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Effect of COVID-19 inpatients with cognitive decline on discharge after the quarantine period: A retrospective cohort study

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Abstract

Background: A new SARS-CoV-2 variant, Omicron, was reported on November 14, 2021, and it altered the COVID-19 epidemic with a different peak timing by region in Japan. Residents in the Hiroshima prefecture, especially the vulnerable elderly, were threatened by this wave in advance of many other prefectures. We evaluated the effect of cognitive decline on discharge extension after the quarantine period.

Methods: Participants of this retrospective cohort study were patients who were admitted to the care unit for COVID-19 treatment at Hiroshima University Hospital between January 1, 2022, and March 1, 2022 (60 days). Our primary outcome was the extended length of stay (LOS) in the hospital after the quarantine period (10 days after onset). A negative binomial regression analysis was performed to assess the extended LOS of patients with cognitive decline, adjusting for age classification, gender, and severity of COVID-19.

Results: The total number of participants was 74. Per the level of cognitive function, there were 56 independent participants, 5 mild declines, and 13 severe declines. For the negative binomial regression analysis, the exponentiated coefficient of mild cognitive decline was 3.05 (95% confidential interval [CI]: 1.43–6.49) and that of severe cognitive decline was 1.95 (95% CI: 1.09–3.53).

Conclusions: Mild cognitive decline and severe cognitive decline elevated the risk of extended LOS after COVID-19 patients finished the quarantine period.

KEYWORDS

cognitive decline, COVID-19, Omicron variant, quarantine period

1 | INTRODUCTION

On November 14, 2021, the appearance of a new SARS-CoV-2 variant (Omicron) was reported from South Africa.[1] Because of the number of mutations, an increase in transmissibility and a change in clinical presentations, the World Health Organization designated Omicron as a variant of concern.[2] The quite rapid spread of Omicron caused an increase in COVID-19 patients around the world. The total number of COVID-19 patients at the end of November 2021 in the world was 290,377,647, which then increased to 444,101,547 at the end of February 2022.[3] The first case in Japan was detected in an asymptomatic patient on November 30, 2021.[4]

The COVID-19 epidemic varied from region to region in Japan. Hiroshima prefecture was threatened by the epidemic in advance of many other prefectures. After a COVID-19 outbreak caused by Omicron at the Marine Corps Air Station Iwakuni in December 2021, a reemergence of the epidemic started in January 2022 in Hiroshima prefecture, which adjoins Iwakuni city.[5] The spread of Omicron was associated with quite sharp increases in reported infections of COVID-19.[6] Semi-emergency coronavirus measures began in Hiroshima prefecture along with Okinawa prefecture and Yamaguchi prefecture on January 9, 2022, which was the first designation against the wave that Omicron would cause in Japan.[7] After a decrease in the epidemic, the designation finished on March 6, 2022.[8]

The risk of death and exacerbation caused by COVID-19 increases with increasing age.[9] Moreover, comorbidities that generally increase with aging also elevated risk.[10,11] The spread of the epidemic would affect older people who had various comorbidities and contexts. When such persons were affected by COVID-19, more elderly needed hospitalization than young people.[12] During the epidemic, to provide hospitalization for new patients, the length of hospital stay should be shortened with a recovery of the patient condition. In Japan, however, older age, an increase in comorbidities, and complicated contexts are related to prolonged stays.[13,14] Particularly, because patients with a decline in cognitive function often need physical and social support from their family or care facility, such provision of services results in an extension of discharge.[15]

In this study, we investigated the effect of cognitive decline on discharge extension of COVID-19 patients after the quarantine period during epidemic outbreaks caused by Omicron. We examined a bottleneck factor for an increase of patients who could not be hospitalized and who stayed at home after being infected by COVID-19. Based on the results, we discuss measures to prepare for future epidemics and disaster outbreaks that will increase medical needs.

2 | METHODS

2.1 | Study design

This study is a retrospective cohort study.

