The Protective Effect of the COVID-19 Vaccine in Cancer Patients

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Abstract. The novel coronavirus pneumonia pandemic has led to bad engulf on public health worldwide. Widespread vaccination with SARS-CoV-2 vaccine (COVID-19 vaccine) has become one of the most potentially effective strategy of ending the epidemic and avoiding the public suffering from both physical and psychological pain. With weak autoimmunity and the complex body condition in different stages of treatment, cancer patients are more vulnerable and sensitive to infect in COVOD-19 pandemics. There are many data indicating that cancer patients usually obtain the higher mobidity, higher rate of the severe illness and higher fatality in COVID-19 pandemic. In that case, they are in greater need of protective measures, of which vaccination is the most convenient and widely accepted protective. Based on the existing clinical studies, this review aims to focus on the safety and efficacy of the COVID-19 vaccine in patients with cancer. After that the immunogenicity of the vaccine itself, adjuvant, doses, times of vaccinations and patient condition are listed to consider how they affet the effect of vaccine. Due to the complexity of the immune function of cancer patients, COVID-19 vaccination in cancer patients is extremely critical to protect from COVID-19 pneumonia, so large-scale clinical studies and real-world research data are still needed to develop a more refined and appropriate vaccination program to achieve better protection of oncology patients.

Keywords: COVID-19, Vaccine, Cancer, Effect.

1. Introduction

Novel coronavirus pneumonia is an emerging acute respiratory disease resulting from infection of the novel coronavirus, now named SARS-CoV-2 (COVID-19), which is a kind of RNA virus. Novel coronavirus pneumonia has give rise to tremendous public health impacts and economic losses around the world. Data published from Center for Systems Science and Engineering (CSSE) at Johns Hopkins University statistics, as of March 10, 2023, there were a total of 676, 609,955 people have been infected, of whom 6,881,955 have died, and a total of 13,338,833,198 doses of vaccine have been administered globally to date. Mass vaccination against SARS-CoV-2 to achieve herd immunity is still a more effective means of protection against pneumonia.

Cancer is the second leading cause of death worldwide, with extremely high morbidity and mortality rates in the population [1]. Because of the average high age of oncology patients, the high number of complications, immune suppression due to antitumor therapy, and repeated trips in the hospitals due to treatment needs, cancer patients are in extreme danger of infection in novel coronavirus pneumonia outbreaks. Therefore, COVID-19 prevention in oncology patients is extremely significant. However, there is an absence of research evidence on novel coronavirus vaccination in cancer patients, and related studies are underway. SARS-CoV-2 vaccination strategies for this population need to be focused and refined. This review aims to summarize the strength of the protection of the COVID-19 vaccine on cancer patients and the current problems.

2. Epidemiological characteristics of COVID-19 in cancer patients

The incidence of COVID-19 pneumonia in 313 cancer patients was increased significantly in comparison with the whole population (1.6% vs 0.37%) during the first quarter in 2020 from Wuhan [2]. Of the 1590 COVID-19 patients with past medical history collected by Liang in China, 9 (50%) of 18 patients with a history of malignancy were confirmed as serious illness, compared with only 16% of those without tumor (245 of 1572) [3], suggesting that the symptoms of cancer patients

infected new coronavirus are more serious. Dai reported that patients with cancer had a higher ICU (Intensive Care Unit) occupancy, higher proportion of severe symptom, and a higher chance of requiring invasive mechanical ventilation, and even obtained a higher facility rate [4], demonstrating cancer patientshad a higher rate of critical conditions in Corona Virus Disease. A study conducted by COVID-19 and Cancer Consortium collected the data of 928 adult cancer patients from Spain, Canada, and the United States who infected with COVID-19, intimating the high proportion of severe illness and mortality in oncology patients [5]. These results indicate that cancer patients are of vulnerability to infection, and have high rates of morbidity and mortality, requiring additional protection and prevention, especially the inoculation of COVID-19 vaccine.

3. Categorization, mechanisms and effects of COVID-19 vaccine

According to different development theories and production processes, the SARS-CoV-2 vaccines presently can be broadly categorized into six types: inactivated vaccines, recombinant protein vaccines, RNA vaccines, DNA vaccines, virus-vectored vaccine and virus-like particle (VLP) vaccines [6].

The mechanisms of active immunization are similar in these six types vaccines. The brief explanation is that the vaccines are capable of inducing T-cell and B-cell-mediated acquired immunity when it enters the human body and produces memory cells with less Virulence and Pathogenicity. Once inoculated with vaccines, the immune system can respond quickly to eliminate the virus when the pathogen invades the body. The most important point in the vaccination process is to ensure that the body does not experience uncomfortable symptoms of infection while developing immunity.

After promotion to the market, the protective effects and adverse reactions of these six types of vaccines produced by different manufacturers are varied (Table 1).

