



Willingness to receive COVID-19 vaccination and adverse effects after vaccination in breast cancer survivors during the COVID-19 pandemic: a cross-sectional retrospective study of a Chinese population

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Background: Breast cancer (BC) patients have a higher mortality rate after COVID-19 infection, but data on vaccination of BC patients and attitude towards COVID-19 vaccination and safety after vaccination are lacking. We wanted to understand the willingness and factors of BC survivors to receive a COVID-19 vaccine, and their adverse reactions. The purpose is to judge the safety of vaccination, and find strategies to promote vaccination in BC patients.

Methods: Offline and online questionnaire surveys were provided in outpatient clinics and on an online follow-up platform, respectively, to collect information. Factors influencing vaccination willingness were analyzed by univariate and multivariate logistic regression. All statistical tests were performed bilaterally, and a P value <0.05 was considered statistically significant. Patients who have been vaccinated need to fill in questions about the impact on quality of life after vaccination, the type and frequency of vaccination, and side effects.

Results: A total of 497 valid questionnaires were collected; 289 (58.1%) BC survivors were vaccinated with a COVID-19 vaccine, and 379 (76.26%) BC survivors had a fully or basically accepting attitude toward vaccination. Survivors over 70 years of age, educated only to high school level, and those receiving chemotherapy had significantly lower levels of acceptance of COVID-19 vaccines. Multivariate logistic regression analyses suggested that treatment status and cognitive attitude were independent factors influencing COVID-19 vaccination among BC survivors. The main reason for being vaccinated was “doctor recommendation” (57.26%). Unwillingness to receive a COVID-19 vaccine was mainly due to “the unknown safety of the vaccine in cancer patients” (67.80%). A total of 97.56% of the survivors believed that vaccination had no or almost no effect on their quality of life. Among the BC survivors, 18 (6.23%) had adverse reactions after vaccination. All adverse reactions were grade 1 or 2, and no adverse reactions of grade 3 or above were reported. The adverse reactions reported by 15 survivors (83.33%) markedly improved within 1 week.

Conclusions: In terms of cognitive attitudes toward COVID-19 vaccines, elderly individuals and those with a lower education level were less receptive to vaccination. Therefore, attention to elderly survivors can help improve the vaccination rate.

Keywords: Adverse reactions; breast cancer (BC); COVID-19 vaccine; epidemiology

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Introduction

COVID-19 is an infectious respiratory tract disease caused by a novel coronavirus. In mild cases, symptoms such as fever, cough, and shortness of breath can occur, but in more severe cases, infection can lead to pneumonia, severe acute respiratory syndrome, and even death. Importantly, since the onset of the COVID-19 pandemic, this new coronavirus has been continuously mutating, resulting in more than 200 variants thus far (1-3). The transmissibility of the virus has also continuously increased, causing infection worldwide and resulting in the declaration of a public health emergency by the World Health Organization. Although some data show that the pathogenicity of variants has weakened and that the proportion of severely ill patients has decreased, many patients still require hospitalization, imposing a substantial burden on medical resources. Effective treatment methods for COVID-19 are still lacking, and symptomatic treatment remains the most common approach. Therefore, vaccination is still considered the most effective preventive measure. Vaccination cannot fully prevent COVID-19 infection

but can significantly reduce the proportion of severely ill patients, the hospitalization rate, and the mortality rate (4). Among those who are infected, breast cancer (BC) patients have a higher mortality rate after COVID-19 infection (5). In addition, treatment delays or interruption due to COVID-19 may also affect patients' prognoses. Moreover, BC survivors are a high-risk population with low immunity due to antitumor treatments such as chemotherapy and radiotherapy; therefore, they are more in need of vaccination against COVID-19 (6-8). However, the numbers of cancer survivors included in clinical trials for different COVID-19 vaccines have been very limited (9-11). Previous studies suggested that vaccination rates of cancer patients ranged from 25.8% to 65% (12-14) and 45.9–69% of them self-reported having related side effects after the first vaccination (13,14). While the main reasons for refusing vaccination include: vaccine related adverse events, conflict with antitumor therapy, the fear of allergic reaction, and so on (15,16). For BC cancer survivors, relevant data on their suitability for COVID-19 vaccination, adverse reactions to COVID-19 vaccines, and effects of COVID-19 vaccination on tumor recurrence and metastasis are lacking. Therefore, we retrospectively investigated the vaccination status of BC survivors and analyzed their willingness to be vaccinated, factors influencing their vaccination willingness, and adverse reactions to COVID-19 vaccines. We present the following article in accordance with the STROBE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-5838/rc>).

Highlight box

Key findings

- Although BC survivors exhibited a high willingness to receive a COVID-19 vaccine, some survivors were still concerned about the safety of and adverse reactions. After vaccination, BC survivors had no serious adverse reactions, and their quality of life and survival were not affected.

What is known and what is new?

- BC survivors, as a special population, need to be vaccinated because of decreased immunity caused by radiotherapy and chemotherapy. In China, approximately 85.64% of the population has completed a COVID-19 vaccination schedule, but cancer survivors have lower confidence in vaccines.
- In this article, we report on the status of COVID-19 vaccination in BC patients, and analyze the willingness and reasons for vaccination. Among vaccinated survivors we assessed adverse events and quality of life.

