



# A web-based survey of SARS-CoV-2 vaccination and its adverse effects in Chinese postoperative patients with breast cancer: a cross-sectional study

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**Background:** Vaccination against SARS-CoV-2 has been the most important strategy for preventing infection and controlling pandemics of coronavirus disease 2019 (COVID-19). Cancer patients have a significantly higher risk of infection with COVID-19 because of their impaired immunity. Breast cancer is the most common female malignant tumor in the world. However, studies on COVID-19 vaccination in breast cancer patients are scarce, so that more information is needed to guide vaccination in these.

**Methods:** We conducted a web-based questionnaire survey on SARS-CoV-2 vaccination in breast cancer patient. Questionnaires completed by non-postoperative patients will be considered invalid. The main variables in the questionnaire including vaccination status, willingness to get the vaccines, candidate factors, and measures of adverse events in vaccinated individuals were used for analysis. Univariate and multivariate logistic regression was used to estimate the associations.

**Results:** Among 947 valid online questionnaires, 341 (36.0%) accepted SARS-CoV-2 vaccination, while 606 (64.0%) did not. There were significant differences in age, current treatment, time since surgery, and symptoms of anxiety and depression between the two groups. Compared to vaccinated patients, we identified current treatment [odds ratio (OR) =0.51 for endocrine therapy; 95% confidence interval (CI): 0.29–0.89], time since surgery (OR =22.49 for 1–2 years; 95% CI: 12.31–41.10; OR =8.49 for 2–5 years; 95% CI: 4.98–14.46; OR =1.79 for >5 years; 95% CI: 1.11–2.89), and symptoms of depression (OR =2.48; 95% CI: 1.19–5.15) as significant factors for being unvaccinated. The overall incidence of adverse reactions was 43.1%, and the most common local and systemic adverse reactions were pain (28.4%) and fatigue (8.8%). However, about 76.6% of the unvaccinated participants were willing to be vaccinated.

**Conclusions:** Compared to the general population, postoperative patients with breast cancer had a lower rate of vaccination for SARS-CoV-2. Receiving treatment, a shorter time since surgery, and symptoms of depression were associated with being unvaccinated. However, about 76.6% of the unvaccinated participants were willing to be vaccinated. Although our study showed that there were adverse effects of SARS-CoV-2 vaccines, such as pain, fatigue, they are common adverse effects of routine vaccination. We believe that vaccination against COVID-19 is safe in postoperative patients with breast cancer.

**Keywords:** Coronavirus disease 2019 (COVID-19); vaccine; unvaccination; breast cancer; adverse reaction

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## Introduction

COVID-19, caused by the novel coronavirus SARS-CoV-2, has spread worldwide, and is characterized by high mortality and unmanageable respiratory symptoms, especially in older patients and patients with pre-existing illnesses such as cancers (1-4). Cancer patients have a significantly higher risk of infection with COVID-19 because of their impaired immunity due to the disease or treatments (5-9). Currently, vaccination against SARS-CoV-2 has been the most important strategy for the prevention and control of COVID-19 (10). Up to now, at least 5 different COVID-19 vaccines, mainly consisting of inactivated and protein subunit vaccines, have been approved for emergency use in China (11). Although a strong willingness to vaccinate in the general population was reported by several cross-sectional studies, some reports showed a high hesitancy rate to receive a COVID-19 vaccine among cancer patients, especially those still in the stage of tumor therapy (12-15). The COVID-19-related mortality has significant differences in between non-cancer and cancer patients (16). Breast cancer, the most common female malignant tumor worldwide, is characterized by better survival (17-19). According to GLOBOCAN statistics in 2020, nearly 2.3 million women have been diagnosed with breast cancer, and the incidence of this disease is increasing year by year in most parts of the world, including China (17). However, studies that systematically investigate the safety profile after vaccination for SARS-CoV-2 in postoperative patients with breast cancer are scarce, and there is no clear recommendation for the timing of vaccination. Real-world data is urgently needed to address public concerns on the side effects of the vaccines. The purpose of the current study is to review the difficulties of this patients population getting the vaccines, such as extreme adverse events and interfere with the anti-cancer treatments, and describe the current status of vaccination in the Chinese general population, which would provide a comparison reference for the vaccination rate in the cancer patients. It is also necessary to review factors associated with non-vaccination to inform the current study. We present the following article in accordance with the SURGE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gs-22-454/rc>).

