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Management of Breast Cancer Patients During the Coronavirus Disease 2019 Pandemic: The Experience From the Epicenter of China, Wuhan

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Abstract

The COVID-19 pandemic has a huge impact on the medical care procedures for breast cancer patients. Here we share our experience in the management of breast cancer patients during the pandemic in Wuhan, and it is found to be correlated to a reduction in chemotherapy-related myelosuppression and hepatic dysfunction, which may provide a reference for other centers.

Background: The coronavirus disease 2019 pandemic is a global public health event. Wuhan used to be the epicenter of China and finally controlled the outbreak through city lockdown and many other policies. However, the pandemic and the prevention strategies had a huge impact on the medical care procedures for patients with breast cancer, leading to the delay or interruption of anticancer therapies. Patients and Methods: To better serve patients with breast cancer under the premise of epidemic control, many strategies have been proposed and optimized in our center. One of the most important parts of these strategies is the promotion of telemedicine, including online consultation, online prescription, and drug mailing services. **Results:** In keeping with the city and hospital policies, we have also introduced stricter ward management policies and more precise care. **Conclusion:** Here, we collected the diagnosis and treatment process of patients with breast cancer in our center during the coronavirus disease 2019 pandemic, which was found to be correlated to a reduction in chemotherapy-related myelosuppression and hepatic dysfunction, hoping to provide a reference for other cancer centers that may suffer from the similar situation.

Clinical Breast Cancer, Vol. 22, No. 1, e1–e7 © 2021 Elsevier Inc. All rights reserved. **Keywords:** Telemedicine, Chemotherapy, Side effects, Myelosuppression, Hepatic Dysfunction

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2, has been a worldwide public health event. Wuhan was the epicenter of China and great efforts have been endeavored to control the outbreak in this city.¹⁻³ Wuhan announced the city lockdown on January 23, 2020, followed by a number of other policies to control the pandemic.⁴ Large amounts of medical resources were also devoted to the patients with COVID-19.^{5,6} These measures have led to the rapid control of COVID-19 in this city. Now, Wuhan has passed the

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most difficult period and the quarantine level has been downgraded significantly. However, the pandemic and the prevention strategies have had and will continue to have a huge impact on the "new normal" health care system.⁷⁻⁹

Under such an unanticipated circumstance, medical care for patients with breast cancer has been postponed or interrupted during the pandemic in Wuhan. Compared with the general population, patients with breast cancer are at increased risk of infection and developing worse outcomes owing to the original malignancies, suppressed immunity, and therapy-related side effects.^{10,11} Patients with breast cancer in Wuhan were exposed to a high risk of delays or interruptions of standard anticancer therapy during the pandemic, owing to the city lockdown and shortage of medical resources. Moreover, the treatment modalities for patients who suffered both breast cancer and COVID-19 would have been interrupted until the Health Management Program for Discharged COVID-19 Patients was met.¹²

To better serve patients with breast cancer on the premise of epidemic control, many strategies have been proposed and optimized in our center, the Department of Breast and Thyroid

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Surgery of Wuhan Union Hospital. One of the most important parts of these strategies is the promotion of telemedicine, including online consultation, online prescription, and drug mailing services. In keeping with the city's and hospital's policies, we have also introduced stricter ward management measures and more precise care.

Here, we collected the diagnosis and treatment process of patients with breast cancer in our center during the COVID-19 pandemic, which was found to be correlated with a decrease in chemotherapyrelated myelosuppression and hepatic dysfunction, in the hope of providing a reference for other cancer centers that may suffer from the similar situation.

Methods

Wuhan announced the lockdown measures on January 23, 2020, followed by a number of other policies to control the pandemic, and we chose this key date as the cut-off time for our analysis in this study. We then collected the outpatient and inpatient programs for confirmed or suspected patients with breast cancer in the Department of Breast and Thyroid Surgery of Wuhan Union Hospital during the pandemic. To explore the response of patients with breast cancer to these strategies, we also retrospectively analyzed consecutive patients with breast cancer who came to our department for chemotherapy from December 1, 2019, to June 15, 2020, using January 23, 2020 as the cut-off date.

