ACTA ONCOLOGICA
2020, VOL. 59, NO. 11, 1393–1396
https://doi.org/10.1080/0284186X.2020.1810313

Taylor & Francis
Taylor & Francis Group

LETTER TO THE EDITOR

Analysis of clinical features of COVID-19 in cancer patients

Wei-Ting Cheng[a], Yu-He Ke[a], Guang-Yan Yang[a], Hong Sun[a], Yu Chen[a], Ren-Yi Ying[a], Xiao-Hu Zeng[a], Dan Shen[a], Kai-Jie Tang[a], Kai Xu[b] and Fang Yu[a]

[a]Medical Department, Wuhan No.1 Hospital, Wuhan, China; [b]Department of Orthopedics, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, China

ARTICLE HISTORY Received 7 July 2020; Accepted 10 August 2020

With the outbreak of SARS-CoV-2, the clinical data of COVID-19 infection in cancer patients need to be further improved

Since December 2019, an outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in China. The new coronavirus has swept across the world in a short period of time, which has led to more than 4692797 cases and 195920 deaths globally as of 25 April 2020 [1]. A total of 85,766 cases have been diagnosed in China as of 16 July 2020. As the initial area of the epidemic, a total of 50007 cases have been confirmed in Wuhan, accounting for 61.3%. Similar to most respiratory viral diseases, most patients infected with COVID-19 are mild patients. With the continuous innovation of treatment methods, the proportion of patients with severe illness began to decline significantly [2]. Most mild patients can heal themselves, but patients with severe COVID-19/disease progress rapidly and have a high mortality rate, who requires our more attention. Previous studies have found that people in poor health, such as cancer patients, were more likely to be infected with COVID-19 [3].

Due to the abnormal immune function of cancer patients, it is unclear whether these patients have a higher susceptibility during the outbreak of COVID-19 and are more likely to develop severe disease. After analyzing 1590 cases of COVID-19 diagnosed from 575 hospitals, Liang et al. found that compared with patients without cancer, the incidence of COVID-19 in cancer patients was higher and the prognosis was also poor [4]. However, the characteristic data of severe COVID-19 patients with cancer remain limited. Our study aimed to collect and analyze the clinical data of severe COVID-19 patients with cancer, and further explore the characteristics of COVID-19 and provide reference for treatment of COVID-19 patients with cancer.

Patients, diagnostic criteria and statistics

This study was approved by the Ethics Committee of Wuhan No.1 Hospital. In this retrospective study, a total of 1476 COVID-19 patients were admitted to Wuhan First Hospital as of 19 March 2020, which served as a hospital designated by the government for patients with severe COVID-19/disease. All the patients were residents of Wuhan, and the diagnostic criteria of COVID-19 was based on the Diagnosis and Treatment Protocol for the 2019 Novel Coronavirus Pneumonia (Seventh Trial Edition) published by the National Health Commission of China.

The newly diagnosed patients were required to meet one of the following conditions: (1) positive signals of COVID-19 nucleic acids were found in the detection of fluorescent real-time RT-PCR; (2) the detection of viral gene sequencing showed a high degree of homology with known new coronavirus COVID-19. In addition, mild patients were required to meet the following conditions: (1) history of epidemiology; (2) fever or other respiratory symptoms; (3) abnormalities on CT images compatible with viral pneumonia. Patients with severe COVID-19/disease need to meet one of the following conditions: (1) shortness of breath, respiratory rate $\geq$ 30 times/min; (2) oxygen saturation (resting state)$\leq$93%; (3) $PaO_2/FIO_2 \leq 300$ mm Hg. Critically ill patients were required to meet one of the following conditions: (1) respiratory failure requiring mechanical ventilation; (2) shock; (3) combined with other organ failure, and ICU treatment was required.

Among these 1476 COVID-19 patients, 29 patients had cancer, including 20 patients with severe COVID-19/disease and 9 mild patients. Five patients died during the treatment. This study was reviewed and approved by Wuhan First Hospital Ethics Committee (No. 202008). All patients signed a written informed consent.

