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Is the vaccine for COVID-19 effective in preventing and treating long COVID?

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ABSTRACT

Currently, various types of vaccines have been developed to prevent COVID-19 infection and prevent progression to severe diseases. After COVID-19 infection, a considerable number of patients are complaining of long COVID. However, it has not yet been specifically defined and there is no effective treatment. Therefore, I tried to find out whether vaccination before infection reduced the incidence or worsening symptoms of long COVID from studies reported so far. In addition, I tried to find out whether post-infectious vaccination also relieved symptoms. Long COVID and vaccine-related studies were searched and investigated through Google and the medical search engine. As a result, a total of 12 papers suitable for analysis were summarized. Five studies examined whether vaccination before infection reduced the incidence or symptoms of long COVID, 6 studies examined whether post-infectious vaccination relieved the symptoms of long COVID, and 1 study examined both. In most studies, pre-infection vaccination significantly reduced the incidence of long COVID and relieved long COVID symptoms compared to non-vaccination controls. In addition, post-infection vaccination could significantly reduce the incidence of long COVID. In particular, there was no significant difference between vaccination group and non-vaccination group in the incidence and symptom mitigation of long COVID according to the type of vaccine. In conclusion, vaccination was helpful in preventing and treating long COVID that occur before and even after COVID-19 infection. These findings will be a good guide to recommend vaccinations to unvaccinated people who are still hesitant to vaccinate.

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection called coronavirus disease 2019 (COVID-19), which began in Wuhan, China in December 2019, has since spread around the world, becoming a pandemic in which more than 500 million people were infected and more than 6 million of them die so far. Most patients with COVID-19 experience mild to severe illness. On the other hand, about 10–15% develop severely illness and 5% become critically ill (Wu & McGoogan, 2020). The world is controlling COVID-19 to some extent owing to the development of vaccines and treatments along with government-level control, including strong containment measures such as wearing masks and social distancing. Fortunately, the high mortality rate is gradually decreasing thanks to large-scale vaccinations as it turns out that various kinds of vaccines prevent COVID-19 infection and prevent serious deterioration even if they become infected (Callaway et al., 2021).

SARS-CoV-2 goes through many mutations over time, and its infectivity tends to increase (Aiyegbusi et al., 2021). After recovering from COVID-19, a considerable number of patients have complained of various symptoms including dry cough, loss of smell, and fatigue. These symptoms, commonly called long COVID, have not yet been specifically defined and there is no effective treatment (Raveendran et al., 2021). Currently, various types of vaccines have been developed to prevent COVID-19 infection and prevent progression to severe diseases. However, there are few studies to find out whether vaccination before COVID-19 helps prevent long COVIDs and relieve

symptoms after COVID-19. In addition, little is known about whether vaccines help improve symptoms as a treatment option for long COVIDs.

Therefore, I investigated whether vaccination before COVID-19 infection reduced the incidence or relieved symptoms of long COVID from studies reported so far. Furthermore, I tried to find out whether post-infectious vaccination also reduced the incidence or relieved symptoms of long COVID.

Methods

Study design

Primary studies related to vaccination against long COVID were searched until Jun 12, 2022 through Google scholar academic search engine and medical search engines such as PubMed, EMBASE, MedRxiv, and Web of Science. The search terms included "COVID-19," "Chronic," "Long," "Post," "Persistent," and "Vaccine." The search parameters included a combination of free text, Medical Subject Headings, and EMTREE terms. In addition, to ensure that all available studies are included, we also scanned the reference list of the original paper to identify additional related articles.

Search strategy and selection criteria

Only studies that satisfy the following inclusion criteria were selected for analysis: study design, randomized clinical trial or cohort study; patients (P), patients who were infected with COVID-19 (test positive or clinically suspected); intervention (I), vaccination for COVID-19; comparator (C), non-vaccination; and outcome (O), prevalence of long COVID or improvement of long COVID symptom. The following papers were excluded because they were judged to be inappropriate for analysis: Review articles, case reports or case-series less than 50 cases, letters to editor, commentaries, laboratory studies. The review process is summarized in Figure 1. The information such as first author, country, study design, study period, population, confirmation methods of COVID-19, vaccine(s), definition of Long COVID, year of publication, publication language was extracted from the database.

Ethical issues

This systematic review does not require ethical approval because only previously published data were included in the review.

