EJMO

DOI: 10.14744/ejmo.2023.18762
EJMO 2023;7(3):255–264

Research Article

Association of COVID-19 with Features of the Peripheral Hemogram Among Cancer Patients Undergoing Chemotherapy

Jia-Yong Su,[1#] Zhen-Jie Guo,[2#] Yao-Hong Liu,[1] Qiong-Mei Li,[3] Yan-Jun Li,[1] Bing-Hua Chen,[1] Yu-Ling Zhao,[1] Bin-Yuan Mo,[1] De-Shen Chen,[1] Yu-Ni Li,[1] Yu-Tong Cai,[1] Qing-Qing Chen,[4] Jian-Hong Zhong[1,5]

[1]Department of Hepatobiliary Surgery, Guangxi Medical University Cancer Hospital, Nanning, China
[2]Medical Records Room, Guangxi Medical University Cancer Hospital, Nanning, China
[3]Nursing College of Guangxi Medical University, Nanning, China
[4]Guangxi Crucial Laboratory of AIDS Prevention and Treatment & School of Public Health, Guangxi Medical University, Nanning, China
[5]Key Laboratory of Early Prevention and Treatment for Regional High Frequency Tumors (Guangxi Medical University), Ministry of Education, Nanning, China
[#]*Jia-Yong Su and Zhen-Jie Guo contributed equally to this work.*

Abstract

Objectives: Future pandemics involving COVID-19 or other respiratory disorders may pose risks to treatment outcomes among cancer patients on chemotherapy. Here we explored whether diagnosis with COVID-19 might influence how chemotherapy alters the peripheral hemogram of cancer patients. To examine changes in the peripheral hemogram before and after chemotherapy depending on whether patients were unexposed to the SARS-CoV-2 virus, had COVID-19, or were recovering from COVID-19.

Methods: We retrospectively reviewed the records of 8,900 patients with solid cancers who underwent chemotherapy between October 10, 2022 and March 1, 2023. We compared hemograms before and after chemotherapy within and across the following three groups: 3,215 patients previously unexposed to SARS-CoV-2, 2,771 patients with COVID-19, and 2,817 patients recovering from COVID-19. We compared counts of white blood cells, red blood cells, and platelets as well as percentages of neutrophils between the first blood sampling after admission and the first sampling after conclusion of chemotherapy.

Results: Of the various parameters examined, only the changes in counts of white blood cells and platelets differed significantly across the three patient groups. White blood cell count before chemotherapy was lower in patients with COVID-19 than in those unexposed to the virus or those recovering from COVID-19. Platelet count after chemotherapy was lower in patients with COVID-19 than in those recovering from COVID-19. Chemotherapy reduced the red blood cell count and increased the neutrophil percentage in all three patient groups, with the largest changes occurring in patients with COVID-19; however, these changes did not achieve statistical significance.

Conclusion: These studies suggest that COVID-19 does not significantly alter the peripheral hemogram of cancer patients who receive effective chemotherapy.

Keywords: COVID-19, tumor chemotherapy, peripheral hemogram

Cite This Article: *Su JY, Guo ZJ, Liu YH, Li QM, Li YJ, Chen BH, et al. Association of COVID-19 with Features of the Peripheral Hemogram Among Cancer Patients Undergoing Chemotherapy. EJMO 2023;7(3):255–264.*

Address for correspondence: Jian-Hong Zhong, MD. Department of Hepatobiliary Surgery, Guangxi Medical University Cancer Hospital, He Di Rd. #71, Nanning 530021, P.R. China
Phone: +86-771-5330855 **E-mail:** zhongjianhong@gxmu.edu.cn

Submitted Date: July 22, 2023 **Accepted Date:** August 17, 2023 **Available Online Date:** October 06, 2023

The COVID-19 pandemic has caused more than 759 million infections and nearly 6.9 million deaths globally.[1] The pandemic poses particularly severe risks for cancer patients, since infection with the causative virus, SARS-CoV-2, increases risk of death much more among them than among individuals without cancer.[2-4] In fact, cancer in patients with COVID-19 independently predicts worse prognosis, higher risk of hospitalization, and higher risk of mortality within 30 days after hospital admission.[5-8] This increased risk of poor outcomes likely reflects the systemic effects of cancer and chemotherapy,[9-11] as well as patients' avoidance of treatment visits due to fear of infection. These considerations highlight the need to understand whether and how COVID-19 may affect cancer patients undergoing treatment and their prognosis, especially since cancer is the second leading cause of death after cardiovascular disease.[12] The findings may be relevant for improving cancer management during a future pandemic of COVID-19 or other respiratory disease.

COVID-19 has been shown to influence cancer progression and patient responses to particular chemotherapy drugs,[13, 14] but how the disease may modulate the effect of chemotherapy on blood hemostasis is lacking. This is important because chemotherapy-induced changes in, for example, counts of white blood cells or platelets can increase risk of complications such as infection or hemorrhage, as well as worsen prognosis.[15, 16] The peripheral hemogram, which simultaneously provides information about the blood's functions of oxygenation, immune responses and coagulation can be a straightforward way to screen patients for risk of complications or poor prognosis.

