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Characteristics and outcomes of COVID-19 infection in 45 patients with breast cancer: A multi-center retrospective study in Hubei, China

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ABSTRACT

Background: The COVID-19 pandemic is a significant worldwide health crisis. Breast cancer patients with COVID-19 are fragile and require particular clinical care. This study aimed to identify the clinical characteristics of breast cancer patients with COVID-19 and the risks associated with anti-cancer treatment.
Methods: The medical records of breast cancer patients with laboratory-confirmed COVID-19 were collected among 9559 COVID-19 patients from seven designated hospitals from 13th January to 18th March 2020 in Hubei, China. Univariate and multivariate analyses were performed to assess risk factors for COVID-19 severity.
Results: Of the 45 breast cancer patients with COVID-19, 33 (73.3%) developed non-severe COVID-19, while 12 (26.7%) developed severe COVID-19, of which 3 (6.7%) patients died. The median age was 62 years, and 3 (6.7%) patients had stage IV breast cancer. Univariate analysis showed that age over 75 and the Eastern Cooperative Oncology Group (ECOG) score were associated with COVID-19 disease severity ($P < 0.05$). Multivariate analysis showed that patients who received chemotherapy within 7 days had a significantly higher risk for severe COVID-19 (logistic regression model: RR = 13.886, 95% CI 1.014 −190.243, $P = 0.049$; Cox proportional hazards model: HR = 13.909, 95% CI 1.086−178.150, $P = 0.043$), with more pronounced neutropenia and higher LDH, CRP and procalcitonin levels than other patients ($P < 0.05$).
Conclusions: In our breast cancer cohort, the severity of COVID-19 could be associated with baseline factors such as age over 75 and ECOG scores. Chemotherapy within 7 days before symptom onset could be a risk factor for severe COVID-19, reflected by neutropenia and elevated LDH, CRP and procalcitonin levels.

1. Introduction

The current coronavirus disease 2019 (COVID-19) pandemic has been active worldwide since December 2019, a period of more than half a year, which brought unprecedented challenges to the health care system. As of 29th August 2020, the total number of laboratory-confirmed cases has risen sharply to almost 25 million globally, with 688,354 (3.3%) deaths [1–3]. The increasing number of newly diagnosed and hospitalized patients with COVID-19 has brought unprecedented challenges and changes to health care

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systems. According to a previous study, patients with malignancy are more susceptible and vulnerable to COVID-19 infection than those without cancer [4]. Although some treatment regimens and recommendations have been proposed for cancer patients during epidemics, identifying the core risk factors for COVID-19 remain necessary and important.

Some researchers have conducted studies to characterize cancer patients with COVID-19 [5–12]. Approximately 1–2.5% of COVID-19 patients have cancer, and their mortality rate ranges from 11.4 to 28.6%, which is much higher than that of the general population [4–12]. Regrettably, many of these studies ignored the effects of different cancer types. As the most common cancer among women, breast cancer has a long treatment cycle resulting in immunosuppression and increased risk of infection [13], thus individuals with breast cancer are at increased risk of COVID-19 infection and should be given increased attention. In our previous study and Kuderer's study, breast cancer patients had the highest proportion among all cancer patients with COVID-19 [9,14]. And their mortality rate was 14%, far below the average of general cancer patients (28%) [5,9]. A study from Paris suggested that the severity of breast cancer patients with COVID-19 resided more in comorbidities [15], however, our previous study found that cancer patients with anti-cancer treatment had a poorer prognosis, which prompted us to assess the relationship between disease severity and anti-cancer treatment among the breast cancer population.

This study aimed to identify the epidemiological and clinical characteristics of breast cancer patients with COVID-19 and risks associated with anti-cancer treatment. This multi-center retrospective study included 45 breast cancer patients with laboratory-confirmed COVID-19 identified among 9559 COVID-19 patients in seven hospitals in Hubei, China.

2. Material and methods

2.1. Study design and participants

In this multi-center retrospective study, 45 breast cancer patients diagnosed with laboratory-confirmed COVID-19 (40 cases from our previous study and 5 from two other hospitals) were identified among 9559 COVID-19 cases referred from the outpatient fever policlinics and admitted between 13th Jan and 18th March 2020 to seven designated hospitals in Hubei, China (Cancer Center of Union Hospital (7/45), Western District of Union Hospital (5/45), Red Cross Hospital of Union Hospital (5/45) and The Central Hospital of Wuhan (5/45), all of which are affiliated with Tongji Medical College of Huazhong University of Science and Technology; Jinyintan Hospital (17/45); Renmin Hospital of Wuhan University (3/45) and the First Renmin Hospital of Jingzhou (3/45). The clinical outcomes of the patients were followed up to 15th April 2020. This study was approved by the Ethics Committee of Union Hospital, Tongji Medical College of Huazhong University of Science and Technology (NA2020-0078).

