



Original Article

Frailty Progression in Older Adults during the Start Phase of Vaccination Programs against COVID-19

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SUMMARY

Background: No studies have so far explored differences in frailty between groups of individuals who are vaccinated/unvaccinated against COVID-19. Therefore, this study aimed to investigate frailty progression in community-dwelling individuals requiring care/support who were using outpatient rehabilitation services during the start phase of vaccination programs against COVID-19.

Methods: A longitudinal survey using the Frailty Screening Index was administered in April 2020, September 2020, and June 2021 to 74 older adults (43 males, 31 females; age, 78.2 ± 7.2 ; mean \pm standard deviation) requiring long-term care/support and using outpatient rehabilitation services. Participants were divided into the vaccinated (those who had received COVID-19 vaccinations; 41 participants) and unvaccinated (those who had not been vaccinated; 33 participants) groups. The Frailty Screening Index and frailty rating (robust, pre-frailty/frailty) at each of the three periods were analyzed using the Cochran's Q test. The resulting items and ratings with significant differences underwent post-hoc testing with the Bonferroni correction.

Results: Concerning the frailty rating (robust, pre-frailty/frailty), pre-frailty/frailty increased significantly only in the unvaccinated group. Its post hoc tests showed that pre-frailty/frailty increased significantly from April 2020 to June 2021 and from September 2020 to June 2021.

Conclusions: We find a difference in frailty progression between groups of vaccinated and unvaccinated community-dwelling older adults requiring care/support who were using outpatient rehabilitation services at the beginning of coronavirus vaccination programs during the COVID-19 pandemic.

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1. Introduction

Coronavirus 2019 (COVID-19) has been spreading worldwide since December 2019 and remains uncontrolled. Japan is currently experiencing a marked increase in cases, surpassing 20,000 infections daily, due to the fifth wave of the virus.¹ The pandemic has forced citizens to refrain from daily activities and change their way of life. Previous studies have shown that due to COVID-19, self-imposed precautions among older adults seriously affect their physical and mental functions.^{2–7} In our first study, we found that restrictions on activities intended to prevent COVID-19 among elderly individuals who have disabilities and require support or care may affect frailty.⁸ Rates of COVID-19 infection, risk of severe cases, and mortality rates are extremely high among older adults, and meta-analyses of COVID-19 patients have shown that frailty is an important predictor of mortality and delirium.^{9–12} Thus, evaluating, preventing, and treating frailty is essential during the COVID-19 pandemic.

Vaccination is currently recommended worldwide to control the COVID-19 pandemic.¹¹ Japan began priority vaccination of medical personnel followed by people ≥ 65 years old in February 2021.¹³ COVID-19 vaccines are highly effective,^{14,15} and several studies have reported medical associations with COVID-19 vaccination, including a decrease in the number of cases, hospitalization rates, and severe cases.^{16–18} Nonetheless, there have been no studies worldwide that explored the progression of frailty in older adults during the start phase of coronavirus vaccination programs. Furthermore, vaccination with COVID-19 is effective in improving mental health in various people.^{19–21} In addition, vaccinated individuals are expected to benefit from resuming previous activities before the pandemic and continue domestic travel.²² It has also been suggested that a vaccination campaign can be an opportunity to return to normal life.²³ We hypothesized that vaccination would prevent infection and reduce severe cases, leading to a return to ordinary life.

Therefore, this study aimed to investigate changes in frailty status in vaccinated and unvaccinated community-dwelling older adults requiring support or care who had no history of COVID-19 infection and were using outpatient rehabilitation services at the beginning of vaccination programs against COVID-19.

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2. Material and methods

2.1. Participants

Participants were members of the dataset of individuals using outpatient rehabilitation services in northern Tochigi Prefecture from our first study.⁸ The outpatient rehabilitation center provides rehabilitation and pick-up and drop-off services based on the long-term care insurance system. Participants can also receive meal and hygiene services depending on their level of care needs.

The study was commenced in April 2020 for all registrants in a facility, followed by the exclusion of those who experienced difficulty in measuring grip strength, walking speed and undergoing interviews for frailty evaluations (Figure 1). Finally, 74 participants were included (43 males, 31 females; age, 78.2 ± 7.2 years; mean \pm standard deviation; Figure 1). The follow-up survey after the vaccination period excluded six individuals < 65 years old (because priority vaccinations were administered to those ≥ 65 years old), three who were hospitalized, two who had died, one taking a long-term break from outpatient services to use home care due to a bone fracture, and five who had difficulty hearing over the phone. None of our participants had a history of COVID-19 at the beginning of the study or was infected during the study period.