2.2 | Setting

The study setting is a 28-bed care unit to treat COVID-19 patients at Hiroshima Univesiry Hospital. The most severe level which can be admitted to this unit was "severe Illness" as defined by the National Institutes of Health (NIH).[16]

2.3 | Data source

We extracted the dataset from the electronic medical record system of Hiroshima University Hospital. There was no missing data in this study.

2.4 | Participants

The participants were all inpatients who were admitted to a special 28-bed care unit for COVID-19 treatment at Hiroshima University Hospital between January 1, 2022, and March 1, 2022 (60 days). The attending physicians belonged to the Department of General Internal Medicine or the Department of Infectious Diseases. The total number of physicians was 17.

We excluded patients who were moved to other care units to treat other diseases after the quarantine period. In Japan, the quarantine period was 10 days from the onset of COVID-19 symptoms except for "critical illness" as defined by NIH. Some patients were discharged from the hospital and stayed at their homes or hotels after the hospitalization during the quarantine period because their severity of COVID-19 was low. The severity of some patients was exacerbated to Critical illness within 10 days, and they were moved to intensive care units in other hospitals. We also excluded them from the study, because we could not follow their discharges. In addition, patients who died during the hospitalization were excluded. Sample size calculation was not conducted because this study was an all cases analysis.

2.5 | Outcome

In Japan, the quarantine period is 10 days from the onset of COVID-19 symptoms, and as such, the outcome of this study was the extended Length of Stay in hospital (LOS) from the end of the quarantine period. The day the quarantine period ended was defined as day 1.

2.6 | Cognitive function

We adopted the Dementia Symptomatology Assessment (DSA) utilized in the Long-Term Care Insurance system as the evaluation tool for cognitive function. At Hiroshima University Hospital, the cognitive function of all patients was evaluated upon admission by nurses, using DSA. DSA is a standardized measure to assess cognitive function in Japan.[17,18] The level of dementia scale correlates with the Mini-Mental State Examination and a level 1 in DSA is equivalent to 0.5 points on the Clinical Dementia Rating.[19,20] DSA had high inter-rater reliability.[21] Confirming the non-linear relationship between extended LOS and the level of DSA, we divided participants into three groups: independent, mild, and severe.[18] The DSA level of the independent group was 1, that of the mild group was 2 and 3, and that of the severe group was 4 and 5.

2.7 | Other variables

We extracted age classification, gender, comorbidity (chronic pulmonary disease, obesity, cardiovascular disease, diabetes, hypertension, and malignant tumor), the severity of COVID-19 on admission defined by NIH, and the date of onset, admission, and discharge from the electronic medical record system.[9,18] For patients whose discharge was postponed, we determined the reason from the electronic medical record.

2.8 | Ethics statement

Ethical approval was granted by the Ethics Committee for Epidemiological Research at Hiroshima University (Ref. no. E-2480). This study was conducted in accordance with the principles of the Helsinki Declaration. Because this was a retrospective cohort study, we did not obtain consent from the patients and have posted information about this research on the Hiroshima University website with the contact address for the rejection of participation. We also described that patient anonymity was ensured on the website.

2.9 | Statistical analysis

2.9.1 | Main analysis

We showed the baseline characteristics of the participants. We used chi-squared tests for the discrete variables.

We calculated the number of inpatients by day, based on the date of admission and discharge. Moreover, we showed the number stratified by the severity of COVID-19 and the level of cognitive function.

Because the distribution of the outcome variable, extended LOS, was skewed to the right, we adopted a negative binomial regression analysis (Figure S1). The adjusted variables were cognitive function, age classification, gender, and severity of COVID-19.

Statistical significance was set at $p < 0.05$.