2.2. Study definitions

Patients with the pathological diagnosis of breast cancer at any time and laboratory confirmation of COVID-19 were included. COVID-19 was diagnosed by RT-PCR of nasal or pharyngeal specimens based on criteria of the World Health Organization [3], or antibody IgM and IgG based on criteria by the National Health Commission (NHC) of China [16]. According to Diagnosis and Treatment Program of 2019 New Coronavirus Pneumonia (v7.0 Feb 8, 2020) by the NHC [16], upon admission, severe cases were characterized as oxygen saturation$\leq$93% at rest or chest imaging with lesion progression>50% within 24–48 h. Critical cases, were the patients with respiratory failure and requiring invasive mechanical ventilation, shock, or organ failure requiring intensive care unit (ICU) care, regardless of age and comorbidities. We categorized severe/critical cases into the severe group, and mild/moderate cases into the non-severe group. Breast cancer staging was based on the American Joint Committee on Cancer (AJCC-8ed) guidelines [17].

2.3. Data collection

Demographic information, clinical manifestations, physical signs, laboratory results, chest radiographs, treatments and outcomes were extracted from electronic medical records using a standardized data collection form and cross-checked by two trained researchers. Clinical outcome data were collected up to 15th April 2020.

2.4. Statistical analysis

Continuous variables, that were not normally distributed, were expressed as the median and interquartile range (IQR) and compared using the Mann-Whitney *U* test. Categorical variables were noted as numbers (%) and compared by the χ^2 test or Fisher's exact test. The risk ratio (RR) and 95% confidence interval (CI) from univariate and multivariate logistic regression models explored risk factors for COVID-19 severity. The hazard ratio (HR) and 95% CI from the Cox proportional hazards model represented effects of risk factors over time. Statistical analyses were conducted using SPSS statistics 22.0 and SAS 9.4 software. A two-sided *P* value less than 0.05 was considered statistically significant.

3. Results

3.1. Clinical characteristics of breast cancer patients with COVID-19

In this study, 45 breast cancer patients with COVID-19 were selected (Table 1), of which 40 (88.9%) patients were diagnosed by PCR and 5 (11.1%) patients were diagnosed by positive serum antibody plus chest CT radiography indicative of COVID-19. Twelve (26.7%) patients were categorized into the severe group, while the rest were categorized into the non-severe group (73.3%). All patients were females with no smoking history; the median age was 62 years (54.0–70.5 years) (Table S1). There were five women >75 years old, four in the severe group, and one in the non-severe group. Only 4.4% (2/45) of the patients had ECOG scores higher than score one. More than half of the patients had underlying diseases (60.0%), mainly hypertension (31.1%). Regarding the characteristics of breast cancer, 3 (6.7%) patients were diagnosed with stage IV disease, 31.6% had HER2 overexpression, and 55.3% had estrogen receptor (ER) positivity. There were 23 patients undergoing anti-cancer treatment, including chemotherapy, radiotherapy, surgery and endocrinotherapy, while 22 patients were followed up only. Among all the patients, 51.5% (23/45) received anti-cancer treatment within one month before symptom onset, and 33.3% (15/45) received anti-cancer treatment within one week, including chemotherapy (4/45, 8.9%), surgery (2/45, 4.4%), radiotherapy (2/45, 4.4%), targeted therapy (2/45, 4.4%) and endocrinotherapy (7/45, 16.3%). Patients undergoing anti-cancer treatment within 7 days were aged 24–69 years old, three of who were treated with taxane-based chemotherapy, and the remaining patient was treated with anthracycline-based chemotherapy (Table S2).

Typical symptoms at illness onset were fever (82.2%), cough (75.6%) and dyspnea (42.2%) (Table 1 and Table S1). Dyspnea and expectoration were more common in the severe group than in the

Table 1
Clinical characteristics and outcomes of patients.