Therefore we examined how chemotherapy altered the peripheral hemogram in three types of cancer patients: those never infected with the SARS-CoV-2 virus, those with COVID-19 and those recovering from COVID-19.

Methods

Study Participants

The protocol of this retrospective study conformed to the Declaration of Helsinki and its later amendments and was approved by the Ethics Review Committee of the Guangxi Medical University Cancer Hospital (LW2023100), which waived the requirement for written informed consent because patients or their legal guardians had consented, upon admission, to analysis and publication of anonymized medical data for research purposes.

We extracted the medical data of all patients with malignant solid tumors who underwent chemotherapy in our hospital between October 10, 2022 and March 1, 2023. Before chemotherapy, tumors were typed and staged based on clinical presentation, laboratory tests, imaging, and histopathology. We did not enroll patients with non-solid tumors, such as leukemia, myelodysplastic syndrome, multiple myeloma or plasmacytoma because their hemograms can show substantial variability independent of chemotherapy (data not shown).

We assigned patients to one of three groups: those admitted between October 10, 2022 and December 6, 2022, before SARS-CoV-2 was circulating in humans;[17] those admitted between December 7, 2022 and January 15, 2023 who were diagnosed with COVID-19;[18] and those admitted between January 16, 2023 and March 1, 2023 who had previously been diagnosed with COVID-19 but were judged to be recovering because they no longer presented any clinical symptoms or chest computed tomography signs, and because two PCR tests for SARS-CoV-2, conducted seven days apart, were negative.[19]

COVID-19 Diagnosis

Patients in the study were diagnosed initially with COVID-19 if they had clinical symptoms and chest radiological signs as specified in the "Chinese Prevention and Control Program for Novel Coronavirus Pneumonia" (9th edition),[20] and if infection with bacteria or virus normally associated with community-acquired pneumonia had been excluded. Diagnosis of COVID-19 was confirmed if a PCR test of a nasopharyngeal swab was positive for SARS-CoV-2.[21]

Data Collection

Medical records on the peripheral hemogram of all patients were extracted from the central hospital database, together with data on sex, age, number of chemotherapy cycles, as well as use of molecular targeted drugs and immune inhibitors. Data were extracted by one investigator and cross-checked by another against the original database. In cases of missing data or apparent errors, the attending clinical physician was contacted for clarification.

Outcome

The primary outcome was changes in the peripheral hemogram between the first blood sampling after admission and the first sampling after conclusion of chemotherapy. In this study, the hemogram comprised counts of white blood cells, red blood cells and platelets, as well as the percentage of neutrophils.

Statistical Analysis

We did not estimate a minimal sample for this study because it was retrospective and designed to describe effects in the actual patient population. Data were analyzed

statistically using SPSS 26.0 (IBM, Chicago, IL, USA) and GraphPad Prism 9.0 (GraphPad Software, San Diego, CA, USA), and results associated with $p<0.05$ were considered significant. Continuous data were expressed as means and standard deviations, while categorical data were reported as frequencies and percentages. Changes in hemograms before and after chemotherapy within each of the three patient groups were assessed for significance using the paired-samples t test, two-sample t test or corrected t test with normal distribution if the data were normally distributed; otherwise, changes were assessed using the Wilcoxon rank-sum test. Differences across patient groups were assessed using analysis of variance if the variables were continuous, or using Pearson's chi-squared or Fisher's exact tests if the variables were categorical.

Results

Of the 8,900 patients whom we screened initially, we excluded 148 (1.7%) with non-solid tumors and allocated the remaining to the following three groups (Fig. 1): patients unexposed to SARS-CoV-2 (n=3,164) because they were admitted to the hospital before the virus was circulating among humans; patients with COVID-19 (n=2,771); and patients recovering from COVID-19 (n=2,817).

Most patients were younger than 60 years, more than half were receiving immune checkpoint inhibitors, while very few were receiving molecular targeted agents. Most patients in the study had received one round of chemotherapy (Table 1). The distribution of tumor types did not differ significantly across the three groups (Supplementary Table 1).

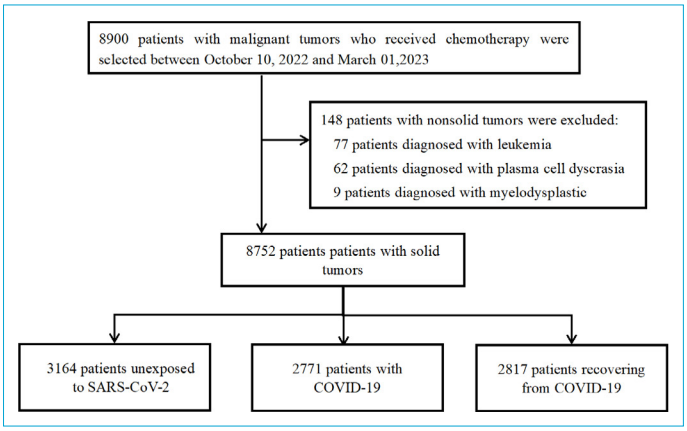


Figure 1. Flow diagram of patient selection. COVID-19, coronavirus disease 2019.