## Methods

### *Study design and population*

A web-based cross-sectional study was conducted among postoperative patients with breast cancer in China. We developed a self-administered online survey for the collection of data. The survey link was created through the Wen-Juan-Xing platform (Changsha Ranxing Information Technology Co., Ltd., Hunan, China), China's largest online survey platform. Postoperative Chinese female patients with breast cancer were recruited via social media platforms such as WeChat groups or the Good Doctor Online Platform. We posted the link on the platform with no incentive measures. Each participant provided informed consent and volunteered to participate in the study. One submission of the questionnaire was allowed for a single I.P. address. For quality control, the questionnaire could not be submitted unless all required questions were answered. This survey was conducted between 4 Sept 2021 and 19 Sept 2021. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was reviewed and approved by the institutional research ethics board of Xiangya Hospital, Central South University (Changsha, China) (No. 202108168).

### *Questionnaires*

We developed the questionnaire based on interviews with breast cancer patients and revised the questionnaire after consultation with epidemiologists and breast surgeons according to the purpose of the current study.

We divided the questionnaire into four parts. In the first part, regardless of whether the patients were vaccinated, we collected demographic information, including age, education, marital status, and comorbidities.

In the second part, we collected information related to breast cancer including the current treatment (chemotherapy, HER2-targeted therapy, radiation therapy, endocrine therapy, Chinese medicine treatment) and the time since surgery.

The third part involved a survey of COVID-19 vaccination. We investigated the patients' attitudes towards vaccines such as the confidence for the efficacy and safety

of the vaccines, and preferences for the type of vaccines. Since the population needs to receive two or three times vaccinations in China, so the time of the vaccination is also important. To investigate the rate of SARS-CoV-2 vaccination, a single question, “have you been vaccinated against SARS-CoV-2 and what was the type of vaccine?” was asked. At the same time, we asked participants if they had consulted a doctor before getting vaccinated and what types of vaccine they were getting. Reasons for being unvaccinated were also investigated, with the options as follows: “a lack of vaccine supply”, “concern about breast cancer deterioration after vaccination”, “concern about adverse reactions of the vaccine”, “concern about interactions between the vaccine and treatment for breast cancer”, “having another disease that is a contraindication”, “don’t belong to the vaccinated population”, “unnecessary to be vaccinated because of good control of the pandemic”, and “other reasons”. Meanwhile, the reasons for patients already being vaccinated were investigated and the options were as follows: “the epidemic prevention and control situation at home and abroad is still grim, and I asked for vaccination”, “at present, the breast cancer condition is stable, and doctors suggest vaccination”, “I thought the condition of breast cancer is stable and asked for vaccination”, “other patients have been vaccinated and asked for vaccination themselves”, “vaccination for national policy requirements”, and “other reasons”. Adverse reactions after SARS-CoV-2 vaccination, including local and systemic reactions, were measured by a single question that allowed for multiple answers, namely “did you have any adverse reactions after the vaccination”, with several responses based on a vaccine-related meta-analysis or survey (20,21).

In the last part, to assess patients’ mental well-being, the symptoms of depression and anxiety were measured by the 2-item Patient Health Questionnaire (PHQ-2) and the 2-item Generalized Anxiety Disorder (GAD-2) scale, respectively, with 3 as the cut-off point for both scales (22,23).

### Statistical analysis

Categorical variables including demographic and clinical information, adverse reactions, and other patient-reported outcomes were displayed as counts (%) and compared using the Chi-square test or Fisher’s exact test. Multivariate logistic regression was used to identify factors for not being vaccinated, and odds ratio (OR) and 95% confidence interval (CI) were presented as the effect sizes. We selected age, current treatment, time since surgery, Anxiety (GAD-2  $\geq 3$ ), and Depression (PHQ-2  $\geq 3$ ) as the influencing factors

to analysis (Ref., reference). All data were analyzed with SPSS 23 (IBM, SPSS Statistics 23). P was considered two-sided, and a value less than 0.05 was considered statistically significant.