Characteristics	Disease Severity			
	All Patients ($N = 45$)	Non-Severe ($N = 33$)	Severe ($N = 12$)	*P* value
Age (years)				0.020
≤75	40 (88.9%)	32 (97.0%)	8 (66.7%)	
>75	5 (11.1%)	1 (3.0%)	4 (33.3%)	
ECOG Score				0.067
0–1	43 (95.6%)	33 (100%)	10 (83.3%)	
≥2	2 (4.4%)	0 (0%)	2 (16.7%)	
Comorbidities	27 (60.0%)	21 (63.6%)	6 (50.0%)	0.409
Hypertension	14 (31.1%)	11 (33.3%)	3 (25.0%)	0.865
Diabetes	7 (15.6%)	5 (15.2%)	2 (16.7%)	>0.999
Chronic Cardiovascular Disease (not including hypertension)	6 (13.3%)	5 (15.2%)	1 (8.3%)	0.921
Hepatitis	4 (8.9%)	3 (9.1%)	1 (8.3%)	>0.999
Cancer (not including breast cancer)	3 (6.7%)	3 (9.1%)	0 (0%)	0.553
Chronic Cerebrovascular Disease	1 (2.2%)	1 (3.0%)	0 (0%)	>0.999
AIDS	1 (2.2%)	0 (0%)	1 (8.3%)	0.267
Others	7 (15.6%)	6 (18.2%)	1 (8.3%)	0.733
Stage				>0.999
I-III	42 (93.3%)	31 (93.9%)	11 (91.7%)	
IV	3 (6.7%)	2 (6.1%)	1 (8.3%)	
Her-2 expression[a]				0.232
HER-2 (+)	12 (31.6%)	8 (26.7%)	4 (50%)	
HER-2 (−)	26 (68.4%)	22 (73.3%)	4 (50%)	
Hormone receptor status[a]				>0.999
ER (+)	21 (55.3%)	17 (56.7%)	4 (50%)	
ER (−)	17 (44.7%)	13 (43.3%)	4 (50%)	
Anti-cancer within 1 month				0.928
Yes	23 (51.1%)	17 (51.5%)	6 (50.0%)	
No	22 (48.9%)	16 (48.5%)	6 (50.0%)	
Chemotherapy within 1 month				0.556
Yes	7 (15.6%)	4 (12.1%)	3 (25.0%)	
No	38 (84.4%)	29 (87.9%)	9 (75.0%)	
Anti-cancer within 7 days[b]	15 (33.3%)	9 (27.3%)	6 (50.0%)	0.153
Surgery	2 (4.4%)	1 (3.0%)	1 (8.3%)	>0.999
Chemotherapy	4 (8.9%)	1 (3.0%)	3 (25.0%)	0.090
Radiotherapy	2 (4.4%)	1 (3.0%)	1 (8.3%)	>0.999
Targeted therapy	2 (4.4%)	0 (0%)	2 (16.7%)	0.067
Endocrinotherapy	7 (16.3%)	6 (19.4%)	1 (8.3%)	0.676
Main symptoms				>0.999
Fever	37 (82.2%)	26 (78.8%)	11 (91.7%)	0.577
Cough	34 (75.6%)	24 (72.7%)	10 (83.3%)	0.734
Dyspnea	19 (42.2%)	10 (30.0%)	9 (75.0%)	0.019
Laboratory findings				
Neutrophil <1.8* 10^9/L	6 (13.3%)	2 (6.1%)	4 (33.3%)	0.042
LDH> 250 U/L	14 (35.9%)	5 (17.9%)	8 (81.8%)	<0.001
AST> 40 U/L	10 (25.0%)	4 (13.8%)	6 (54.4%)	0.025
CRP> 10 mg/L	23 (47.7%)	14 (42.4%)	9 (81.8%)	0.055
CT changes				0.448
Unilateral	9 (20.0%)	8 (24.2%)	1 (8.3%)	
Bilateral	36 (80.0%)	25 (75.8%)	11 (91.7%)	
Clinical outcomes				0.016
Discharge	42 (93.3%)	33 (100%)	9 (75.0%)	
Death	3 (6.7%)	0 (0%)	3 (25.0%)	

[a] Results of 7 patients in HER2 and HR expression were missing.
[b] One patient received chemotherapy and targeted therapy together; another patient received radiotherapy and targeted therapy together.

non-severe group ($P < 0.05$). Body temperature upon admission and during hospital stay was significantly higher in the severe group ($P < 0.05$) (Table S1). All the four patients who received chemotherapy within 7 days had a fever (Table S2).

3.2. Laboratory results, CT imaging findings and patient outcomes

The laboratory tests performed upon admission showed that the levels of neutrophils and platelets in the severe group were significantly lower than those in the non-severe group ($P < 0.05$) (Table 1 and S1). In contrast, the levels of LDH, AST and CRP in the severe group were significantly higher than those in the non-severe group ($P < 0.05$) (Table 1 and S1, Fig. 2).

