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Expected Usefulness of Fourth Dose of COVID-19 Vaccine for Patients with Underlying Solid Tumor who Previously Received the Primary Heterologous COVID-19 Vaccine

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Abstract

Coronavirus disease 2019 (COVID-19) immunization frequently requires two standard doses. Due to the likelihood that the population may lose immunity after receiving a standard mass vaccination and the potential for the introduction of a new strain, several scientists are currently advocating the use of a booster dosage of the vaccine. The authors of this retrospective study used a clinical model for immune response prediction to forecast how solid cancer patients will respond to the fourth dosage of the COVID-19 immunization. In the case of homologous primary backgrounds, the prospective rates of extension of protective efficacy for using viral vector and messenger ribonucleic acid (mRNA) COVID-19 vaccines for vaccinees with underlying solid tumor are equal to 11.5 and 16.5%, respectively. In the event of heterologous primary backgrounds, the prospective rates of extension of protective efficacy for using viral vector and mRNA COVID-19 vaccines are equal to 2.2 and 7.2%, respectively, for patients with underlying solid cancer. In conclusion, the fourth dose of the COVID-19 vaccine regimen had an effect on the immunogenicity of vaccine recipients with underlying malignancy.

Keywords
- COVID-19
- dose
- fourth
- vaccine
- cancer

Introduction

Coronavirus disease 2019 (COVID-19) has affected the entire world.[1] Vaccination is the finest disaster management strategy.[2] Traditionally, two vaccination doses are required for complete immunization. Several experts advise administering an additional COVID-19 booster dose when there is an emerging variant and a possible drop in protective immunity occurs after a normal vaccine administration.[3–5]

After vaccination, antibody levels may drop, necessitating practice to prevent infection. The effectiveness of the COVID-19 vaccine in certain populations of vaccine recipients with background personal illnesses is a significant clinical problem. Immune responses to standard immunizations are poor in immunocompromised people and those with problematic autoimmunity (such as lupus and cancer).[1] Patients with compromised immune systems are at a higher risk of developing significant vaccine resistance.[1] Despite the fact that many people are still concerned, the third and second COVID-19 vaccination doses are occasionally used as booster doses. The additional dose of COVID-19 vaccine is on its way, and the next injection is already planned.

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Some scientists advocate for an additional vaccination dose in the event of the emergence of a new type of pathogen as well as the anticipated loss of public immunity after regular mass immunization. Because the efficacy of the additional dosage of the COVID-19 vaccine is unknown, any research into its efficacy is intriguing. The third dosage of the vaccination for patients who have malignancy is the topic for further discussion right now in clinical oncology.[6–11] According to some recent clinical trial findings,[12–15] the third vaccination dose may be beneficial. Increased immunity is usually observed after the third dose immunization, and there is no significant increase in the incidence of postvaccination adverse events.[12–15] Those studies, however, are frequently based on a small number of participants and focus on a specific COVID-19 vaccine type. The impact of confounding variables, such as previous asymptomatic COVID-19, is typically not excluded in those studies.[12–17] Those who have had the recommended vaccinations are also becoming ill as a result of the unusual pathogen strain.

Adding to the third dose of the basic vaccine, several countries, particularly those with a history of nonstandard heterologous vaccination for the first and second doses, are still dealing with an uncontrolled COVID-19 outbreak. A third vaccine is already in use, but an additional booster is still required. Many countries, including those in Southeast Asia, have already declared and implemented the additional fourth dose policy. The precise efficacy of the fourth dose vaccine is an intriguing issue that has received little attention. The data on subjects with underlying diseases, such as solid tumors, is also extremely limited. Cancer patients will be given the fourth dose of the COVID-19 vaccine here, and the researchers will use a clinical model to predict how they will react.

Materials and Methods

Study Design

The response of cancer patients to the fourth dose of the COVID-19 vaccine was predicted by the researchers using a clinical model. The emphasis is concentrated on mathematical model application in medicine. The method is a typical in silico mathematical modeling tool that is unaffected by complex environmental variables, according to an in vitro and in vivo evaluation. "Primary data"[18] refers to the fundamental data regarding the infection protection effectiveness rates of different types of vaccine. It is crucial to understand that each vaccination has a different immunogenicity mechanism. Vaccines made with various biotechnologies comprise a wide range of necessary components, resulting in a wide range of immunoprotection inductions. Following routine immunization, the maximal level of infection protection efficacy, or effective immune response, will be derived. The immune system's effectiveness will rise with the addition of the dose.

