Article

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Clinical Characteristics of COVID-19 in Gynecological Cancer Patients during Chemotherapy—An Observational Study

Yao Li[1], Cuiqin Sang[1], Xiaoli Ru[1], Shuzhen Wang[1,*], Hong Wang[1,*]

[1]Department of Obstetrics and Gynecology, Beijing Chaoyang Hospital, The Affiliated Hospital of Capital Medical University, 100020 Beijing, China
*Correspondence: darrywang2003@163.com (Shuzhen Wang); Wanghongwh188@sina.com (Hong Wang)
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Background: Infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affects multiple organs throughout the body, which puts chemotherapy patients at even greater risk. This study aims to identify the clinical characteristics of gynecological cancer patients infected with SARS-CoV-2 during chemotherapy.

Methods: Gynecological cancer patients infected with SARS-CoV-2 during chemotherapy from August 1, 2022, to January 31, 2023, were enrolled in this observational cohort study. Patients in the control group were not infected with SARS-CoV-2. All continuous variables, including blood cells (leukocytes, neutrophils, lymphocytes) and biochemical indices (alanine transaminase (ALT), Aspartate transferase (AST), lactate dehydrogenase (LDH), albumin and creatinine) were repeatedly measured and analyzed statistically by the generalized additive mixed model (GAMM). Latent class analysis was estimated for the high-risk factors of severe COVID-19. The primary outcome was to develop a severe condition.

Results: During the study period, there were 71 patients with chemotherapy in our center. Of the 57 cases infected with SARS-CoV-2, 14 patients without infection, the infection rate was 80.28%. 52 cases out of the 57 infected patients were included in this study, 9.62% (5/52) cases showed severe disease, and 1 patient died. 51 cases survived during the acute coronavirus disease 2019 (COVID-19) phase. If chemotherapy is given after SARS-CoV-2 infection, tissues and organs that are sensitive to chemotherapy are more likely to be re-damaged by COVID-19. The plasma levels of leukocytes, neutrophils, lymphocytes, ALT, and AST decreased; LDH and creatinine in plasma showed a linear increase, while plasma albumin decreased, and platelets showed no apparent trend. The changes in blood cells and biochemical indices were most evident in relapsed patients and patients with COVID-19 within 2 weeks after chemotherapy. Latent class analysis showed that all severe COVID-19 patients were classified into class 1; the patients of class 1 showed a shorter interval between chemotherapy and COVID-19, and the higher baseline of AST, ALT, and LDH, the more cycles of chemotherapy and the advanced stage.

Conclusions: The interval between chemotherapy and COVID-19 is associated with damage to tissues and organs. Clinical factors and laboratory factors indicate poor health conditions among patients with gynecological cancer and COVID-19.

Keywords: gynecological cancer; COVID-19; SARS-CoV-2; observational study; a generalized additive mixed model; latent class analysis

Introduction

The World Health Organization (WHO) declared the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and it announced the coronavirus disease 2019 (COVID-19) as a pandemic on 11 March 2020 [1]. Cancer patients are more vulnerable to infections because of the presence of comorbidities, poor health status, and immunosuppression caused by both cancer and anticancer treatment. Many studies focused on the risk of cancer patients infected with SARS-CoV-2. They showed that preexisting comorbidities, for example, cancer, constitute a risk factor associated with severe COVID-19 and intensive care unit (ICU) admission [2,3]. The pandemic has affected outcomes for patients with cancer in many ways; for example, surgeries, treatments, scheduled physician appointments, laboratory tests, and imaging had to be delayed. However, postoperative chemotherapy is important and necessary for patients with ovarian cancer (OC) and some patients with uterine and cervical malignancies, which may lead to suffering from bacterial and viral infections during their course of chemotherapy [4,5]. Delays in chemotherapy for malignant patients may lead to emotional problems and disease development. And cancer patients suffer from the double whammy of chemotherapy and COVID-19. This interaction between these two factors may aggravate the side effects of chemotherapy, which may be life-threatening and make the treatment of patients needing chemotherapy into a dilemma. Presently, there is rare literature discussing the clinical presence of COVID-19 in gynecological cancer patients during chemotherapy.

Wu and McGoogan [3] reported a 2.3% death rate in the general population vs 5.6% among cancer patients. Liang W [6] reported that compared with the general population, cancer patients infected with SARS-CoV-2 are more likely to develop severe COVID-19, which may lead to increased mortality. Therefore, it is necessary to understand the clinical characteristics and prognosis of cancer patients infected with SARS-CoV-2 after chemotherapy.

