JCN Open Access ORIGINAL ARTICLE

pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2022;18(1):79-86 / https://doi.org/10.3988/jcn.2022.18.1.79

Impact of Dementia on Mortality Due to Coronavirus Disease 2019: Propensity-Score-Matching Study

Jin Pyeong Jeon[a]
Su Jung Lee[b]
Chulho Kim[c]

Departments of [a]Neurosurgery and [c]Neurology, Hallym University Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea
[b]School of Nursing, Hallym University, Chuncheon, Korea

Background and Purpose Patients with dementia are particularly vulnerable to coronavirus disease 2019 (COVID-19) because they tend to be older and often have concomitant diseases. Previous studies have investigated the impact of dementia on COVID-19 outcomes, but the evidence is not robust for Asian populations. We aimed to determine the relationship between dementia and COVID-19 outcomes using data from a large-scale nationwide public database.

Methods Data on patients with COVID-19 who were released from quarantine between January 1, 2020 and April 30, 2020, published by the Korea Disease Control and Prevention Agency, were divided into two groups based on the dementia status. Propensity-score matching was used to adjust for multiple confounders between the dementia and no-dementia groups. Binary, ordinal logistic regression and multivariate Cox proportional-hazards models were used to compare mortality, quarantine duration, and clinical deterioration according to the dementia status in the two groups.

Results Males and older individuals (age ≥60 years) constituted 41.5% and 32.9%, respectively, of the 5,299 patients. The prevalence of dementia was 4.2%, and 4.5% of the participants died during hospitalization. In multivariate analysis, dementia was significantly associated with increased mortality (odds ratio [OR]=2.80, 95% confidence interval [CI]=1.60−4.60), longer duration of quarantine (hazard ratio=1.69, 95% CI=1.16−2.45), and larger shift to a worse clinical severity (common OR=1.74, 95% CI=1.18−2.61).

Conclusions After adjusting for important clinical predictors, dementia was associated with increased in-hospital mortality, duration of quarantine, and clinical deterioration during hospitalization in COVID-19 patients.

Keywords COVID-19; dementia; mortality.

INTRODUCTION

Coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has massively affected the world, with there being 197,767,859 cases and 4,215,888 deaths as of August 1, 2021 (https://www.worldometers.info/coronavirus/). The first COVID-19 patient was reported in January 2020 in Korea,[1] and the cumulative total numbers were 198,345 patients and 2,095 deaths as of July 31, 2021 (http://ncov.mohw.go.kr/). Advanced age is a well-known risk factor for mortality in COVID-19 patients.[2] Soneji et al.[2] reported that the age-standardized death rate per 100,000 person-years increased from 0.1 deaths in patients aged 30−39 years, to 9.5 deaths in those older than 80 years. In addition to older age, pre-existing comorbidities such as hypertension and cardiovascular and pulmonary diseases have been reported to be associated with higher rates of mortality.[3]

Received February 16, 2021
Revised July 14, 2021
Accepted July 14, 2021

Correspondence
Chulho Kim, MD, PhD
Department of Neurology, Hallym University Chuncheon Sacred Heart Hospital, 77 Sakju-ro, Chuncheon 24253, Korea
Tel +82-33-240-5255
Fax +82-33-255-6244
E-mail gumdol52@naver.com

Patients with dementia are particularly vulnerable to COVID-19 because they tend to be older, often have concomitant diseases, and in many cases live in chronic-care facilities.[4] Bauer et al.[5] reported that dementia patients were more likely to have comorbidities such as stroke, diabetes, atherosclerosis, electrolyte imbalance, and pneumonia. It has consistently been shown that dementia increases mortality in Western countries.[6,7] Docherty et al.[6] reported a dementia rate of 13.5% in 17,459 COVID-19 patients in the United Kingdom, and found that the presence of COVID-19 increased the mortality rate significantly (hazard ratio [HR]=1.40, 95% confidence interval [CI]=1.28−1.52). However, information on the association between dementia and coronavirus disease outcomes in Korea has been scarce and contradictory. Hwang et al.[8] found that dementia increased the risk of mortality, in contrast to the findings of another study.[9] We think that the small number of enrolled patients (11 out of 103 in one study and 35 out of 352 in the other), the inclusion of small regional cohort studies, racial differences, and analyses performed without adjusting for confounding factors contributed to these conflicting results. In addition, a community-based study showed that mortality risk due to COVID-19 differs with race,[10] with an Asian population exhibiting a higher mortality rate than non-Hispanic white people (relative risk [RR]=1.38, 95% CI=1.25−1.53). However, in patients without COVID-19, the mortality rate due to dementia in the Asian population has been found to be lower than in non-Hispanic white patients with dementia, especially in those younger than 70 years.[11] In-hospital mortality in patients with dementia has been associated with advanced age, concomitant cardiovascular diseases, and malnutrition, which are risk factors that also strongly overlap with poor outcomes from COVID-19. It is therefore necessary to adjust for confounding factors when attempting to accurately assess the association between dementia and mortality.