Assessment of a Booster Dose of a Vaccination

Mathematical modeling is used to assess the efficacy of a booster vaccination.[19] The current study is retrospective in nature and uses a mathematical model method. Human test subjects are not required for the evaluation of a novel vaccine whose safety has not yet been established, according to the procedure described for evaluating vaccine efficacy in silico.[19] According to in vitro and in vivo studies, mathematical modeling can generate a reasonable prediction result without the influence of environmental confounding factors.[19]

The arithmetic mathematical model is used in this study to evaluate a booster dose of a vaccination. The model is static and linear in structure. Data that was previously accessible is used as the model's main input. The impact of a booster was examined in a prior clinical experiment that employed the same modeling strategies as this one. The protective effectiveness following the booster dose will probably be regarded as background infection protection efficacy for modeling purposes. When administered as a booster dosage, the additional dose may raise the protective efficacy rate and boostering activity, but it would not exceed the baseline protective efficacy rate. Contrary to popular belief, the background protective efficacy of the booster immunization will not be greater than the ultimate protective efficacy. According to the previously indicated calculation, the final projected infection protection efficacy rate after the fourth dose will be computed as "background protective effect after the third dose + additional protection from the fourth dose." This model can be used to forecast the immune response to the fourth booster vaccine in vaccine recipients with a baseline solid tumor. The model can be run using straightforward arithmetic operations. The model's mathematical methodology allows for the elimination of biological confounding variables.

This model simulates and forecasts the action of the fourth dosage of the COVID-19 vaccination using fundamental data from a developing Asian nation with a problem of highly endemic, uncontrollable infection.

Background: Some individuals in this condition received two heterologous COVID-19 shots in addition to two booster doses of the vaccine. An inactivated-inactivated, messenger ribonucleic acid (mRNA) viral vector is often utilized for the fundamental doses of the COVID-19 vaccination (https://www.prachachat.net/marketing/news-837033). In brief, in this setting, the primary backgrounds, the first and second doses, are either inactivated vaccine and inactivated vaccine, which is called homologous path, or inactivated vaccine plus viral vaccine, which is called the heterologous path. The third dose is generally an mRNA vaccine. The following modeling study is based on the most recent publicly available data on the protection ability of the third booster. Utilizing earlier data on the immunization's effectiveness in cancer cases, changes to the vaccine's reported efficacy are also made.[20]

The model was developed using a retrospective analysis of clinical data that was made available to the public. Therefore, there are no confounding factors in the effectiveness analysis of the current study. Additionally, there are no human or animal subjects, and therefore informed consent or ethical approval is not required. As discussed earlier, a mathematical model can be developed and used to predict how the fourth

dose of the immunization will affect young people who are at risk for developing cancer.

Primary and Secondary Outcome

The primary outcome in this study is the predicted protection rate after the fourth dose. The secondary outcome is the possible expansion of protective efficacy.

Inclusion and Exclusion Criteria

In the present clinical mathematical model study, the purposive inclusion is done in order to get the primary data for further simulation, as earlier mentioned. In the event that there is no complete data, an exclusion is set.

Statistical Analysis

Basic mathematics and descriptive statistics are employed in this investigation. A percentage calculation serves as the foundation for the direct arithmetic computation. The estimate of a potential growth of preventive efficacy is based on the mathematical model, which uses arithmetic subtraction. "Possible expansion of protective efficacy" is calculated using the formula "Expected greatest protective efficacy rate after the fourth dose – Background protective effect after the third dose."

Ethics

All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study is a clinical mathematical model study and does not directly deal with patients, and therefore, ethical approval is not applicable, and the consent form is also not applicable.

Results

Protection Rare after the Fourth Dose

A clinical model study indicates that varied fourth dosage regimens can provide varying protection rates, which is according to varying projected infection protection efficacy for various background immunizations (►**Table 1**). Vaccination recipients with underlying solid tumors may experience altered immune responses to all vaccine kinds. The greatest protective efficacy rates for the viral vector and mRNA COVID-19 in cases with homologous primary backgrounds are predicted to be 89% and 94%, respectively, after the fourth immunization. The greatest protective efficacy rates for the viral vector and mRNA vaccines in cases with heterologous primary backgrounds are anticipated to be 89 and 94%, respectively, following the fourth immunization.

Possible Expansion of Protective Efficacy

Compared to the viral vector vaccine, the mRNA COVID-19 can more effectively stimulate the immune system. The prospective rates of expansion of protective efficacy for using viral vector and mRNA vaccines are examined for recipients with underlying solid tumors.

The background protection impact after the third dose and the expected viral vector vaccine's maximal protective efficacy rate are equal to 77.5 and 89% in the case of homologous primary backgrounds, respectively. As a result, 11.5% is the theoretical rate of protective effectiveness extension. The mRNA vaccine's highest anticipated protective efficacy rate is predicted to be 94%, with a background protective effect of 77.5% following the third dose. As a result, 16.5% is the potential rate of protective effectiveness extension.

The background protection impact after the third booster and the expected maximal protective efficacy rate for the viral vector vaccine for the case with heterologous main backgrounds are equivalent to 86.7 and 89%, respectively. As a result, 2.2% will be the theoretical rate of protective efficacy extension. The mRNA vaccine's highest anticipated protective efficacy rate is predicted to be 94%, with a background protective effect of 62.34% following the second vaccine administration. The potential rate of infection protection efficacy extension is expected to be 7.2%.