Differences in Hemogram Features

Chemotherapy had obviously different effects across the three patient groups, although all the indicators after chemotherapy were within the expected range and all patients achieved satisfactory chemotherapy benefits. Of the various parameters examined, only the changes in counts of white blood cells and platelets differed significantly across the three patient groups (Fig. 2). White blood cell count before chemotherapy in patients with COVID-19 (5.7×10^9 /L) was lower than the counts in those unexposed to the virus

Table 1. Clinicodemographic and treatment characteristics of the three patient groups.

Characteristic	Unexposed to SARS-CoV-2 (n=3164)	With COVID-19 (n=2771)	Recovering from COVID-19 (n=2817)	p
Sex				0.621
Male	1404 (44.4)	1198 (43.2)	1222 (43.4)	
Female	1760 (55.6)	1573 (56.8)	1595 (56.6)	
Age, yr				0.683
<60	2263 (71.5)	2009 (72.7)	2021 (71.7)	
≥60	901 (28.5)	762 (27.3)	796 (28.3)	
Number of chemotherapy cycles				
1	2337 (73.9)	1969 (71.1)	2101 (74.6)	0.064
2	745 (23.5)	717 (25.9)	649 (23.0)	
3	61 (1.9)	65 (2.3)	46 (1.6)	
≥ 4	21 (0.7)	20 (0.7)	21 (0.7)	
Molecularly targeted drugs				0.120
Yes	120 (3.8)	83 (3.0)	111 (3.9)	
No	3044 (96.2)	2688 (97.0)	2706 (96.1)	
Immune checkpoint inhibitors				0.429
Yes	1407 (44.5)	1216 (43.9)	1206 (42.8)	
No	1757 (55.5)	1555 (56.1)	1611 (57.2)	

Values are n (%), unless otherwise noted.

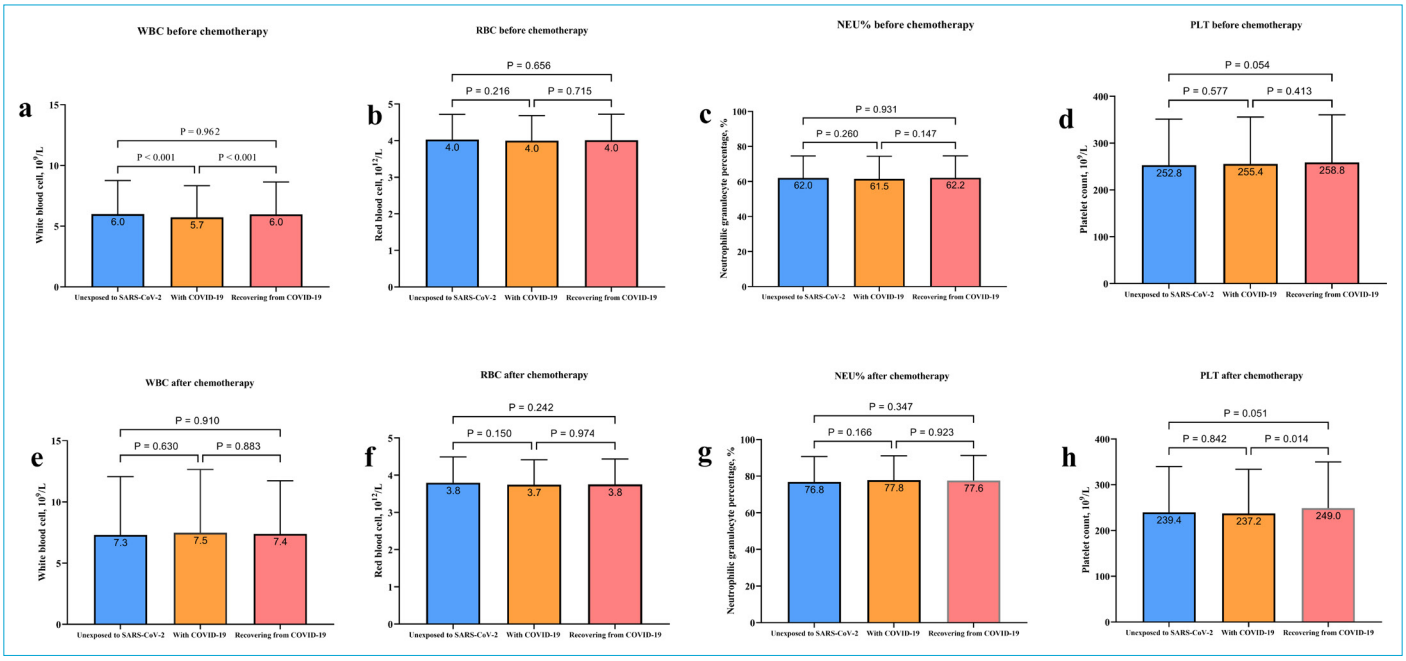


Figure 2. Peripheral hemogram of cancer patients before and after chemotherapy in different states of infection. **(a-d)** Comparison of white blood cell count (WBC), red blood cells (RBC), percentage of neutrophils (NEU%), and platelets (PLT) before chemotherapy in different states of infection of cancer patients. **(e-h)** Comparison of WBC, RBC, NEU%, and PLT after chemotherapy in different states of infection of cancer patients. COVID-19, coronavirus disease 2019.