This study performed a detailed analysis of how dementia influences outcomes in the Korean population using a large-scale nationwide public data set. We accounted for factors that could contribute to outcomes, and performed a propensity-score matching (PSM) analysis to adjust for confounding variables.

METHODS

Data sources

The Institutional Review Board of Hallym University Chuncheon Sacred Heart Hospital (No. 2020-07-016) and the Korea Disease Control and Prevention Agency (KDCA) approved this study and waived the need to obtain informed consents. The Korea National Committee for Clinical Management of COVID-19 had previously constructed a registry to collect the clinical data of patients hospitalized for COVID-19. That registry utilizes a standardized clinical record form (CRF) that is a modified version of the World Health Organization global CRF for COVID-2019 (https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19).[12] We extracted data for our analysis from patients confirmed as being released from quarantine between January 1, 2020 and April 30, 2020, according to clinical epidemiological information of COVID-19-confirmed patients published by the KDCA (http://www.kdca.go.kr/).[13] Dementia was defined based on the judgement of the clinician who had made the past diagnosis, as well as the medication history. Clinical severity is recorded on a 10-point scale score in the WHO CRF.[14] However, we revised this score and divided it into three classes: 1) no need for oxygen therapy, 2) need for oxygen therapy, and 3) ventilator support or death.

The primary outcome was a comparison of in-hospital mortality rates in COVID-19 patients with and without dementia. Secondary outcomes were how the duration of quarantine and the need for admission to an intensive-care unit (ICU) due to clinical deterioration differed according to the dementia status. In particular, the duration of quarantine was defined as the period of release from isolation from the general treatment center where patients with mild symptoms stayed, or as the period from hospital admission to discharge.

Statistical analysis

We compared baseline clinical and demographic characteristics between COVID-19 patients with and without dementia using the χ^2 test, *t*-test, or Mann-Whitney U test, as appropriate. Missing values were sparsely distributed in our COVID-19 cohort, and so we applied multiple imputation (5 repetitions with 10 cycles) in such cases. The baseline mortality, quarantine duration, and maximum clinical severity during hospitalization differed significantly between the dementia and no-dementia groups. We compared these clinical outcomes after applying PSM (1:1 ratio).

Binary logistic regression analysis was performed to compare predictors of in-hospital mortality between the two groups. A multivariate logistic regression model was applied to independent variables for which the *p* value was <0.05 in the univariate model or that had clinical relevance. We used a Cox proportional-hazards (CPH) survival model of in-hospital mortality and quarantine at the end of the follow-up period, according to the dementia status. All independent variables were entered into the CPH model for mortality, and significance was assessed using the HR and 95% CI. Cumulative survival plots for the quarantine duration were created using Kaplan-Meier statistics to compare the quarantine duration

Table 1. Comparison of clinicodemographic differences between the dementia and no-dementia groups before and after PSM