We present the cases of gynecological cancer who had undergone chemotherapy and suffered from COVID-19. The current study aims to describe the clinical characteristics of patients with gynecological cancer who were infected with SARS-CoV-2 during chemotherapy so that severe COVID-19 may be identified as soon as possible in gynecological cancer patients, leading to reduced mortality.

Patients and Method

Setting

We conducted the observational descriptive study at the Gynecologic Oncology Center, Beijing Chaoyang Hospital, Capital Medical University. We obtained the data of all gynecological cancer patients who were treated with chemotherapy and had a positive test result for the SARS-CoV-2 virus from analysis of nasopharyngeal or oropharyngeal swab specimens obtained at any point during their hospitalization or an outpatient setting from August 1, 2022, to January 31, 2023. Follow-up continued through January 31, 2023.

During the study period, a total of 71 tumor patients in our center received postoperative chemotherapy, and 57 cases were infected with SARS-CoV-2, of which 5 cases were excluded from the study for lost follow-up, and 52 patients with gynecological cancer during chemotherapy were finally included in this study. Inclusion criteria, exclusion criteria, and the flow chart of the study population are shown in Fig. 1. 14 patients who were not infected after chemotherapy were in the control group. The inclusion criteria were as follows: (1) SARS-COV-2 negative after chemotherapy; (2) the date of follow-up is available. The patients were excluded from the control group when the patients were lost to follow-up. (Fig. 1 was created by EmpowerStats (http://www.empowerstats.com, X and Y Solution, Inc., Boston, MA, USA) and WPS Office V12.1.0.16120 (Kingsoft Office, Beijing, China)).

Data Sources

We obtained data from the clinical data warehouse. We obtained the following data elements for each patient: demographic data, tumor treatment and pathological data, disease status at infection with SARS-CoV-2 (treatment modality and tumor status), and cardinal symptoms, in particular, oxygen support. The interval between chemotherapy and viral infection was recorded. Blood biochemical indices were tested regularly. Historical and current medication lists, historical and current diagnoses, clinical notes, and historical discharge dispositions for previous in-patient hospitalizations were collected.

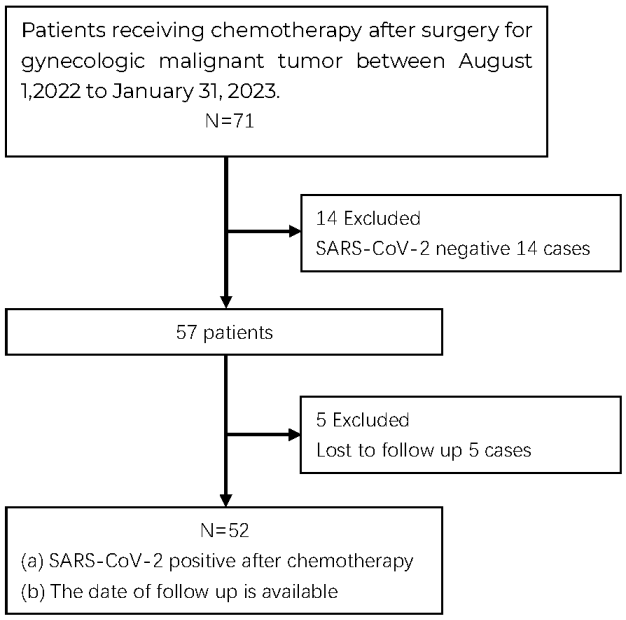

Fig. 1. The flow chart of the patient selection process.

End Point

COVID-19 is classified according to WHO standards [7] as severe and no-severe. The primary endpoint was the diagnosis of severe COVID-19, or the patient died. Patients without a primary end-point event had their data censored on January 31, 2023.

Variables Assessed

All continuous variables, including blood cells (leukocytes, neutrophils, lymphocytes) and biochemical indices (alanine transaminase (ALT) Aspartate transferase (AST), lactate dehydrogenase (LDH), albumin, and creatinine), were repeatedly measured to describe the clinical features of SARS-CoV-2 infecting patients with gynecological cancer in chemotherapy. We calculated the interval between COVID-19 and operation or recurrence, the interval between chemotherapy and COVID-19, and the dynamic changes of biochemical indices after COVID-19.

Statistical Analysis

Data management and statistical analysis were performed with SPSS software version 27.0 (IBM, Corp. in Armonk, NY, USA) and R software (version 3.6.1, R Project for Statistical Computing, Lucent, Mount Jasmine, NJ, USA), and EmpowerStats (http://www.empowerstats.com, X and Y Solution, Inc., Boston, MA, USA).