What is the implication, and what should change now?

- Doctor recommendation and popular science education can help BC survivors become more willing to receive a COVID-19 vaccine.

Methods

Research subjects

For BC survivors who had completed or were receiving treatment, the inclusion criteria were as follows: (I) BC confirmed by histological pathology; (II) no distant metastasis at the time of receiving the first vaccination; and (III) comprehension and voluntary completion of the questionnaire. The exclusion criteria were: (I) positivity for SARS-CoV-2 nucleic acid, as detected by real-time fluorescence reverse transcription-polymerase chain reaction (RT-PCR); and (II) failure to complete the questionnaire.

Survey content

This study was a retrospective cross-sectional study, and the sampling method was convenience sampling. A self-designed anonymous questionnaire was used. BC survivors were notified of the questionnaire through social media and outpatient clinics from January 1 to March 31, 2022. Each participant could submit responses to the questionnaire only once. The questionnaire consisted of multiple questions designed to obtain the following information: (I) general patient information (age, education level, tumor type and stage, etc.); (II) whether the BC survivor was willing to receive a COVID-19 vaccine and the reasons; (III) the type of COVID-19 vaccine; (IV) adverse reactions to the COVID-19 vaccine; (V) the effect of vaccination on quality of life (statistically analyzed using a 4-point Likert scale); and (VI) survival outcome after vaccination. BC survivors were asked whether they were willing to take a COVID-19 vaccine and whether they had taken the COVID-19 vaccine. Persons who choose completely accept or basically accept about taking the vaccine were vaccine-accepting individuals, while persons who choose basically reject or completely reject were vaccine-hesitant individuals. Then a question was used to ask reasons for accepting or hesitant vaccination. This option is multiple while other answers can be filled out. Use three questions to understand the specifics of vaccination, including type of vaccination, number of times, and whether to complete the vaccination. The quality of life of the vaccinated survivors was rated using a 4-level Likert scale, where a score of 1 represented a serious impact, and a score of 4 represented no impact at all. The remaining three questions ask about the presence, timing, and duration of side reactions. Survivors after vaccination were asked if recurrent metastases had occurred. Active contact with physician if this occurs (*Table 1*).

Statistical analysis

R Program (ver.4.0.5) was used to analyze the data. Count data are expressed as the number of survivors or percentages. Relevant influential factors of vaccination among BC survivors were analyzed using logistic regression. We analyzed all relevant factors using univariate logistic regression. When $P < 0.05$, the factor was included in the multivariate logistic regression, and the method of stepwise forwards was used for statistical analysis. Correlation strength was expressed as the odds ratio (OR) and the 95% confidence interval (CI). Pearson's chi-square test or Fisher's exact test was used to test differences

between specific groups. All statistical tests were performed bilaterally. A P value < 0.05 was considered statistically significant.

Ethics

The questionnaire was submitted to the Ethical Committee of Xijing Hospital (Xi'an, Shaanxi) for review. The committee determined that ethical approval was not needed for this anonymous survey as the risk was not greater than the minimum risk (not higher than the risk or discomfort of the study object in the routine examination/test of daily life, physical or psychological) and did not involve routine treatment, and exemption from informed consent would not have adverse effects on the rights of subjects. The voluntary nature of this study was clearly relayed to participating patients before they completed the questionnaire. All patients provided verbal consent then checked in the questionnaire that they "voluntarily participate in this study and have a preliminary understanding of this study." and did not receive any financial compensation. All steps were performed in accordance with the Declaration of Helsinki (as revised in 2013).

Results

General characteristics of the population

A total of 529 questionnaires were collected. After excluding 32 questionnaires with obvious missing content and errors, 497 valid questionnaires, all of which were completed by women, were included in the analysis. Among them, 289 (58.2%) survivors had received at least 1 dose of a COVID-19 vaccine, and 208 survivors (41.9%) had not received any COVID-19 vaccine (*Table 2*).

The proportions of vaccinated BC survivors were significantly different among survivors across different ages, treatment status, and cognitive attitude toward COVID-19 vaccines (*Figure 1A-1C*). The proportion of vaccinated BC survivors decreased as age increased ($P = 0.037$). The proportion of vaccinated survivors among those receiving chemotherapy was significantly lower than among survivors who had finished treatment or received only endocrine or anti-HER2 treatment (30.00% *vs.* 62.01%; $P < 0.001$). In addition, survivors' attitudes toward COVID-19 vaccination were significantly correlated with vaccination status ($P < 0.001$). However, no significant difference was found between survivors with different education levels, tumor grades, or molecular subtypes.

