



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

Xiaoxiao Wang^{1,2,3#}, Minxue Shen^{3,4#}, Qian Zhang^{1,2,3}, Xiaomin Wang^{1,2,3}, Hanghao Zhang^{1,2,3}, Tingxuan Li^{1,3}, Yuanping Hu^{1,3}, Fan Xia^{1,3}, Liqiu Liao^{1,2,3}

¹Department of Breast Surgery, Xiangya Hospital, Central South University, Changsha, China; ²Clinical Research Center For Breast Cancer (Xiangya Hospital), Changsha, China; ³National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, China; ⁴Department of Social Medicine and Health Management, Xiangya School of Public Health, Central South University, Changsha, China

Contributions: (I) Conception and design: L Liao, Xiaoxiao Wang; (II) Administrative support: L Liao; (III) Provision of study materials or patients: Xiaoxiao Wang, M Shen; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: M Shen, Xiaoxiao Wang; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work and should be considered as co-first authors.

Correspondence to: Liqiu Liao, Department of Breast Surgery, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha, China.
Email: liaoliqiu@csu.edu.cn.

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

Submitted Jul 22, 2022. Accepted for publication Sep 06, 2022.

doi: 10.21037/gs-22-454

View this article at: <https://dx.doi.org/10.21037/gs-22-454>

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 ≥ 3), and Depression (PHQ-2 ≥ 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 ≥ 3), n (%)	72 (7.6)	56 (9.2)	16 (4.7)	0.011
Depression (PHQ-2 ≥ 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 ≥ 3)	2.07 (1.17, 3.67)	0.013	0.83 (0.38, 1.82)	0.649
Depression (PHQ-2 ≥ 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 ≥ 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.

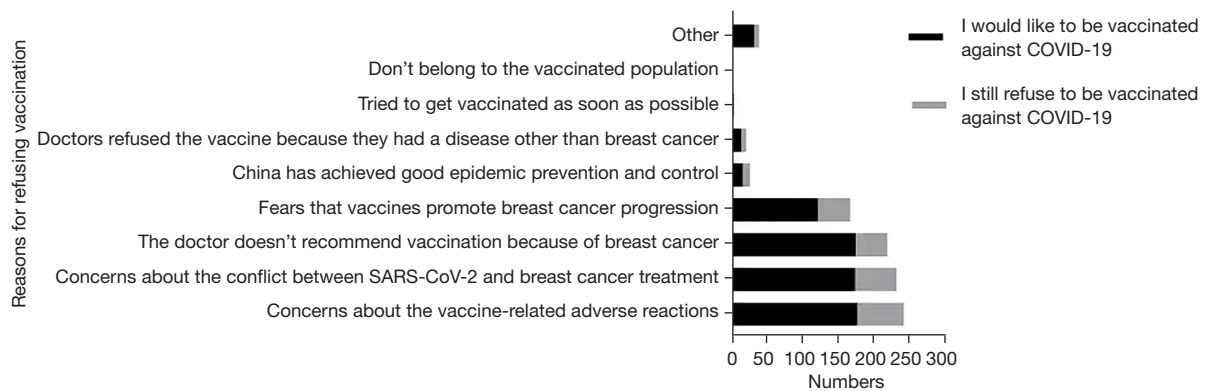


Figure 1 Reasons for being unvaccinated and acceptance of vaccination.

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.

Acknowledgments

The authors wish to thank Shouman Wang, Yuhui Wu, Jian Hai, Juan Huang, Lei Guo, Na Luo, Yehong Kuang, and Qiaolin Wang (from Xiangya Hospital Central South University), Wenjun Yi, Feng Xu, and Haiyan Zou (from the Second Xiangya Hospital of Central South University), Ning Xie (from Hunan Cancer Hospital), Chaojie Zhang and Xu Dai (from Hunan Provincial People's Hospital), Tao Wu (from the First People's Hospital of Changde City), Li Ding (from the First People's Hospital of Huaihua City), Jie Yan and Xiongqiang Hu (from the First People's Hospital of Chenzhou City), and Taohong Shen (from Huarong County People's Hospital) for disseminating the survey. The authors would also like to thank all participants for

their assistance in the online survey.

Funding: This work was supported by the National Natural Science Foundation of China (No. 81974420). The funder did not participate in the study.

Footnote

Reporting Checklist: The authors have completed the SURGE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gc-22-454/rc>

Data Sharing Statement: Available at <https://gs.amegroups.com/article/view/10.21037/gc-22-454/dss>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gc-22-454/coif>). The authors have no conflicts of interest to declare.