Table 1. Summary of the efficacy and safety of the COVID-19 vaccin

Categorization	Vaccine Name	Manufacturer	Number of Inoculations	Disease Prevention Rate	Rate of Prevent Severe Illness and Hospitalization	Adverse Reaction
Inactivated Vaccine	BBIBP-CorV	Beijing Institute of Biological Products of Sinopharm Group	2	78.10% higher in the elderly	No data currently available	Not available
	CoronaVac	SINOVAC	2	83.70%	100.00%	Local redness and induration, dizziness, headaches and muscle aches, as well as fatigue or diarrhea
Virus-vectored Vaccine	Ad26.COV2.S	Johnson & Johnson	1	52.90%	85.00%	Injection site pain, fatigue, headache, pain in muscle, joints, chills, enlarged arm lymph nodes, nausea and vomiting, and fever,GBS,TTS
	Vaxzevria	AstraZeneca	3	79.00%	100.00%	Headache, nausea, myalgia, arthralgia, injection site pain and fever, fatigue, malaise, fever, and chills
RNA Vaccines	BNT162b2	Pfizer - BioNTech SE	3	91.30%	96.70%	Injection site pain, fatigue and headache, myocarditis, allergic reaction
DNA Vaccines	Zycov-D	Zydus Cadila's	3	66.60%	100.00%	Headache, nausea, myalgia, arthralgia, pain at the injection site, stroke, cerebral infarction
Recombinant Protein Vaccines	NVX-CoV2373	Novavax	2	90.40%	100.00%	Headache, nausea or vomiting, myalgia, arthralgia, injection site pain, fatigue and malaise,myocarditis or pericarditis
(VLP) Vaccines	CoVLPs	Medicago	In the research and development			

4. Efficacy and safety of the COVID-19 vaccine in cancer patients

Cancer patient are usually more susceptible to viral infections and are in a more dangerous situation in epidemics due to their own immune deficiencies or low immunity. Whether vaccination will produce the expected immune response in cancer patients and whether there will be any other serious side effects in addition to the common adverse reactions, such as redness, swelling, and pain in the site of inoculation, are the reasons for cancer patients' tangled consideration in the vaccination. Existing COVID-19 vaccine clinical program research, in different treatment stages of tumor patients mostly do not meet the experimental inclusion criteria [1]. So for the vaccine safety and effectiveness

of tumor patients with less data and analysis, there are still some studies carried out to draw relevant conclusions.

In a thesis by Ayse Irem Yasin et al. on the efficacy of CoronaVac, a kind of inactivated vaccine, in tumour patients, the positive ratio and antibody levels in serum are used as representative indicators of immune response. The average antibody titer is 363.9AU/ml in the group of cancer patients, wherase the ratio the group of controls enhances to 656.5AU/ml. Simultaneously, seropositive rate in cancer patients decreases by 12.3% [7]. Compared with ordinary controls, the seroprevalence ratio and antibody levels of cancer patient group are significantly lower. This result is not surprising, as the suppressed immune system of cancer patients can have a negative effect on the immune response, but the high seroprevalence rate (85.2%) still proves the effectiveness of the vaccine. Moreover, the data on untoward reaction after administration displays that the ratio of adverse reactions is 15.9% in the cancer patients in comparison with 22.5% in the controls after the first immunization[8]. However, the results of adverse reactions are similar after the second challenge, emphasizing that the vaccine is reliably safe for cancer patients.

The research from David J. Pinato showed that the cancer patients with a complete immunization diminished morbidity in compared to invaccination patients. The proportion of symptomatic, specific therapy, acute complications, hospitalizations and demanding of oxygen therapy with COVID-19 decreased about 9.4% ($p=0.0070$), 28.3% ($p<0.0001$), 10.8% ($p=0.0379$), 10.3% ($p=0.0007$) and 16.3% ($p=0.0036$), respectively[8].Comparisons of the different vaccines shows that vaccinated cancer patients have improved outcomes and less frequent sequelae after SARS-CoV-2 infections.

Wang's research, targeting to BNT162b2 (one of the RNA vaccine), demonstrates that five weeks after inoculation, 95% patients of solid tumors produce antibodies, while only 60% of patients with hematologic tumors do so [1]. The serological response of patients with solid tumors vaccinated with the COVID-19 vaccine is weaker than that of the healthy population, while the level on patients with hematologic tumors vaccinated is minimum [1]. Meanwhile the overall short-term security of COVID-19 vaccination in tumor patients was no significant different in compared to healthy population [1].

It is also reported that among cancer patients, vaccination on whom developed tumor metastasis are slightly less effective, and the effectiveness of the COVID-19 vaccine is slightly worse in oncology patients who received traditional treatment, including chemotherapy, immunotherapy (IT), or targeted therapy, than in the untreated group, with the lowest seropositivity rate (76.8%) in chemotherapy patients, due to significant bone marrow suppression and impaired immune function [7]. Beside that, compared with those lung cancer patients who receiving chemotherapy, treating with IT and tyrosine kinase inhibitor (TKI), a type of targeted therapy, have a higher rate of adverse events at each vaccination (three doses of vaccine in total) [9]. As supplementary evidence, among the different types of cancer treatment, antibody levels are numerically higher in patients who stop treatment than that in the curing duration [10], but without statistically significant differences.