On chest CT scans, 80.0% (36/45) of patients showed bilateral involvement (Table 1). The typical patterns were ground-glass opacity (29/42, 69.0%), diffuse patchy shadowing (6/42, 14.3%) and local patchy shadowing (5/42, 11.9%) (Fig. 1, Table S1), however, radiography between the severe group and the non-severe group did not significantly differ (Table 1).

Treatments for COVID-19 included routine physical therapy and medical therapy (Table S1). During hospitalization, 7 patients developed complications, mainly ARDS (4/41, 9.8%), and 4 patients developed severe events (4/45, 8.9%), including admission to the ICU, mechanical ventilation, or death [4] (Table S1). The median time from symptom onset until severe events was 8.5 days. For the patients who developed severe disease, the median time mentioned above was 4.0 days, while for the non-severe patients, it was 12.0 days (Table S1). Three patients (6.7%) in the severe group

had died as of April 15th, 2020; one of these patients had received chemotherapy within 7 days prior to symptom onset (Table 1).

3.3. Risk factors for disease severity

To explore the clinical factors affecting COVID-19 severity, univariate and multivariate logistic regression models were applied. In the univariate logistic analysis, age over 75 years and ECOG score were associated with disease severity ($P < 0.05$) (Fig. 2). Notably, chemotherapy within 7 days showed a tendency towards an association with severe illness ($P = 0.051$). After adjusting for age and other anti-cancer treatments within 7 days (including surgery, radiotherapy, targeted therapy and endocrinotherapy), patients undergoing chemotherapy within 7 days had a significantly higher risk of severe illness (RR = 19.457, 95% CI: 1.147–329.997, $P = 0.040$) (Table 2). Moreover, among patients with ongoing anti-cancer treatment within one month, the multivariate Cox proportional hazards model showed that chemotherapy within 7 days was an independent risk factor for developing severe illness after adjusting for age (HR = 13.909, 95% CI 1.086–178.150, $P = 0.043$) (Table 3, Fig. 3A).

3.4. Correlations of chemotherapy with laboratory findings

Next, we evaluated the correlation of chemotherapy and laboratory findings. The results showed that patients undergoing chemotherapy within 7 days had lower leukocyte and neutrophil counts, and higher LDH, CRP and procalcitonin levels than other patients ($P < 0.05$) (Fig. 3B, Table S3). Similar results were observed between the severe and non-severe groups, that is, neutrophil and platelet counts, and LDH, CRP and procalcitonin levels significantly differed ($P < 0.05$) (Fig. 3C, Table S3).

4. Discussion

With the rapid progression of COVID-19 worldwide, large numbers of cancer patients are inevitably affected by this pandemic [5–10], which leads to grave concerns about standard-of-care treatment regimens in the COVID-19 era and the adoption of protective measures, such as postponing active cancer treatments. However, a set of universal guidelines for all types of cancer is unlikely, especially for patients receiving active life-saving therapy or undergoing active treatment to achieve a probable cure. Breast cancer, the most common malignancy among women, is commonly identified in early stages, with slow progression and a high rate of survival [18]. Based on our recent report, we focused on the effects of COVID-19 on breast cancer patients and determined risk factors for severe COVID-19 in this population.

To date, several studies on the epidemiological characteristics of COVID-19 in cancer patients have been published, but most have focused on general cancer patients, with only two reports on breast cancer [5–10,15,19]. The proportion of breast cancer patients with COVID-19 in our study (0.47%) was lower than that reported by Hershman (0.62%), the difference possibly being related to the higher incidence of breast cancer in the United States [10]. Remarkably, breast cancer patients with COVID-19 had lower disease severity and mortality than general cancer patients. Compared with the similar works of breast cancer patients with COVID-19 in