## Results

In all, 947 valid online questionnaires were collected from postoperative female patients with breast cancer. The numbers of vaccinated and unvaccinated patients were 341 (36.0%) and 606 (64.0%), respectively. Among them, 84.8% received inactivated vaccines, while 15.2% received protein subunit vaccines, and 27.7% had completed the vaccination. Characteristics of patients who were unvaccinated and vaccinated for SARS-CoV-2 are shown in *Table 1*. There were significant differences between the two groups in age, current treatment, current state, concerns, anxiety, and depressive symptoms.

Among the unvaccinated participants, the top 3 reasons for their decision included concerns about the vaccine-related adverse reactions (39.9%), concerns about the conflict between SARS-CoV-2 and breast cancer treatment (38.3%), and the doctor does not recommend vaccination because of breast cancer (36.1%). We then carried out multivariate logistic regression and identified that current treatment, the time since surgery, and symptoms of depression were significant factors for being unvaccinated (*Table 2*). Patients receiving endocrine therapy were more likely to be vaccinated than untreated patients (OR =0.51 for endocrine therapy; 95% CI: 0.29–0.89). In addition, the shorter the time since surgery, the more likely patients were vaccinated. We also investigated whether the breast cancer patients were willing to be vaccinated against SARS-CoV-2 if their disease was under control. Among the unvaccinated patients, 76.6% were willing to be vaccinated. These data demonstrated that the postoperative breast cancer patients had a strong willingness for vaccination if the disease was stable (*Figure 1*).

*Table 3* shows the reasons for getting vaccinated in participants. Vaccination of patients was mainly influenced by national policies and the status of breast cancer.

*Table 4* shows the post-vaccination adverse reactions by types of vaccination. The overall incidence of adverse reactions was 43.1% (147/341), the incidence of local adverse reactions was 33.7% (115/341), and the incidence of systemic adverse reactions was 15.2% (52/341). Furthermore, 38.7% (132/341) of the adverse reactions occurred after receiving the first shot, and no severe adverse

**Table 1** Characteristics of participants vaccinated and unvaccinated for SARS-CoV-2

Characteristic	Total (n=947)	Unvaccinated (n=606, 64.0%)	Vaccinated (n=341, 36.0%)	P
Age (years), n (%)				0.049
<30	11 (1.2)	8 (1.3)	3 (0.9)	
30–39	174 (18.4)	128 (21.1)	46 (13.5)	
40–49	395 (41.7)	248 (40.9)	147 (43.1)	
50–60	309 (32.6)	186 (30.7)	123 (36.1)	
>60	58 (6.1)	36 (5.9)	22 (6.5)	
Education, n (%)				0.109
Primary/middle school	386 (40.8)	247 (40.8)	139 (40.8)	
High school	264 (27.9)	157 (25.9)	107 (31.4)	
College or above	297 (31.4)	202 (33.3)	95 (27.9)	
Marital status, n (%)				0.284
Unmarried	18 (1.9)	13 (2.1)	5 (1.5)	
Married	848 (89.5)	534 (88.1)	314 (92.1)	
Divorced	60 (6.3)	43 (7.1)	17 (5.0)	
Widowed	21 (2.2)	16 (2.6)	5 (1.5)	
Current treatment, n (%)				<0.001
CT	75 (7.9)	60 (9.9)	15 (4.4)	
TT	52 (5.5)	50 (8.3)	2 (0.6)	
RT	13 (1.4)	13 (2.1)	0	
ET	540 (57.0)	319 (52.6)	221 (64.8)	
CMT	51 (5.4)	31 (5.1)	20 (5.9)	
≥ Two therapy methods	79 (8.3)	72 (11.9)	7 (2.1)	
NT	137 (14.5)	61 (10.1)	76 (22.3)	
Comorbidities, n (%)				0.194
Hypertension	90 (9.5)	52 (8.6)	38 (11.1)	
Hyperlipidemia	81 (8.6)	46 (7.6)	35 (10.3)	
Obesity	49 (5.2)	30 (5.0)	19 (5.6)	
Digestive diseases	40 (4.2)	29 (4.8)	11 (3.2)	
Hepatitis	36 (3.8)	28 (4.6)	8 (2.3)	
Respiratory diseases	31 (3.3)	20 (3.3)	11 (3.2)	
Time since surgery, n (%)				<0.001
<1 year	317 (33.5)	290 (47.9)	27 (7.9)	
1–2 years	208 (22.0)	160 (26.4)	48 (14.1)	
2–5 years	305 (32.2)	125 (20.6)	180 (52.8)	
>5 years	117 (12.4)	31 (5.1)	86 (25.2)	