Patients with breast cancer who came to our department for chemotherapy underwent routine selective blood tests or liver function tests as recommended by their attending physicians. To calculate the incidence of chemotherapy-related side effects during the pandemic, we collected the results of all patients' first blood routine or liver function tests in each cycle of chemotherapy, including adjuvant chemotherapy and neoadjuvant chemotherapy. If the patient exhibits moderate or greater myelosuppression or hepatic dysfunction, chemotherapy may be delayed until the results are almost normal, and the reexamination results of blood routine or liver function in this chemotherapy cycle were excluded in this study.

The results of blood routine test and liver function test were divided into the before pandemic group and during pandemic group according to their test time using January 23, 2020, as the cut-off value. Leukopenia, neutropenia and thrombocytopenia were defined as white blood cell count of less than 3.5×10^9 cells/L, neutrophils of less than 1.5×10^9 cells/L, and platelets of less than 125×10^9 cells/L, respectively. Hepatic dysfunction was defined as any abnormally elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), or gamma-glutamyl transpeptidase. The normal ranges of AST, ALT, and gamma-glutamyl transpeptidase were defined as 8 to 40 U/L, 5 to 35 U/L, and 7 to 32 U/L, respectively.

Results of blood routine or liver function tests were compared using Kruskal-Wallis test and the abnormal data were organized by frequency (%). The Pearson χ^2 test was used to compare the categorical data between the before and during pandemic groups. Logistic regression was used to calculate the odds ratios (ORs). A *P* value of less than .05 was considered significant in this study and all statistical analyses were performed using Statistical Product and Service Solutions (SPSS, IBM Company, version 24.0, Armonk, NY).

Results

Revolutionary Telemedicine: Online Consultation, Prescription, and Drug Mailing Services

Wuhan had strict traffic control measures during the lockdown period from January 23 to early April, making it difficult for patients to get to the hospital. To make it easier for patients to get medical advice and minimize visits to the hospital, medical institutions have launched or strengthened their telemedicine services based on the phone, website, and some other interactive communication mobile applications.

The process of diagnosis and treatment of confirmed or suspected patients with breast cancer during the pandemic is shown in Figure 1. For patients in our center, we provide online consultation through a public platform of our hospital in *Wechat* for routine follow-up. For the patients who need oral medications, such as endocrine therapy drugs, oral chemotherapy drugs, and so on, we provide online prescription with real name authentication and drug mailing services, which may decrease the risk related to the patients visiting the hospital. For patients who still require an on-site outpatient visit after the online consultation and prescription, including patients who need imaging and laboratory tests, patients are advised to go to the hospital with proper personal protection, as well as receiving temperature screening and epidemiological investigation before entering the outpatient center.

As shown in Figure 2A, the frequency of online consultations increased slightly after the city lockdown, and it increased robustly on the day we introduced the online prescription and drug mailing system. A total of 6720 online consultations with our center were recorded in this study, with a daily number (mean \pm standard deviation) of 6.88 \pm 3.65 before the lockdown and 29.38 \pm 13.33 during the pandemic (Figure 2B; *P* < .001).

Strict Admission Requirements and Ward Management

For patients requiring hospitalization for surgery, periodic chemotherapy, radiation, or targeted therapy, careful prehospital COVID-19 screening is recommended. To decrease the patients' financial burden, the city residents' health insurance covers most of the costs of the above screening methods. As shown in Figure 1, temperature screening, epidemiological investigation, history taking, clinical symptoms of COVID-19, physical examination, severe acute respiratory syndrome coronavirus disease 2 nucleic, and antibody tests are required to get the permission to the inpatient department. According to different screening results, the patients were divided into 3 groups as follows: positive, suspected, and negative. As shown in Figure 1, the positive patients are confirmed COVID-19 patients according to the Standard Diagnosis and Therapy Schema of COVID-19 of China. These patients were sent to specialized hospitals for treatment of COVID-19 and were not allowed to go to other hospitals until they are confirmed cured. Their anticancer therapy, especially chemotherapy, was usually interrupted to some extent during this period. The suspected patients should have some of these screening tests again, especially the nucleic acid test. Only patients with confirmed negative screening results are admitted to the inpatient wards of our center.