All participants were given a written explanation of the eva-

luation, provided written informed consent, and consented to the study. This study was approved by the International University of Health and Welfare Institutional Review Board (Approval No.: 17-lo-189-7) and was conducted in accordance with the guidelines proposed by the Declaration of Helsinki.

2.2. Evaluation of frailty

In our first study, we conducted frailty evaluations in April and September 2020.⁸ This was supplemented in the present study with a follow-up survey conducted in June 2021. Data were collected as previously described in Hirose and Sawaya study.⁸ Specifically, the Frailty Screening Index asks the following questions: for weight loss, "Have you lost 2 kg or more in the past 6 months?" (Yes = 1 point); for walking speed decline, "Do you think you walk slower than before?" (Yes = 1 point); for exercise, "Do you go for a walk for your health at least once a week?" (No = 1 point); for memory, "Can you recall what happened 5 minutes ago?" (No = 1 point); and for feeling fatigued, "In the last 2 weeks, have you felt tired without a reason?" (Yes = 1 point). The scores were defined as follows: ≥ 3 , frailty; 1 or 2, pre-frailty; and 0, robust.²⁴

We referenced baseline (April 2020) medical chart information for age, height, weight, long-term care level, body mass index, living alone, medical conditions (cerebrovascular disease, hypertension, orthopedic disease, cancer, and diabetes), and grip strength and walking