**Table 1** (continued)

Table 1 (continued)

Characteristic	Total (n=947)	Unvaccinated (n=606, 64.0%)	Vaccinated (n=341, 36.0%)	P
Consult a doctor, n (%)	639 (67.5)	401 (66.2)	238 (69.8)	0.253
Anxiety (GAD-2 $\geq 3$ ), n (%)	72 (7.6)	56 (9.2)	16 (4.7)	0.011
Depression (PHQ-2 $\geq 3$ ), n (%)	84 (8.9)	68 (11.2)	16 (4.7)	0.001

CT, chemotherapy; TT, HER2-targeted therapy (such as trastuzumab, pertuzumab, and pyrotinib, among others); RT, radiation therapy; ET, endocrine therapy (such as tamoxifen, toremifene, anastrozole, exemestane); CMT, Chinese medicine treatment; NT, not receiving a treatment; Comorbidities, other diseases besides breast cancer; 1–2 years, including the second year after surgery; 2–5 years, the second year after surgery is not included; Consult a doctor, consult a breast doctor or oncologist before COVID-19 vaccination; GAD-2, 2-item Generalized Anxiety Disorder scale; PHQ-2, 2-item Patient Health Questionnaire.

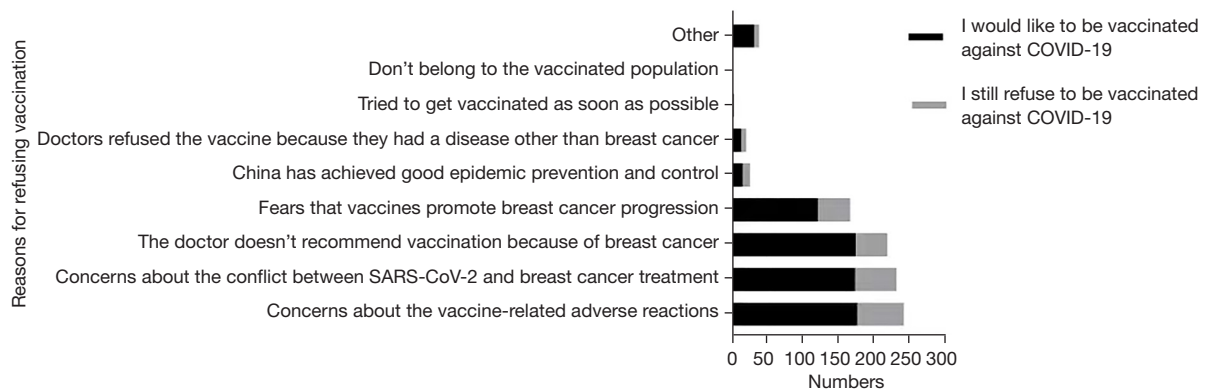
Table 2 Factors for being unvaccinated in participants

Factors	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age (years)				
<30	Ref.		Ref.	
30–39	1.63 (0.39, 6.80)	0.503	0.88 (0.16, 4.75)	0.877
40–49	1.70 (0.91, 3.19)	0.098	1.37 (0.65, 2.89)	0.405
50–60	1.03 (0.58, 1.82)	0.916	1.12 (0.57, 2.21)	0.734
>60	0.92 (0.52, 1.65)	0.789	1.09 (0.55, 2.16)	0.810
Current treatment				
NT	Ref.		Ref.	
ET	0.16 (0.10, 0.25)	<0.001	0.51 (0.29, 0.89)	0.017
Others	0.28 (0.19, 0.41)	<0.001	0.68 (0.44, 1.07)	0.096
Time since surgery				
<1 year	Ref.		Ref.	
1–2 years	29.80 (16.86, 52.65)	<0.001	22.49 (12.31, 41.10)	<0.001
2–5 years	9.25 (5.49, 15.59)	<0.001	8.49 (4.98, 14.46)	<0.001
>5 years	1.93 (1.20, 3.08)	0.006	1.79 (1.11, 2.89)	0.017
Anxiety (GAD-2 $\geq 3$ )	2.07 (1.17, 3.67)	0.013	0.83 (0.38, 1.82)	0.649
Depression (PHQ-2 $\geq 3$ )	2.57 (1.46, 4.50)	0.001	2.48 (1.19, 5.15)	0.015