Strict entry and management requirements are also implemented in the inpatient ward, with a maximum of 1 permanent

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Figure 1 Flow chart of diagnosis and treatment process of patients with breast cancer in our center during the pandemic. COVID-19, coronavirus disease-2019; G-CSF, granulocyte-colony stimulating factors; SARS-CoV-2, severe acute respiratory syndrome coronavirus disease-2.







companion per patient allowed into the wards. The patient's companion should also undergo the same screening procedure before entering the inpatient ward. Visitors are not allowed into the inpatient building. The patients were accommodated in a private room as much as possible to decrease the possibility of crossinfection among patients. Even with these precautions, patients and their companions still must wear masks during hospitalization and nurses disinfected the air and the floor of the ward twice a day. Our center provides free masks for these patients and their companions.

Changes in Clinicopathologic Characteristics

We collected the clinicopathologic characteristics of all patients who came to our center for chemotherapy from December 1, 2019, to June 15, 2020, using January 23, 2020, as the cut-off date. A total of 358 patients were included in this study and they were divided into 2 groups based on when they were diagnosed with breast cancer. There were 6 patients among them who contracted COVID-19 and were cured. As shown in Table 1, 177 patients were diagnosed with breast cancer before the pandemic and 181

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Table 1 Clinicopathologic Characteristics of the Included Patients.

Characteristics	Diagnosed Time					
	Before Pandemic ($n = 177$)	During Pandemic ($n = 181$)	Value			
Age, years (median, range)	48 (26-73)	48 (26-75)	.788			
T stage			.189			
1 (%)	68 (38.4)	62 (34.3)				
2 (%)	89 (50.3)	96 53.0)				
3 (%)	12 (6.8)	20 (11.0)				
4 (%)	8 (4.5)	3 (1.7)				
N stage			.611			
0 (%)	74 (41.8)	76 (42%)				
1 (%)	80 (45.2)	70 (40.9)				
2 (%)	16 (9.0)	24 (13.3)				
3 (%)	7 (4.0)	7 (3.9)				
M stage			.767			
0 (%)	168 (94.9)	173 (95.6)				
1 (%)	9(5.1)	8 (4.4)				
Molecular subtype			.001			
Luminal-A like (%)	28 (15.8)	57 (31.5)				
Luminal-B (HER2–) (%)	66 (37.3)	63 (34.8)				
Luminal-B (HER2+) (%)	22 (12.4)	27 (14.9)				
HER2-amplified (%)	38 (21.5)	16 (8.8)				
TNBC (%)	23 (13.0)	18 (9.9)				
Surgery regimen			.018			
Not yet	12 (6.8)	29 (16.0)				
Mastectomy	141 (79.7)	134 (74.0)				
Breast-conserving surgery	24 (13.6)	18 (9.9)				
Chemotherapy regimen			.143			
Containing A (%)	2 (1.1)	1 (0.6)				
Containing T (%)	39 (22.0)	56 (30.9)				
A+T combination (%)	136 (76.8)	124 (68.5)				
Chemotherapy schedule			.023			
Every 3 weeks (%)	172 (97.2)	181 (100.0)				
Weekly (%)	5 (2.8)	0				
Targeted therapy			.096			
No or refused (%)	121 (68.4)	138 (76.2)				
Yes (%)	56 (31.6)	43 (23.8)				
Radiation			.478			
No or refused (%)	70 (39.5)	65 (35.9)				
Yes (%)	107 (60.5)	116 (64.1)				
	I	I				

Note: The TNM stages were divided according to the eighth edition of the American Joint Committee on Cancer (AJCC) staging manual for breast cancer. Boldface entries indicate statistical significance.