Continuous variables were expressed as mean ± standard deviation (normal distribution) or median (quartile) (skewed distribution). Categorical variables were expressed in frequency or as a percentage. Latent class analysis (LCA) was employed to identify the potential class of severe COVID-19 by the organ of tumor origin, age, interval between chemotherapy and COVID-19, and hematological and biochemical markers. A generalized additive mixed model (GAMM) was used for repeated measurement data. LCA and GAMM were performed using R software (version 3.6.1, R Project for Statistical Computing, Lucent, Mount Jasmine, NJ, USA). The significance level was set at 0.05. We calculated the proportion of major symptoms of COVID-19 using multiple responses. We did not calculate the relevant factors in severe patients because the number of cases was limited. Multiple imputation was used to account for missing data.

Results

Clinical Characteristics of Gynecological Cancer Patients with COVID-19

Of 71 consecutive patients with COVID-19 who were admitted to the hospital between August 1, 2022, to January 31, 2023, 5 patients were excluded from this study because they were lost to follow-up and discharged after inpatient admission. A total of 52 gynecological cancer patients with COVID-19 were included in our analysis. The other 14 patients who were not infected with SARS-CoV-2 during the observation period after postoperative chemotherapy were used as a control group. Detailed patient characteristics are shown in Table 1 and Table 2 (Ref. [7]).

The death case of a 74-year-old female had a history of ovarian cancer treated by surgery and platinum-based combination chemotherapy weekly, with a cumulative dose of 270 mg paclitaxel and carboplatin 600 mg (AUC = 5). She suffered from pulmonary infection and pleural effusion during the interval of chemotherapy. Tumor treatment had to be discontinued, and she presented a high fever (40 °C) 59 days after the last chemotherapy and was diagnosed with COVID-19 by nucleic acid assay. On the third day of diagnosis, respiratory and hemodynamic functions deteriorated, with acute renal function deteriorating and anemia, which progressed rapidly, and death occurred 8 days after diagnosis. During this period, the tumor was well controlled. According to her clinical manifestations, the direct cause of death was multiple organ failure, respiratory failure, and hemodynamic functions deteriorated, which had nothing to do with tumor and tumor treatment.

Another severe patient, a 39-year-old female, suffered from ovarian cancer treated by surgery and platinum-based combination chemotherapy; before the fifth chemotherapy, she presented a low fever, cough, and difficulty breathing, accompanied by progressive peripheral blood thrombocytopenia, and was diagnosed with COVID-19 by nucleic acid test, Nirmatrelvir and ritonavir were administered on the third day, she presence danger signs, so we classified to the severe group.

Another 3 cases present breathing difficulties and need oxygen support. Of the five severe patients, two patients over 80 years old were treated with antiviral therapy, and the other patients had no record of viral treatment.

No patients had a smoking history. The median age was 64 years (ranged 36–83 years) (Table 1). 26 of 52 patients had underlying diseases (50.0%), mainly hypertension (18/52, 34.61%). Diabetes mellitus (DM) 11/52 (21.15%), 5 patients were diagnosed with pulmonary embolism (PE), 3 patients had multiple primary cancers (tongue cancer and parotid gland cancer, breast cancer, and endometrial cancer, one case of cervical cancer combined with ovarian cancer), and 2 patients had asthma.

Based on the baseline values of hematological and biochemical indicators, latent class analysis was used to identify the potential class of severe COVID-19 by organ of tumor origin, age, interval between chemotherapy and COVID-19, and hematological and biochemical markers with the use of R software, version 3.6.1 (R Project for Statistical Computing, Lucent, Mount Jasmine, NJ, USA). The result shows that 5 severe cases were all in class 1, and no one was in class 2. Posterior probabilities for severe COVID-19 in the class 1 was 0.9426 (0.5560–1.0000), in the class 2 was 0.0570 (<0.0001–0.4236), Posterior probabilities for no- severe COVID-19 in the class 2 was 0.9430 (0.5764–1.0000), and in the class 1 was 0.0574 (<0.0001–0.4440). The results of LCA show population characteristics by class. From the results, we can see that the difference between the two classes mainly occurred in the biochemical indicators, based on baseline values of hematological and biochemical indicators, and ignoring the repeated measurement data.