	Before PSM			After PSM		
	Dementia (*n*=224)	No dementia (*n*=5,075)	*p*	Dementia (*n*=224)	No dementia (*n*=224)	*p*
Age, years			<0.001			0.986
0–9	0 (0.0)	66 (1.3)		0 (0.0)	0 (0.0)	
10–19	0 (0.0)	195 (3.8)		0 (0.0)	0 (0.0)	
20–29	0 (0.0)	1,009 (19.9)		0 (0.0)	0 (0.0)	
30–39	0 (0.0)	523 (10.3)		0 (0.0)	0 (0.0)	
40–49	1 (0.5)	684 (13.5)		1 (0.5)	1 (0.4)	
50–59	9 (4.0)	1,068 (21.0)		9 (4.0)	10 (4.5)	
60–69	22 (9.8)	857 (16.9)		22 (9.8)	21 (9.4)	
70–79	52 (23.2)	489 (9.6)		52 (23.2)	56 (25.0)	
≥80	140 (62.5)	184 (3.6)		140 (62.5)	136 (60.7)	
Sex, male	71 (31.7)	2,126 (41.9)	0.003	71 (31.7)	90 (40.2)	0.076
BMI, kg/m^2						0.501
<18.5	33 (14.7)	296 (5.8)		33 (14.7)	24 (59.8)	
18.5–22.9	121 (54.0)	2,118 (41.7)		121 (54.0)	116 (51.8)	
23.0–24.9	39 (17.4)	1,204 (23.8)		39 (17.4)	48 (21.4)	
25.0–29.9	27 (12.1)	1,209 (23.8)		27 (12.1)	29 (12.9)	
≥30	4 (0.4)	248 (4.9)		4 (0.4)	7 (3.1)	
Outcome				149 (66.5)	174 (77.7)	
Death	75 (33.5)	166 (3.3)	<0.001	75 (33.5)	50 (22.3)	0.008
Duration of quarantine (days)	24.0 (13.0–33.2)	24.0 (18.0–32.0)	0.065	24.0 (13.0–33.3)	23.0 (17.0–33.0)	0.372
ICU admission	16 (7.1)	176 (3.5)	<0.001	16 (7.1)	26 (11.6)	0.145
Clinical severity score			<0.001			0.056
No need for oxygen therapy	107 (47.8)	4,377 (86.2)		107 (47.8)	123 (54.9)	
Need for oxygen therapy	41 (18.3)	500 (9.9)		41 (18.3)	48 (21.4)	
Ventilator support or death	76 (33.9)	198 (3.9)		76 (33.9)	53 (23.7)	
BPsys ≥130 mm Hg	133 (59.4)	2,744 (54.1)	0.136	133 (59.4)	154 (68.8)	0.049
BPdia ≥80 mm Hg	118 (52.7)	3,152 (62.1)	0.004	118 (52.7)	132 (58.9)	0.216
Body temperature (°C)	36.8±0.6	36.9±0.6	<0.001	36.8±0.6	36.9±0.6	0.157
Comorbidities						
Diabetes	63 (28.1)	618 (12.2)	<0.001	63 (28.1)	57 (25.4)	0.594
Hypertension	126 (56.2)	1,045 (20.6)	<0.001	126 (56.2)	125 (55.8)	1.000
Heart failure	12 (5.4)	47 (0.9)	<0.001	12 (5.4)	11 (4.9)	1.000
Coronary artery disease	15 (6.7)	162 (3.2)	0.007	15 (6.7)	16 (7.1)	1.000
Asthma	8 (3.6)	116 (2.3)	0.308	8 (3.6)	7 (3.1)	1.000
COPD	8 (3.6)	32 (0.6)	<0.001	8 (3.6)	4 (1.8)	0.380
CKD	10 (4.5)	45 (0.9)	<0.001	10 (4.5)	8 (3.6)	0.810
Malignancy	5 (2.2)	140 (2.8)	0.792	5 (2.2)	3 (1.3)	0.721
Chronic liver disease	6 (2.7)	76 (1.5)	0.261	6 (2.7)	8 (3.6)	0.786
Rheumatic/autoimmune disease	0 (0.0)	38 (0.7)	0.370	0 (0.0)	0 (0.0)	-
Laboratory parameters						
Hemoglobin (g/dL)	12.0±1.9	13.3±1.7	<0.001	12.0±1.9	12.2±1.9	0.230
Lymphocytes (%)	35.7±5.7	39.4±4.9	<0.001	24.6±13.1	23.3±11.9	0.291
Platelet count (×10^3/μL)	204±81	238±82	<0.001	204±81	224±91	0.016
White blood cell count (×10^3/μL)	6.1±3.0	6.1±2.8	0.922	6.1±3.1	6.7±3.4	0.040

Categorical variables are number (percentage), and continuous variables are mean±standard-deviation or median (interquartile range) values.
BMI, body mass index; BPdia, diastolic blood pressure; BPsys, systolic blood pressure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ICU, intensive-care unit; PSM, propensity-score matching.

between the dementia and no-dementia groups. The maximum clinical severity scores during admission were divided into tertiles, after which ordinal logistic regression analysis was performed to identify predictors of a larger shift in the distribution of the maximum clinical severity. All statistical analyses were performed with R software (version 3.6.3, R Core Team, R Foundation for Statistical Computing, Vienna, Austria), with statistical significance set at $p<0.05$.

RESULTS

Among the 5,628 patients who were confirmed as having COVID-19, 329 for whom information on dementia was not available were excluded. Supplementary Table 1 (in the online-only Data Supplement) compares the clinical characteristics of confirmed COVID-19 patients with dementia (n=224) and those without dementia (n=5,075). The proportion of patients with dementia was 4.2% (224 out of 5,299), 2,197 subjects were male (41.5%), 32.9% of the subjects were aged ≥60 years, and 192 subjects were hospitalized in ICUs. The most common COVID-19 symptom was sore throat (84.6%), followed by fever and cough.