Table 1 Questions used for understanding vaccination status, attitudes and reasons towards vaccination, side effects after vaccination

Variables	Questions	Response option
COVID-19 vaccination	Do you agree that persons with mental disorders should take COVID-19 vaccines?	Completely accept; basically accept; basically reject; completely reject
	Have you taken the COVID-19 vaccine?	Yes; no
Reasons of breast cancer patients receive the new crown vaccine or not		
Vaccine-accepting individuals	Reasons for agreeing to vaccination	Doctor recommendation; belief that the vaccine is effective; vaccination is a social responsibility; desire to return to normal life; the ideal protective strategy; belief in mass immunization; others____
Vaccine-hesitant individuals	Reasons for not being vaccinated	Vaccine safety is unknown; doctor did not recommend; not in a high-risk group; no confidence in the vaccine; personal history of allergy; belief that the vaccine does not work; others____
The details of vaccination		
If vaccinated	The type of vaccine you received	Sinovac COVID-19 vaccine; Sinopharm COVID-19 vaccine; Zifivax COVID-19 vaccine; CanSinoBIO COVID-19 vaccine; unknown; others____
If vaccinated	Have you been vaccinated?	Yes; no
If vaccinated	How many times have you been vaccinated?	1;2;3
Adverse effects		
If vaccinated	Is there any adverse effect on life after being vaccinated?	1;2;3;4
If vaccinated	Whether there are adverse reactions or side effects after vaccination?	Yes; no
If there are adverse reactions	The time of occurrence of adverse reactions	Within 24 hours after vaccination; within 3 days of vaccination; within a week of vaccination; others____
If there are adverse reactions	How long does the adverse reaction last?	Within 24 hours; within 3 days; within a week; others____
Recurrence or metastasis		
After vaccination	Whether there has been recurrence or metastasis of breast cancer?	Yes; no

In case of recurrence and metastasis, please contact the doctor for follow-up consultation in time.

Factors influencing COVID-19 vaccination

We divided the BC survivors into a vaccinated group (n=289) and an unvaccinated group (n=208). For the two groups, univariate logistic regression analysis suggested a P value of less than 0.05 for treatment status and cognitive attitude. Multivariate logistic regression analysis suggested that treatment status (chemotherapy; OR =0.41; 95% CI: 0.2–0.87; P=0.02; anti-HER2 or endocrine therapy; OR =2.01; 95% CI: 1.21–3.32; P=0.007) and cognitive attitude

(negative: OR =0.01; 95% CI: 0–0.03; P<0.001) toward COVID-19 vaccines were independent factors influencing COVID-19 vaccination among BC survivors (*Table 3*).

Cognitive attitudes toward COVID-19 vaccines

A total of 379 (76.26%) survivors were completely or basically accepting of COVID-19 vaccines; 118 (23.74%) survivors basically or completely rejected COVID-19 vaccines.

Table 2 Basic characteristics of breast cancer survivors

Variables	All	Vaccinated	Not vaccinated	P value
N (%)	497 (100.00)	289 (58.15)	208 (41.85)	–
Age, years (%)				
20–29	6 (1.21)	4 (0.80)	2 (0.40)	0.037
30–49	260 (52.31)	158 (31.79)	102 (20.52)	
50–69	210 (42.25)	121 (24.35)	89 (17.91)	
≥70	21 (4.23)	6 (1.21)	15 (3.02)	
Education (%)				
Low ^a	272 (54.73)	159 (31.99)	113 (22.74)	0.9512
High ^b	225 (45.27)	130 (26.16)	95 (19.11)	
Grade (%)				
CIS	19 (3.82)	15 (3.02)	2 (0.40)	0.093
BRCA N0 ^c	239 (48.09)	131 (26.36)	108 (21.73)	
BRCA N+ ^d	239 (48.09)	143 (28.77)	96 (21.73)	
Treatment (%)				
None	172 (34.61)	91 (18.31)	81 (16.30)	<0.0001
CHT	60 (12.07)	18 (3.62)	42 (8.45)	
Other ^e	265 (53.32)	180 (36.22)	85 (17.10)	
Type (%)				
HER2–/HR+	212 (42.66)	123 (24.75)	89 (17.91)	0.21
HER2+/HR+	181 (36.42)	113 (22.74)	68 (13.68)	
HER2+/HR–	66 (13.28)	36 (7.24)	30 (6.04)	
HER2–/HR–	38 (7.65)	17 (3.42)	21 (4.23)	
Cognitive attitudes (%)				
Completely accept	228 (45.88)	205 (41.25)	23 (4.63)	<0.0001
Basically accept	151 (30.38)	80 (16.10)	71 (14.29)	
Basically reject	101 (20.32)	2 (0.40)	97 (19.52)	
Completely reject	17 (3.42)	0 (0.00)	17 (3.42)	

^a, less than high school; ^b, high school and above; ^c, no regional lymphadenectomy (imaging or clinical examination); ^d, regional lymph node metastasis (imaging or clinical examination); ^e, anti-HER2 or endocrine therapy. CIS, carcinoma in situ; BRCA, breast invasive carcinoma; CHT, chemotherapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor.