Table 1 Expected immunoprotection after the fourth dose of COVID-19 vaccine for cases with underlying cancer

The fourth dose vaccine		Protective efficacy rate (%)				
Type	Specific boostering[a] activity (%)	Background protective effect after the third dose[b] (%)		Expected highest protective efficacy rate after the fourth dose (%)	Possible expansion of protective efficacy (%)	
		Homologous Primary background[c]	Heterologous primary background[c]		Homologous Primary background	Heterologous primary background
Viral vector	35.9	77.5	86.7	89	11.5	2.2
mRNA	23.3	77.5	86.7	94	16.5	7.2

Abbreviations: COVID-19, coronavirus disease 2019; mRNA, messenger ribonucleic acid.

[a]If a vaccine is given as a second dose, a certain booster activity can increase the protective efficacy rate of the first dose.

[b]The background protective effect following the second dose of the vaccine is the immunoprotection rate, and data are based on an open report from a developing Southeast Asian country.[19]

[c]Primary background in the setting: homologous = inactivated + inactivated vaccine + mRNA vaccine, heterologous = inactivated + viral vector + mRNA vaccine.

Discussion

Even after receiving both doses of the vaccine, a coronavirus infection is still possible, so preventive action is essential. Additionally, for some vaccine recipients, protection is limited after two vaccine doses. As a result, booster vaccine doses have been recommended and are being given in a variety of situations. Few studies have looked into the efficacy of the subsequent booster, with a majority focusing on immune-compromised populations. Many experts now agree that a vaccine booster dose can improve immune responses, though it is not always necessary.[3–5]

Due to an inability to control the disease, some regions, particularly those in Indochina, historically used a second dose of the immunization. Individuals with cancer are also among those receiving the second boost.[20] The vaccination's effectiveness is still being debated after the second dose. Because the developed immunity is still modest, a third dose is recommended.

In immunocompromised individuals, further COVID-19 immunization is commonly administered to strengthen immunity and guard against the constantly evolving COVID-19 variation.[3–5] Some regions, especially those in Indochina, historically required a second dose of the vaccine since the sickness was uncontrollable. Patients with cancer are recommended for boosters as well.[8] After the second dose, there is still disagreement on the vaccine's efficacy. A fourth dose is advised because the already-established immunity is still underwhelming. Many healthy individuals have already received an additional dose of the vaccine since the first and second doses were of poor quality. Current best practices recommend booster whenever an underlying illness is present. The primary COVID-19 prevention method for the population of cancer patients should, in accordance with the Centers for Disease Control and Prevention's recommendations, be immunization. It can demonstrate that in subjects with preexisting malignancies, the booster COVID-19 vaccination dosage can still offer additional immunoprotection. There is an immunological gap that the additional dose of vaccine may fill because the background immunization in this situation does not follow the regular mRNA vaccine schedule.

The predicted immunoprotection after the fourth dosage may differ in patients with hybrid immunity, particularly those with a history of past COVID-19 infection and heterologous immunization, due to a variety of circumstances. Individuals with hybrid immunity may have a higher and more robust immune response after getting the fourth dose of the vaccination. The combination of spontaneous infection and subsequent heterologous vaccination may result in a more diversified and comprehensive immune response, including both cellular and humoral immunity. Previous research has found that individuals with hybrid immunity have higher levels of neutralizing antibodies than those with only spontaneous infection or vaccination. As a result, it is reasonable to believe that following the fourth treatment, patients with hybrid immunity will have increased antibody levels, perhaps giving an additional layer of protection against COVID-19. Another theory is that those with hybrid immunity have a longer immunological memory response. The combination of prior infection and subsequent vaccination may result in a more persistent and long-lasting immunological memory, resulting in long-term protection against COVID-19 even after the fourth dosage. Natural infection combined with heterologous vaccination may result in a more diversified antibody repertoire that can better recognize and neutralize variant strains. It should be noted that these are hypothetical notions that would necessitate additional study and clinical trials to determine the real immunoprotection offered by the fourth vaccine dosage in patients with hybrid immunity.

The authors state that the current study can offer crucial data for clinical oncology planning for immunization. The ability of cancer cases to establish immunity against severe acute respiratory syndrome coronavirus 2 has been found to be enhanced by receiving a third dosage of the vaccine, according the current study.[8] Consideration should be given to the mRNA vaccine, which among a variety of vaccine types has the best immunogenicity. The booster immunization using the mRNA vaccine should be helpful in terms of preventive oncology given the current state of the outbreak and the future guidelines on immunizing a patient with an underlying cancer.

Conclusion

In this study, the immunogenicity of vaccinees with an underlying solid malignancy was found to be impacted by the fourth dose of the vaccine. There are several choices to think about if a fourth dose is scheduled.

Patient Consent

This study is a clinical mathematical model study and does not directly deal with patients, and therefore, ethical approval is not applicable, and the consent form is also not applicable.

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None.

Conflict of Interest

None declared.

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