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.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507-13.
- Luo L, Fu M, Li Y, et al. The potential association between common comorbidities and severity and mortality of coronavirus disease 2019: A pooled analysis. *Clin Cardiol* 2020;43:1478-93.
- Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis* 2020;20:533-4. Erratum in: *Lancet Infect Dis* 2020;20:e215.
- Kamboj M, Sepkowitz KA. Nosocomial infections in patients with cancer. *Lancet Oncol* 2009;10:589-97.
- Li JY, Duan XF, Wang LP, et al. Selective depletion of regulatory T cell subsets by docetaxel treatment in patients with nonsmall cell lung cancer. *J Immunol Res* 2014;2014:286170.
- Longbottom ER, Torrance HD, Owen HC, et al. Features of Postoperative Immune Suppression Are Reversible With Interferon Gamma and Independent of Interleukin-6 Pathways. *Ann Surg* 2016;264:370-7.
- Sica A, Massarotti M. Myeloid suppressor cells in cancer and autoimmunity. *J Autoimmun.* 2017;85:117-25.
- Schmidt T, Jonat W, Wesch D, et al. Influence of physical activity on the immune system in breast cancer patients during chemotherapy. *J Cancer Res Clin Oncol* 2018;144:579-86.
- Hodgson SH, Mansatta K, Mallett G, et al. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. *Lancet Infect Dis* 2021;21:e26-35.
- Callaway E. The race for coronavirus vaccines: a graphical guide. *Nature* 2020;580:576-7.
- Lazarus JV, Ratzan SC, Palayew A, et al. A global survey of potential acceptance of a COVID-19 vaccine. *Nat Med* 2021;27:225-8.
- Wang J, Jing R, Lai X, et al. Acceptance of COVID-19 Vaccination during the COVID-19 Pandemic in China. *Vaccines (Basel)* 2020;8:482.
- Zhang Y, Luo X, Ma ZF. Willingness of the general population to accept and pay for COVID-19 vaccination during the early stages of COVID-19 pandemic: a nationally representative survey in mainland China. *Hum Vaccin Immunother* 2021;17:1622-7.
- Barrière J, Gal J, Hoch B, et al. Acceptance of SARS-CoV-2 vaccination among French patients with cancer: a cross-sectional survey. *Ann Oncol* 2021;32:673-4.
- Pathania AS, Prathipati P, Abdul BA, et al. COVID-19 and Cancer Comorbidity: Therapeutic Opportunities and Challenges. *Theranostics* 2021;11:731-53.

17. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021;71:209-49.
18. Matsen CB, Neumayer LA. Breast cancer: a review for the general surgeon. *JAMA Surg* 2013;148:971-9.
19. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet* 2018;391:1023-75.
20. So ACP, McGrath H, Ting J, et al. COVID-19 Vaccine Safety in Cancer Patients: A Single Centre Experience. *Cancers (Basel)* 2021;13:3573.
21. McDonald I, Murray SM, Reynolds CJ, et al. Comparative systematic review and meta-analysis of reactogenicity, immunogenicity and efficacy of vaccines against SARS-CoV-2. *NPJ Vaccines* 2021;6:74.
22. Liu ZW, Yu Y, Hu M, et al. PHQ-9 and PHQ-2 for Screening Depression in Chinese Rural Elderly. *PLoS One* 2016;11:e0151042.
23. Plummer F, Manea L, Trepel D, et al. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. *Gen Hosp Psychiatry* 2016;39:24-31.
24. Wang Q, Yang L, Jin H, et al. Vaccination against COVID-19: A systematic review and meta-analysis of acceptability and its predictors. *Prev Med* 2021;150:106694.
25. Desai A, Sachdeva S, Parekh T, et al. COVID-19 and Cancer: Lessons From a Pooled Meta-Analysis. *JCO Glob Oncol* 2020;6:557-9.
26. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol* 2020;21:335-7.
27. Gasparri ML, Gentilini OD, Lueftner D, et al. Changes in breast cancer management during the Corona Virus Disease 19 pandemic: An international survey of the European Breast Cancer Research Association of Surgical Trialists (EUBREAST). *Breast* 2020;52:110-5.
28. Dietz JR, Moran MS, Isakoff SJ, et al. Recommendations for prioritization, treatment, and triage of breast cancer patients during the COVID-19 pandemic. the COVID-19 pandemic breast cancer consortium. *Breast Cancer Res Treat* 2020;181:487-97.
29. Izcovich A, Ragusa MA, Tortosa F, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. *PLoS One* 2020;15:e0241955.
30. Ribas A, Sengupta R, Locke T, et al. Priority COVID-19 Vaccination for Patients with Cancer while Vaccine Supply Is Limited. *Cancer Discov* 2021;11:233-6.
31. Noor FM, Islam MM. Prevalence and Associated Risk Factors of Mortality Among COVID-19 Patients: A Meta-Analysis. *J Community Health* 2020;45:1270-82.
32. Rubin LG, Levin MJ, Ljungman P, et al. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. *Clin Infect Dis* 2014;58:e44-100.
33. Carreira H, Williams R, Müller M, et al. Associations Between Breast Cancer Survivorship and Adverse Mental Health Outcomes: A Systematic Review. *J Natl Cancer Inst* 2018;110:1311-27.
34. Maasz SW, Roorda C, Berendsen AJ, et al. The prevalence of long-term symptoms of depression and anxiety after breast cancer treatment: A systematic review. *Maturitas* 2015;82:100-8.
35. Carreira H, Williams R, Funston G, et al. Associations between breast cancer survivorship and adverse mental health outcomes: A matched population-based cohort study in the United Kingdom. *PLoS Med* 2021;18:e1003504.
36. Anderson EJ, Roupael NG, Widge AT, et al. Safety and Immunogenicity of SARS-CoV-2 mRNA-1273 Vaccine in Older Adults. *N Engl J Med* 2020;383:2427-38.
37. Hwang JK, Zhang T, Wang AZ, et al. COVID-19 vaccines for patients with cancer: benefits likely outweigh risks. *J Hematol Oncol* 2021;14:38.

(English Language Editor: C. Betlazar-Maseh)

Cite this article as: Wang X, Shen M, Zhang Q, Wang X, Zhang H, Li T, Hu Y, Xia F, Liao L. A web-based survey of SARS-CoV-2 vaccination and its adverse effects in Chinese postoperative patients with breast cancer: a cross-sectional study. *Gland Surg* 2022;11(9):1497-1506. doi: 10.21037/gs-22-454