(6.0×10^9 /L, p<0.001) or those recovering from COVID-19 (6.0×10^9 /L, p<0.001). In contrast, white blood cell count after chemotherapy did not differ significantly across the three groups. Platelet count after chemotherapy in patients with COVID-19 (237.2×10^9 /L) was lower than the count in those recovering from COVID-19 (249.0×10^9 /L, p=0.014). In contrast, platelet count before chemotherapy did not differ significantly across the three groups. Similarly, neither red blood cell count nor percentage of neutrophils differed significantly across the three groups, whether before or after chemotherapy.

Found in the comparison before and after chemotherapy in each patients group itself, chemotherapy significantly reduced counts of red blood cells and platelets, while significantly increasing white blood cell count and neutrophil percentage (Supplementary Fig. 1). These effects of chemotherapy were largest among patients with COVID-19.

Differences in Clinical Interventions

Patients with COVID-19 were significantly less likely to receive leukocyte-depleted red blood cells or recombinant human erythropoietin injection than the other two patient groups, but significantly more likely to receive human granulocyte colony-stimulating factor to restore white blood cell count or neutrophil percentage (Table 2). Patients with COVID-19 were also more likely to receive caffeic acid tab-

Table 2. Comparison of frequencies of clinical interventions in the three patient groups.*

Intervention	Unexposed to SARS-CoV-2 (n=985)	With COVID-19 (n=1482)	Recovering from COVID-19 (n=1281)	p
Transfusion of leukocyte-depleted red blood cells	32 (3.2)	26 (1.8)	26 (2.0)	0.039
Injection of recombinant human erythropoietin	24 (2.4)	13 (0.9)	15 (1.2)	0.003
Injection of granulocyte colony-stimulating factor	621 (63.0)	995 (67.1)	806 (62.9)	0.031
Injection of mecapegfilgrastim	66 (6.7)	101 (6.8)	88 (6.9)	0.990
Caffeic acid tablets	153 (15.5)	276 (18.6)	260 (20.3)	0.015
Transfusion of platelets from apheresis	15 (1.5)	11 (0.7)	10 (0.8)	0.113
Injection of recombinant thrombopoietin	20 (2.0)	8 (0.5)	7 (0.5)	<0.001
Injection of interleukin-11	74 (5.5)	52 (3.5)	69 (5.4)	<0.001

* Values are n (%) in terms of the total numbers of interventions, not patients.

lets and/or injection with recombinant thrombopoietin or interleukin-11 to restore platelet count (Fig. 3).

Differences in Medications After Discharge

The three groups were prescribed similar distributions of preventive medications after discharge (Table 3, Supplementary Table 2). For example, many were prescribed injections of granulocyte colony-stimulating factor or mecapegfilgrastim to restore white blood cell count and neutrophil percentage, while many received injections of recombinant thrombopoietin or interleukin-11 to improve platelet count.

Discussion

This retrospective study suggests that COVID-19 does not influence the peripheral hemogram of cancer patients on chemotherapy to a clinically significant extent. Regardless of whether patients had never been infected with SARS-CoV-2, had COVID-19 or were recovering from COVID-19, all the indicators after chemotherapy were within the expected range and patients achieved satisfactory chemotherapy benefits. This implies that cancer patients with COVID-19 should be treated in similar ways as those without the disease.

Cancer patients may be more vulnerable to severe complications and death from COVID-19 than patients with other chronic diseases.[7, 22, 23] This reflects that the immune system can be damaged by cancer itself[24-26] and by chemotherapy,[27, 28] and such damage can be exacerbated by complications and immune failure caused by COVID-19.[29-31] In addition, chemotherapy can inhibit formation of red blood cells and platelets from bone marrow.[32, 33] These considerations imply that clinicians should exercise caution when formulating treatment plans for patients with COVID-19, yet our results with a large patient sample presenting a broad range of tumor types suggests that significant deviations from standard cancer treatment and management are unlikely to be necessary.

We found that of the various parameters examined for COVID-19 patients, only the changes in counts of white blood cells and platelets differed significantly across the three patient groups. White blood cell count before chemotherapy was lower in patients with COVID-19 than in those unexposed to the virus or those recovering from COVID-19, but white blood cell count after chemotherapy did not differ significantly across the three groups, although there was a trend towards higher values in patients with COVID-19. Platelet count after chemotherapy was lower in patients with COVID-19 than those recovering from COVID-19, but it was still well within the normal range. Furthermore, chemotherapy reduced the red blood cell count and increased