SAS9.3 statistical analysis software was used to analyze the data. Normally distributed data were expressed as mean ± standard deviation (SD), while non-normally distributed data were expressed as median (interquartile range), and comparisons were examined by Student's t test and Wilcoxon two sample test. The categorical data were expressed as n(%), and 95% confidence interval (95% CI) was estimated using the asymptotic method. The differences between the two groups were examined by Pearson χ^2 test

CONTACT Kai Xu godocoto@163.com Department of Orthopedics, Tongji Hospital, Huazhong University of Science and Technology, No. 1095 Jiefang Ave., Qiaokou District, Wuhan, 430030, Hubei, China; Fang Yu whsyufang@126.com Medical Department, Wuhan No.1 Hospital, No. 215 Zhongshan Ave., Qiaokou District, Wuhan, 430022, China

Supplemental data for this article can be accessed here.

or Fisher's exact test. The U-test was used to compare the individual rate with the overall rate. A two-tailed $p < .05$ was considered statistically significant.

Demographic and clinical characteristics of COVID-19 patients accompanied by cancer

In this study, a total of 1476 patients (673 males and 803 females) were diagnosed with COVID-19, including 29 patients with cancer and 1447 non-cancer patients. Totally 757 patients had severe COVID-19, including 20 patients with cancer and 737 non-cancer patients; meanwhile, 719 patients were diagnosed as mild COVID-19, including 9 patients with cancer and 710 non-cancer patients. The average age of these 1476 patients was 57.8 ± 15.9 years old, and the average hospital stay was 19.6 ± 9.7 days.

Among these 1476 COVID-19 patients, 29 patients had cancer, accounting for 1.96% (95% CI: 1.26–2.67). COVID-19 patients with cancer (15 males and 14 females) had an average age of 67.2 ± 10.1 years and an average hospital stay of 24.9 ± 13.7 days, including 20 patients with severe COVID-19/disease and 9 mild patients. The proportion of patients with severe COVID-19/disease (20/29) was significantly higher compared with the proportion of severe cases among COVID-19 patients with cancer in the report of China (39%, $\chi^2 = 4.813$, $p = .028$) [4], and was also significant higher compared with the proportion of severe cases among COVID-19 patients with cancer in other oncology departments in Wuhan (25%, $\chi^2 = 6.662$, $p = .010$) [5] (Table 1).

In this study, we found that the average length of stay of cancer patients was significantly higher than that of non-cancer patients (25.4 ± 9.8 vs. 19.6 ± 9.7 days, $t = 2.612$, $p = .009$), and the proportion of patients with severe COVID-19/disease among cancer patients was significantly higher than that among non-cancer patients (20/29 vs. 737/1447, $\chi^2 = 3.987$, $p = .046$). In addition, the mortality rate of cancer patients was also significantly higher than that of non-cancer patients (5/29 vs. 68/1447, $\chi^2 = 9.513$, $p = .002$). However, the time from hospitalization to death was higher in cancer patients than that in non-cancer patients (24.9 ± 14.1 vs. 12.8 ± 11.9 days), but there was no significant difference ($p > .05$).

Compared with non-cancer patients, cancer patients were older (67.0 vs. 59.0 years old, $t = 36.003$, $p < .001$), and there were 23 cancer patients older than 60 years. It is worth noting that there was a total of 19 cases within 5 years of cancer. All the dead patients were cancer patients with a survival time of less than 5 years, and the mortality rate reached 26.32% (95% CI: 6.52–46.12). In addition, according to the history of treatment, we found that 7 patients underwent surgery, chemotherapy, radiotherapy, targeting, endocrine therapy and other anti-cancer treatments within 1 month before the onset of COVID-19, of which 5 were patients with severe COVID-19/disease and 3 patients died; meanwhile, 22 patients did not undergo anti-cancer treatment, of which 15 were patients with severe COVID-19/disease and 2 patients died.

Laboratory testing indicators and radiological examination results of COVID-19 patients with cancer

The laboratory test results of patients after admission showed that the absolute value of peripheral blood leukocytes in 13 patients decreased, the absolute value of neutrophils increased in 2 patients, and the absolute count of lymphocytes in 15 patients decreased significantly (Si. 1). Furthermore, the average level of neutrophil to lymphocyte ratio (NLR) in cancer patients was significantly higher than that in non-cancer patients, and 23 (23/29) cancer patients had NLR ≥ 2. In addition, among cancer patients, the NLR of patients with severe COVID-19/disease was higher than that of mild patients [3.9 (2.4, 5.5) vs. 2.7 (1.4, 3.4)] (Si. 1). We found that the absolute value of lymphocytes in dead patients was also lower than that in surviving patients (0.59 ± 0.18 vs. 1.21 ± 0.55) (Si. 1).