Abbreviations: A = anthracyclines HER2 = human epidermal growth factor receptor 2;; T = taxanes; TNBC = triple negative breast cancer.

were diagnosed during the pandemic. Characteristics of the patients are compared between these 2 subgroups. There are some significant differences in molecular subtype (P < .001), but no significant differences are found between the age at diagnosis, T stage, N stage, M stage, chemotherapy regimen, targeted therapy, and radiation. As for the difference in surgery regimen, it might be because a proportion of patients diagnosed during the pandemic were still undergoing neoadjuvant chemotherapy until June 15, 2020. Although most of the patients diagnosed before the pandemic had finished neoadjuvant chemotherapy, except for a few patients with advanced breast cancer who were not suitable candidates for surgery. To decrease the risk related to frequent hospital visits of the patients, we decreased the use of weekly chemotherapy schedules (2.8% vs 0%; P = .023).

Decrease of Chemotherapy-related Side Effects

To calculate the incidence of chemotherapy-related side effects during the pandemic, we collected the routine blood and liver function test results of 358 patients with breast cancer receiving chemotherapy. None of these patients had been diagnosed with liver metastasis or active hepatitis. These patients had a median age of 49

Table 2 Blood Routing	ne Test Results at Different Times.		
Variables	Before Pandemic ($n = 495$)	During Pandemic (<i>n</i> = 906)	<i>P</i> Value
WBC (g/L)	5.44 (4.05-6.97)	5.24 (4.41-6.51)	.287
NE (g/L)	3.54 (2.45-4.87)	3.38 (2.48-4.42)	.133
PLT (g/L)	261 (193-330)	245 (195-296)	.004
Leukopenia			
No	413 (83.4%)	794 (87.6%)	.029
Yes	82 (16.6%)	112 (12.4%)	
Neutropenia			
No	445 (89.9%)	842 (92.9%)	.047
Yes	50 (10.1%)	64 (7.1%)	
Thrombocytopenia			
No	460 (92.9%)	857 (94.6%)	.210
Yes	35 (7.1%)	49 (5.4%)	

Abbreviations: NE = neutrophil; PLT = platelet ; WBC = white blood cell.

Table

Data of WBC, NE, and PLT are shown as medians (quartiles). Boldface entries indicate statistical significance

Logistic Regression Analysis of time of blood Routine lest Dysfunction.									
Time	Leukopenia			Neutropenia			Thrombocytopenia		
	OR	95% CI	<i>P</i> Value	OR	95% CI	<i>P</i> Value	OR	95% CI	P Value
Before pandemic	Ref	-	-	Ref	-	-	Ref	-	-
During pandemic	0.710	0.522-0.967	.03	0.676	0.459-0.997	.048	0.751	0.480-1.177	.212

Abbreviations: CI = confidence interval; OR = odds ratio. Boldface entries indicate statistical significance.

years (25-77 years) and the median number of chemotherapy cycles during the time of our study was 4 (2-10). The routine blood and liver function tests were performed according to the patient's condition and the doctor's consideration. No severe myelosuppression and liver dysfunction were observed in this study.

Chemotherapy-related Myelosuppression. The routine blood test results are summarized in Table 2. Within the whole period included in this study, we collected 495 results of routine blood tests before the pandemic and 906 during the pandemic. As shown in Table 2, there is no significant difference in the exact counts of white blood cell count and neutrophils between these 2 periods, although the platelet counts decreased slightly but remained generally within the normal range. However, the incidence of leukopenia (16.6% vs 12.4%; P = .029) and neutropenia (10.1% vs 7.1%;P = .047) both decreased significantly. Although there is no signifiicant difference in thrombocytopenia, the incidence of thrombocytopenia decreased slightly (7.1% vs 5.4%; P = .210). To calculate the ORs between these 2 periods, univariate logistic regression was performed. As shown in Table 3, the pandemic period was correlated with leukopenia (OR, 0.710; 95% CI, 0.522-0.967; P = .030) and neutropenia (OR, 0.676; 95% CI, 0.459-0.997; P = .048), although there was limited involvement in thrombocytopenia (OR, 0.751; 95% CI, 0.480-1.177; *P* = .212).