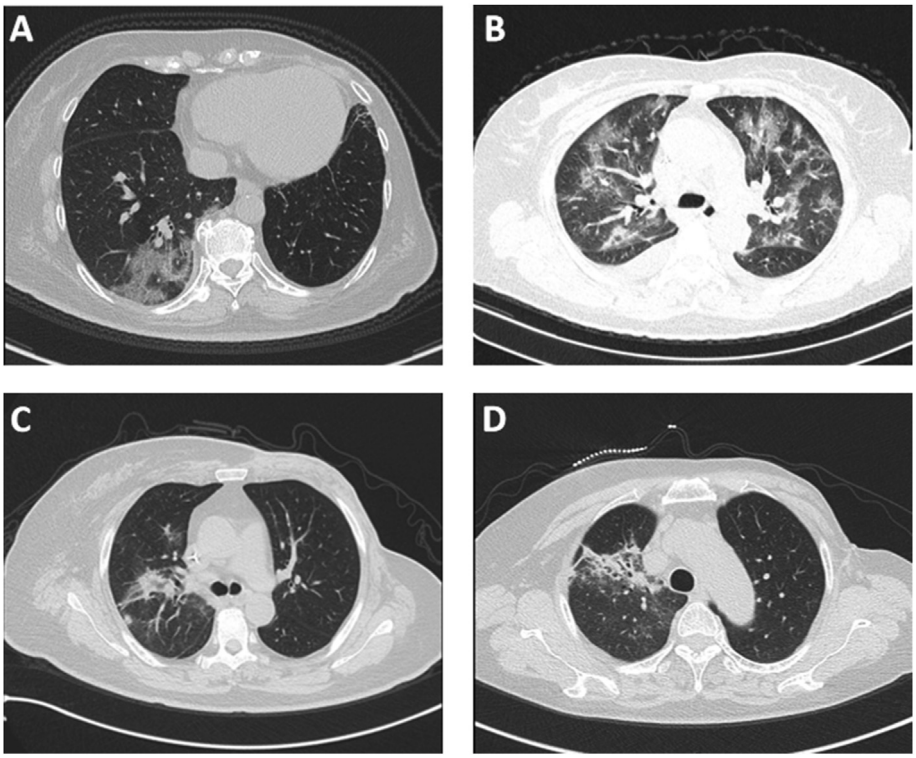

Fig. 1. Typical chest CT scan radiologic findings. A. Sporadic patchy ground-glass opacities in the right lower lobe. B. Diffuse patchy ground-glass opacities bilaterally. C. A mixed pattern of ground-glass opacities and consolidation in the right lung. D. Patchy consolidation in the right upper lobe with obvious predominant reticular change.