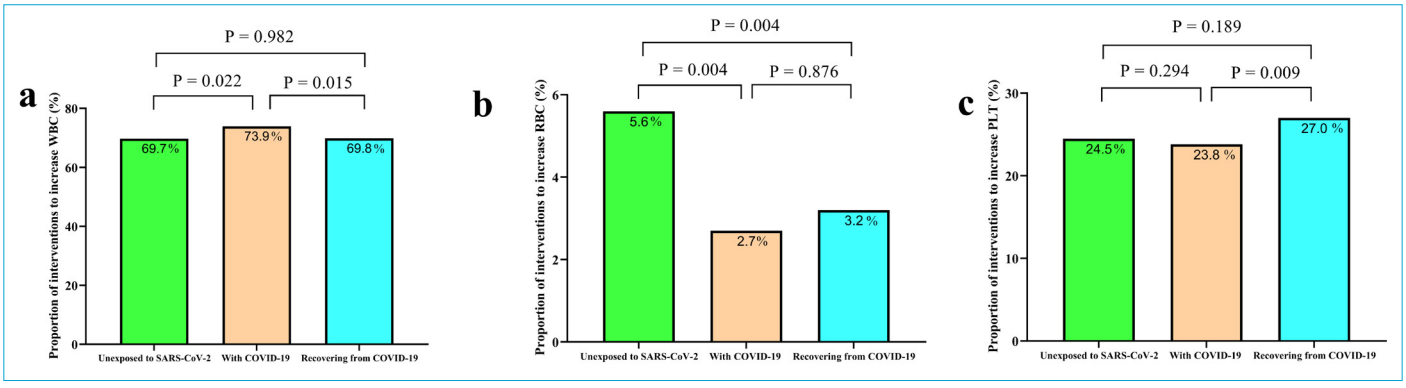


Figure 3. Comparison of frequencies of clinical interventions to increase **(a)** white blood cell count, **(b)** red blood cell count, or **(c)** platelet count in the three patient groups.

Table 3. Comparison of frequencies of prophylactic medications prescribed to the three patient groups after discharge.*

Medication	Unexposed to SARS-CoV-2 (n=208)	With COVID-19 (n=373)	Recovering from COVID-19 (n=325)	p
Injection of granulocyte colony-stimulating factor	99 (47.6)	185 (49.6)	155 (47.7)	0.853
Mecapegfilgrastim injection	10 (4.8)	26 (7.0)	19 (5.8)	0.130
Caffeic acid tablets	96 (46.2)	156 (41.8)	147 (45.2)	0.521
Injection of recombinant thrombopoietin	1 (0.5)	2 (0.5)	1 (0.3)	1.000
Human interleukin-11 injection	2 (1.0)	4 (1.1)	3 (0.9)	1.000

* Results are presented as n (%) in terms of the number of interventions, not patients.

the neutrophil percentage in all three patient groups and to a greater extent in patients with COVID-19, although the magnitude of these changes did not differ significantly among the three groups. This indicates that COVID-19 does not significantly interfere with the peripheral hemogram of cancer patients after chemotherapy, and that chemotherapy can be planned similarly as for patients without COVID-19.

Among the various treatments and prevention strategies that can be effective against COVID-19,[34-36] anti-inflammatory corticosteroids have been shown to improve survival in patients with severe COVID-19.[37] Whether steroid therapy affects the peripheral hemogram of cancer patients during chemotherapy should be explored in future work. Relatively few of our patients received blood transfusion, reflecting uncertainty about the impact of COVID-19 on the safety and efficacy of blood transfusion for cancer patients.[38, 39] Future work should also explore the potential effects of blood transfusion on the peripheral hemogram during chemotherapy.

Studies should continue to explore the long-term effects of COVID-19.[40-42] and the implications for long-term cancer management. Studies should also explore whether and how SARS-CoV-2 may interact with other viruses circulating in humans, and whether such interactions affect the safety and efficacy of cancer treatments. This type of research should also be extended to patients with non-solid tumors.

Strengths and Limitations

Our study has several strengths. Our cancer center is one of the largest in China, allowing us to perform a comprehensive assessment of patients with a broad range of solid cancers in order to provide insights relevant to real-world clinical practice. On the other hand, our findings should be interpreted with caution in light of our study's retrospective and single-center design, and the fact that we collected data during only about four months of chemotherapy, even though such treatment can last far longer. We did not take into account the potential influence of nursing care, exact type and number of cycles of chemotherapy, interactions between synchronous chemotherapy regimes, or other factors that may affect the peripheral hemogram.

Conclusion

These studies suggest that COVID-19 does not significantly alter the peripheral hemogram of cancer patients undergoing effective chemotherapy. The impact of the COVID-19 pandemic is ongoing, although it may become as common as other viral infections in the future. More and longer studies are needed to determine whether the COVID-19 pandemic can lead to other adverse outcomes in patients on chemotherapy. Continuous monitoring of the impact of the COVID-19 pandemic and other global health crises on the hemogram of cancer patients undergoing chemotherapy is essential for optimizing prognosis of cancer patients.

Disclosures

Ethics Committee Approval: The study was approved by the Guangxi Medical University Cancer Hospital Ethics Committee in June 20, 2023 (LW2023100).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Funding: This study was supported by the Specific Research Project of Guangxi for Research Bases and Talents (GuiKe AD22035057), the National Natural Science Foundation of China (82060510 and 82260569), and Guangxi Undergraduate Training Program for Innovation and Entrepreneurship (S202310598204 and S202310598205).

Role of the funding source: The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript. The corresponding authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data Availability Statement: Original data can be obtained from the corresponding authors in accordance with privacy/ethical restrictions.