Results

A total of 12 studies on the effectiveness of vaccination against long COVID were finally searched in the databases. Of them, 4 studies were conducted in the UK (Antonelli et al., 2022; Arnold et al., 2021; Garber et al., 2020; Ayoubkhani et al., 2021), 4 studies in the US (Wisnivesky et al., 2022; Taquet et al., 2022; Wanga et al., 2021; Simon et al., 2021), 1 study in France (Scherlinger et al., 2021), 1 study in India (Arjun et al., 2022), 1 study in Israel (Kuodi et al., 2021) and 1 international study (Strain et al., 2022). Five studies investigated whether vaccination before infection reduced the incidence or symptoms of long COVID (Kuodi et al., 2021; Wisnivesky et al., 2022; Antonelli et al., 2022; Taquet et al., 2022; Arjun et al., 2022), 6 studies investigated whether post-infectious vaccination relieved the symptoms of long COVID (Arnold et al., 2021; Garber et al., 2020; Ayoubkhani et al., 2021; Strain et al., 2022; Wanga et al., 2021; Scherlinger et al., 2021), and 1 study investigated both (Simon et al., 2021). Table 1 shows the characteristics of each included study.

Effect of the vaccination before COVID-19 infection on long COVID

Of the total 12 studies, 5 studies investigated the incidence and symptomatic change of long COVID after receiving a vaccine prior to COVID-19 infection.

Kuodi et al. evaluated the effect of pre-infectious vaccination on the long-term consequences of COVID-19. Among 951 COVID-19 infected adults who tested positive in RT-PCR for COVID-19, 340 (36%) received one dose of vaccine and 294 (31%) received at least two doses of vaccine. Of them, 636 (67%) had at least one symptom when COVID-19 was diagnosed and 337 (35%) were suspected of having long COVID symptom in the study. When adjusted according to the follow-up period and presence of symptoms, vaccinated participants were 54-83% less likely to report 7 of 10 most commonly reported symptoms than unvaccinated. Furthermore, those who had two doses of vaccine were no more likely to have symptoms than those who were uninfected with COVID-19.

Winsnivesky et al. made a prospective Post-COVID-19 registry to investigate whether receiving a vaccine for COVID-19 affected the symptom changes in long COVID participants. In total, 453 COVID-19 patients were followed up for 6 months since they got vaccinated for COVID-19. Of them, 324 (72%) were vaccinated during the 6 month follow-up. Propensity score-adjusted analyses did not show any significant differences in symptoms such as in anosmia, dyspnea, cough, phlegm, and wheezing between vaccinated and unvaccinated patients ($p>0.05$). They suggested that vaccination did not seem to improve the long COVID symptoms in post-COVID patients.

Antonelli et al. evaluated symptoms of COVID-19 lasting ≥ 28 days in adults testing positive on RT-PCR or antigen test for COVID-19 through app-based survey. Among 1,240,009 COVID Symptom Study app users, two doses vaccinated participants had about a half of symptoms lasting ≥ 28 days than unvaccinated (odds ratio [OR] = 0.51, 95% confidence interval [CI]: 0.32-0.82, p=0.005), whereas one dose vaccinated participants were about as likely to have symptoms lasting ≥28 days than unvaccinated (OR = 1.04, 95% CI: 0.86-1.25, p=0.69). One dose vaccinated participants had similar number of symptoms lasting ≥28 days comparing with unvaccinated (OR = 1.04, 95% CI: 0.86-1.25, p=0.69). Among COVID-19 infected individuals, almost all symptoms developed less frequently in vaccinated than unvaccinated individuals. Furthermore, vaccinated individuals were more likely to be asymptomatic.

Taquet et al. evaluated the incidence of COVID-19 results for 6 months depending on the vaccination status between vaccinated and unvaccinated individuals against COVID-19. A total of 9,479 infected and vaccinated individuals (2,996 with partially vaccinated and 6,957 with fully vaccinated) were matched to the same number of infected and unvaccinated controls in the study. As a result, there was no association between fully vaccinated and unvaccinated individuals that long COVID symptoms lasted for 6 months after infection: 64.9% vs 65.6%, (hazard ratio [HR] = 1.00, 95% CI: 0.95-1.06). However, comparing with unvaccinated, fully vaccinated individuals were less likely to have anosmia (HR = 0.68, 95% CI: 0.55-0.84, p=0.0004), fatigue (HR = 0.86, 95% CI: 0.77-0.96, p=0.005), hair loss (HR = 0.66, 95% CI: 0.54-0.81, p<0.0001), myalgia (HR = 0.70, 95% CI: 0.59-0.84, p<0.0001), and other pain (HR = 0.85, 95% CI: 0.76-0.96, p=0.007).