Among the survivors who had received at least 1 dose of a COVID-19 vaccine, 99.30% held a supportive attitude, while among the survivors who had not received a vaccine, 45.19% held a supportive attitude, and the difference between the two was significant ($P < 0.001$). In addition, acceptance of COVID-19 vaccines was significantly

different among BC survivors with different ages, different levels of education, and different treatment statuses ($P = 0.0048$, $P = 0.0356$, and $P = 0.0019$, respectively). Survivors over 70 years of age, not educated beyond high school, and survivors receiving chemotherapy had significantly lower acceptance levels of COVID-19 vaccines (*Figure 2A–2C*),

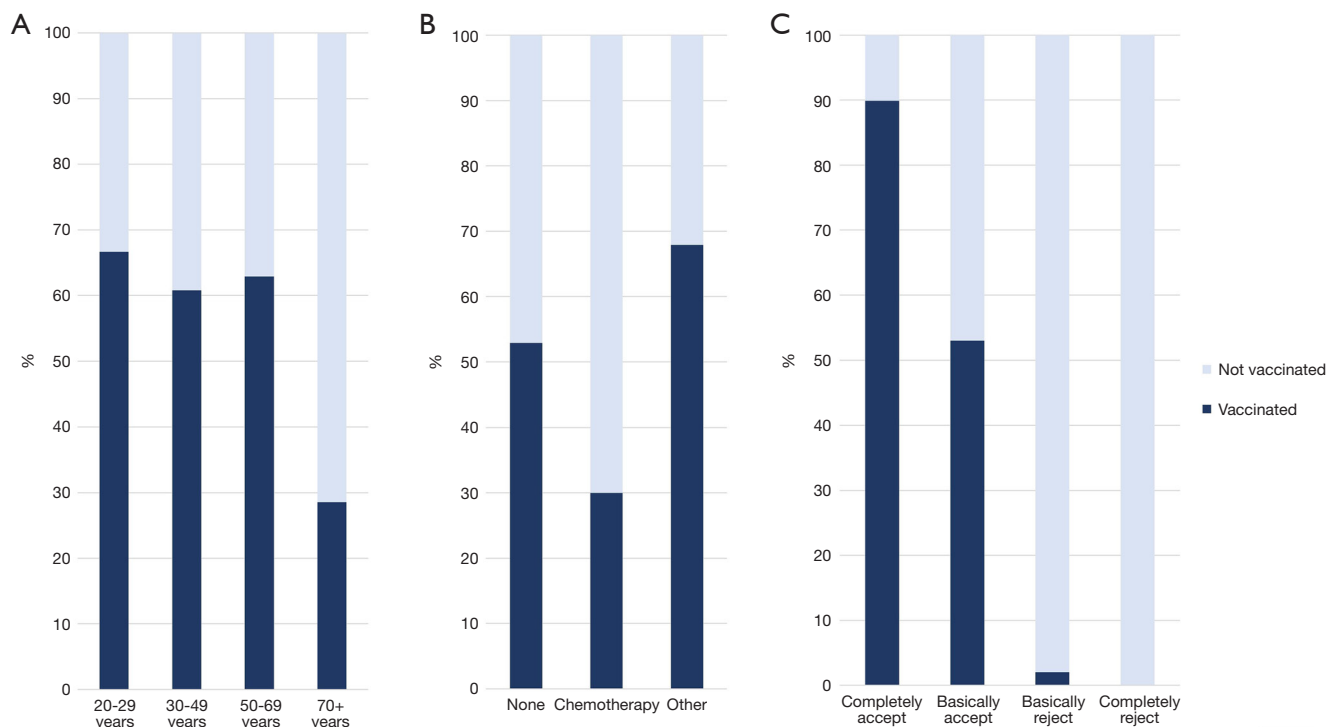


Figure 1 Stacked histogram of the proportions of vaccinated BC survivors at different groups. (A) Stacked histogram of the proportions of vaccinated BC survivors at different ages. (B) Stacked histogram of the proportions of vaccinated BC survivors with different treatment statuses. (C) Stacked histogram of the proportion of vaccinated BC survivors with different cognitive attitudes toward COVID-19 vaccines. BC, breast cancer.

and survivors with different molecular subtypes and tumor stages had similar cognitive attitudes toward COVID-19 vaccines ($P=0.1783$ and $P=0.6723$, respectively) (Table 4).

Reasons for willingness/unwillingness to receive a COVID-19 vaccine

For patients who were willing to receive a COVID-19 vaccine, the main reasons for acceptance were “doctor recommendation” (57.41%) and “belief in the protective effect of the vaccine” (55.15%), and other reasons included “belief in vaccination as a social responsibility” (48.02%), “eagerness to return to normal life” (29.55%), “belief in vaccination as the current ideal protection strategy” (22.43%), and “belief in herd immunity” (12.14%) (Figure 3A). For patients who were unwilling to receive a COVID-19 vaccine, the main reason was “the unknown safety of the vaccine in cancer patients” (67.80%), and other reasons included “no doctor recommendation” (23.73%), an allergy history (13.56%), “not a member of a high-risk

population” (12.71%), and “no confidence in the vaccine” (5.08%) (Figure 3B). Among the vaccinated survivors, 0.69% basically or completely rejected COVID-19 vaccines but still chose to vaccinate because it was recommended by their doctor; in contrast, 45.19% of survivors who were not vaccinated were receptive to COVID-19 vaccines (Table 5).