In-hospital mortality

The in-hospital mortality rate was 4.5% (241 out of 5,299 patients). Supplementary Fig. 1 (in the online-only Data Supplement) shows that missing variables were randomly distributed. After multiple imputation, we compared the clinical characteristics and laboratory values between the dementia and no-dementia groups (Table 1).

There were significant differences in clinical characteristics between the two groups, and so we applied PSM (1:1 ratio) to the independent variables. Supplementary Table 2 (in the online-only Data Supplement) indicates that the independent variables were balanced for matched data after PSM, with the variables used having similar distributions in the dementia and no-dementia groups. Table 2 lists the results of the multivariate logistic regression analysis of predictors of in-hospital mortality in the matched population. Dementia was a significant predictor of mortality after adjusting for significant variables (odds ratio [OR]=2.80, 95% CI=1.60−4.90) and in the CPH model (HR=1.85, 95% CI=1.27−2.70) (Fig. 1). Body mass index (BMI), lymphocyte count, and platelet count were also significant predictors of mortality in the CPH model.

Duration of quarantine

Participants were treated in isolation for a median of 24.0 days. The Kaplan-Meier plot analysis revealed that patients with dementia had a higher probability of being quarantined than did no-dementia patients (p in log-rank test=0.004) (Fig. 2).

Table 2. Results of the binary logistic regression analysis of predictors of mortality in the participants

Model	OR (95% CI)	p
Dementia (crude model)	1.90 (1.24–2.90)	0.003
Model 1	2.12 (1.35–3.32)	0.001
Model 2	2.18 (1.36–3.48)	0.001
Model 3	2.80 (1.60–4.90)	<0.001

Model 1 was adjusted for variables included in the crude model and additionally for age and sex. Model 2: Model 1 + BMI, diabetes, hypertension, heart failure, coronary artery disease, bronchial asthma, COPD, CKD, malignancy, and chronic liver disease. Model 3: Model 2 + hemoglobin and lymphocytes.
CI, confidence interval; OR, odds ratio.

In the CPH model, dementia was a significant predictor of the duration of quarantine in matched data (HR=1.69, 95% CI=1.16−2.45) (Supplementary Fig. 2 in the online-only Data Supplement).

Distribution of maximum clinical severity

Fig. 3 compares the distributions of maximum clinical severity scores between the dementia and no-dementia groups during hospitalization. The proportion of patients who received ventilator support or who died was higher for those with dementia than for those without dementia. Table 3 presents the association between dementia and a higher maximum clinical severity score. Dementia was a significant predictor in the ordinal logistic regression model (common OR=1.74, 95% CI=1.18−2.61).

DISCUSSION

Dementia is believed to be closely associated with mortality in COVID-19 patients. A recent meta-analysis revealed that dementia significantly increased mortality due to COVID-19 (RR=2.62, 95% CI=2.04−3.36).[3] However, the results of that study may be unreliable since it did not adjust for confounding factors such as patient age and comorbidities that can affect the prognosis. In addition, high heterogeneity (I^2=96%) was observed across the studies included in that meta-analysis, and it also did not accurately reflect outcomes in the Asian population because it included only 3 studies involving a total of 17 dementia patients from Asian countries.[3] We therefore considered it necessary to investigate how dementia affects outcomes after SARS-CoV-2 infection in a study design that adjusted for confounding variables and drew from a Asian population.

Our study found that the baseline characteristics of COVID-19 patients differed significantly between those with and without dementia. Patients with dementia were older, less obese, more likely to be female, and had higher maximum