An Indian study by Arjun et al. showed that in a total of 487 COVID-19 adult participants, 287 participants (58.9%) received two doses of vaccines, 81 (16.6%) received one dose of vaccine, and 119 (25%) were unvaccinated. Overall, 142 (29.2%) of individuals reported long COVID symptoms. Two doses vaccinated individuals were more likely to have long COVID symptoms 4 weeks after infection than unvaccinated individuals (OR = 2.32, 95% CI: 1.17-4.58, p=0.01). Furthermore, two doses vaccinated patients were more serious status than unvaccinated (OR = 5.71, 95% CI: 3.00-10.89, p<0.001). These results were the opposite of those of other studies. Those who received two doses vaccinated were more likely to show long COVID-19 symptoms later.

Effect of the vaccination after COVID-19 infection on long COVID

Six studies have investigated the incidence of long COVID or symptom changes by vaccination after COVID-19 infection.

Arnold et al. investigated a total of 66 unvaccinated patients who were hospitalized for COVID-19 and followed up those who remained unvaccinated or vaccinated. Fifty four participants (82%) experienced long COVID symptoms at 8 months in both groups. At 1 month after vaccination or corresponding time for unvaccinated, vaccinated participants reported improvement of their symptoms more than unvaccinated (23.2% vs 15.4%). In addition, vaccinated participants reported less worsening of their symptoms than unvaccinated (5.6% vs 14.3%). However, there was no difference in their symptoms unchanged between vaccinated and unvaccinated participants (71.1% vs 70.3%). Interestingly, no difference in response was identified between Pfizer and AstraZeneca vaccines.

Gaber et al. investigated 67 healthcare workers with long COVID who had post-infectious vaccination. Among them, 75% had fatigue, 53% had shortness of breath, and 18% had anxiety, respectively. Several weeks after vaccination, 45 subjects (67%) had no change in symptoms while 14 subjects (21%) had improved symptoms. However, 8 subjects (12%) reported worsening of symptoms, especially fatigue.

Ayoubkhani et al. assessed a total of 6,729 participants who reported long COVID symptoms of varying degrees of severity. Of them, 4,747 participants reported activity limitation caused by long COVID at least once during follow-up. The odds of most symptoms decreased after each vaccination. Overall, the odds of suffering from most individual symptoms decreased after the first vaccination. In general, there was an increase between the first and second vaccinations, and most of them turned to a decline or steady after the second vaccination. In particular, the second vaccination decreased odds to report long COVID symptoms ($p=0.03$). There was no significant difference in the type of vaccine.

Strain et al. investigated people from the international long COVID support groups (Long COVIDSOS). As a result, 57% of participants improved their symptoms after vaccination, 25% of participants showed no change in symptoms, and 19% of participants showed worsening symptoms. There were significant individual differences in responses. Compared to the Astrazeneca vaccine, there was a greater improvement in the symptom severity score in Moderna vaccine.

Wanga et al. evaluated the long-term changes in symptoms after vaccination in US adults regardless of whether they were infected with COVID-19 infection. Respondents who received positive test results reported significantly more long-term symptoms than those who received negative test results (65.9% vs. 42.9%; $p<0.05$). Respondents who tested positive were less likely to receive ≥1 dose of COVID-19 vaccine than those who tested negative (28.3% vs. 39.4%). Respondents who tested positive for COVID-19 were more likely to report that the vaccine improved their long-term symptoms than those who tested negative (28.7% versus 15.7%, $p=0.023$).

According to a nationwide online survey by Scherlinger et al., a total of 567 people responsed. Of the 397 vaccinated participants, 255 (64.2%) received one vaccine dose and 142 (35.8%) received 2 vaccine doses. On the other hand, 170 of 567 patients (30%) remained unvaccinated. With regard to the effects of vaccines lasting more than 2 weeks for long COVID symptoms, 72.6% of patients had improved symptoms whilst 63.7% had worsened. Interestingly, the overall frequency of improvement after vaccination showed no significant difference between patients with virologically confirmed and those who were non-virologically confirmed long COVID (20.2% vs. 24.3%, $p = 0.35$). Furthermore, 21.8% of them reported improvement (including anosmia and brain fog), and 31% reported worsening symptoms (including fever/chills, gastro-intestinal symptoms, paraesthesia and arthralgia), respectively. However, there was no difference depending on the type of vaccine used ($p = 0.60$).