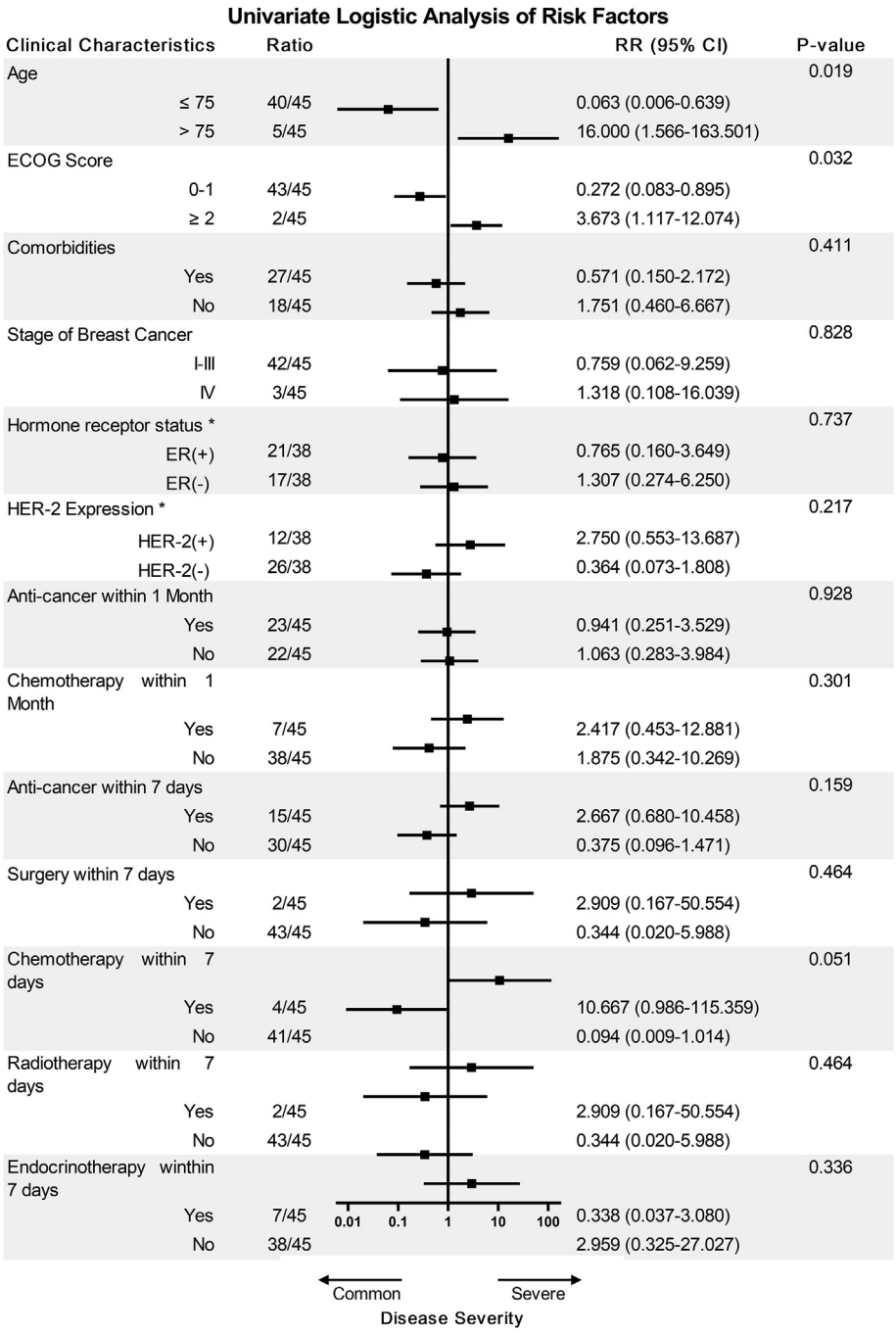

Fig. 2. Forest Plot of Univariate Analysis for Clinical Characteristics as Potential Risk Factors. * HER2 and hormone receptors expression were available in 38/45 patients. The results of 7 patients were missing.

Table 2
Logistic multivariate analysis of risks for COVID-19 severity in 45 patients.

Clinical Factors	RR	95% CI	*P* value
Age	1.027	0.960–1.099	0.436
Chemotherapy within 7 days	19.457	1.147–329.997	0.040
Other anti-cancer treatment within 7 days[a]	1.938	0.342–10.994	0.455

[a] Other anti-cancer treatment includes surgery, radiotherapy, targeted therapy and endocrinotherapy.

Table 3
Cox proportional hazard analysis of risks for COVID-19 severity in patients undergoing anti-cancer treatment within one month.

Clinical Factors	HR	95% CI	*P* value
Age	0.914	0.821–1.017	0.100
Chemotherapy within 7days	13.909	1.086–178.150	0.043