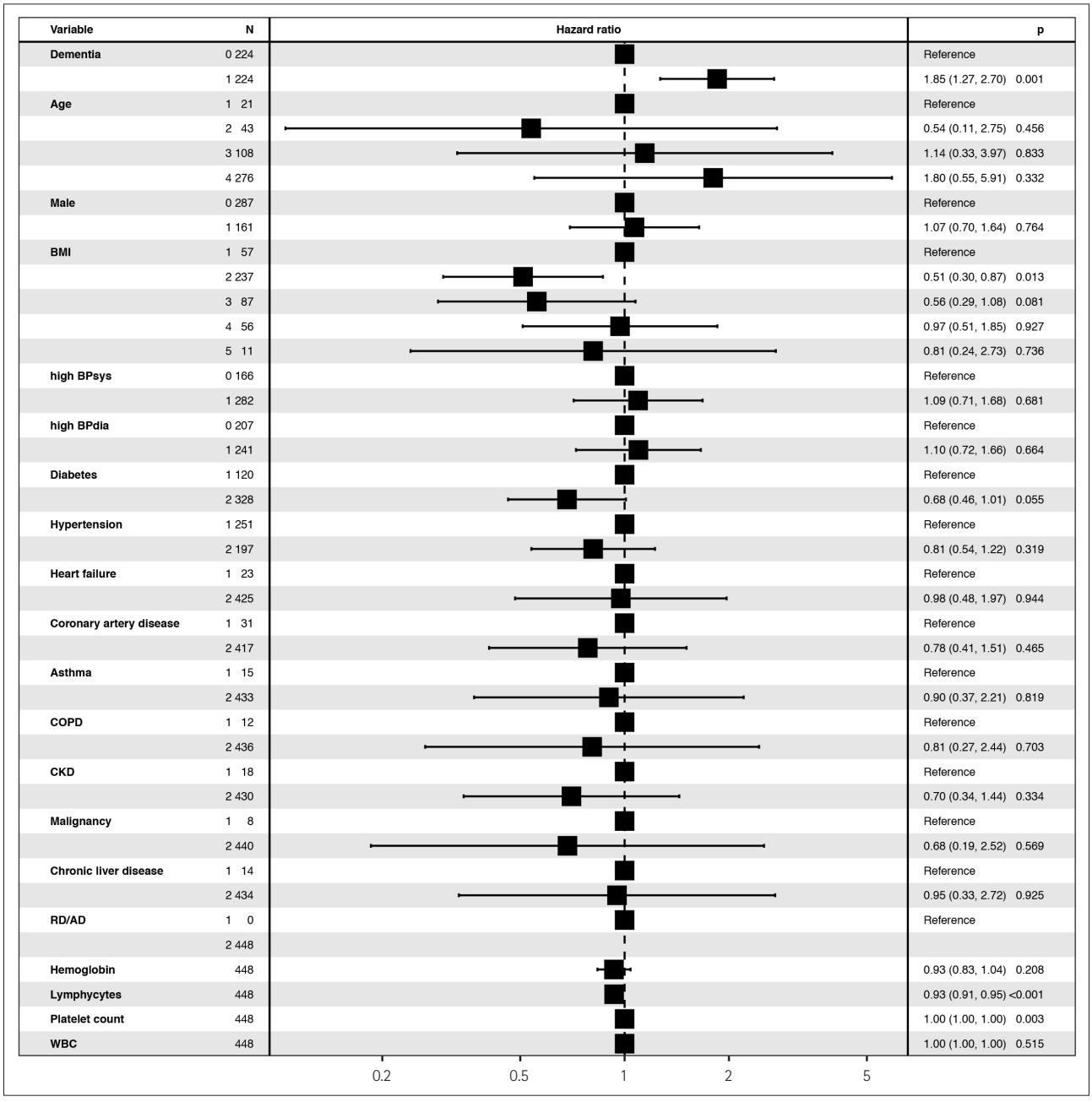

Fig. 1. Results from the multivariate Cox proportional-hazards model for in-hospital mortality in the participants. Each black rectangle represents the hazard ratio (HR) for in-hospital mortality. Horizontal bars represent the 95% confidence intervals. An HR of 1 is equivalent to no difference in the hazard rate of each risk factor versus control. HRs higher than 1 indicate increased hazard rates of in-hospital mortality resulting from the risk factor, while HRs lower than 1 indicate decreased hazard rates of in-hospital mortality. BMI, body mass index; BPdia, diastolic blood pressure; BPsys, systolic blood pressure; WBC, white blood cell count.

clinical severity scores and a higher rate of comorbidities (Table 1). In particular, higher mortality rates in COVID-19 patients have been found to be associated with medical comorbidities, advanced age, and female sex.[6] Thus, confounding variables should be adjusted for when assessing the impact of dementia on mortality. In our analysis, after adjusting for possible confounding variables in the matched population using PSM, we observed that dementia was still a significant risk factor for in-hospital mortality (OR=2.80, 95% CI=1.60–4.90). This was true in various statistical models (Table 2), which provides robust evidence for this relationship being present in Korean subjects.