Simon et al. examined whether vaccination for COVID-19 before or after infection was related to the clinical course of long COVID. Among 2,392 patients who received first vaccination prior to diagnosis, 382 (15.9%) had any symptoms of long COVID. Of 17,796 patient with post-infection vaccination 5,529 (31.0%) had any symptoms of long COVID. On the contrary, 84,408 (38.2%) had any symptoms of long COVID in 220,460 unvaccinated. As a result, vaccination after infection as well as prior to COVID-19 infection were significantly less likely to have long COVID symptoms. Furthermore, a single dose of any vaccine showed a beneficial effect compared with unvaccinated even if it was administered up to 12 months after infection.

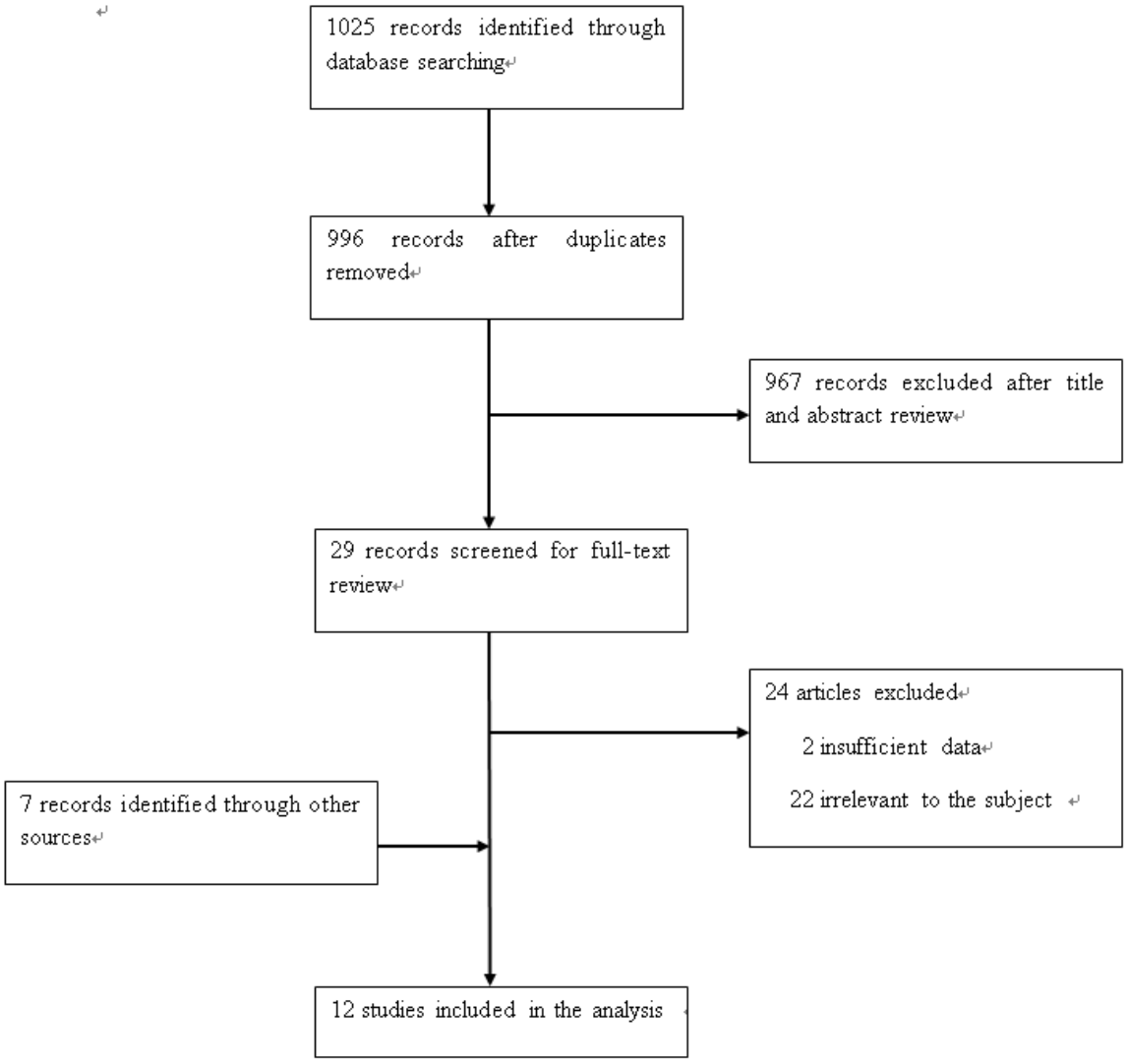

Figure 1. Flowchart of the study selection

A total of 1032 records were searched from the databases. After rigorous review, 12 studies were finally selected for analyses.