The Characteristics of the Gynecological Cancer

Three-fourths of the patients had ovarian cancer (34/52, 65.38%), 16 had endometrial cancer (16/52, 30.77%), and 2 had cervical cancer (2/52, 3.85%) in the infection group. 10 cases of ovarian cancer cases, 3 cases of endometrial cancer, and 1 case of cervical cancer in the control group. Of the 52 cases, 10 had recurrent tumors, and 42 had initial treatment. 14 control cases were initial treatment; none had recurrent tumors. Most of them were advanced (35/52). All the patients received chemotherapy before COVID-19. And 21.15% (11/52) were diagnosed with COVID-19 after chemotherapy within one week, 17.31% (9/52) more than 1 week, within two weeks, 17.31% (9/52) more than 2 weeks, within four weeks, 19.23% (10/52) more than 4 weeks, within 8 weeks, 20.08% (12/52) more than 8 weeks, the longest interval is 80 days. 47 patients received taxon-based chemotherapy, including 43 patients for 3-week intervals, 3 patients at weekly intervals, and 1 patient receiving only paclitaxel therapy. Among these pa-

Table 1. The baseline and oncological characteristics of gynecological cancer patients with COVID-19 and control cases.

Characteristics	No-severe	Severe/Critical	Control group
N	47	5	14
Averages of age and range	60.71 ± 11.60	65.60 ± 9.53	63.89 ± 8.75
≤60 years	19	3	6
>60 years	28	2	8
Type of tumor			
Initial treatment	37	5	10
Relapse	10	0	4
Complication			
PTE	5/47	0	0/14
Diabetes (yes/all)	9/47	5/5	5/14
Hypertension (yes/all)	17/47	1/5	7/14
Site of Cancer[&]			
Ovarian cancer	29	5	10
Carcinoma of the endometrium	16	0	3
Cervical cancer	2	0	1
Stage of tumor			
I–II	16	1	5
III	16	2	9
IV (lung metastasis 3 cases)	15	2	
Chemotherapy regimens			
TC or T	42	5	13
PEB, VP16, MTX	3	0	1
Radiochemotherapy	2	0	0
Combination therapy (targeting)			
Yes	27	2	5
No	20	3	9
Number of cycles of chemotherapy			
≤4 cycles	25	3	3
≥5 cycles	22	2	11

Abbreviation: COVID-19, coronavirus disease 2019; TC, Paclitaxel and Carboplatin; T, Paclitaxel; PEB, Cisplatin (DDP) + Etoposide (VP16) + Bleomycin (BLM); MTX, methotrexate; PTE, pulmonary thromboembolism.

&: 3 cases of multiple primary cancer, one case of ovarian cancer and cervical cancer was included in ovarian cancer, and 1 case of endometrial cancer combined the tongue cancer and parotid gland cancer when another endometrial cancer combined breast cancer was included in endometrial cancer.

tients, one received treatment with PEB (Cisplatin (DDP) + Etoposide (VP16) + Bleomycin (BLM)), another with Etoposide (VP16), and a third with methotrexate (MTX). Additionally, two cervical cancer patients underwent postoperative chemoradiotherapy. The cycles of chemotherapy before SARS-CoV-2 infection were 1–8 cycles, 29 cases received maintenance treatment and anti-angiogenesis targeted therapy.

Among the 52 patients included in the analysis, the primary endpoint of severe developed in 5 patients (9.62%); 1 patient died from COVID-19 on the eighth day after diagnosis. 4 cases of severe out-of-danger and discharged follow-up 46, 51, 56, 61 days, 47 cases patients of no-severe recovery from the acute phase of the COVID-19 (ranged 1–31 days), followed up for 9–80 days, 5 cases occurred the pulmonary thromboembolism (PTE), 2 cases asthma. There was some delay in anti-cancer treatment after infection, ranging from 5 to 14 days; no tumor progression was found during the observation period.

Interaction between SARS-CoV-2 Infection and Anti-Cancer Treatment

The Dynamic Changes of the Peripheral Blood Cells and Biochemical Indices with the Interval COVID-19 in Patients with Recurrence and Primary Gynecological Cancers

There was an interaction between dynamic changes in blood cells and the interval of COVID-19 diagnosis, both in recurrent and primary patients (all $p < 0.0001$). However, the features of interaction were different. After COVID-19, leukocytes (WBC), neutrophils, platelets, and hemoglobin

Table 2. Clinical features of COVID-19 in patients with gynecological malignant tumors undergoing chemotherapy.