Authorship Contributions: Concept – J.-H.Z.; Design – J.-H.Z., J.-Y.S.; Supervision – Z.-J.G.; Materials – Y.-H.J.; Data collection &/or processing – Q.-M.L., Y.-J.L., B.-H.C., Y.-L.Z., B.-Y.M., D.-S.C.; Analysis and/or interpretation – Y.-N.L., Y.-T.C.; Literature search – Q.Q.C.; Writing –J.-Y.S.; Critical review – J.-H.Z.

References

1. World health statistics 2023: monitoring health for the SDGs, Sustainable Development Goals. Geneva: World Health Organization; 2023. Licence: CC BY-NC-SA 3.0 IGO.
2. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. BMJ. 2020;368:m1198.
3. Westblade LF, Brar G, Pinheiro LC, Paidoussis D, Rajan M, Martin P, et al. SARS-CoV-2 Viral Load Predicts Mortality in Patients with and without Cancer Who Are Hospitalized with COVID-19. Cancer Cell. 2020;38(5):661-71 e2.
4. Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet. 2020;395(10241):1907-18.
5. Belsky JA, Tullius BP, Lamb MG, Sayegh R, Stanek JR, Auletta JJ. COVID-19 in immunocompromised patients: A systematic review of cancer, hematopoietic cell and solid organ transplant patients. J Infect. 2021;82(3):329-38.
6. Sun L, Surya S, Le AN, Desai H, Doucette A, Gabriel P, et al. Rates of COVID-19-Related Outcomes in Cancer Compared With

Noncancer Patients. JNCI Cancer Spectr. 2021;5(1):Pkaa120.
7. Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020;21(3):335-7.
8. Li LQ, Huang T, Wang YQ, Wang ZP, Liang Y, Huang TB, et al. COVID-19 patients' clinical characteristics, discharge rate, and fatality rate of meta-analysis. J Med Virol. 2020;92(6):577-83.
9. Kamboj M, Sepkowitz KA. Nosocomial infections in patients with cancer. Lancet Oncol. 2009;10(6):589-97.
10. Zhang L, Zhu F, Xie L, Wang C, Wang J, Chen R, et al. Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. Ann Oncol. 2020;31(7):894-901.
11. Key NS, Khorana AA, Kuderer NM, Bohlke K, Lee AYY, Arcelus JI, et al. Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol. 2020;38(5):496-520.
12. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17-48.
13. Fujii K, Chihara Y, Mishima C, Yamamoto M. [Concurrent COVID-19 and Pneumocystis Jirovecii Pneumonia in a Patient with Breast Cancer Receiving Adjuvant Dose-Dense Chemotherapy]. Gan To Kagaku Ryoho. 2022;49(13):1941-3.
14. Mechal H, Benmalek R, Choukrallah H, Maaroufi A, Habbal R, Benouna EGM, et al. Cardiac involvement in cancer patients under chemotherapy and diagnosed with COVID-19: case report and literature review. Pan Afr Med J. 2022;41:45.
15. Chen LP, Lin SJ, Yu MS. Prognostic value of platelet count in diffuse large B-cell lymphoma. Clin Lymphoma Myeloma Leuk. 2012;12(1):32-7.
16. Nagashima K, Tanaka H, Nagai Y, Sugita Y. Immune pancytopenia after chemotherapy in a patient with diffuse large B-cell lymphoma. BMJ Case Rep. 2016;2016.
17. Zhou J, Sun H, Wang Z, Cong W, Wang J, Zeng M, et al. Guidelines for the Diagnosis and Treatment of Hepatocellular Carcinoma (2019 Edition). Liver Cancer. 2020;9(6):682-720.
18. Curran MP, Robinson DM. Aprepitant: a review of its use in the prevention of nausea and vomiting. Drugs. 2009;69(13):1853-78.
19. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.
20. European Association for the Study of the Liver. Electronic address eee, European Association for the Study of the L. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. J Hepatol. 2018;69(1):182-236.
21. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395(10223):497-506.
22. Lievre A, Turpin A, Ray-Coquard I, Le Malicot K, Thariat J, Ahle G, et al. Risk factors for Coronavirus Disease 2019 (COVID-19) severity and mortality among solid cancer patients and impact of the disease on anticancer treatment: A French nationwide cohort study (GCO-002 CACOVID-19). Eur J Cancer. 2020;141:62-81.
23. Grivas P, Khaki AR, Wise-Draper TM, French B, Hennessy C, Hsu CY, et al. Association of clinical factors and recent anticancer therapy with COVID-19 severity among patients with cancer: a report from the COVID-19 and Cancer Consortium. Ann Oncol. 2021;32(6):787-800.
24. Wang X, Lu XJ, Sun B. The pros and cons of dying tumour cells in adaptive immune responses. Nat Rev Immunol. 2017;17(9):591.
25. Mortezaee K, Majidpoor J. CD8(+) T Cells in SARS-CoV-2 Induced Disease and Cancer-Clinical Perspectives. Front Immunol. 2022;13:864298.
26. McKinney EF, Smith KG. T cell exhaustion and immune-mediated disease-the potential for therapeutic exhaustion. Curr Opin Immunol. 2016;43:74-80.
27. Wu MY, Li CJ, Yiang GT, Cheng YL, Tsai AP, Hou YT, et al. Molecular Regulation of Bone Metastasis Pathogenesis. Cell Physiol Biochem. 2018;46(4):1423-38.
28. Kang DH, Weaver MT, Park NJ, Smith B, McArdle T, Carpenter J. Significant impairment in immune recovery after cancer treatment. Nurs Res. 2009;58(2):105-14.
29. Marfella R, Sardu C, D'Onofrio N, Prattichizzo F, Scisciola L, Messina V, et al. Glycaemic control is associated with SARS-CoV-2 breakthrough infections in vaccinated patients with type 2 diabetes. Nat Commun. 2022;13(1):2318.
30. Napoli C, Tritto I, Mansueto G, Coscioni E, Ambrosio G. Immunosenescence exacerbates the COVID-19. Arch Gerontol Geriatr. 2020;90:104174.
31. Grimaldi V, Benincasa G, Moccia G, Sansone A, Signoriello G, Napoli C. Evaluation of circulating leucocyte populations both in subjects with previous SARS-COV-2 infection and in healthy subjects after vaccination. J Immunol Methods. 2022;502:113230.
32. Corbeau A, Kuipers SC, de Boer SM, Horeweg N, Hoogeman MS, Godart J, et al. Correlations between bone marrow radiation dose and hematologic toxicity in locally advanced cervical cancer patients receiving chemoradiation with cisplatin: a systematic review. Radiother Oncol. 2021;164:128-37.
33. Newman NB, Sidhu MK, Baby R, Moss RA, Nissenblatt MJ, Chen T, et al. Long-Term Bone Marrow Suppression During Postoperative Chemotherapy in Rectal Cancer Patients After Preoperative Chemoradiation Therapy. Int J Radiat Oncol Biol Phys. 2016;94(5):1052-60.
34. Yuan Y, Jiao B, Qu L, Yang D, Liu R. The development of COVID-19 treatment. Front Immunol. 2023;14:1125246.
35. Harris E. FDA Grants Full Approval to Paxlovid, COVID-19 Antiviral Treatment. JAMA. 2023;329(24):2118.
36. Tomazini BM, Maia IS, Cavalcanti AB, Berwanger O, Rosa RG,