Table 1. Study characteristics

Author (year of publication)	Country	Study Design	Period Observed	Population	Confirmation of COVID-19	Sample Size	Vaccine(s)	Definition of Long COVID
Kuodi (2022)	Israel	Cross-sectional, prospective cohort study	Mar to Jun 2021(COVID-19 infection), Jul to Nov 2021 (survey completion)	Adults	RT-PCR	N=951 (317 unvaccinated, 294 fully vaccinated)	NR	Long-term symptoms fully recovered from infection
Wisnivesky (2022)	USA	Prospective cohort study	Jul 2020 to Feb 2021	Adults	Laboratory-documented infection	N=453 (324 vaccinated, 129 unvaccinated)	Pfizer, Moderna Johnson & Johnson	Symptoms to 6 months
Antonelli (2022)	UK	Prospective, nested case-control study	Dec 2020 to July 2021	Adults	RT-PCR or LFAT	N=4,740 (2,370 unvaccinated, 2,370 fully vaccinated)	BNT162b2, ChAdOx1nCoV-19, mRNA-1273	Long duration ≥28 days
Tarquet (2022)	USA	Matched case-control study	Jan to Aug 2021	Any age	RT-PCR	N=18,958 (9479 unvaccinated, 2996 partially vaccinated, 6957 fully vaccinated)	Pfizer, Moderna, Janssen, unspecified	Symptoms in the 6 months after infection
Arjun (2022)	India	Retrospective cohort study	Apr to Sep 2021	Adults	RT-PCR	N=487 (122 unvaccinated, 287 vaccinated [doses NR]	Covaxin (majority)	Symptoms 4 weeks from the date of diagnosis
Arnold (2021)	UK	Prospective cohort study	Apr to May 2020 (COVID-19 hospitalisation), Jan to Feb 2021 (vaccination)	Adult	RT-PCR	n-66 (22 unvaccinated, 44 partially vaccinated)	Pfizer, AstraZeneca	Persistent symptoms
Gaber (2021)	UK	Prospective cohort study	Dec 2020 to Jan 2021	Healthcare workers	NR	N=77 (10 unvaccinated, 67 partially vaccinated)	Pfizer	NR
Ayoubkhani (2021)	UK	Prospective cohort study	Feb to Sep 2021	Adults	RT-PCR and symptoms	N=28,356 (all partially vaccinated, 23,753 fully vaccinated)	mRNA vaccine, adenovirus vector vaccine	Long duration ≥28 days
Simon (2021)	USA	Retrospective cohort study	Jan to Apr 2021	Any age	NAAT or antigen test	N=240,648 (220,460 unvaccinated, 17,796 fully vaccinated)	Pfizer, AstraZeneca, Moderna	Symptoms between 12 and 20 weeks after infection
Strain (2022)	UK	Online survey (LongCovid-SOS)	Mar to Apr 2021	Adults	RT-PCR/serology or suspected COVID-19	N=812 (698 partially vaccinated, 114 fully vaccinated)	AstraZeneca, Pfizer, Moderna	Symptoms lasting ≥12 weeks
Wanga (2021)	USA	Online survey	Apr 2021	Adults	Test positive	N=3,135 (698 test postive, 2,437 test negative)	NR	Symptoms lasting >4 weeks since onset
Scherlinger (2021)	France	Online survey	Nov 2020 to May 2021	Adults	RT-PCR/serology or suspected COVID-19	N=567 (170 unvaccinated, 255 partially vaccinated, 142 fully vaccinated)	Pfizer, Moderna, AstraZeneca, mRNA/vector vaccine combination	Post-acute sequelae (≥28 days)

NR, not reported; LFAT, lateral flow antigen test; NAAT, nucleic acid amplification test

Discussion

This study evaluated the effect of vaccination before and after COVID-19 infection on the course of long COVID. In order to find out whether vaccination before and after COVID-19 significantly reduce long COVID, the effect of the vaccine was divided into before and after COVID-19 infection. As a result, vaccination before COVID-19 infection reduced the occurrence of long COVID and worsening of the symptoms, and post-infectious vaccination also improved the symptoms of long COVID. In particular, there was no significant difference between vaccinated group and unvaccinated group in the incidence and symptom mitigation of long COVID according to the type of vaccine (Pfizer, AstraZeneca, Moderna, etc.).

The novel SARS-CoV-2 has resulted in a global pandemic of COVID-19. SARS-CoV-2 is a positive-sense single-stranded RNA virus. It is one of the seven coronaviruses that can infect humans (Corman et al., 2018). Typical cases of acute COVID-19 include fever, respiratory symptoms, and gastrointestinal problems (Larsen et al., 2020). However, patients can present with a wide range of length and severity. Most patients are asymptomatic, while others require hospitalization and intensive care (Cunningham et al., 2021).