OR, odds ratio; CI, confidence interval; NT, not receiving a treatment; ET, only endocrine therapy (such as tamoxifen, toremifene, anastrozole, exemestane); Others, CT or TT or RT or CMT or  $\geq 2$  therapy methods; CT, chemotherapy; TT, HER2-targeted therapy (such as trastuzumab, pertuzumab, and pyrotinib, among others); RT, radiation therapy; CMT, Chinese medicine treatment; 1–2 years, including the second year after surgery; 2–5 years, the second year after surgery is not included; GAD-2, 2-item Generalized Anxiety Disorder scale; PHQ-2, 2-item Patient Health Questionnaire.

reactions were reported. Inactivated vaccines and protein subunit vaccines showed similar traits of adverse reactions. There was no significant correlation between different treatment regimens and adverse reactions. In addition, we

also investigated the changes in breast cancer conditions after vaccination. The findings demonstrated that SARS-CoV-2 vaccination showed good safety for postoperative patients with breast cancer.



**Figure 1** Reasons for being unvaccinated and acceptance of vaccination.

**Table 3** Reasons for getting vaccinated in vaccinated participants

Reasons	Total (n=341)
Vaccination for national policy requirements (%)	122 (35.8)
The breast cancer condition is stable, and I asked for vaccination (%)	119 (34.9)
The breast cancer condition is stable, and doctors suggest vaccination (%)	96 (28.2)
The epidemic is still grim, and I asked for vaccination (%)	86 (25.2)
Followed other patients who have been vaccinated (%)	31 (9.1)
Others (%)	4 (1.2)

## Discussion

We conducted a cross-sectional study through social media and reported a relatively low rate of vaccination for SARS-CoV-2 in postoperative patients with breast cancer compared to the general population (24). Compared with the vaccinated group, the unvaccinated group showed a shorter time since surgery, more patients received treatment, and more patients had symptoms of anxiety and depression. Receiving breast cancer-related treatment, time since surgery, and symptoms of depression were significant factors for being unvaccinated. A lower rate of vaccine-related adverse reactions was shown.

The unexpected epidemic of COVID-19 is a challenge in the field of oncology. Although the percentage of COVID-19 among cancer patients was only 2%, there are limited studies on COVID-19 vaccination in postoperative patients with breast cancer (25). According to a large meta-

analysis from Luo *et al.*, a significantly increased risk of death in COVID-19 patients with cancer versus those without cancer was observed, with an OR of 1.90 (95% CI: 1.57–2.30) (3). A nationwide analysis confirmed that patients with cancer had a higher risk of severe events [a composite endpoint defined as the percentage of patients being admitted to the intensive care unit requiring invasive ventilation, or death; 39% *vs.* 8%, hazard ratio (HR) =5.34; 95% CI: 1.80–16.18; P=0.0026] and deteriorated more rapidly than those without cancer (median time to severe events, 13 *vs.* 43 days, HR =3.56; 95% CI: 1.65–7.69; P<0.0001) (26). Meanwhile, they confirmed that patients who were undergoing chemotherapy or surgery over the past month had a higher risk of clinically severe events (75% *vs.* 43%) (26). This prompted the management of breast cancer to change significantly during the COVID-19 pandemic, including modification of the treatment protocol, extending the waiting time for breast surgery, and increasing the use of genomic profile analysis based on an international survey named EUBREAST (27). At present, most clinicians use the American Society of Breast Surgeons (ASBrS), National Accreditation Program for Breast Centers (NAPBC), National Comprehensive Cancer Network (NCCN), the Commission on Cancer (CoC), and the American College of Radiology (ACR) guidelines as the global COVID-19 clinical decision stream (28).