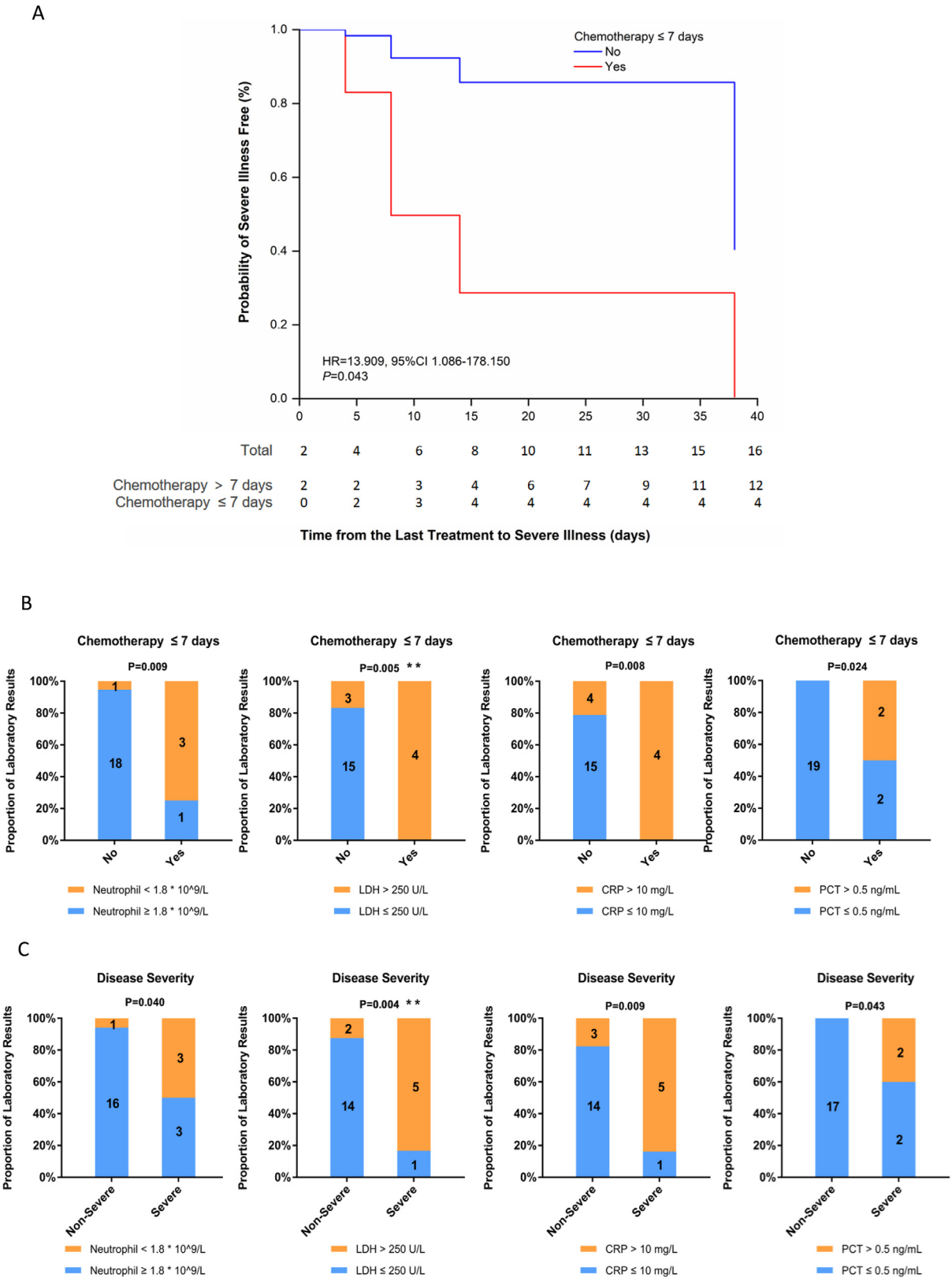

Fig. 3. Chemotherapy, state and disease severity. A. Cox survival analysis for the risk of severe illness with chemotherapy within 7 days. Breast cancer patients with COVID-19 who underwent chemotherapy within 7 days had a higher risk of developing severe illness. The number of patients at each time point is represented below. B. Patients treated with chemotherapy within 7 days before symptom onset had distinct abnormalities in neutrophils, LDH, CRP and procalcitonin (PCT). The number of patients is represented in each column. C. The severe group of patients who underwent chemotherapy within 7 days showed significant differences in neutrophils, LDH, CRP and PCT. The number of patients is represented in each column. * The results in Fig 3. C were analyzed in the population of patients who received anti-cancer treatment within one month before symptom onset. ** The LDH result of one patient was missing in the Non-severe group.

the world, the mortality in our study was 6.7%, which is similar to that in Vuagnat's study (6.7%) and higher than Kalinsky's study (3.7%) [15,19]. These different outcomes among breast cancer patients could be explained by the different regional distributions and availability of medical treatments, testing methods, subtypes and virulence of COVID-19. A current report indicated that the COVID-19 variant with spike D614 to G614 increased COVID-19 infectivity [20]. However, the mortality of our study (6.7%) was much lower than that of general cancer patients (11.4–18.6%) [5,8–10]. In addition, regarding to disease severity, 26.7% of breast cancer patients in our study had severe disease, which was still lower than that of general cancer patients observed by H. Zhang (47.8%), Ma (54.1%), and Dai (34.3%) [7,8,21]. In addition, there was a similar trend in the comparison of critical case rates. A total of 8.9% (4/45) of breast cancer patients developed events of admission to the ICU/mechanical ventilation/death in our study, which was lower than that of general cancer patients in the studies of L. Zhang (53.6%), and Liang (39%) [5,6]. The discrepancies above may be due to different strategies for combating the pandemic, cancer types, and basic characteristics (e.g., sex, age, general health and comorbidities). Taken together, cancer type seems to be a major determinant of the mortality rate, and we can speculate that breast cancer patients with COVID-19 have better outcomes than the general cancer population.

Recent sessions of chemotherapy or other anti-cancer treatment appear to be a risk factor for the severity of COVID-19 in cancer patients [5,6,9]. Potential reasons being breast cancer patients' specificities, reported also in previous papers, such as female gender, longer time since diagnosis (beyond one year, 65.1%), and cancer stage (I-III, 93.3%) [9]. A study by L. Zhang indicated that undergoing anti-cancer treatment within 14 days showed an effect [6], and our previous study showed that chemotherapy within 4 weeks was a risk factor for fatal outcomes [9]. Notably, in this study, we observed breast cancer patients undergoing chemotherapy within 7 days were more likely to develop severe disease. This discrepancy in timing may be due to different cancer types, anti-cancer strategies and intensities. Breast cancer patients are generally female, relatively young, and with no history of smoking [18,22–24], indicating a better baseline condition. Moreover, breast cancer patients are usually treated with mild chemotherapy regimens, in which induced hematological disorders resolve in approximately one week [25]. Breast cancer patients have been reported to have a better prognosis and faster recovery from chemotherapy than those with other solid tumors, such as lung cancer [26]. Our study focused on the relationship between anti-tumor treatment and the disease severity of breast cancer patients with COVID-19. Remarkably, according to univariate and multivariate analyses, our study identified the risk and effect of chemotherapy on severe COVID-19 in breast cancer patients, reaching a profound and meaningful conclusion and emphasizing the effect of cancer therapy. Notably, in Vuagnat's study, univariate analysis showed that the ongoing cancer therapy (within 30 days) was not associated with disease severity, and there was no further analysis of cancer therapy within 7 or 14 days. In addition, the number of patient events in their study was too small to perform multivariate analysis [15]. Our study demonstrated that age over 75 was a distinct risk factor for severity, which is similar to Vuagnat's report (age over 70).