'Long COVID' is a term used to describe the presence of various symptoms, even weeks or months after acquiring SARS-CoV-2 infection with or without the virus (Raveendran et al., 2021). It is also called "post-acute COVID-19 syndrome (PACS)" or "post-acute sequelae of COVID-19 (PASC)" (Proal et al., 2021). It includes both ongoing symptomatic COVID-19 (from 4 to 12 weeks) and post-COVID-19 syndrome (12 weeks or more) (NICE, 2020). In October 2021, the World Health Organization (WHO) defined long COVID as "A condition which occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually three months from the onset of COVID-19 with symptoms that last for at least two months and cannot be explained by an alternative diagnosis.

Common symptoms include not only fatigue, shortness of breath, and cognitive dysfunction but also others involving the musculo-skeletal, cardiac and central nervous systems, which generally have an impact on everyday functioning" (WHO, 2021). Symptoms of long COVID may fluctuate or relapse over time. These symptoms may appear after an initial recovery from an acute COVID-19 episode, or may be persistent symptoms that are not resolved after an initial COVID-19 disease (Salamanna et al., 2021). In this study, most of the studies used different definitions of long COVID, which are also given in Table 1.

The underlying mechanism of the long COVID is not fully elucidated. It could be related to at least one of the following mechanisms: 1) presence of a persistent viral reservoir; 2) the presence of viral fragments stimulating the immune system; or 3) development of an autoimmune response induced by the infection itself (Massey et al., 2021). Risk factors for long COVID have not been fully revealed. So far, increasing age, underlying medical conditions including hypertension, obesity, psychiatric disorders, and immunosuppression have been associated with development of long COVID (Barda et al., 2021). At present, there are no established treatments for Long COVID (Strain et al., 2022).

Various interventions, including mask-wearing, quarantining, and social distancing, have played a significant role in monitoring and regulating the COVID-19 pandemic; nevertheless, vaccination is considered a highly cost-effective intervention to mitigate the pandemic.

Pre-infectious vaccination has been found to be significantly more effective than unvaccinated controls because vaccination promotes the removal of coronavirus remaining in the body or reduces some of the body's immune responses related to the occurrence of long COVID. Recently it is suggested that COVID-19 vaccination might improve patients' symptoms by reducing potential viral reservoirs and/or viral fragments (Massey et al., 2021). A recent systematic review reported that a single dose of vaccines showed about 40–60% effectiveness at preventing any clinical status of COVID-19 and that two doses showed 85% or more effectiveness (Liu et al., 2021). The safety of COVID-19 vaccines is regarded as acceptable for mass vaccination, but long-term monitoring of the safety is required, especially in older population with underlying diseases.

So far, there have been many reports that vaccines are helpful for prevention of COVID-19 infection or serious deterioration. Unfortunately, until now, studies on whether vaccines help prevent and treat long COVID are

rare, and it has not yet been clarified. Therefore, this study revealed that vaccination before or after COVID-19 infection reduced the incidence and relieved symptoms of long COVID. Especially, this study is important in that it was investigated through real world studies on how vaccines affect the progress of long COVID based on before and after COVID-19 infection.

Conclusion

In conclusion, this study elucidated that vaccination not only prevents COVID-19, but also reduces long COVID that occur before and after COVID-19 infection. I hope that this study could be a good guide to encouraging unvaccinated people who are still hesitant to get vaccinated.

Limitations

This study has some limitations. First, different definitions of long COVID were used for each study. For this reason, accurate comparisons between studies could not be made. Second, some studies include cases in which the diagnosis of infection was diagnosed only with the patient's symptoms. Furthermore, in a few studies confirming the effectiveness of the vaccine before infection, some patients who had already been infected were included. Third, the method of collecting information was different, such as collecting necessary data from the hospital's medical records or inputting it by app-based patients themselves. Finally, the types of vaccines inoculated are different for each study, and some studies have not clearly described the types of vaccines inoculated. Therefore, more standardized data collection or well-designed prospective large-scale research is needed.