So far, vaccination remains an important strategy to prevent infection and control in the pandemic. An effective vaccine is considered essential to prevent further morbidity and mortality (10). However, according to our survey, the vaccination rate of postoperative patients with breast cancer was only 36.0%. Furthermore, only 27.7% completed the vaccination. This can be explained by the results presented

**Table 4** Adverse reactions of different types of vaccines and the relationship between different treatment regimens and adverse reactions

Adverse reactions	Total (n=341)	Type of vaccination			Current treatment						
		Inactivated vaccine (n=289, 84.8%)	Protein subunit vaccine (n=52, 15.2%)	P	CT (n=15)	TT (n=2)	ET (n=221)	CMT (n=20)	≥ Two therapy methods (n=7)	NT (n=76)	P
Any	147 (43.1)	124 (42.9)	23 (44.2)	0.859	6 (40.0)	0	101 (45.7)	8 (40.0)	3 (42.9)	29 (38.2)	0.781
Local	115 (33.7)	95 (32.9)	20 (38.5)	0.433	4 (26.7)	0	81 (36.7)	3 (15.0)	2 (28.6)	25 (32.9)	0.414
Pain	97 (28.4)	83 (28.7)	14 (26.9)	0.791	3 (20.0)	0	69 (31.2)	2 (10.0)	1 (14.3)	22 (28.9)	0.339
Induration, swelling	18 (5.3)	13 (4.5)	5 (9.6)	0.168	0	0	12 (5.4)	1 (5.0)	1 (14.3)	4 (5.3)	0.666
Itch	14 (4.1)	10 (3.5)	4 (7.7)	0.243	1 (6.7)	0	8 (3.6)	0	0	5 (6.6)	0.630
Systemic	52 (15.2)	45 (15.6)	7 (13.5)	0.697	3 (20.0)	0	33 (14.9)	17 (85.0)	1 (14.3)	10 (13.2)	<0.001
Fatigue	30 (8.8)	28 (9.7)	2 (3.8)	0.284	3 (20.0)	0	21 (9.5)	2 (10.0)	0	4 (5.3)	0.457
Headache, dizziness	11 (3.2)	8 (2.8)	3 (5.8)	0.227	1 (6.7)	0	5 (2.3)	2 (10.0)	0	3 (3.9)	0.227
Stuffy, runny nose	9 (2.6)	8 (2.8)	1 (1.9)	1.000	0	0	5 (2.3)	2 (10.0)	0	2 (2.6)	0.373
Itch	7 (2.1)	6 (2.1)	1 (1.9)	1.000	1 (6.7)	0	5 (2.3)	0	1 (14.3)	0	0.099
Rash	3 (0.9)	2 (0.7)	1 (1.9)	0.392	0	0	2 (0.9)	0	0	1 (1.3)	1.000
Arthralgia	3 (0.9)	2 (0.7)	1 (1.9)	0.392	0	0	2 (0.9)	1 (5.0)	0	0	0.406
Fever	3 (0.9)	2 (0.7)	1 (1.9)	0.392	0	0	2 (0.9)	1 (5.0)	0	0	0.406
Diarrhea	2 (0.6)	2 (0.7)	0	1.000	0	0	2 (0.9)	0	0	0	1.000
Appetite impaired	2 (0.6)	2 (0.7)	0	1.000	0	0	1 (0.5)	1 (5.0)	0	0	0.291
Other	6 (1.8)	6 (2.1)	0	0.596	1 (6.7)	0	4 (1.8)	0	0	1	0.513

The data are expressed as n (%). CT, chemotherapy; TT, HER2-targeted therapy (such as trastuzumab, pertuzumab, and pyrotinib, among others); ET, endocrine therapy (such as tamoxifen, toremifene, anastrozole, exemestane); CMT, Chinese medicine treatment; NT, not receiving a treatment.

in *Table 2*. For example, the time since surgery was closer, and they were more reluctant to be vaccinated. Most participants' concerns were regarding the vaccine-related adverse reactions or the conflict between SARS-CoV-2 and breast cancer treatment. Antibodies cannot be produced effectively because of the decreased function of the patient's immune system during chemotherapy. Additionally, patients with cancer are more vulnerable to adverse outcomes from COVID-19, as indicated by meta-analyses, and hospitalized patients with cancer and COVID-19 infection are at higher risk of mortality (29-31). Therefore, according to the Clinical Practice Guidelines for Immune Disabled Vaccination issued by the Infectious Diseases Society of America (IDSA), we still recommend that patients be