Vaccination status and adverse reactions

A total of 289 (58.1%) BC survivors were vaccinated against COVID-19; 251 had completed the vaccination schedule. The types of vaccine received by these patients included the Sinovac COVID-19 vaccine, Sinopharm COVID-19 vaccine, and Zifvax COVID-19 vaccine. None were vaccinated with the CanSinoBIO COVID-19 vaccine (Table 6).

Among the BC survivors who had received at least 1 dose of a COVID-19 vaccine, 18 had adverse reactions after vaccination, including injection site discomfort, fever, cough, rash, and fatigue. The overall incidence of adverse reactions was 6.23% (Table 7). All adverse reactions were

Table 3 Univariate and multivariate logistic regression analyses of whether breast cancer survivors are willing to receive a vaccine

Variables	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	P value	OR	95% CI	P value
Age, years						
20–29	Ref	–	–	–	–	–
30–49	0.77	0.14–4.31	0.77	–	–	–
50–69	0.68	0.12–3.79	0.66	–	–	–
≥70	0.2	0.03–1.40	0.105	–	–	–
Education						
Low ^a	Ref	–	–	–	–	–
High ^b	0.97	0.68–1.39	0.879	–	–	–
Grade						
CIS	Ref	–	–	–	–	–
BRCA N0 ^c	0.32	0.1–1	0.051	–	–	–
BRCA N+ ^d	0.4	0.13–1.23	0.11	–	–	–
Treatment						
None	Ref	–	–	–	–	–
CHT	0.38	0.2–0.71	0.003	0.41	0.2–0.87	0.02
Other ^e	1.88	1.27–2.8	0.002	2.01	1.21–3.32	0.007
Type						
HER2–/HR+	Ref	–	–	–	–	–
HER2+/HR+	1.2	0.8–1.8	0.374	–	–	–
HER2+/HR–	0.87	0.5–1.51	0.619	–	–	–
HER2–/HR–	0.59	0.29–1.17	0.132	–	–	–
Cognitive attitudes						
Supportive	Ref	–	–	–	–	–
Negative	0.01	0–0.03	<0.001	0.01	0–0.03	<0.001

^a, less than high school; ^b, high school and above; ^c, no regional lymphadenectomy (imaging or clinical examination); ^d, regional lymph node metastasis (imaging or clinical examination); ^e, anti-HER2 or endocrine therapy. CIS, carcinoma in situ; BRCA, breast invasive carcinoma; CHT, chemotherapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor.

grade 1 or 2, and no adverse reactions of grade 3 or above were reported. No significant difference in the incidence of adverse reactions was identified among patients who received different types of vaccines. Thirteen (72.22%) adverse reactions occurred within 3 days after vaccination, and five (27.78%) occurred within 1 week after vaccination. The adverse reactions reported by 15 survivors (83.33%) markedly improved within 1 week. One of the survivors with cough had a history of radiation pneumonia. The

incidence of adverse reactions to COVID-19 vaccination did not significantly differ among survivors in different age groups.

Effect of vaccination on quality of life

The median score was 3, and the mean score was 3.208±0.505. A total of 97.56% of the survivors considered that vaccination had no or almost no effect on their quality