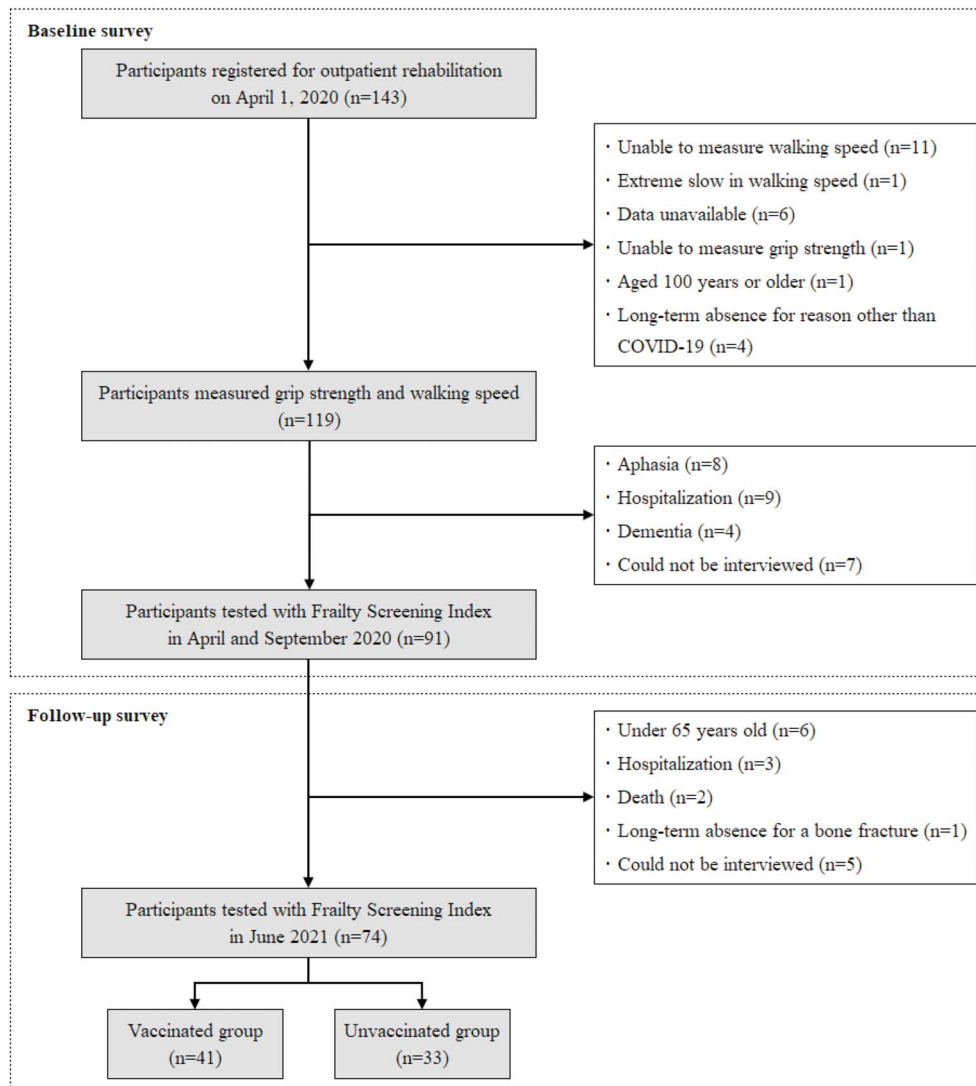


Figure 1. Flowchart of research participants.

speed as measures of physical function. Grip strength and walking speed were measured in accordance with previous studies.^{8,25,26}

2.3. The vaccinated and unvaccinated groups

Participants were classified into two groups as follows: those who had been vaccinated against COVID-19 (vaccinated group) and those who had not been vaccinated against COVID-19 (unvaccinated group). In the region where this study was conducted, voluntary vaccination began with community-dwelling adults ≥ 65 years old on May 9, 2021. Therefore, a benchmark for the start of the survey was determined before the third Frailty Screening Index was performed on all participants. In total, 62 patients who continued to use outpatient rehabilitation services were asked whether they had been vaccinated, and the survey was set to start when $> 50\%$ responded that they had received at least one vaccine dose. The vaccinated group surpassed 50% in June 2021, at which point we began our third frailty survey using the Frailty Screening Index administered face-to-face or over the phone. The survey of the vaccinated group was administered at least 2 weeks after vaccination (16.9 ± 3.7 ; mean number of days \pm standard deviation), considering the question “In the last 2 weeks, have you felt tired without a reason?” as vaccination side effects include localized reactions of pain and generalized reactions of fever, fatigue, and headache.^{14,15,27} The number of participants was 41 in the vaccinated group and 33 in the unvaccinated group. Pfizer vaccine was administered to 40 participants and Moderna vaccine to one participant. The reasons for non-vaccination in the unvaccinated group were difficulty booking a vaccination appointment (15 participants), anxiety (12 participants), illness (one participant), belief (two participants), and others (three participants).

2.4. Statistical analysis

Basic attributes at baseline were compared between the two groups using the unpaired *t*-test for age, height, weight, body mass index, grip strength, and normal walking speed; the χ^2 test for sex, living alone, and medical conditions; the Wilcoxon rank-sum test for the level of care; and Fisher’s exact test for frailty rating. The level of care was treated as a seven-category ordinal scale.²⁸ Next, to compare longitudinal changes in frailty in the vaccinated and unvaccinated groups, each item of the Frailty Screening Index and frailty rating (robust, pre-frailty/frailty) at each of the three time periods (April 2020, September 2020, and June 2021) were analyzed using the Cochran’s Q test. Items found to have a significant difference were subsequently subjected to post hoc testing using the Bonferroni adjustment. IBM SPSS Statistics V25.0 was used for all statistical analyses, with a statistical significance level of 5%.

3. Results

Figure 1 shows the flowchart of the participants. The basic attributes for each group as of April 2020 are listed in Table 1. No significant differences were found in any of the items at baseline. Tables 2 and 3 show the Frailty Screening Index results by time period (April 2020, September 2020, and June 2021) for the vaccinated and unvaccinated groups. Concerning frailty rating, pre-frailty/frailty ratings increased significantly only in the unvaccinated group. In its post hoc testing, pre-frailty/frailty ratings increased significantly from April 2020 to June 2021 and from September 2020 to June 2021. Response to the questionnaire items in both groups showed the same trends; over time, both were more likely to answer “no” to the ex-

ercise-related question, “Do you go for a walk for your health at least once a week?” and to the memory-related question, “Can you recall what happened 5 minutes ago?” In post hoc testing, participants in both groups were significantly more likely to answer “no” to the exercise-related question, “Do you go for a walk for your health at least once a week?” in June 2021 compared to September 2020. No severe side effects of the vaccine were observed in the vaccinated group.