vaccinated 2 weeks before the start of chemotherapy and 3 months after the end of chemotherapy (32). Furthermore, some of the American Society of Clinical Oncology (ASCO)'s recommendations about clinical oncology in the FAQs document can be adopted to reduce the risk of infection in unvaccinated patients, such as: (I) patients can collect routine laboratory samples and even inject chemotherapy drugs at home whenever possible; (II) for hormone receptor-positive breast cancer, patients may be delayed for up to 2 months. About 77% of unvaccinated patients were willing to be vaccinated when the breast cancer was stable, which is lower than in previous study (12). This might be related to our premise that breast cancer is stable.

Patients with breast cancer are susceptible to mental health problems, such as anxiety and depression (33). A systematic review reported that the prevalence of depression and anxiety among breast cancer survivors was 9.4% to 66.1% and 17.9% to 33.3%, respectively (34). Moreover, breast cancer survivorship was positively associated with anxiety (HR =1.33; 95% CI: 1.29–1.36; P<0.001) and depression (HR =1.35; 95% CI: 1.32–1.38; P<0.001) (35). In our findings, the unvaccinated group showed more significant anxiety (9.2% vs. 4.7%, P=0.011) and depression (11.2% vs. 4.7%, P=0.001) compared with the vaccinated group. Besides, patients who were in states of depression were more reluctant to be vaccinated. Therefore, we encouraged patients to keep effective communication with their breast surgeon or oncologist, such as increasing the frequency of follow-up and holding lectures on knowledge related to the epidemic. This will bring some benefits, including professionally assessing the patient's ability to tolerate vaccines to determine the approximate time of vaccination and reduce unnecessary anxiety or depression about the vaccination.

Although the main trials showed efficacy in more than 90% of individuals and favorable safety in healthy but also older populations, current knowledge of the safety and efficacy of authorized COVID-19 vaccines in patients with cancer, particularly those receiving active treatment, is limited (36). Most guidelines recommend COVID-19 vaccination for cancer patients and make general assumptions that benefits outweigh the risks (37). Encouragingly, there has been no other safety questions for cancer patients until now. Our survey showed a 43.1% incidence of adverse reactions, which is lower than the 76.1% incidence previously reported in cancer patients (20). This may be caused by the small sample size, the bias in patient recall, or the limited type of vaccination in our survey. Besides, inactivated vaccines and protein subunit vaccines showed similar traits of adverse reactions. More importantly, these adverse reactions were mild and self-limiting, such as pain, fatigue, hardening, and swelling at the injection site, and no severe adverse reactions were reported. This generally agrees with previous findings (20,21). The above results suggested that COVID-19 vaccination has a good safety profile in postoperative patients with breast cancer. Therefore, we advocate that postoperative patients with breast cancer in good physical condition should accept COVID-19 vaccination as soon as possible, as delayed vaccination may place this vulnerable group at an increased risk of infection. However, breast

imaging at disease assessment still needs to be performed in hospitals with adequate resources because pandemics can be prolonged and potentially life-threatening in the long run.

## Conclusions

In conclusion, we reported a relatively low rate of vaccination against SARS-CoV-2 in postoperative patients with breast cancer. The unvaccinated group showed a shorter time since surgery, more patients received treatment, and more patients had symptoms of anxiety and depression than the vaccinated group. Time since surgery and symptoms of depression were significant factors for being unvaccinated. Our study demonstrates the favorable safety profile of SARS-CoV-2 vaccines, and the benefits of vaccination should not be underappreciated.

## Limitations

The limitations of this study is the limited variables on factors directly associated with vaccination status such as whether the family members of the patients have got vaccinated and worry about the re-outbreak of the pandemic and death due to the pandemic. However, the study has strengths, including a large sample size, a systematic assessment of demographic, clinical, and psychological factors in the context of real-world clinical practice, and providing needed data to elucidate the factors associated with being unvaccinated in postoperative patients with breast cancer. In addition, we are unable to observe the long-term effects of novel coronavirus vaccine on breast cancer due to the short period of widespread application.

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was reviewed and approved by the institutional research ethics board of Xiangya Hospital, Central South University (Changsha, China) (No. 202108168). Each participant provided informed consent to participate in the study.

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