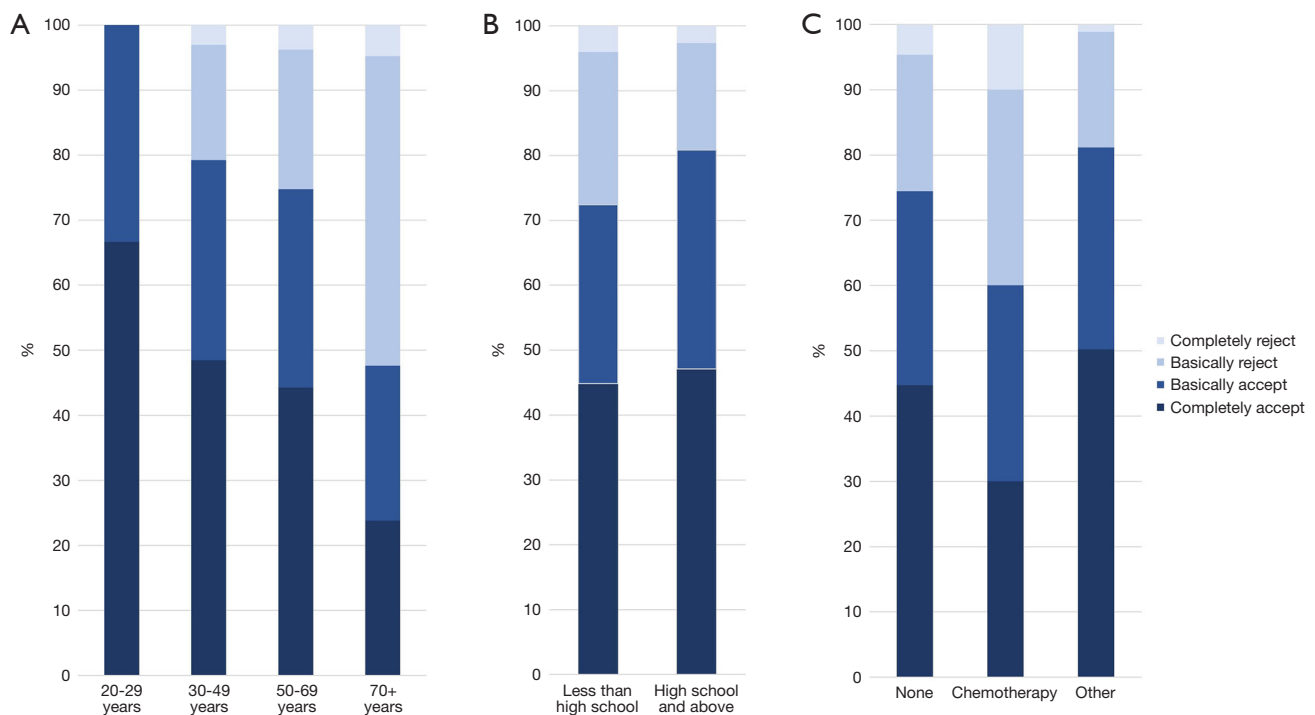


Figure 2 Stacked histogram of the proportion of BC survivors with different cognitive attitudes toward COVID-19 vaccines among BC survivors at different groups. (A) Stacked histogram of the proportion of BC survivors with different cognitive attitudes toward COVID-19 vaccines among BC survivors at different ages. (B) Stacked histogram of the proportion of BC survivors with different cognitive attitudes toward COVID-19 vaccines among BC survivors with different education levels. (C) Stacked histogram of the proportion of BC survivors with different cognitive attitudes toward COVID-19 vaccines among BC survivors at different treatment statuses. BC, breast cancer.

of life. A lower score significantly correlated with the incidence of adverse reactions to the vaccine ($P < 0.001$) (Figure 4). The median score for survivors with adverse reactions to the vaccine was 3, and the mean score was 2.722 ± 0.6691 .

Vaccination and tumor survival

After vaccination, two patients (0.69%) experienced recurrence and metastasis. One patient had ipsilateral tumor recurrence (molecular subtype, HR+/HER2-luminal A BC), and one patient had bone metastasis (HR-/HER2 basal-like BC). A review of the disease history showed that the two patients were in a late disease stage and had large tumors, >four lymph node metastases, and a mild response to neoadjuvant chemotherapy.

Discussion

Effective preventive and therapeutic drugs for COVID-19

are lacking, so vaccination remains the most important preventive strategy. Although some evidence shows that vaccination has not reduced the infection rate for COVID-19 BC survivors, it reduces the risk of severe disease and hospitalization. BC survivors, as a special population, need to be vaccinated because of decreased immunity caused by radiotherapy and chemotherapy. BC survivors often need to receive long-term endocrine or anti-HER2 treatment, and whether vaccination has an effect on antitumor treatment is an issue that needs to be addressed. In China, approximately 85.64% of the population has completed a COVID-19 vaccination schedule, but cancer survivors have lower confidence in vaccines (13). In this study, 58.15% of BC survivors had received at least 1 dose of a COVID-19 vaccine, a percentage that may be higher than the actual vaccination rate for BC survivors. We published information regarding whether BC survivors can receive a COVID-19 vaccine and recommended that patients who are not currently receiving chemotherapy should receive a vaccine if their physical condition permits

Table 4 Clinical characteristics of breast cancer survivors with different cognitive attitudes

Variables	Overall	Supportive	Negative	P value
N (%)	497 (100.00)	379 (76.26)	118 (23.74)	
Vaccinated (%)				
Yes	289 (58.15)	285 (57.34)	4 (0.80)	<0.0001
No	208 (41.85)	94 (18.91)	114 (22.94)	
Age, years (%)				
20–29	6 (1.21)	6 (1.21)	0 (0.00)	0.0048
30–49	260 (52.31)	206 (41.45)	54 (10.87)	
50–69	210 (42.25)	157 (31.59)	53 (10.66)	
≥70	21 (4.23)	10 (2.01)	11 (2.21)	
Education (%)				
Low ^a	272 (54.73)	197 (39.64)	75 (15.09)	0.0356
High ^b	225 (45.27)	182 (36.62)	43 (8.65)	
Grade (%)				
CIS	19 (3.82)	16 (3.22)	3 (0.60)	0.6723
BRCA N0 ^c	239 (48.09)	180 (36.22)	59 (11.87)	
BRCA N+ ^d	239 (48.09)	183 (36.82)	56 (11.27)	
Treatment (%)				
None	172 (34.61)	128 (25.75)	44 (8.85)	0.0019
CHT	60 (12.07)	36 (7.24)	24 (4.83)	
Other ^e	265 (53.32)	215 (43.26)	50 (10.06)	
Type (%)				
HER2–/HR+	212 (42.66)	165 (33.20)	47 (9.46)	0.1783
HER2+/HR+	181 (36.42)	143 (28.77)	38 (7.65)	
HER2+/HR–	66 (13.28)	46 (9.26)	20 (4.02)	
HER2–/HR–	38 (7.65)	25 (5.03)	13 (2.62)	

^a, less than high school; ^b, high school and above; ^c, no regional lymphadenectomy (imaging or clinical examination); ^d, regional lymph node metastasis (imaging or clinical examination); ^e, anti-HER2 or endocrine therapy. CIS, carcinoma in situ; BRCA, breast invasive carcinoma; CHT, chemotherapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor.