Chemotherapy-related Hepatic Dysfunction. A total of 444 liver function tests are included in this study; 247 were performed before the pandemic and 197 during the pandemic. As shown in Table 4, there were significant reductions in levels of both AST (P < .001) and ALT (P = .012) during the pandemic. The incidence of hepatic dysfunction (45.3% vs 34.0%; P = .016) and ALT elevation (37.2% vs 20.3%; P < .001) both decreased significantly. The incidence of AST elevation decreased slightly with no significance (16.2% vs 13.2%; P = .378). As shown in Table 5, the pandemic period correlated with hepatic dysfunction (OR, 0.621; 95% CI, 0.422-0.915; P = .016) and ALT elevation (OR, 0.429; 95% CI, 0.279-0.662; P < .001).

Discussion

To the best of our knowledge, few studies¹³ have shared their preparedness plans for the care of patients with breast cancer during the COVID-19 pandemic, especially in an epicenter like Wuhan. In this study, we described the strategies of breast cancer care in our center. We have made these adjustments to the management of patients with breast cancer without compromise to their long-term oncologic outcomes, and the incidence of chemotherapy-related myelosuppression and hepatic dysfunction was even significantly decreased during the pandemic.

There are 2 key points that need to be considered during the pandemic according to the severity of the pandemic, local policies, and the patients' condition. One key point is the balance between hospital visits and the risk of exposure to severe acute respiratory syndrome coronavirus 2, and another is the balance between side effects induced by anticancer treatments and the risk of poor outcomes once the patient was infected.^{14,15} A review from Singapore¹⁶ suggested a universal framework and it may be applied to pandemic planning guideline development in other parts of the world. The specific strategies in different areas may differ,

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Table 4Liver Fun	ction Test Results at Different Times.		
Variables	Before Pandemic ($n = 247$)	During Pandemic ($n = 197$)	<i>P</i> Value
ALT (U/L)	29 (20-44)	16 (23-33)	<.001
AST (U/L)	21 (26-35)	19 (23-31)	.012
Hepatic dysfunction			
No	135 (54.7%)	130 (66.0%)	.016
Yes	112 (45.3%)	67 (34.0%)	
ALT dysfunction			
No	155 (62.8%)	157 (79.7%)	<.001
Yes	92 (37.2%)	40 (20.3%)	
AST dysfunction			
No	207 (83.8%)	171 (86.8%)	.378
Yes	40 (16.2%)	26 (13.2%)	

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase. Data for ALT and AST are shown as medians (quartiles). Boldface entries indicate statistical significance.

Logistic Regression Analysis of Time of Liver Function Dysfunction.									
Time	Hepatic Dysfunction				ALT Dysfunction		AST Dysfunction		
	OR	95% CI	<i>P</i> Value	OR	95% CI	<i>P</i> Value	OR	95% CI	<i>P</i> Value
Before pandemic	Ref	-	-	Ref	-	-	Ref	-	-
During pandemic	0.621	0.422-0.915	.016	0.429	0.279-0.662	<.001	0.787	0.461-1.342	.379

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; CI = confidence interval; OR = odds ratio. Boldface entries indicate statistical significance.

but common topics include classification of patient prioritization, minimizing hospital visits, telemedicine, and modifying acceptable managements.^{17,18}

Online consultation is an important part of telemedicine, but its capabilities are relatively limited. With our data, we demonstrated that even after the city lockdown, the number of online consultations has increased only by a small margin. The online consultation system can only realize the communication function, but not the physical examination, imaging or laboratory testing, or prescription or pharmacy. In addition to answering patients' questions and relieving anxiety, the more practical value of telemedicine is the online prescription and drug delivery services. For patients with chronic diseases, such as malignant tumors, this system can significantly decrease the need to go out for medical care services and purchase drugs, thus decreasing the possibility of their exposure to COVID-19 infection risk. However, online prescription and drug delivery services require policy support from the government and competent administrative departments for health.^{19,20} These administrators need to strike a balance between the needs of patients and important issues such as drug safety. This may be an important development direction for telemedicine services in the future.