Blood biochemical tests found that serum albumin levels decreased in 19 patients, D-Dimer levels increased in 18 patients, CRP levels increased in 15 patients, lactate dehydrogenase levels increased in 14 patients, and creatine kinase levels increased in 10 patients (Si. 1).

The results showed significant differences in CRP and ALB between the severe group and the mild group ($p < .05$) (Si. 1). Besides, the CRP/ALB of patients with severe COVID-19/disease was higher than that of mild patients [1.13 (0.09, 1.81) vs. 0.09 (0.08, 0.11)], but there was no significant difference between the two groups ($p > .05$). However, the CRP/ALB of dead patients was higher than that of surviving patients [1.81 (1.57, 2.75) vs. 0.10 (0.08, 1.06)] (Si. 1).

After admission, the patients underwent chest CT scan, and all showed abnormal imaging findings of varying degrees. Imaging data were not obtained in 3 patients due to critical illness or death (Si. 2). After testing, there was no significant difference in CT results between severe and mild patients ($p > .05$) (Si. 2).

Treatment of patients

In our study, 28 patients received antiviral therapy, of which 21 received a combination of two antiviral drugs and 8 received one antiviral drug. Among these drugs, arbidol was the most widely used drug, which was applied in 19 (19/29) patients, with an average duration of 8 ± 2.5 days. Twenty-five patients received traditional Chinese medicine, with an average duration of 14.8 ± 4.3 days. The proportion of mechanical ventilation in cancer patients was significantly higher than that in non-cancer patients (10/29 vs. 81/1447, $p < .05$) (Table 2).

Discussion

Currently, studies have confirmed that patients with cancer have become a high-risk group of COVID-19. COVID-19 has become a fatal factor for cancer patients due to poor immunity or immune disorder caused by anti-cancer therapy [6]. The number of cancer patients in our hospital was also

Table 1. Analysis of baseline data of 29 patients.

		Comparison between mild and severe COVID-19 patients			Death group and survival group	
Baseline data	Patients ($N = 29$)	Severe patients ($N = 20$)	Mild patients ($N = 9$)	p Value	Death Group ($N = 5$)	Survival Group ($N = 24$)
Age (years old)	67.0 ± 10.0	70.3 ± 8.9	59.8 ± 8.9	.006	75.2 ± 3.1	65.3 ± 10.2
Duration of tumor (years)	3(1.5,6)	2.50(1.25,6.00)	4.00(2.00,6.00)	.670	1.00 (0.90,1.50)	3.00 (1.75,7.00)
Length of stay (days)	21(13,32)	26.00(15.50,36.00)	13.00(11.00,30.00)	.131	32.00 (21.00,34.00)	19.50 (13.00,31.00)
Gender (male/female)	15/14	12/8	3/6	.245	5/0	10/14
Combined with basic diseases						
Basic pulmonary diseases	2	2	0	>.999	2	0
Hypertension	12	8	4	>.999	2	10
Cardiovascular diseases	4	3	1	>.999	2	2
Diabetes mellitus	6	6	0	.137	4	3
Thyroid diseases	5	2	3	.287	2	0
Clinical symptoms of admission						
Fever	16	11	5	>.999	3	13
Cough	20	12	8	.201	2	18
Expectoration	10	8	2	.431	2	8
Fatigue	12	11	1	.043	4	8
Chest tightness	11	9	2	.412	2	9
Shortness of breath	10	9	1	.107	2	8
Sore throat	4	3	1	>.999	1	3
Chills	2	2	0	>.999	0	2
Sore muscles and joints	4	4	0	.280	1	3
Nausea and vomiting	1	1	0	>.999	1	0

Table 2. Analysis of treatment of 29 patients.