(17–20), which might have led to more survivors choosing to receive a vaccine, thus resulting in a high percentage of vaccinated participants in this study.

Previous reports in the literature show that age and education level correlate with vaccination rates. Younger people with higher education levels have higher COVID-19 vaccination rates (13,16). Our data showed no difference in COVID-19 vaccination rates between survivors in different age groups and with different education levels, perhaps

because some of our data were collected through an online platform and data for elderly survivors were not collected because of their unfamiliarity with the online platform. However, the level of acceptance of COVID-19 vaccines significantly affected the vaccination rate. The analysis showed that vaccination acceptance among survivors with different ages and education levels significantly differed. Survivors over 70 years of age and those with a low education level reported significantly lower acceptance of

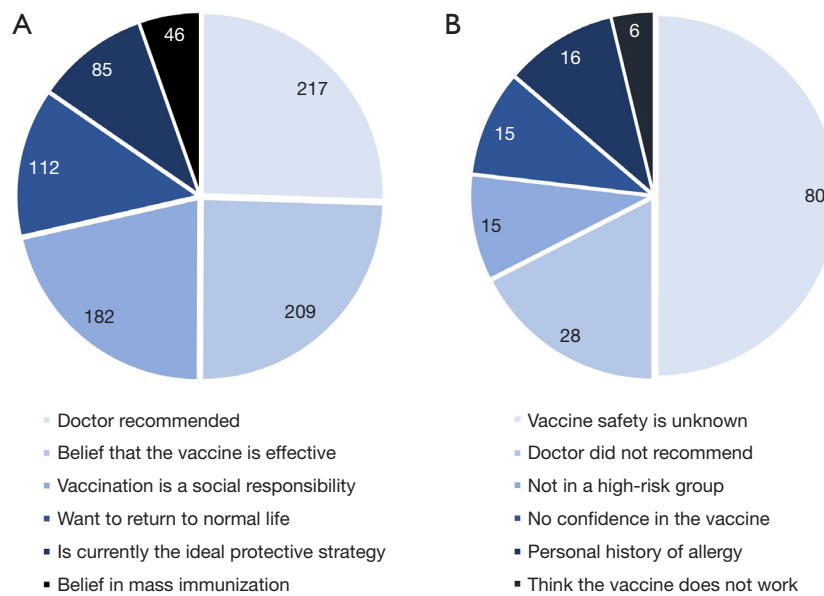


Figure 3 Reasons of breast cancer patients receive the new crown vaccine or not. (A) Pie chart of reasons for agreeing to vaccination. (B) Pie chart of reasons for not being vaccinated.

Table 5 Assessment of vaccination willingness: reasons for agreeing to vaccination or not being vaccinated

Reasons	n	%
Reasons for agreeing to vaccination		
Doctor recommendation	217	57.26
Belief that the vaccine is effective	209	55.15
Vaccination is a social responsibility	182	48.02
Desire to return to normal life	112	29.55
The ideal protective strategy	85	22.43
Belief in mass immunization	46	12.14
Reasons for not being vaccinated		
Vaccine safety is unknown	80	67.80
Doctor did not recommend	28	23.73
Not in a high-risk group	15	12.71
No confidence in the vaccine	15	22.71
Personal history of allergy	16	13.56
Belief that the vaccine does not work	6	5.08

COVID-19 vaccines, and these survivors were also at a high risk for COVID-19 infection. Therefore, improving COVID-19 vaccine acceptance will help increase the

vaccination rate among BC survivors. In addition, treatment status is an independent factor influencing whether BC survivors received a COVID-19 vaccine. Most patients undergoing chemotherapy did not receive a COVID-19 vaccine. However, endocrine therapy or anti-HER2 therapy had no effect on vaccination. Therefore, whether survivors receiving chemotherapy are suitable to receive a COVID-19 vaccine requires further investigation.

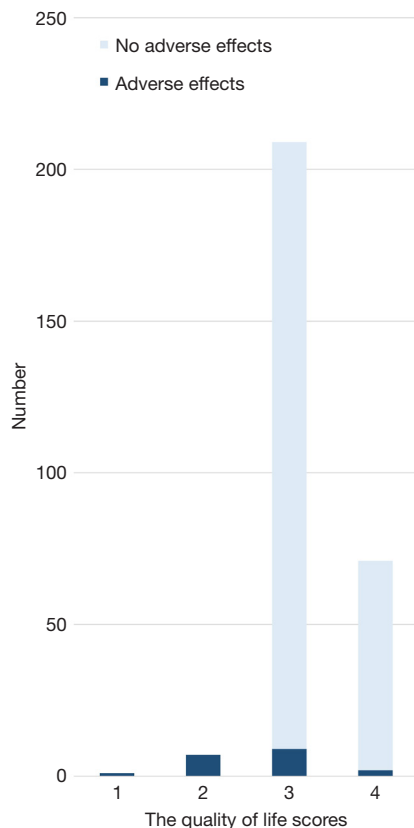
Similar to the findings of Villarreal-Garza *et al.* (16), 57.26% of the survivors were willing to be vaccinated because it was recommended by their doctor. Among the people who were unwilling to vaccinate, the main reason was “the unknown safety of the vaccine in cancer patients.” High-quality evidence on the efficacy and safety of COVID-19 vaccines is still lacking, but some studies have confirmed the effectiveness (21-25) and safety (23,26-28) of COVID-19 vaccination for cancer survivors. More than 60% of the BC survivors had sex hormone receptor-positive tumors and require at least 5 years of endocrine therapy. Endocrine therapy often leads to dyslipidemia and an increased risk of thrombotic events. Adenovirus vaccines may cause rare venous or arterial thrombosis events associated with thrombocytopenia (17). Therefore, BC survivors should avoid adenovirus vaccines (29). In this study, all survivors received inactivated vaccines or recombinant protein vaccines and no adenovirus vaccines. The correlation between immune