Thanks to China's adequate medical resources, in our center, all the screening tests can be completed in 1 day or even 6 hours for certain cases. Rapid and comprehensive screening makes it easier for patients to get proper medical care on the premise that reduces the risk of COVID-19 infection. No nosocomial infection of COVID-19 was reported in our center since the strict screening strategies were taken during the pandemic. As the pandemic rapidly spreads and changes, we recognize that our recommendations in this study should be optimized based on the specific situations of other medical centers. In the absence of sufficient medical resources to ensure rapid and adequate screening, hospital administrators need to comprehensively assess the need for anticancer treatment and the potential risk of COVID-19 in patients with cancer, and then adjust the screening procedures.

The main measures to control an epidemic are to control the source of infection, cut off the transmission route, and protect the susceptible population.²⁰⁻²² Patients with cancer as a special susceptible group need special care during the pandemic. It is suggested by many oncologists that a designed postponing of elective surgery, cytotoxicity chemotherapy, or immune checkpoint inhibitors for some stable cancer could be considered in high-risk areas.²³⁻²⁵ A survey of 343 oncologists from 28 countries also indicated that most participants would use less aggressive therapy to avoid potential risk during the pandemic.²⁶ For patients receiving periodic chemotherapy in our department, we appropriately changed the diagnosis and treatment strategies according to the actual condition. Although some measures have not been documented or quantified, we still found significant decreases in chemotherapy-related side effects during the pandemic. The decrease may be correlated with ward visit limitation, or less use of weekly chemotherapy schedule, or greater use of long-acting granulocyte-colony stimulating factors, or masks, or strengthened public health awareness, or other potential factors. Limited by our working conditions, we were not able to record detailed information, including patients' other clinicopathologic information, therapeutic drugs and doses, other chemotherapy-related side effects, and long-term follow-up. These

Table



factors lead to limited findings on the specific and elaborate relationship between the measures we took during the pandemic and the therapeutic response of the patients.

Conclusions

Considering the current situation and development trend of COVID-19 all over the world, it is difficult to assess its final impact and consequences. This pandemic has brought great challenges in the management of those who are infected or affected. In this study, we collected the diagnosis and treatment process for patients with breast cancer in our center during the COVID-19 pandemic, in the hope of providing a reference for other cancer centers that may suffer from a similar situation. And we further analyzed the short-term chemotherapy-related side effects of patients with breast cancer, as a result of the current strategies, which have never been reported, detailed follow-up for long-term outcomes remains crucial.

Clinical Practice Points

- · Wuhan was the epicenter in China and great efforts have been undertaken to control the outbreak of coronavirus disease 2019 (COVID-19).
- · Now Wuhan has passed the most difficult period, but the accompanying sacrifices are also noteworthy, and the ongoing pandemic has had and will continue to have a huge impact on the normal running of health care systems.
- · The medical care for patients with breast cancer is greatly affected by pandemic prevention strategies.
- · In this study, we collected the diagnosis and treatment process of patients with breast cancer in our center during the COVID-19 pandemic, in the hope of providing a reference for other cancer centers that may encounter a similar situation.
- Revolutionary telemedicine, such as online consultation, prescription, and drug mailing services, was launched or strengthened during the pandemic to make it easier for patients to get medical advice and minimize visits to the hospital.
- · For patients requiring hospitalization for surgery, periodic chemotherapy, or targeted therapy, careful prehospital COVID-19 screening and strict ward management were recommended.
- · We also found that the incidence of chemotherapy-related myelosuppression and hepatic dysfunction was significantly decreased because we took these measures during the pandemic.
- · In this study, we have exhibited some newly proposed and improved management strategies for patients with breast cancer, and these may have the potential to reduce chemotherapy-related side effects during the pandemic; however, the long-term effects of the COVID-19 still need more detailed clinical and pathophysiologic studies to confirm and explain.

Disclosure

The authors have stated that they have no conflicts of interest.

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