivor	16 (40)
Non-survivor	
Inflammatory indexes	Median(min-max.)
Neutrophil:lymphocyte ratio (NLR)	6.2 (1.4–34.5)
Platelet:lymphocyte ratio (PLR)	243.4 (71-1305)

Characteristic	n (%)
Baseline laboratory parameters	Median(min-max.)
Total white blood cell count (x10 ³ /uL)	6.34 (1.21–27.48)
Hemoglobin (g/dL)	11 (6,5-15.7)
Platelet count (x10 ³ /uL)	248 (41–710)
Neutrophil (x10 ³ /uL)	4.8 (0.8–25)
Lymphocytes (x10 ³ /uL)	0.85 (0.33–2.7)
Monocytes (x10 ³ /uL)	0.4 (0.04–1.3)
Albumin (g/dL)	3.7 (2-4.7)
C reactive protein (mg/dl)	6 (0.3–30)
Uric acid (mg/dL)	5 (2–14)
D-dimer	1.35 (0.3–18)

Univariate analysis of survival time was performed on a total of 27 parameters. 3 out of 27 parameters were found to be statistically significant in the univariate analysis: mechanical ventilation requirement (p = 0.05), serum fibrinogen level (p = 0.046), receiving radiotherapy in the last 28 days (p = 0.000).

Univariate analysis results are shown in Table 2.

Table 2
Univariate Analysis of Survival Time by Categorical Variable

Variable	Log-rank test value	p-value
Age (< 65 / ≥65)	0.034	0.853
Sex (Female/male)	0.045	0,832
Metastasis	0.429	0.513
Comorbidities (< 2/ ≥2)	0.578	0.447
Hypertension	1.130	0.288
Diabetes mellitus	1.092	0.298
Cardiovascular disease	0.001	0.976
Receiving chemotherapy in the last 28 days	0.121	0.728
Receiving radiotherapy in the last 28 days	16.50	0.000
Hospitalization in the intensive care unit	3.108	0.078
Thorax computed tomography involvement (mild/severe)	0.010	0.922
Mechanical ventilation requirement	3.732	0.050
COVID 19 corticosteroid treatment doses (≤ 1 mg/kg/>1 mg/kg)	0.752	0.386
Total white blood cell count	3.296	0.192
Hemoglobin	1.678	0.195
Platelet count	5.245	0.073
Neutrophil	3.197	0.202
Lymphocytes	0.097	0.755
Monocytes	0.577	0.447
D-dimer	2.569	0.109
Fibrinogen	3.971	0.046
Albūmin	2.514	0.113
C reactive protein	0.119	0.730
Uric acid	2.115	0.347
Neutrophil:lymphocyte ratio (NLR)	3.346	0.067
< 6/ ≥6		

Variable	Log-rank test value	p-value
Platelet:lymphocyte ratio (PLR) < 270/ ≥270	0.250	0.617
Prognostic Index (PI) 0/2	3.553	0.169
Modified Glasgow prognostic score(mGPS)	2.462	0.292

Multivariate analysis included the three prognostic significance factors observed to be significant on univariate analysis: Mechanical ventilation requirement, serum fibrinogen level, receiving radiotherapy in the last 28 days. Multivariate analysis by Cox proportional hazard model showed that mechanical ventilation requirement was considered an independent prognostic factor for survival (P = 0.042). The results of multivariate analysis are shown in Table 3.

Table 3
Multivariate Analysis Results for Prognostic Factors

Parameter	p-value	OR	%95 CI
Mechanical ventilation requirement	0.042	14.03	1.1-178.5
Serum fibrinogen level	0.395	3.36	0.2–54.8
Receiving radiotherapy in the last 28 days	0.382	6.17	0.1-363.7

Discussion

In cancer cases, COVID-19 morbidity and mortality are higher than the normal population (11,12). Therefore, various studies have been conducted to determine the factors that can predict mortality. Our study aimed to investigate the factors affecting survival in gastrointestinal cancer patients with COVID-19 disease. In addition, we aimed to examine the effects of various inflammatory parameters on survival, which may be an indicator of the hyper-inflammatory state caused by COVID-19 in patients with genitourinary cancer.

Hyper-inflammatory state during COVID-19 in cancer patients is one of the main reasons that increase mortality. The negative acute-phase reaction, driven by interleukin 6 and other cytokines; causes lymphocytopenia, hypoalbuminemia, and cytokine excess (13–15). Systemic

inflammation destroys CD4 + T lymphocytes and increases suppressor CD8 + T lymphocytes, thus leading to an increase in neutrophil-lymphocyte ratio. A recent study found that neutrophil-lymphocyte ratio, on Covid Inflammatory Score, prognostic index, prognostic index, modified Glasgow prognostic score were associated with survival (10). In our study, however, no statistically significant relationship was found between inflammatory parameters and survival. This result may be due to our study's small

number of patients. In addition, while the other study included all cancer types, our study only included patients with genitourinary cancer. This may have changed the results.

Cancer patients are immunosuppressed due to malignancy and anti-tumor therapy. Therefore they have a predisposition for respiratory diseases and severe pneumonia. The need for mechanical ventilation may therefore be associated with prognosis. In a previous study, a statically significant relationship was found between the need for mechanical ventilation and mortality (15,16). In our study, a significant relationship was found in the univariate analysis ($p = 0.05$). Multivariate analysis by Cox proportional hazard model showed that mechanical ventilation requirement was considered an independent prognostic factor for survival. While other studies included general cancer groups, only patients with genitourinary cancer were included in our study (15,16). The relationship between mechanical ventilation and survival may also vary in cancer subgroups. There are very few studies in the literature regarding the factors affecting the prognosis of COVID-19 in cancer subgroups. Larger, prospective studies are needed to clarify this situation.

In severe COVID-19; infection-induced coagulopathy and secondary hyperfibrinolysis have been demonstrated (17). In our study, while fibrinogen level was significant in univariate analysis, it was statistically insignificant in multivariate analysis. This result may be related to the small sample size.

Also, the other study included non-cancer patients. The results may not have been significant because cancer patients already have hypercoagulopathy. Further studies are needed on this subject.

However, our findings are also based on some study limitations. First, the study was retrospective and based on a small sample size.

Conclusion

In conclusion, mechanical ventilator requirement may be an independent risk factor for prognosis in COVID-19 patients with genitourinary cancer. Also, an increase in fibrinogen due to hypercoagulopathy may be a prognostic independent predictor of survival. Larger, prospective studies are needed.

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