The results of the above studies altogether suggest that the vaccine has a protective effect on patients with tumors in terms of COVID-19, although experimental data from different species of the vaccine indicates that even if not as good as in the common mass, the COVID-19 vaccine is still highly effective in cancer patients and is relatively safe and reliable. Different cancer stages and classes of lines can also lead to differences in vaccine effectiveness, with hematologic tumors being less effective than solid tumors, and patients in the treatment phase, especially chemotherapy, being less effective with the vaccine. In contrast, there is a rebound in the effect of the COVID-19 vaccine in oncology patients who stopped treatment.

5. Problems and recommendations of different vaccines

The types of vaccines administered to tumor patients in the above mentioned studies were inactivated vaccine, RNA vaccine, and virus-vector vaccine. The methodology and the reference

index representing efficacy are not standardized among the three types, so it is not possible to make a cross-sectional comparison of which vaccine is more effective in cancer patients.

The immunogenicity of the vaccine itself, adjuvant, doses, times of vaccinations and patient condition will affect the effectiveness and safety of the COVID-19 vaccine for tumor patients, and careful consideration is needed in the selection of vaccination in order to achieve the expected results.

For cancer patients, live virus vaccines should be avoided in the first place. Considering their low immunity, the immune response and protective effect after vaccination may be reduced. What's more, some reports suggest that adenoviral vector vaccines ChAdOx1nCoV-19, Ad26.COV2.S may be associated with rare cases of post-vaccination thrombosis [1], and tumor cells can directly activate the coagulation system, secrete mucin and tissue factor, destroying vascular endothelial cells, increasing thrombin activity, and leading tumor patients in a hypercoagulable state. In that case, vaccines with the potential to trigger thrombosis should be avoided, so before the mechanism of thrombus generation after such vaccination is completely clarified, it is recommended that tumor patients should choose with careful consideration.

In terms of adjuvants, the application of aluminum adjuvant is relatively mature, and its safety has been used in the development of several types of new coronavirus vaccines. Existing studies suggest that there is great potential for enhancing the vaccine immune response in immunocompromised populations on oil-in-water adjuvants as well as complex adjuvants consisting of some aluminum hydroxide adjuvants and CpGs [11], maybe used as universal adjuvants for neocoronavirus vaccine development in the future.

Due to the defective immune function of tumor patients who can not produce the same level of antibodies as normal populations, it is necessary to follow up the continuous vaccination. A number of studies have suggested that after the second, third and even the fourth vaccination, the standard of the patient's immune response has increased [12]. In order to avoid the uncertainty that may be brought about by a single dose of vaccination, it is recommended that patients with tumors be vaccinated with multiple doses of the COVID-19 vaccine.

As for the patient situation, in the previously mentioned study it is shown that the vaccination of patients during the chemotherapy period is unsatisfactory and vaccination during this period is not recommended. Immunotherapy patients, on the other hand, although the effect of vaccination is slightly lower than that of untreated patients and the potential for adverse effects is higher, is still in a vaccineable state. Targeted therapies need to be discussed in different situations. When immunotargeted therapies with anti-CD20 monoclonal antibodies (e.g., rituximab) are used, the drugs will affect the function of B cells, so vaccination is not recommended during this process. While Bruton's tyrosine kinase have been proved that have different effects on other vaccines (it will attenuate the effect of ab initio immune response after hepatitis B-CpG vaccine, while there is no significant effect on re-immune response after recombinant zoster vaccine [13]), so it is hard to say what effect BTK will have on COVID-19 vaccine and is necessary to carry out a targeted study.

In addition to this, the duration of the vaccine effect relates to issues such as whether or not the patient undergoes further treatment, and is one of the considerations in the selection of cancer patients. It is shown that three months after completion of the mRNA ChAdOx1 nCoV-19 vaccine in a batch of patients with solid cancers, diminished immunogenicity is observed, which is insufficient to prevent infection with the newer variants [10], and an additional dose had to be vouchsafed to this susceptible population in an effort to maitain the effect.

6. Conclusion and Discussion

Cancer patients are riding a wave of the vaccine as a protection against COVID-19 infection, whose effectiveness and safety are at a high level. The type, adjuvant, the times, doses and the condition of patient will all affect the effectiveness of the COVID-19 vaccine.

At present, COVID-19 vaccine still has the problem of slightly poor persistence and not very good effect to new variants. For cancer patients, the method of increasing the number of vaccinations or

increasing the dose is not of great significance because of vlunerable immune system, but rather poses other dangers, so further research is needed to focus on the persistence and variant aspects.

The question of which type of vaccine is better and more recommended for oncology patients has never been convincingly answered, and at this stage it can only be ruled out on the basis of the problems that exist, so in the future parallel experiments with uniformly comparable parameters need to be put on the agenda in order to draw the appropriate conclusions.

As a kind of respiratory infection disease, the conclusion about the vaccine effect of COVID-19 can be partly suggestive for the future research on vaccines for influenza and other respiratory diseases.

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