Characteristics	No-severe	Severe/Critical*
N	47	5
The median interval between the latest chemotherapy and infection of SARS-CoV-2 (days)		
Relapse	19 (1–116)	No, any one#
Initial operation	126 (20–510)	107 (39–130)
Duration of the acute phase of COVID-19 (median, days)	7 (2–32)	11 (4–15)
COVID-19–clinical presence in the registry*		
Fever, ≥38.0 °C	30/47 (63.83%)	4/5
Cough	29/47 (61.70%)	4/5
Gastrointestinal dysfunction	9/47 (19.15%)	3/5
Dyspnea or Decreased O_2 saturation, <96%	0	5/5
Anosmia/dysgeusia	11/47 (23.4%)	2/5
Headache	8/47 (17.02%)	2/5
Weak	4/47 (8.51%)	0
Death	0	1/5

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

* No percentage is calculated for a total of less than 10.

None of the relapsed patients developed severe disease.

Based on World Health Organization (WHO)'s classification of COVID-19 severity [7], 5 cases were classified into the severe group. One patient died of severe COVID-19, and 47 cases were categorized into the no-severe group.

in the relapse group plummeted, and the slope of the straight line was significantly different from that in the primary group ($p < 0.0001$). In both initial treatment and recurrence groups, peripheral blood lymphocytes increased after the diagnosis of COVID-19 (Fig. 2).

Plasma albumin in patients with primary or recurring gynecological cancer decreased linearly after SARS-CoV-2 infection. However, the decrease was more rapid in the recurrence group; the slopes of the two lines are significantly different. ALT increased after COVID-19 in patients with newly treated tumors and decreased within a short time, while ALT increased linearly after COVID-19 in patients with recurrent tumors. AST showed a similar change trend to ALT in newly treated and relapsed patients. LDH and creatinine show a curve decline in the primary group, while the relapsed group shows all increased linearly (Fig. 2).

The Association between Blood Cells and Biochemical Indices and the Interval of COVID-19 after Chemotherapy

We divided the patients infected with SARS-CoV-2 into three groups, according to the duration of chemotherapy, and into three groups: group 1, less than 2 weeks after chemotherapy; group 2, 15 days to 31 days; and group 3, more than 31 days. The patients of control group (no COVID-19) were excluded from this analysis. Of the 52 cases, 20 were in group 1, 9 in group 2, and 23 in group 3. There were no significant differences in the biochemical and hematological indicators among the three groups at the time of COVID-19 diagnosis (all p values > 0.05).

The WBC decreased rapidly and linearly after SARS-CoV-2 infection within 2 weeks after chemotherapy. Both groups 2 and 3 show that the WBC increased slowly; these two lines are very close but a little different, and group 2 had a smaller slope.

As the lymphocytes and granulocytes infected with SARS-CoV-2 within 14 days after chemotherapy decreased rapidly and linearly if the interval was more than 15 days, while lymphocytes and granulocytes increased slowly. Group 2 and group 3 of the neutrophils almost overlapped. Lymphocytes are a little different; the difference between group 2 and group 3 of the lymphocytes displayed a rising slope.

The effect of chemotherapy on platelets showed that the infection with SARS-CoV-2 within 2 weeks after chemotherapy resulted in a sharp decrease in platelets, and at the interval more than 15 days after chemotherapy, there is no adverse effect, even if infected with the SARS-CoV-2.

Infected the SARS-CoV-2 within 15 days after chemotherapy, plasma albumin rapidly decreased, ALT and AST also showed a linear decline, AST decreased more obviously, as did the LAP, an appreciable elevation when the creatinine (CRE) and LDH showed a sharp increase. After 15 days, the albumin, AST, ALT, and LAP trends were not linear. It hasn't shown any regularity (Fig. 3).

Discussion

This analysis involved a small sample of consecutive patients who had gynecological cancer-infected SARS-CoV-2 after chemotherapy. Gynecological cancer with COVID-19 seems to be very similar to those observed in the general population, most commonly present with non-specific symptoms of fever, dyspnoea, and chest tightness. Consistent with the presentation of COVID-19 in non-cancer patients [3,6,8].