Veiga VC, et al. Effect of Dexamethasone on Days Alive and Ventilator-Free in Patients With Moderate or Severe Acute Respiratory Distress Syndrome and COVID-19: The CoDEX Randomized Clinical Trial. JAMA. 2020;324(13):1307-16.
37. Group WHOREAfC-TW, Sterne JAC, Murthy S, Diaz JV, Slutsky AS, Villar J, et al. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. JAMA. 2020;324(13):1330-41.
38. O'Brien SF, Lieshout-Krikke RW, Lewin A, Erikstrup C, Steele WR, Uzicanin S, et al. Research initiatives of blood services worldwide in response to the covid-19 pandemic. Vox Sang. 2021;116(3):296-304.
39. Piechotta V, Chai KL, Valk SJ, Doree C, Monsef I, Wood EM, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. Cochrane Database Syst Rev. 2020;7(7):CD013600.
40. Huang L, Li X, Gu X, Zhang H, Ren L, Guo L, et al. Health outcomes in people 2 years after surviving hospitalisation with COVID-19: a longitudinal cohort study. Lancet Respir Med. 2022;10(9):863-76.
41. Global Burden of Disease Long CC, Wulf Hanson S, Abbafati C, Aerts JG, Al-Aly Z, Ashbaugh C, et al. Estimated Global Proportions of Individuals With Persistent Fatigue, Cognitive, and Respiratory Symptom Clusters Following Symptomatic COVID-19 in 2020 and 2021. JAMA. 2022;328(16):1604-15.
42. Chen AK, Wang X, McCluskey LP, Morgan JC, Switzer JA, Mehta R, et al. Neuropsychiatric sequelae of long COVID-19: Pilot results from the COVID-19 neurological and molecular prospective cohort study in Georgia, USA. Brain Behav Immun Health. 2022;24:100491.

Table S1. Comparison of the frequencies of different types of solid tumor in the three patient groups.