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References

Aiyegbusi, O. L., Hughes, S. E., Turner, G., Rivera, S. C., McMullan, C., Chandan, J. S., Haroon, S., Price, G., Davies, E. H., Nirantharakumar, K., Sapey, E., Calvert, M. J., & TLC Study Group (2021). Symptoms, complications and management of long COVID: a review. Journal of the Royal Society of Medicine, 114(9), 428–442. https://doi.org/10.1177/01410768211032850

Antonelli, M., Penfold, R. S., Merino, J., Sudre, C. H., Molteni, E., Berry, S., Canas, L. S., Graham, M. S., Klaser, K., Modat, M., Murray, B., Kerfoot, E., Chen, L., Deng, J., Österdahl, M. F., Cheetham, N. J., Drew, D. A., Nguyen, L. H., Pujol, J. C., Hu, C., … Steves, C. J. (2022). Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. The Lancet. Infectious diseases, 22(1), 43–55. https://doi.org/10.1016/S1473-3099(21)00460-6

Arjun, M. C., Singh, A. K., Pal, D., Das, K., Gajjala, A., Venkateshan, M., ... & Subba, S. H. (2022). Prevalence, characteristics, and predictors of Long COVID among diagnosed cases of COVID-19. *medRxiv*.
Arnold, D. T., Milne, A., Samms, E., Stadon, L., Maskell, N. A., & Hamilton, F. W. (2021). Are vaccines safe in patients with Long COVID? A prospective observational study. *MedRxiv*.

Ayoubkhani, D., Bermingham, C., Pouwels, K. B., Glickman, M., Nafilyan, V., Zaccardi, F., ... & Walker, A. S. (2021). Changes in the trajectory of Long Covid symptoms following COVID-19 vaccination: community-based cohort study. *medRxiv*.

Barda, N., Dagan, N., Cohen, C., Hernán, M. A., Lipsitch, M., Kohane, I. S., Reis, B. Y., & Balicer, R. D. (2021). Effectiveness of a third dose of the BNT162b2 mRNA COVID-19 vaccine for preventing severe outcomes in Israel: an observational study. Lancet (London, England), 398(10316), 2093–2100. https://doi.org/10.1016/S0140-6736(21)02249-2

Callaway E. (2021). Fast-spreading COVID variant can elude immune responses. Nature, 589(7843), 500–501. https://doi.org/10.1038/d41586-021-00121-z

Chen, M., Yuan, Y., Zhou, Y., Deng, Z., Zhao, J., Feng, F., Zou, H., & Sun, C. (2021). Safety of SARS-CoV-2 vaccines: a systematic review and meta-analysis of randomized controlled trials. Infectious diseases of poverty, 10(1), 94. https://doi.org/10.1186/s40249-021-00878-5

Corman, V. M., Muth, D., Niemeyer, D., & Drosten, C. (2018). Hosts and Sources of Endemic Human Coronaviruses. Advances in virus research, 100, 163–188. https://doi.org/10.1016/bs.aivir.2018.01.001

COVID-19 rapid guideline: managing the long-term effects of COVID-19. (2020). National Institute for Health and Care Excellence (NICE).

Cunningham, J. W., Vaduganathan, M., Claggett, B. L., Jering, K. S., Bhatt, A. S., Rosenthal, N., & Solomon, S. D. (2020). Clinical Outcomes in Young US Adults Hospitalized With COVID-19. JAMA internal medicine, 181(3), 379–381. Advance online publication. https://doi.org/10.1001/jamainternmed.2020.5313

Gaber, T. A. K., Ashish, A., Unsworth, A., & Martindale, J. (2021). Are mRNA covid 19 vaccines safe in long covid patients? A health care workers perspective. British Journal of Medical Practitioners, 14(1), NA-NA.

Klugar, M., Riad, A., Mohanan, L., & Pokorná, A. (2021). COVID-19 Vaccine Booster Hesitancy (VBH) of Healthcare Workers in Czechia: National Cross-Sectional Study. Vaccines, 9(12), 1437. https://doi.org/10.3390/vaccines9121437

Kuodi, P., Gorelik, Y., Zayyad, H., Wertheim, O., Wiegler, K. B., Abu Jabal, K., Dror, A. A., Nazzal, S., Glikman, D., & Edelstein, M. (2022). Association between BNT162b2 vaccination and reported incidence of post-COVID-19 symptoms: cross-sectional study 2020-21, Israel. NPJ vaccines, 7(1), 101. https://doi.org/10.1038/s41541-022-00526-5

Larsen, J. R., Martin, M. R., Martin, J. D., Kuhn, P., & Hicks, J. B. (2020). Modeling the Onset of Symptoms of COVID-19. Frontiers in public health, 8, 473. https://doi.org/10.3389/fpubh.2020.00473

Ling, Y., Zhong, J., & Luo, J. (2021). Safety and effectiveness of SARS-CoV-2 vaccines: A systematic review and meta-analysis. Journal of medical virology, 93(12), 6486–6495. https://doi.org/10.1002/jmv.27203

Massey, D., Berrent, D., Akrami, A., Assaf, G., Davis, H., Harris, K., ... & Iwasaki, A. (2021). Change in symptoms and immune response in people with post-acute sequelae of SARS-Cov-2 infection (PASC) after SARS-Cov-2 vaccination. *MedRxiv*.