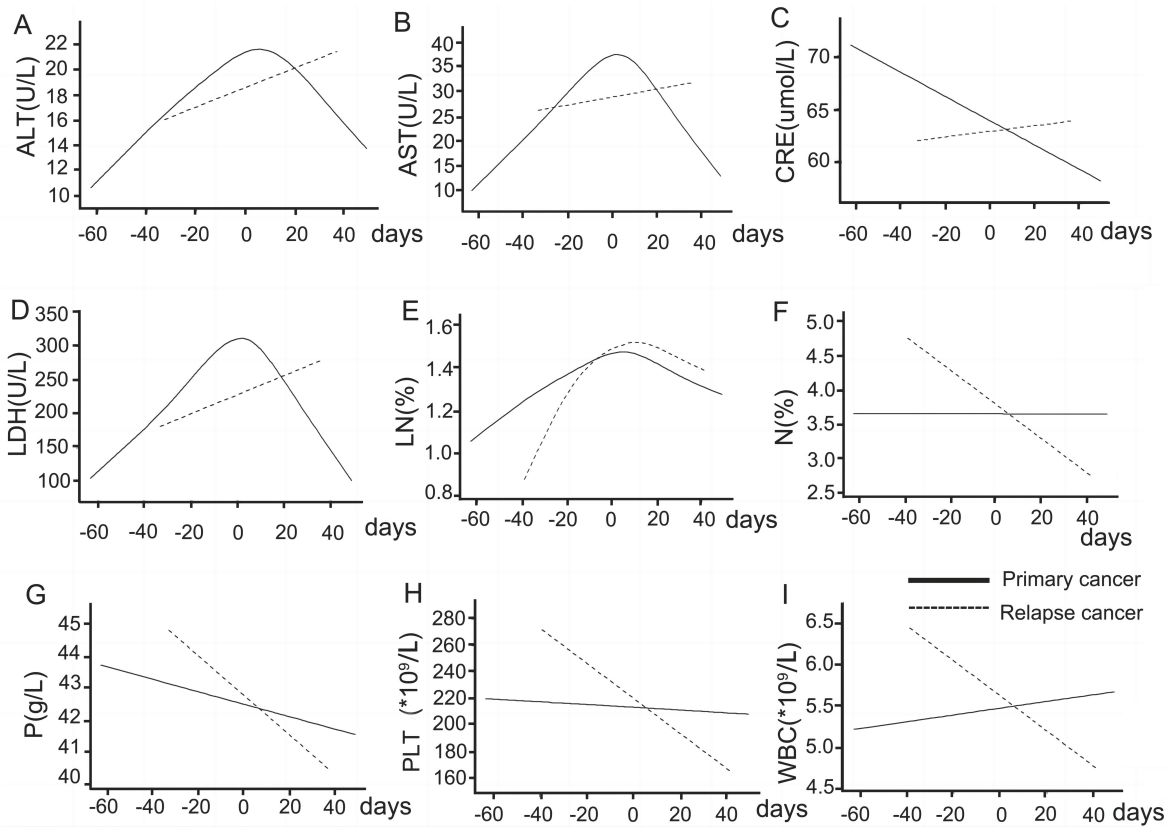

Fig. 2. Dynamic changes of blood cells and biochemical indices after infected SARS-CoV-2 in relapsed patients and newly treated patients. In all of the pictures (A–H). The horizontal coordinate means the period corresponding to the duration of COVID-19 diagnosis, the "zero" is the day when COVID-19 was diagnosed; the left of zero, a negative value means the period before SARS-CoV-2 infection; right of zero, a positive value means the period after COVID-19 diagnosed, and the vertical coordinate is the unit of measurement of corresponding indicators. (A) Alanine transaminase (ALT). (B) Aspartate transferase (AST). (C) Creatinine (CRE). (D) Lactate dehydrogenase (LDH). (E) Lymphocyte (LN). (F) Peripheral blood neutrophil count (N). (G) Plasma albumin (P). (H) Peripheral blood platelet count (PLT). (I) Total number of peripheral blood leukocytes (WBC).

Laboratory findings showed that hematopoietic function and liver and kidney tissues are impacted by SARS-CoV-2 to different degrees for patients. Although these changes are caused by chemotherapy or COVID-19, the dynamic change characteristics of indicators after infection suggest that organs damaged by chemotherapy may be aggravated easily after SARS-CoV-2, such as bone marrow, liver, and kidney. In the present cohort, a death case was infected with COVID-19 56 days after chemotherapy and died of hematopoietic failure and acute renal failure 9 days later. The baseline data of this study are similar to those of Nath SS, but there is a lack of literature with repeated data on COVID-19 patients after chemotherapy for reference [9].

In the present descriptive study, all subjects were patients undergoing surgery, radiotherapy, and chemotherapy in our center. Most cases were diagnosed with COVID-19 in the hospital, while some were outside. Five severe patients and two patients over 80 years old were treated with antiviral therapy, and the other patients had no record of viral treatment. Wu [3] reported that laboratory characteristics of severe COVID-19 show thrombocytopenia 3 days after infection. In this study, 3 of the 5 severe cases showed thrombocytopenia, which was identified in time and avoided more serious conditions. Still, it could not be salvaged in one case of multiple organ failure. Thrombocytopenia may be one of the hallmarks of severe-type patients.