Laboratory examinations on patients undergoing chemotherapy within 7 days showed distinct abnormalities in infection indicators (neutrophil counts, CRP, LDH, and PCT) compared with those not receiving chemotherapy within 7 days, which was consistent with laboratory changes found in severe patients to a rather large extent. It is worth mentioning that, the cutoff chosen for neutropenia (1.8 G/L) is consistent with the minimum normal value in our clinic practice. Only one patient had grade 3–4 leucopenia (<2.0 G/L) according to the CTCAE grading classification and none had grade 3–4 neutropenia (<1.0 G/L), preventing any inclusion of the values in the uni- or multivariate analyses. Neutropenia has been linked to the chemotherapy effects of myelosuppression [27–29], which in turn worsens the immune condition. Additionally, immunosuppression by chemotherapy possibly prolongs the time of viral shedding [30], which provides an explanation for our study, indicating that chemotherapy within 7 days may have led to myelosuppression and secondary infection, resulting in an aggravated illness and poor COVID-19 outcomes.

Therefore, our results can serve as a basis for proposing some recommendations for oncologists. Because intravenous chemotherapy has been identified as a potential risk factor, when available, oral chemotherapy agents should preferentially be administered to contain tumor progression [31–34]. If intravenous chemotherapy must be administered, measures should be taken under strict assessments of individuals, for example, less-toxic agents in myelosuppression [35–38], intensive examinations before and after chemotherapy, prophylactic administration of G-CSF, and close monitoring for any symptom indicative of COVID-19 infection for at least 7 days. The G-CSF might reduce the risk of additional infections [39,40]. But it should be used with caution in case of active COVID for the risk of increased production of inflammatory cytokines [41].

To the best of our knowledge, this study is the first analysis of the clinical characteristics and risk factors for breast cancer patients with COVID-19 in Asia. However, this study has several limitations. First, the sample size of 45 cases was insufficient to reach significance in some respects. For example, only two patients received targeted therapy, and therefore could not to be analyzed in multivariate models. Thus, more patients undergoing anti-cancer treatment should be included in future studies, especially those with targeted therapy. Second, this study did not delve into different regimens of chemotherapy, and extended follow-up and close observation are recommended. In addition, how to balance a delay in cancer treatment against the risk of contracting COVID-19 remains unsettled.

5. Conclusions

In this study, we focused on the clinical characteristics and potential risk factors for COVID-19 in breast cancer patients. Compared with other aggressive types of cancer, breast cancer patients had lower rates of COVID-19-related mortality and severity, the latter of which was related to age over 75 and ECOG scores. In addition, receiving chemotherapy within 7 days before symptom onset was strongly associated with severe COVID-19 in breast cancer patients, reflected by abnormalities in infectious indicators, indicating that ideal preventive care and supportive treatments are warranted.

Declaration of competing interest

The authors declare that they have no competing interests.

Acknowledgments

We thank all patients and healthcare workers who were involved in this study.

ABBREVIATIONS

COVID-19	Coronavirus Disease 2019
CT	Computed tomography

ECOG	Eastern Cooperative Oncology Group
RR	Risk ratio
HR	Hazard ratio
CI	Confidence interval
LDH	Lactic dehydrogenase
CRP	C-reactive protein
PCT	Procalcitonin
RT-PCR	Real time Polymerase Chain Reaction
NHC	National Health Commission
ICU	Intensive care unit
AJCC	American Joint Committee on Cancer
IQR	Interquartile ranges
HER2	Human epidermal growth factor receptor 2
ER	Estrogen receptor
AST	Aspartate aminotransferase
ARDS	Adult respiratory distress syndrome
G-CSF	Granulocyte colony stimulating factor

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Author contributions

YZ and CC designed the study. JW, MW, JL, XW, LP, YH, HY, and ZX contributed to data acquisition. JW and PX summarized the data and performed statistical analysis. JW, MW, JL, PX, YZ, and CC were involved in data interpretation. JW and MW drafted the manuscript. YZ, CC, JL, XW, CL, and ZX critically revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2021.06.006.

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