Table 6 Vaccine choices among breast cancer survivors

Trade name	Types of vaccine	Vaccinated (%)	Completely vaccinated (%)
Sinovac COVID-19 vaccine	Inactivated vaccine	177 (61.25)	162 (56.06)
Sinopharm COVID-19 vaccine	Inactivated vaccine	71 (24.57)	61 (21.11)
Zifivax COVID-19 vaccine	Recombinant protein vaccine	18 (6.23)	14 (1.84)
Unknown	–	23 (7.96)	14 (4.84)
CanSinoBIO COVID-19 vaccine	Adenovirus vector vaccines	0 (0.00)	0 (0.00)

Table 7 Profile of adverse effects after vaccination against COVID-19

Variables	All	Injection site discomfort	Fever	Cough	Rash	Fatigue
All	18 (6.22%)	9	5	3	2	2
Sinovac COVID-19 vaccine	11 (3.80%)	6	3	1	2	1
Sinopharm COVID-19 vaccine	4 (1.38%)	1	2	1	0	1
Zifivax COVID-19 vaccine	1 (0.34%)	0	0	1	0	0
Unknown	2 (0.69%)	2	0	0	0	0

**Figure 4** Stacked histogram of the quality of life scores and adverse reactions of vaccinated BC survivors. BC, breast cancer.

status and vaccination safety is still unclear, but vaccination is not recommended for people with markedly impaired immune function. Our results showed that a doctor's recommendation played a key role in whether BC survivors received a COVID-19 vaccine. Interestingly, 45.19% of the survivors were receptive to COVID-19 vaccines but still did not choose to be vaccinated against COVID-19. Therefore, physicians should make personalized judgments based on the clinical and pathological characteristics of each tumor, the treatment process, and the general condition of each survivor, inform survivors in detail such that they can decide whether to vaccinate, and monitor these survivors on a regular basis.

Our results showed that the incidence of short-term adverse reactions among BC survivors after COVID-19 vaccination was similar to that among the general population. The overall incidence of adverse events was 6.22%. All adverse reactions were grade 1 or 2, and no adverse reactions of grade 3 or above were reported. Most adverse reactions were common vaccination reactions, such as fever, local redness and swelling, and rash. COVID-19 vaccination had no significant effect on quality of life, further demonstrating the safety of the COVID-19 vaccines. Because of the short time-to-market for COVID-19 vaccines, no definite and sufficient data are available to verify whether the risks of recurrence and metastasis increase in BC survivors after vaccination. In this

study, two patients reported recurrence or metastasis after vaccination, but a retrospective analysis of their disease history showed that they were in the late disease stage at initial diagnosis, with a heavy tumor burden and a poor response to treatment. Therefore, recurrence in these two patients may be due to the tumor rather than vaccination. But because survival data were not systematically collected in our study, further studies need to be conducted to draw a solid conclusion.

This study has limitations: bias in data collection, the small sample size (especially the small number of patients receiving specific treatments, such as chemotherapy), and the lack of data on vaccine effectiveness. These findings await confirmation through larger studies.

Conclusions

Most BC survivors were supportive of COVID-19 vaccines, and more than half of them were vaccinated. The main reason for a willingness to be vaccinated was doctor recommendations and belief in the safety of the vaccine. Some BC survivors chose not to receive a COVID-19 vaccine mainly due to concerns about the safety of the vaccine, but they were still willing to accept their doctor's advice. In terms of cognitive attitudes toward COVID-19 vaccines, elderly individuals and those with a lower education level were less receptive to vaccination. Unfortunately, elderly BC survivors are at a high risk for COVID-19 infection. Therefore, attention to elderly survivors can help improve the vaccination rate. The vaccine types received by the BC survivors had good safety profiles. No serious adverse reactions were observed, and the incidence of adverse reactions among the elderly population was not higher than the rates in other age groups. Tumor survival needs further investigation.

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Footnote

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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 questionnaire was submitted to the Ethical Committee of Xijing Hospital (Xi'an, Shaanxi) for review. The committee determined that ethical approval was not needed for this anonymous survey. All patients provided verbal consent then checked in the questionnaire that they "voluntarily participate in this study and have a preliminary understanding of this study."

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