Most previous studies have focused on simple associations between mortality and dementia in COVID-19 patients.[8] In

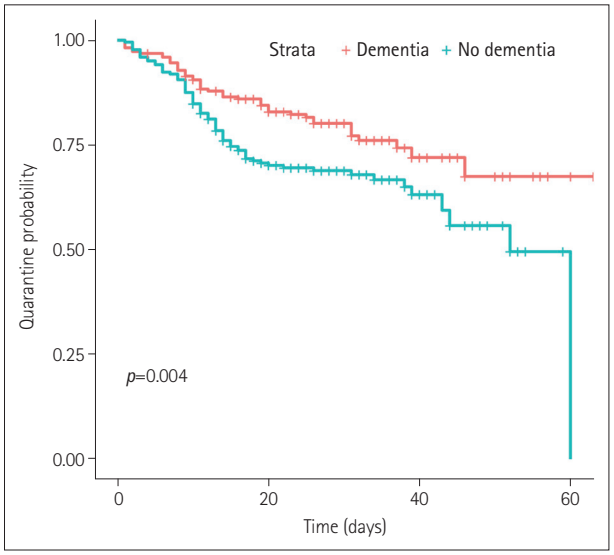

Fig. 2. Kaplan-Meier curves displaying the estimated quarantine duration probability for the dementia and no-dementia groups. Each vertical step in the curve indicates the event (end of quarantine period). A *p* value of <0.05 indicates a significant difference in the log-rank test between the survival curves.

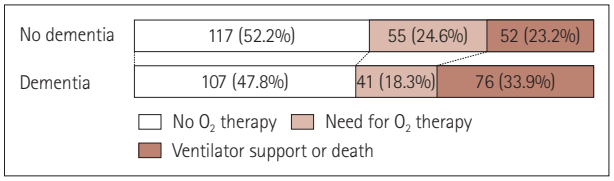

Fig. 3. Distribution of the maximum clinical severity in the participants during hospitalization. Ventilator support indicates the use of a high-oxygen-flow-rate nasal cannula or mechanical ventilation. The number (percentage) of the patients with the maximum clinical severity during hospitalization is given in each cell. The data show that a larger proportion of patients in the dementia group received oxygen or ventilatory support, or died.

addition to the current evidence, we further analyzed associations of dementia with the quarantine duration and the maximum clinical severity during hospitalization. Our study clearly demonstrated that COVID-19 patients with dementia require a longer quarantine duration than those without dementia. Moreover, the need for ventilator support and the occurrence of death were both more frequent among those with dementia. These findings indicate that hospital admissions of COVID-19 patients with concomitant dementia require significant additional medical resources and longer inpatient stays. This can contribute significantly to the likelihood of healthcare management systems being overwhelmed when the number of COVID-19 patients continues to increase, especially if dementia patients are not being managed efficiently. The cognitive decline of dementia patients makes it difficult for them to follow hygiene rules, and they are more susceptible to infection because they often live in chronic-care facilities. It is therefore important for dementia caregivers and medical professionals to cooperate in order to develop protocols for preventing COVID-19 in these patients, and actively comply with them.

Table 3. Results of the ordinal logistic regression analysis of a larger shift in the maximum clinical severity during hospitalization of the participants

Model	OR (95% CI)	*p*
Dementia (crude model)	1.36 (0.96–1.93)	0.088
Model 1	1.46 (1.02–2.10)	0.041
Model 2	1.44 (1.00–2.09)	0.001
Model 3	1.74 (1.18–2.61)	0.006

Model 1 was adjusted for variables included in the crude model and additionally for age and sex. Model 2: Model 1 + BMI, diabetes, hypertension, heart failure, coronary artery disease, bronchial asthma, COPD, CKD, malignancy, and chronic liver disease. Model 3: Model 2 + hemoglobin and lymphocytes.
CI, confidence interval; OR, odds ratio.

The impact of dementia on long-term outcomes has not received sufficient attention in COVID-19 patients. COVID-19 patients have accompanying neurological symptoms and complications. Reportedly 36% of COVID-19 patients experience decreased consciousness, seizures, and acute cerebrovascular diseases, and such symptoms are more pronounced in the presence of severe infection.[15] Due to its structural similarity with SARS-CoV, SARS-CoV-2 is believed to bind to angiotensin-converting enzyme 2 (ACE2), which is expressed in various organs including the lungs, blood vessels, and brain.[4,16,17] Brain injury can result from excessive immune and inflammatory responses and an altered coagulation system, which can in turn contribute to vascular injury and subsequent damage to the blood-brain barrier.[4,15] The SARS-CoV-2 protein also interacts with age-related proteins.[18] Neuroinflammation involving reactive gliosis, oxidative damage, and mitochondrial dysfunction is a common feature of dementia,[19,20] and so brain damage and inflammatory reactions caused by COVID-19 could exacerbate existing dementia. Long-term follow-up of changes in cognitive function and brain structures using radiological tests—even after COVID-19 patients are released from quarantine—is becoming necessary.