Proal, A. D., & VanElzakker, M. B. (2021). Long COVID or Post-acute Sequelae of COVID-19 (PASC): An Overview of Biological Factors That May Contribute to Persistent Symptoms. Frontiers in microbiology, 12, 698169. https://doi.org/10.3389/fmicb.2021.698169

Raveendran, A. V., Jayadevan, R., & Sashidharan, S. (2021). Long COVID: An overview. Diabetes & metabolic syndrome, 15(3), 869–875. https://doi.org/10.1016/j.dsx.2021.04.007

Riad, A., Hocková, B., Kantorová, L., Slávik, R., Spurná, L., Stebel, A., Havriľak, M., & Klugar, M. (2021). Side Effects of mRNA-Based COVID-19 Vaccine: Nationwide Phase IV Study among Healthcare Workers in Slovakia. Pharmaceuticals (Basel, Switzerland), 14(9), 873. https://doi.org/10.3390/ph14090873

Salamanna, F., Veronesi, F., Martini, L., Landini, M. P., & Fini, M. (2021). Post-COVID-19 Syndrome: The Persistent Symptoms at the Post-viral Stage of the Disease. A Systematic Review of the Current Data. Frontiers in medicine, 8, 653516. https://doi.org/10.3389/fmed.2021.653516

Scherlinger, M., Pijnenburg, L., Chatelus, E., Arnaud, L., Gottenberg, J. E., Sibilia, J., & Felten, R. (2021). Effect of SARS-CoV-2 Vaccination on Symptoms from Post-Acute Sequelae of COVID-19: Results from the Nationwide VAXILONG Study. Vaccines, 10(1), 46. https://doi.org/10.3390/vaccines10010046

Simon, M. A., Luginbuhl, R. D., & Parker, R. (2021). Reduced Incidence of Long-COVID Symptoms Related to Administration of COVID-19 Vaccines Both Before COVID-19 Diagnosis and Up to 12 Weeks After. *medRxiv*.

Strain, W. D., Sherwood, O., Banerjee, A., Van der Togt, V., Hishmeh, L., & Rossman, J. (2022). The Impact of COVID Vaccination on Symptoms of Long COVID: An International Survey of People with Lived Experience of Long COVID. Vaccines, 10(5), 652. https://doi.org/10.3390/vaccines10050652

Taquet, M., Dercon, Q., & Harrison, P. J. (2022). Six-month sequelae of post-vaccination SARS-CoV-2 infection: A retrospective cohort study of 10,024 breakthrough infections. Brain, behavior, and immunity, 103, 154–162. https://doi.org/10.1016/j.bbi.2022.04.013

Wanga, V., Chevinsky, J. R., Dimitrov, L. V., Gerdes, M. E., Whitfield, G. P., Bonacci, R. A., Nji, M., Hernandez-Romieu, A. C., Rogers-Brown, J. S., McLeod, T., Rushmore, J., Lutfy, C., Bushman, D., Koumans, E., Saydah, S., Goodman, A. B., Coleman King, S. M., Jackson, B. R., & Cope, J. R. (2021). Long-Term Symptoms Among Adults Tested for SARS-CoV-2 - United States, January 2020-April 2021. MMWR. Morbidity and mortality weekly report, 70(36), 1235–1241. https://doi.org/10.15585/mmwr.mm7036a1

Wisnivesky, J. P., Govindarajulu, U., Bagiella, E., Goswami, R., Kale, M., Campbell, K. N., Meliambro, K., Chen, Z., Aberg, J. A., & Lin, J. J. (2022). Association of Vaccination with the Persistence of Post-COVID Symptoms. Journal of general internal medicine, 37(7), 1748–1753. https://doi.org/10.1007/s11606-022-07465-w

Soriano, J. B., Murthy, S., Marshall, J. C., Relan, P., Diaz, J. V., & WHO Clinical Case Definition Working Group on Post-COVID-19 Condition (2022). A clinical case definition of post-COVID-19 condition by a Delphi consensus. The Lancet. Infectious diseases, 22(4), e102–e107. https://doi.org/10.1016/S1473-3099(21)00703-9

Wu, Z., & McGoogan, J. M. (2020). Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA, 323(13), 1239–1242. https://doi.org/10.1001/jama.2020.2648