4. Discussion

The progression of frailty at the beginning of coronavirus vaccination programs can only be studied accurately during a vaccination campaign in the presence of both vaccinated and unvaccinated individuals. To our knowledge, this is the first such study to be conducted globally. In general, collecting accurate information about vaccination status and vaccination dates in a large-scale survey of older adults is not feasible. Therefore, we focused on a single outpatient rehabilitation center to collect accurate information in this study. Moreover, we analyzed longitudinal changes in the vaccinated and unvaccinated groups using frailty surveys at three time points. Our findings showed a significant increase in pre-frailty/frailty ratings only in the unvaccinated group from April 2020 to June 2021 and from September 2020 to June 2021, suggesting there were differences in frailty progression between groups during the early vaccination campaign, despite no differences in frailty status, physical function, family structure, morbidity, and care level at baseline.

There was a decline in physical activity and cognition in the Frailty Screening Index questionnaire in the unvaccinated group

Table 1
Basic attributes of the participants at baseline.

	Vaccinated group (n = 41)	Unvaccinated group (n = 33)	p value
Age (years)	78.4 \pm 6.3	77.9 \pm 8.3	0.753
Number by females	18 (44)	13 (39)	0.696
Height (cm)	159.2 \pm 8.2	159.2 \pm 9.1	0.995
Weight (kg)	57.7 \pm 11.1	57.2 \pm 10.2	0.844
Body mass index (kg/m ²)	22.7 \pm 3.7	22.6 \pm 3.7	0.889
Grip strength (kg) ^a	22.7 \pm 7.6	23.0 \pm 9.1	0.895
Normal walking speed (m/s)	0.64 \pm 0.4	0.71 \pm 0.3	0.358
Living alone	2 (5)	3 (9)	0.651
Morbidity			
Cerebrovascular disease	20 (49)	16 (48)	0.980
Hypertension	19 (46)	14 (42)	0.736
Orthopedic disease	18 (44)	17 (52)	0.514
Cancer	9 (22)	2 (6)	0.098
Diabetes mellitus	7 (17)	8 (24)	0.446
Frailty screening index			0.946
Robust	17 (41)	15 (45)	
Pre-frailty	19 (46)	14 (42)	
Frailty	5 (12)	4 (12)	
Long-term care level			0.679
Needs support 1	10 (24)	10 (30)	
Needs support 2	8 (20)	5 (15)	
Needs care 1	10 (24)	10 (30)	
Needs care 2	10 (24)	4 (12)	
Needs care 3	2 (5)	3 (9)	
Needs care 4	1 (2)	1 (3)	
Needs care 5	0	0	

Data are presented in average value \pm standard deviation or N (%).

^a: Measurements were taken twice on both the left and right sides, with the maximum values of the right and left sides having been used as the representative values.

Table 2
Comparison of Frailty Screening Index for the vaccinated group by time period.

Item	Questions	Answer		April 2020 Frailty Screening Index	September 2020 Frailty Screening Index	June 2021 Frailty Screening Index	p value	Multiple comparison test
Weight loss	Have you lost 2 kg or more in the past 6 months?	No	0	35 (85)	30 (73)	34 (83)	0.199	
		Yes	1	6 (15)	11 (27)	7 (17)		
Low physical function	Do you think you walk slower than before?	No	0	25 (61)	24 (59)	24 (59)	0.931	
		Yes	1	16 (39)	17 (41)	17 (41)		
Low physical activity	Do you go for a walk for your health at least once a week?	Yes	0	33 (80)	38 (93)	29 (71)	0.017*	**
		No	1	8 (20)	3 (7)	12 (29)		
Cognition	Can you recall what happened 5 minutes ago?	Yes	0	38 (93)	37 (90)	33 (80)	0.050*	
		No	1	3 (7)	4 (10)	8 (20)		
Exhaustion	In the last 2 weeks, have you felt tired without a reason?	No	0	32 (78)	32 (78)	27 (66)	0.103	
		Yes	1	9 (22)	9 (22)	14 (34)		
Robust				17 (41)	16 (39)	11 (27)	0.109	
Pre-frailty/frailty				24 (59)	25 (61)	30 (73)		

Values are expressed as N (%).

*: Significant p value set at 0.05.