2.9.2 | Sensitivity analysis

We used propensity score adjustment to control for covariates. The propensity score was constructed with the use of multivariable logistic regression, with age, gender, comorbidity (chronic pulmonary disease, obesity, cardiovascular disease, diabetes, hypertension, and malignant tumor), and the severity of COVID-19 as the independent variables. Because we need the conversion of "cognitive function," which was the categorical variable, into a binary outcome to adopt the outcome variable in the logistic regression, we divided this variable into two groups: the independent group (DSA: 1) and the cognitive declined group (DSA: 2–5). To confirm the robustness of the result, we conducted a negative binomial regression analysis with propensity score adjustment for all participants (Sensitivity analysis 1) and for participants who were older than 65 years old (Sensitivity analysis 2).

We conducted Sensitivity analysis 3 to confirm the robustness of the result. In Sensitivity analysis 3, we added the excluded patients who died and patients who were transferred to other care units. Because patients that were moved to the ICU were transferred to another hospital, it was not possible to follow the LOS. The extended LOS of patients who died were also defined as the day from the end of the quarantine period to the day when they died and were discharged from the hospital.

We performed all statistical analyses using STATA/MP version 16 (StataCorp, 2019).

3 | RESULTS

Five patients were excluded from the participants. Two of them died and three of them were transferred to other care units. We showed participant characteristics (Table 1). The total number of participants was 74. Per the level of cognitive decline, there were 56 independent, 5 mild, and 13 severe participants. All participants whose cognitive function declined were 65 years old and over ($p < 0.001$). There was no significant difference in gender and comorbidities. The severity of COVID-19 was significantly different among the groups of cognitive function ($p = 0.003$). The median (interquartile range) of extended LOS was 1 day[1-3] in the independent group, 5 days[5,6] days in the mild group, and 3 days[1-6] in the severe group, respectively ($p = 0.001$). We also showed participant characteristics of Sensitivity analysis 3 (Table S2).

Figure 1 shows the number of total inpatients by severity on admission and day. During the first 8 days, a rapid increase in patients was observed. On day 9, participants with severe illness were admitted. Day 30 had the highest number of inpatients and patients with serious illness. From day 8 to day 51, the number of patients remained above 15.

Table 2 shows reasons for the extended discharge of participants. The most frequent reason was the coordination of transfer to another place ($N = 17$, 48.6%).

Figure 2 shows the number of total inpatients by cognitive function and day. Patients with severe cognitive decline were initially admitted on day 7. In the latter half of the observation period, patients with mild cognitive decline increased relatively. As with the case severity of COVID-19, day 30 had the highest number of inpatients and patients with cognitive decline.

Table 3 shows the results of negative binomial regression analysis on the extended LOS. The exponentiated coefficient of mild cognitive decline was 3.05 (95% Confidential Interval [CI]: 1.43–6.49). The exponentiated coefficient of severe cognitive decline was 1.95 (95%CI: 1.09–3.53).

Table S2 shows the results of sensitivity analysis. In the propensity score-adjusted model, cognitive decline was statistically

TABLE 1 Participant Characteristics

		Cognitive function, *n*		
		Independent	Mild	Severe
Total number	56	5	13	
Elderly ≥65 years old	23	5	13	$p < 0.001$*
(%)	(41.1)	(100.0)	(100.0)	
Female, *n*	25	4	8	$p = 0.21$*
(%)	(44.6)	(80.0)	(61.5)	
Chronic pulmonary disease	9	0	1	$p = 0.48$*
(%)	(16.1)	(0)	(7.7)	
Obesity	7	0	0	$p = 0.29$*
(%)	(12.5)	(0)	(0)	
Cardiovascular disease	6	2	3	$p = 0.14$*
(%)	(10.7)	(40.0)	(23.1)	
Diabetes	15	2	2	$p = 0.52$*
(%)	(26.8)	(40.0)	(15.4)	
Hypertension	22	3	6	$p = 0.63$*
(%)	(39.3)	(60.0)	(46.2)	
Malignant tumor	15	3	4	$p = 0.30$*
(%)	(26.8)	(60.0)	(30.8)	
Severity of COVID-19				
Moderate illness	11	1	2	$p = 0.003$*
(%)	(19.6)	(20.0)	(15.4)	
Severe illness	11	4	8	
(%)	(19.6)	(80.0)	(61.5)	
Extended LOS, median	1	5	3	$p = 0.001$**
(IQR)	1–3	5–6	1–6	

Note: **p* values were the results of a chi-squared test. ***p* value was the result of a Kruskal–Wallis equality-of-populations rank test.