Despite the small number of cases, the proportion of severe cases was significantly lower than that reported in the literature [8,10,11]. The description of clinical characteristics and dynamic observation of laboratory tests from 52 patients with gynecological malignant tumors infected with COVID-19 after chemotherapy provided very valuable clinical data. Our study suggests that infecting SARS-CoV-2 after chemotherapy increases further damage to chemotherapy-damaged organs. The interval of chemotherapy and the infected SARS-CoV-2 was important; at less than 2 weeks of the interval, the peripheral blood cells decreased, the plasma albumin level decreased too, and when the serum creatinine and LDH increased significantly, more than 2 weeks of the interval, the changes of peripheral blood cells and blood biochemistry tended to be gentle.

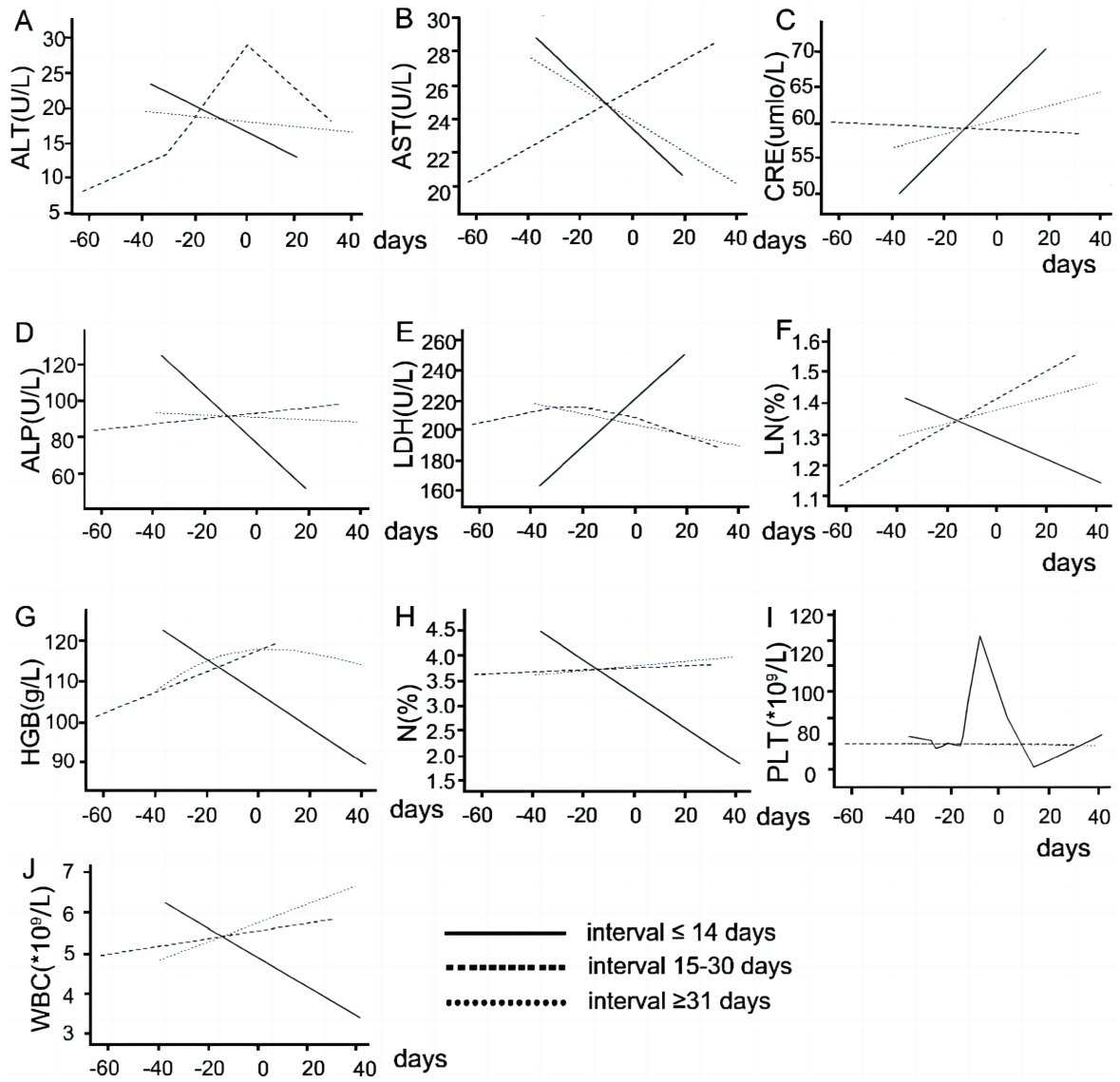

Fig. 3. Dynamic evolution of peripheral blood cells and biochemical factors in SARS-CoV-2 patients after chemotherapy. For all of the pictures (A–J). The horizontal coordinate means the period corresponding to the duration of COVID-19 diagnosis, the "zero" is the day when COVID-19 was diagnosed; left of zero, the negative value means the period before SARS-CoV-2 infection; right of zero, the positive value means the period after COVID-19 diagnosed, and vertical coordinate is the unit of measurement of corresponding indicators. (A) ALT. (B) Glutamic oxalacetic transaminase (AST). (C) CRE. (D) Alkaline phosphatase (ALP). (E) LDH. (F) Peripheral blood lymphocyte count. (G) Total hemoglobin (HGB) in peripheral blood. (H) Peripheral blood neutrophil count (N). (I) Peripheral blood platelet count. (J) Total number of peripheral blood leukocytes (WBC). The pictures of (C,E,F,G,H,J), show that infection with SARS-CoV-2 within 2 weeks after chemotherapy, N, LN, and HGB decreased rapidly in the short term. CRE and LDH were significantly higher; all indicators had no significant changes in SARS-CoV-2 infection more than 2 weeks after chemotherapy.

The risk from chemotherapy can be aggravated by COVID-19. The present study showed that there was no significant difference in the biochemical and hematological indicators among the three groups at the time of COVID-19 diagnosis, but the dynamic changes showed significant differences among the three groups after COVID-19 infection; we can see the effects of interval time on various indicators, the adverse effects of chemotherapy on the body did not recover from the infection before the new coronavirus, aggravating the negative effects. Regarding the low proportion of severe cases, we speculated reasons, including the virulence of the virus decreased, the infection SARS-CoV-2 occurred in the third year of the global COVID-19 epidemic, the emergence of effective therapeutic drugs, and the effect of the COVID-19 vaccine. Despite the short follow-up period, we had the outcomes of SARS-CoV-2 in all the individuals in this cohort. Long-term prognosis requires extended follow-up.