We found a U-shaped relationship between BMI and mortality in COVID-19 patients (Fig. 1). Since it was reported that high BMI was associated with an increase in influenza mortality during the H1N1 pandemic in 2009,[21] a relationship between obesity and COVID-19 mortality is not unexpected. Soeroto et al.[22] found that obesity was associated with increases in ICU admissions, acute respiratory distress syndrome, COVID-19 severity, hospital admissions, and mortality in a systematic review of 16 studies. In addition, obesity can reportedly affect the immune system and impair the host defence mechanism.[23] Therefore, our result is consistent with

previous reports of obesity being associated with poor outcome in COVID-19 patients. Additionally, the platelet count was negatively associated with COVID-19 mortality (Fig. 1, Table 1). COVID-19 patients often have mild thrombocytopenia and appear to exhibit increased platelet consumption,[24] and low platelet count has been associated with severe SARS-CoV-2 infection.[25] Our finding of an association between platelet count and COVID-19 mortality can be interpreted similarly to those previous observations.

This study was subject to some limitations. First, it did not analyze data from a large number of laboratory tests. Compared with non-COVID pneumonia, COVID-19 pneumonia significantly decreases the leukocyte, neutrophil, and platelet counts.[26] Although multiple imputation was performed to handle missing data, individual risk assessments performed using laboratory tests would have yielded more accurate information. Second, there was unreliable information about the place of residence of the patients before they were infected by SARS-CoV-2. Matias-Guiu et al.[27] reported that the place of residence is more closely associated with COVID-19 than dementia, suggesting that it can affect mortality. However, residence information was missing from the KDCA database, making it impossible for us to evaluate its association with mortality. Third, we did not distinguish between different dementia subtypes. Compared with Alzheimer's disease, frontotemporal dementia can occur at a younger age and have a lower mortality rate after COVID-19.[27] Accordingly, future studies are needed of mortality rates in COVID-19 patients while taking dementia subtypes into account.

In conclusion, this study found dementia to be associated with increased in-hospital mortality in COVID-19 patients. Longer duration of quarantine as well as clinical deterioration during hospitalization were also closely associated with dementia status in COVID-19.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2022.18.1.79.

Availability of Data and Material

The datasets generated or analyzed during the study are not publicly available because this data was generated by Korea Disease Control and Prevention Agency (KDCA) and allowed to assess with the reasonable request.

ORCID iDs

Jin Pyeong Jeon https://orcid.org/0000-0001-8543-6855
Su Jung Lee https://orcid.org/0000-0001-9495-8014
Chulho Kim https://orcid.org/0000-0001-8762-8340

Author Contributions

Conceptualization: all authors. Data curation: Jin Pyeong Jeon, Su Jung Lee. Methodology: all authors. Formal analysis: Jin Pyeong Jeon, Chulho Kim. Investigation: Su Jung Lee, Chulho Kim. Validation: all authors. Writing—original draft: Jin Pyeong Jeon, Chulho Kim. Writing—review & editing: all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Funding Statement

This research was supported by the National Research Fund of Korea (NRF-2019R1G1A1097707) and the Ministry of Education (2020R1l1A3070726).

Acknowledgements

We would like to acknowledge all the healthcare workers involved in the diagnosis and treatment of COVID-19 patients in South Korea. We also would like to thank Korea Disease Control and Prevention Agency, National Medical Center, and the Health Information Managers in the hospitals for their effort in collecting the medical records.