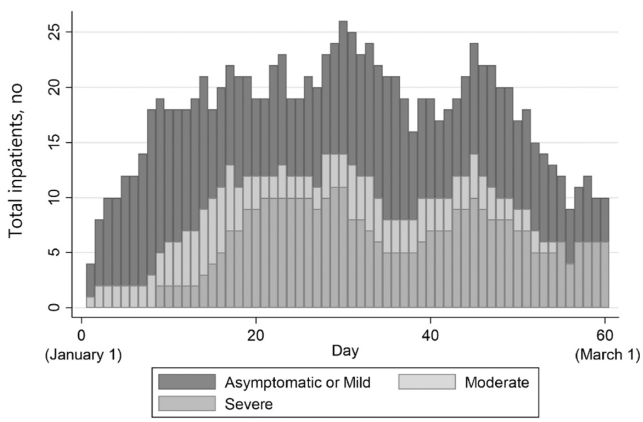

FIGURE 1 Total participants by COVID-19 severity. Number of participants by day and severity of the COVID-19 during the observation period

TABLE 2 Reasons for the extended discharge of participants

	N	(%)
Coordination of transfer	17	(48.6)
Hospital	9	(25.7)
Care facility	4	(11.4)
Private home	4	(11.4)
Continuation of COVID-19 treatment	14	(40)
Complications of aspiration pneumonia	2	(5.7)
Others	2	(5.7)
Total	35	(100)

significant with extended LOS (Sensitivity analysis 1: $p = 0.004$, Sensitivity analysis 2: $p = 0.009$). Sensitivity analysis 3 also showed that cognitive decline was statistically significant with extended LOS (mild cognitive decline: $p = 0.002$, severe cognitive decline: $p = 0.01$).

4 | DISCUSSION

The mild and severe cognitive decline of COVID-19 inpatients was related to discharge extension during the Omicron outbreak. In addition, as the number of inpatients increased, the number of severe patients and patients with cognitive decline increased belatedly. Both

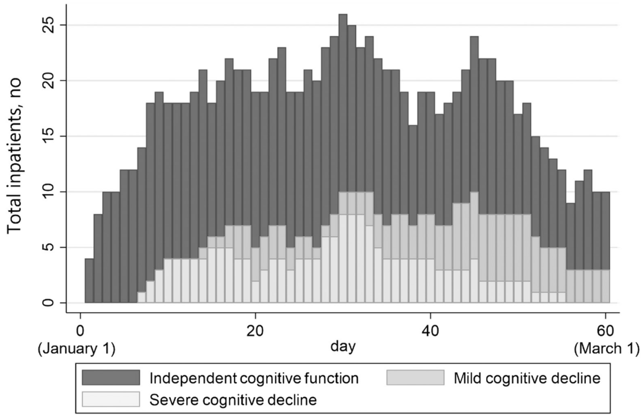

FIGURE 2 Total participants by cognitive function. Number of participants by day and cognitive function during the observation period

TABLE 3 Results of negative binomial regression analysis on the day after the discharge extension

			95% CI	
	Exp Coef	*p* value	Under	Upper
Age				
<64 years old	Reference			
≥65 years old	1.07	0.79	0.66	1.73
Gender				
Male	Reference			
Female	1.01	0.96	0.66	1.55
Cognitive function				
Independent	Reference			
Mild decline	3.05	0.004	1.43	6.49
Severe decline	1.95	0.03	1.09	3.53
Severity				
Mild	Reference			
Moderate	1.16	0.62	0.65	2.06
Severe	1.25	0.41	0.74	2.12

Abbreviations: CI, confidential interval; Exp Coef, exponentiated coefficient.

numbers peaked on day 30 when the number of inpatients was also at a maximum.