** : Significant difference between September 2020 and June 2021.

Multiple comparison test was performed using Bonferroni adjustment.

Table 3
Comparison of Frailty Screening Index for the unvaccinated group by time period.

Item	Questions	Answer		April 2020 Frailty Screening Index	September 2020 Frailty Screening Index	June 2021 Frailty Screening Index	p value	Multiple comparison test
Weight loss	Have you lost 2 kg or more in the past 6 months?	No	0	25 (76)	28 (85)	25 (76)	0.526	
		Yes	1	8 (24)	5 (15)	8 (24)		
Low physical function	Do you think you walk slower than before?	No	0	22 (67)	22 (67)	16 (48)	0.120	
		Yes	1	11 (33)	11 (33)	17 (52)		
Low physical activity	Do you go for a walk for your health at least once a week?	Yes	0	29 (88)	32 (97)	24 (73)	0.012*	***
		No	1	4 (12)	1 (3)	9 (27)		
Cognition	Can you recall what happened 5 minutes ago?	Yes	0	33 (100)	33 (100)	30 (91)	0.050*	
		No	1	0 (0)	0 (0)	3 (9)		
Exhaustion	In the last 2 weeks, have you felt tired without a reason?	No	0	27 (82)	26 (79)	23 (70)	0.236	
		Yes	1	6 (18)	7 (21)	10 (30)		
Robust				15 (45)	15 (45)	6 (18)	0.006*	**, ***
Pre-frailty/frailty				18 (55)	18 (55)	27 (82)		

Values are expressed as N (%).

*: Significant p value set at 0.05.

** : Significant difference between April 2020 and June 2021. ***: Significant difference between September 2020 and June 2021.

Multiple comparison test was performed using Bonferroni adjustment.

showing a progression of frailty status. In a coronavirus pandemic, it is only natural that more people will refrain from engaging in activities to avoid infection regardless of their physical condition. In addition, it is uncertain whether the question, "Do you go for a walk for your health at least once a week?" holds the same relevance during a pandemic as under normal circumstances. Therefore, it is speculated that "cognitive decline" may be a key factor for the frailty progression. Some reports supported the result of this study regarding cognitive decline during the COVID-19 pandemic.^{29–31} However, further study will be needed to verify which frailty items were affected by vaccination because of the multifaceted factors involved in frailty.

According to previous studies on vaccination, the desired normalization against the COVID-19 pandemic is supposed to be accomplished by vaccines.³² Individuals can participate in many of the activities that they performed before the pandemic.²² COVID-19 vaccination has been reported to alleviate psychological distress and provide mental health benefits.³³ Moreover, it has been suggested that vaccination helps not only the mental health of the patient but also other people's mental health.³³ A cutting-edge review focusing on the correlation between frailty and immunity in the older populations found that a well-functioning immune sys-

tem can prevent frailty, and vice versa, demonstrating that following a preventative vaccination not only prevents frailty but also maintains immune homeostasis.³⁴ The widespread use of COVID-19 vaccines can lead to a decrease in disease risk and an increase in social and economic activities.²⁰ Thus, vaccination may have had a positive effect. On the other hand, this study suggests that it is possible that the vaccinated group was originally more active and motivated to go out, which is why participants in this group received their vaccine early during the vaccination campaign. Additional research that takes social backgrounds into account is needed to corroborate this assumption.

This study has some limitations. First, this was a single-center longitudinal study, and the number of participants was small. Second, although several previous studies have shown that vaccination is associated with mental health benefits during the COVID-19 pandemic, we could not conduct a psychological assessment in this study. In addition, the participants were not interviewed about their original activity levels and willingness to go out. In a further longitudinal study, we will assess Geriatric Depression Scale scores and social background factors to further investigate differences between groups. Third, similar to previous research, there are various reasons one might choose to receive or refuse the vaccine.³⁵ Fourth, al-

though pre-frailty/frailty ratings increased in the unvaccinated group, rates of frailty could increase with age, even in the absence of the pandemic.^{36–38} Despite these limitations, our results could hold great significance for public health and policy.

5. Conclusions

Our findings reveal a difference in frailty progression between a vaccinated and an unvaccinated group of community-dwelling older adults requiring care/support who used outpatient rehabilitation services during the start phase of vaccination programs against COVID-19.

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Declarations of interest

The authors declare no conflict of interest.

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