REFERENCES

1. Kim JY, Choe PG, Oh Y, Oh KJ, Kim J, Park SJ, et al. The first case of 2019 novel coronavirus pneumonia imported into Korea from Wuhan, China: implication for infection prevention and control measures. *J Korean Med Sci* 2020;35:e61.
2. Soneji S, Beltrán-Sánchez H, Yang J, Mann C. Population-level mortality rates from novel coronavirus (COVID-19) in South Korea. *medRxiv* 2020 Mar 27 [Preprint]. Available from: https://doi.org/10.1101/2020.03.23.20041814.
3. Hariyanto TI, Putri C, Arisa J, Situmeang RFV, Kurniawan A. Dementia and outcomes from coronavirus disease 2019 (COVID-19) pneumonia: a systematic review and meta-analysis. *Arch Gerontol Geriatr* 2020;93:104299.
4. Ryoo N, Pyun JM, Baek MJ, Suh J, Kang MJ, Wang MJ, et al. Coping with dementia in the middle of the COVID-19 pandemic. *J Korean Med Sci* 2020;35:e383.
5. Bauer K, Schwarzkopf L, Graessel E, Holle R. A claims data-based comparison of comorbidity in individuals with and without dementia. *BMC Geriatr* 2014;14:10.
6. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: prospective observational cohort study. *BMJ* 2020;369:m1985.
7. Bianchetti A, Rozzini R, Guerini F, Boffelli S, Ranieri P, Minelli G, et al. Clinical presentation of COVID19 in dementia patients. *J Nutr Health Aging* 2020;24:560-562.
8. Hwang JM, Kim JH, Park JS, Chang MC, Park D. Neurological diseases as mortality predictive factors for patients with COVID-19: a retrospective cohort study. *Neurol Sci* 2020;41:2317-2324.
9. Moon SS, Lee K, Park J, Yun S, Lee YS, Lee DS. Clinical characteristics and mortality predictors of COVID-19 patients hospitalized at nationally-designated treatment hospitals. *J Korean Med Sci* 2020;35:e328.
10. Jin J, Agarwala N, Kundu P, Harvey B, Zhang Y, Wallace E, et al. Individual and community-level risk for COVID-19 mortality in the United States. *Nat Med* 2020;27:264-269.
11. Hummer RA, Benjamins MR, Rogers RG. Racial and ethnic disparities in health and mortality among the U.S. elderly population. In: Anderson NB, Bulatao RA, Cohen B, editors. *Critical Perspectives on Racial and Ethnic Differences in Health in Late Life.* Washington, DC: The National Academies Press, 2004;53-94.
12. Sung HK, Kim JY, Heo J, Seo H, Jang YS, Kim H, et al. Clinical course and outcomes of 3,060 patients with coronavirus disease 2019 in Korea, January-May 2020. *J Korean Med Sci* 2020;35:e280.
13. Kim SR, Nam SH, Kim YR. Risk factors on the progression to clinical outcomes of COVID-19 patients in South Korea: using national

data. *Int J Environ Res Public Health* 2020;17:8847.
14. WHO Working Group on the Clinical Characterisation and Management of COVID-19 infection. A minimal common outcome measure set for COVID-19 clinical research. *Lancet Infect Dis* 2020;20:e192-e197.
15. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020;77:683-690.
16. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020;395:565-574.
17. Hamming I, Timens W, Bulthuis ML, Lely AT, Navis G, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol* 2004;203:631-637.
18. Lippi A, Domingues R, Setz C, Outeiro TF, Krisko A. SARS-CoV-2: at the crossroad between aging and neurodegeneration. *Mov Disord* 2020;35:716-720.
19. López-Valdés HE, Martínez-Coria H. The role of neuroinflammation in age-related dementias. *Rev Invest Clin* 2016;68:40-48.
20. Pasqualetti G, Brooks DJ, Edison P. The role of neuroinflammation in dementias. *Curr Neurol Neurosci Rep* 2015;15:17.
21. Moser JS, Galindo-Fraga A, Ortiz-Hernández AA, Gu W, Hunsberger S, Galán-Herrera JF, et al. Underweight, overweight, and obesity as independent risk factors for hospitalization in adults and children from influenza and other respiratory viruses. *Influenza Other Respir Viruses* 2019;13:3-9.
22. Soeroto AY, Soetedjo NN, Purwiga A, Santoso P, Kulsum ID, Suryadinata H, et al. Effect of increased BMI and obesity on the outcome of COVID-19 adult patients: a systematic review and meta-analysis. *Diabetes Metab Syndr* 2020;14:1897-1904.
23. Frasca D, McElhaney J. Influence of obesity on pneumococcus infection risk in the elderly. *Front Endocrinol (Lausanne)* 2019;10:71.
24. Connors JM, Levy JH. COVID-19 and its implications for thrombosis and anticoagulation. *Blood* 2020;135:2033-2040.
25. Jiang SQ, Huang QF, Xie WM, Lv C, Quan XQ. The association between severe COVID-19 and low platelet count: evidence from 31 observational studies involving 7613 participants. *Br J Haematol* 2020;190:e29-e33.
26. Soraya GV, Ulhaq ZS. Crucial laboratory parameters in COVID-19 diagnosis and prognosis: an updated meta-analysis. *Med Clin (Engl Ed)* 2020;155:143-151.
27. Matias-Guiu JA, Pytel V, Matías-Guiu J. Death rate due to COVID-19 in Alzheimer's disease and frontotemporal dementia. *J Alzheimers Dis* 2020;78:537-541.