Mild cognitive decline and severe cognitive decline were factors for COVID-19 inpatients that precluded discharge on the day the quarantine period ended. Taking into account the reasons for extended discharge, this relationship included both symptoms of COVID-19, and also needed coordination services for living environment or care after discharge.[22,23] Generally, elderly inpatients needed a proper discharge planning and transition program.[24] Lacking this would cause a quick re-admission and a negative effect on their quality of life. To avoid these risks, the planning and coordination of discharge required appropriate communication between hospital, home care, and community settings and the formalization of designated teams.[25] A past study reported on a remote patient monitoring program for COVID-19 patients after hospital discharge. Based on the results, a discharge transition program and the team should be established to accommodate cognitively declined patients.[26] For future epidemics or disasters, frail elderly will need hospitalization with a rapid increase in medical demands as with this wave.[9] While medical facilities and professionals are utilized in their capacity to confront such a wave, interprofessional work could be the key solution to discharging patients without delay.[27] It is necessary to establish a specialized system of well-coordinated discharge during epidemics or disasters.

The number of inpatients with severe symptoms or cognitive decline increased later than others. Although there was a time lag, the number of total inpatients, severe patients and cognitive declined patients peaked on the same day in this wave (day 30). This would cause a synergistic burden on the medical staff. The COVID-19 pandemic exacerbated a decline in mental health and increased burnout among medical professionals.[28] Additionally, patients with the complex context or cognitive impairment were also affected in terms of the mental health and burnout of medical professionals.[29,30] A past study suggested the necessity of care focused on COVID-19 patients with cognitive impairment.[31] Guidelines for treatment and care considering the severity of COVID-19 and cognitive function are needed to reduce the burden on medical professionals during an epidemic. Moreover, regional bed control should take into account these factors and the characteristics of each medical facility.

This study was the first to examine the effect of cognitive decline on the discharge of COVID-19 patients caused by the Omicron breakout. Even during the epidemic, medical professionals have to beware of cognitive function, not only the severity of COVID-19.

This study has several limitations. First, since the participants of this study were inpatients of a single facility, the sample size was small. Moreover, the facility was a university hospital. There are no other university hospitals in Hiroshima prefecture, thus, there is a selection bias to choose a university hospital. Hiroshima University Hospital adopts a Diagnosis Procedure Combination/Per-Diem Payment System, which is a fixed payment system based on per day of hospitalization by the main disease, and thus, the length of hospital stay at such hospitals tends to be stricter and shorter than in other hospitals.[32] Therefore, we could have underestimated the effect of cognitive decline as a tendency of the hospital. Second, the cognitive decline might cause hypoxia-induced disorientation as a result of the worsening respiratory status. Since the cognitive function at discharge was not assessed, the effect of hypoxia on admission was uncertain. Third, the effect of the small number of participants would cause insufficient power in this study. Lastly, we evaluated cognitive function upon admission without assessing the cause. We could not judge whether the cognitive decline was caused by another disease before the admission or due to the severity of COVID-19. Because our study did not contain critical illnesses, the cause would be an existing condition prior to admission. For future studies, it would be useful to assess cognitive function after COVID-19 symptoms improve or at discharge.

5 | CONCLUSIONS

Mild and severe cognitive decline elevated the risk of discharge extension on the day after COVID-19 patients finished the quarantine period. During the Omicron outbreak, the number of total inpatients, severe patients, and cognitive declined patients peaked on the same day.

AUTHOR CONTRIBUTIONS

SY contributed to the study concept, design, acquisition of data, analysis, interpretation of data, and drafting of the manuscript. MM contributed to the analysis, interpretation of data, and critical revision of the manuscript. KI contributed to the acquisition of data, interpretation of data, and critical revision of the manuscript for important intellectual content. MI and HO contributed to the study concept, acquisition of data, and critical revision of the manuscript for important intellectual content. The authors read and approved the final manuscript.

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CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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