Several significant limitations of the descriptive study restrict the inferences that can be drawn from these findings. Herein, we review the limitations of the available data and then address specific measures that should be undertaken to ensure a correct summary of the actual situation. First, it is a small sample, descriptive study, single-center study. We set up a vertical database and used a generalized additive mixed model for the data of repeated measurements of biochemical indicators and blood cells to show the dynamic change of the indicators of COVID-19 after chemotherapy. Repeated measurements increase the reliability of the results. Second, we set up a control group of patients with gynecological cancers who were not infected with SARS-CoV-2; only 14 subjects met the criteria during the study period. The baseline data of the 14 uninfected patients were similar to the infected groups, which was too small for statistical analysis. The impact of COVID-19 on tumor outcomes requires continued follow-up. We compared the clinical manifestations of cancer patients with COVID-19 with those of general patients with COVID-19 with literature reports [10–13]. Third, we did not analyze the risk factors of patients with severe or died; only 5 of the 52 patients were classified into the severe group during the follow-up period, which was much lower than reported in the literature [14–17], and we could not eliminate confounding by regression analysis. We made a latent class analysis with the data in the existing database. The result showed that 5 severe cases were all in class 1, and no one was in class 2. From these results, we speculated that the interval of infection of SARS-CoV-2 after chemotherapy, cycles, and stage of cancer may be correlated to severe COVID-19, and the patients with gynecological cancer during chemotherapy who suffer from COVID-19 were more likely lead to liver and kidney damage and hematopoietic abnormality. An increase of Cre/LDH at baseline may be the risk factor for severe COVID-19 cases for gynecological cancers during chemotherapy [18]. The present study showed that we should focus on the trend of change.

Conclusions

In conclusion, the hematopoietic function and liver and kidney damage caused by chemotherapy may be aggravated by SARS-CoV-2 infection. The interval between chemotherapy and SARS-CoV-2 infection, cycles of chemotherapy, and stage of cancer may be associated with the poor prognosis.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

YL, SZW and HW conceived the idea of the study; SZW and HW made the design; YL, CQS and XLR acquired the data; all authors analyzed the data and interpreted the results; YL is responsible for illustration. All authors drafted and revised the paper. All authors read and approved the final manuscript and take responsibility for all aspects of this work.

Ethics Approval and Consent to Participate

This study was approved by the ethics committee of Beijing Chaoyang Hospital (2021-Science-639). All participants in the experiment signed informed consent. This experiment complies with the Declaration of Helsinki.

Acknowledgment

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

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