Treatment	Patients ($N = 29$)
Non-invasive mechanical ventilation	5(17.24)
Invasive mechanical ventilation	5(17.24)
Antibiotics	19(65.52)
Chinese patent medicine	20(68.97)
Chinese medicine decoction	21(72.41)
Antiviral therapy	28(96.55)
Treatment of drugs	
Arbidol	17(58.62)
Arbidol + interferon	2(6.90)
Arbidol + hydroxychloroquine	1(3.45)
Oseltamivir phosphate + Arbidol	2(6.90)
Ganciclovir	1(3.45)
Ganciclovir + interferon	1(3.45)
Lopinavir/ritonavir (Kaletra)	1(3.45)
Lopinavir/ritonavir (Kaletra) + hydroxychloroquine	1(3.45)
Ribavirin + Arbidol	1(3.45)
Hydrochloroquine	1(3.45)
No drugs applied in treatment	1(3.45)

significantly larger than the number reported by other studies [4,5], which further confirms that cancer patients have a higher risk of COVID-19 and the possibility of developing severe disease is greater.

Previous studies have suggested that lung cancer patients were at high risk of COVID-19 [5]. We have found that not only lung cancer patients, but also patients with a variety of cancers were high-risk groups of severe COVID-19 patients; meanwhile, the shorter the duration of the cancer is, the higher the risk of death after the occurrence of COVID-19 is. Especially in patients who received anti-cancer treatment within six months, the risk of developing severe disease was higher, and the risk of death was extremely high.

Pathological tests found inflammatory infiltration of interstitial mononuclear cells, mainly lymphocytes, in both lungs of COVID-19 patients. It has also been found that peripheral blood lymphocytes decreased, suggesting that the absolute value of lymphocytes may be related to the severity of the disease and mortality [7]. We found that the absolute value of lymphocytes of dead patients with cancer was significantly lower than that of surviving patients with cancer. The magnitude of decrease in lymphocyte count also reflects the degree of damage to the immune system caused by viral infection. Qin C et al. [6] reported that compared with non-critically ill patients, critically ill patients had higher neutrophil counts but lower lymphocyte counts, so NLR was higher among severely infected patients. NLR, as a prognostic biomarker based on inflammation, has been tested in a variety of cancers and can be considered as an independent factor with predictive value in cancer prognosis. Thus, NLR can be used as a useful factor to reflect the imbalance and immune response of COVID-19 patients. In this study, we found that NLR and CRP/ALB of dead patients were significantly higher than those of surviving patients. The NLR and CRP/ALB of patients with severe COVID-19/disease were higher than those of mild patients, but the difference was not statistically significant. These results suggested that NLR and CRP/ALB were closely related to the death of COVID-19 patients with cancer, but may be related to the severity of the disease, which needs to be confirmed in further studies by expanding the sample size. Meanwhile, our research found that CRP and ALB were closely related to severity and death of patients, suggesting that they can become important indicators of COVID-19 severity and mortality. This study will help clinicians to better elucidate immune dysfunction and potential immune pathogenesis during SARS-CoV-2 infection, so that they can intervene in COVID-19 in time.

There are some limitations in this study. First, the sample size is very limited, and it is a single-center retrospective study. In order to verify our results, further studies of the expanded population in multicenters are still needed. Second, the indicators we included remain limited, so the findings of our research may be biased. Third, long-term follow-up of patients is still necessary to investigate the long-term impact of these factors on the prognosis of patients. Future research will expand the sample size to explore the severity of disease and risk factors of death in COVID-19 patients with cancer.

In conclusion, patients with cancer, especially those who were recently diagnosed with cancer, may be potential high-risk groups of Severe COVID-19 patients. By detecting laboratory and blood biochemical indicators, peripheral blood neutrophils, lymphocytes, NLR, CRP and ALB can be used as prognostic indicators of immune function in COVID-19 patients with cancer, which aim to clarify the disease characteristics of COVID-19 and provide timely intervention for COVID-19 patients with cancer.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This study was supported by National Administration of Traditional Chinese Medicine "Emergency fund for Covid-19" (No. 2020ZYLCYJ03-11) and Natural Science Foundation of Hubei Province (No. 2019CFB641).

References

[1] Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet. 2020;395(10236):1569–1578.

[2] Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. BMJ. 2020;369:m1849.

[3] Dai M, Liu D, Liu M, et al. Patients with cancer appear more vulnerable to SARS-CoV-2: a multicenter study during the COVID-19 outbreak. Cancer Discov. 2020;10(6):783–791.

[4] Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020; 21(3):335–337.

[5] Yu J, Ouyang W, Chua MLK, et al. SARS-CoV-2 transmission in patients with cancer at a Tertiary Care Hospital in Wuhan, China. JAMA Oncol. 2020;6(7):1108.

[6] Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020;71(15):762–768.

[7] Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8(4):420–422.