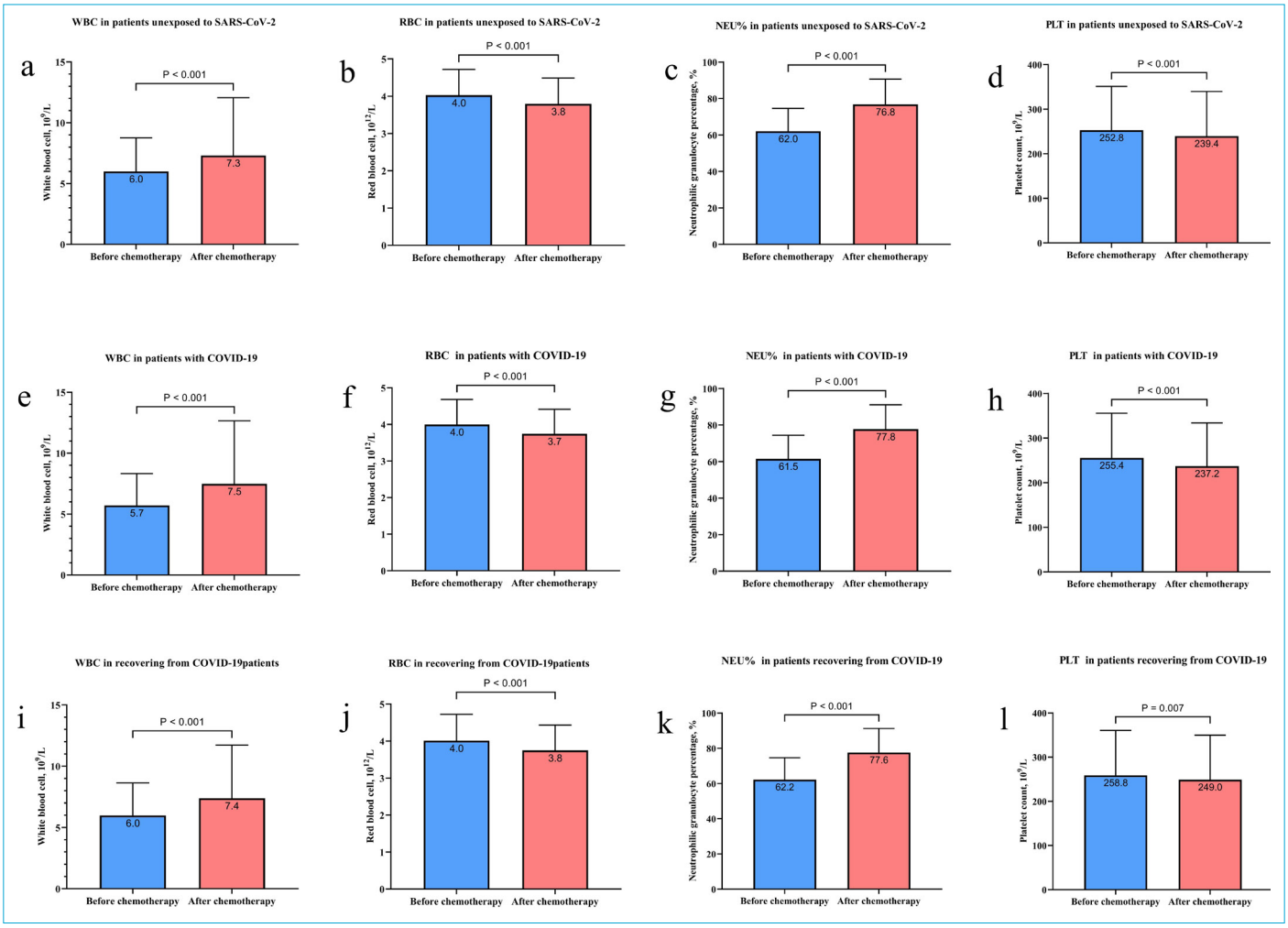
Solid cancer	Unexposed to SARS-CoV-2 (n=3164)	With COVID-19 (n=2771)	Recovering from COVID-19 (n=2817)	p
Central nervous system	10 (0.3)	12 (0.4)	9 (0.3)	0.696
Head and neck	349 (11.0)	323 (11.7)	305 (10.8)	0.596
Thoracic	1196 (37.8)	995 (35.9)	1094 (38.8)	0.076
Digestive system	825 (26.1)	733 (26.5)	803 (28.5)	0.088
Urinary system or male genital organs	39 (1.2)	41 (1.5)	35 (1.2)	0.653
Female genital organs	429 (13.6)	382 (13.8)	348 (12.4)	0.227
Soft tissue and bone	79 (2.5)	61 (3.4)	70 (2.5)	0.098
Lymphoid tissue	210 (6.6)	192 (6.9)	165 (5.9)	0.246
Skin	13 (0.4)	16 (0.6)	11 (0.4)	0.549
Unknown	14 (0.4)	16 (0.6)	7 (0.2)	0.160

Values are n (%), unless otherwise noted.

Table S2. Comparison of in-hospital interventions and post-discharge medication in the three patient groups.*

Measure	Unexposed to SARS-CoV-2 (n=1193)	With COVID-19 (n=1855)	Recovering from COVID-19 (n=1606)	p
In-hospital interventions	985 (82.6)	1482 (79.9)	1281 (79.8)	0.115
After-discharge medications	208 (17.4)	373 (20.1)	325 (20.2)	

* Results are presented as n (%) in terms of the number of interventions, not patients.



Supplementary Figure 1. Comparison of hemogram indexes of each patients group itself before and after chemotherapy. **(a-d)** white blood cell count (WBC), red blood cells (RBC), percentage of neutrophils (NEU%), and platelets (PLT) among patients unexposed to SARS-CoV-2. **(e-h)** WBC, RBC, NEU%, and PLT among patients with COVID-19. **(i-l)** WBC, RBC, NEU%, PLT among patients recovering from COVID-19. COVID-19, coronavirus disease 2019.