

Review Article
Neuroscience



Coping with Dementia in the Middle of the COVID-19 Pandemic

Nayoung Ryoo ¹, Jung-Min Pyun ¹, Min Jae Baek ², Jeewon Suh ³,
Min Ju Kang ⁴, Min Jeong Wang ⁵, Young Chul Youn ⁶, Dong Won Yang ⁷,
Seong Yoon Kim ⁸, Young Ho Park ¹ and SangYun Kim ¹

¹Department of Neurology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea

²Clinical Neuroscience Institute, Seoul National University Bundang Hospital, Seongnam, Korea

³Department of Neurology, National Medical Center, Seoul, Korea

⁴Department of Neurology, Veterans Medical Research Institute, Veterans Health Service Medical Center, Seoul, Korea

⁵Roa Neurology Clinic, Seongnam, Korea

⁶Department of Neurology, Chung-Ang University College of Medicine, Seoul, Korea

⁷Department of Neurology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

⁸Department of Psychiatry, Asan Medical Center, Seoul, Korea



Received: Jul 28, 2020

Accepted: Oct 15, 2020

Address for Correspondence:

SangYun Kim, MD, PhD

Department of Neurology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, 82 Gumi-ro 173-beon-gil, Bundang-gu, Seongnam 13620, Korea.

E-mail: neuroksy@snu.ac.kr

© 2020 The Korean Academy of Medical Sciences.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.


ORCID iDs

Nayoung Ryoo 


<https://orcid.org/0000-0001-5145-115X>

Jung-Min Pyun 


<https://orcid.org/0000-0002-8391-5729>

Min Jae Baek 


<https://orcid.org/0000-0001-8215-6081>

Jeewon Suh 

<https://orcid.org/0000-0003-3509-6447>

Min Ju Kang 


<https://orcid.org/0000-0001-9966-3581>

Min Jeong Wang 

<https://orcid.org/0000-0001-7215-4883>

Young Chul Youn 

<https://orcid.org/0000-0002-2742-1759>

Dong Won Yang 

<https://orcid.org/0000-0002-4733-7298>


ABSTRACT

Multiple neurological complications have been associated with the coronavirus disease-19 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2. This is a narrative review to gather information on all aspects of COVID-19 in elderly patients with cognitive impairment. First, the following three mechanisms have been proposed to underlie the neurological complications associated with COVID-19: 1) direct invasion, 2) immune and inflammatory reaction, and 3) hypoxic brain damage by COVID-19. Next, because the elderly dementia patient population is particularly vulnerable to COVID-19, we discussed risk factors and difficulties associated with cognitive disorders in this vulnerable population. We also reviewed the effects of the patient living environment in COVID-19 cases that required intensive care unit (ICU) care. Furthermore, we analyzed the impact of stringent social restrictions and COVID-19 pandemic-mediated policies on dementia patients and care providers. Finally, we provided the following strategies for working with elderly dementia patients: general preventive methods; dementia care at home and nursing facilities according to the activities of daily living and dementia characteristics; ICU care after COVID-19 infection; and public health care system and government response. We propose that longitudinal follow-up studies are needed to fully examine COVID-19 associated neurological complications, such as dementia, and the efficacy of telemedicine/telehealth care programs.


Keywords: COVID-19; SARS-CoV-2; Neurology; CNS Complications; Dementia Care; Dementia Prevention

INTRODUCTION


World pandemics have occurred throughout the history of mankind. Despite the brilliant advances of modern medicine, we suffered from outbreaks of Spanish Flu, H5N1 bird flu, severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome (MERS) coronavirus, and now, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Seong Yoon Kim 

<https://orcid.org/0000-0002-1077-6289>

Young Ho Park 

<https://orcid.org/0000-0002-2756-1786>

SangYun Kim 

<https://orcid.org/0000-0002-9101-5704>

Disclosure

The authors have no potential conflicts of interest to disclose.

Author Contributions

Data curation: Pyun JM. Formal analysis: Baek MJ, Suh J. Investigation: Wang MJ, Youn YC. Resources: Kang MJ, Yang DW. Supervision: Kim S. Validation: Park YH. Writing - original draft: Ryoo N. Writing - review & editing: Kim SY.

In December 2019, unexplained pneumonia cases were reported in Wuhan, China, and rapidly overwhelmed the whole world. The novel virus has been confirmed as SARS-CoV-2 and this coronavirus disease 2019 (COVID-19) pandemic produced 38,752,924 patients and 1,100,823 deaths worldwide as of October 15, 2020.¹ Each country responded closely to COVID-19 with lock down of economic activities and social relations. Starting with the first COVID-19 patient confirmed after arrival in Korea from Wuhan,² South Korea also experienced 24,988 confirmed cases of COVID-19 including 439 decedents as of October 15, 2020.³ Prompt responses such as drive-through screening centers, active quarantine measures, requirements of face masks and social distancing in public places were done for slowing down the propagation.^{4,5} Research in China and South Korea indicates that early governmental action and cooperation by the population can mitigate the uncontrolled spread of the pandemic.^{6,7}

These rapidly changing environments and newly created policies are not easy for dementia patients to understand and follow. Furthermore, there are growing concerns that SARS-CoV-2 may cause neurological complications, and elderly patients with dementia are particularly vulnerable for COVID-19. Herein, we investigated current research for possible mechanism of central nervous system (CNS) involvement of SARS-CoV-2 and proposed strategies for physicians, patients, families and caregivers who are struggling with dementia in the middle of COVID-19 pandemic.

SEARCH STRATEGY AND METHODS

This article is a narrative review to investigate information on CNS involvement of COVID-19 and proposes strategies for physicians, patients, families and caregivers related with cognitive impairment. We searched all articles from December 2019 up to July 2020 in PubMed, Scopus, ScienceDirect, and Google Scholar search engines using the following keywords: “COVID-19,” “coronavirus,” “SARS-CoV-2” in combination with “CNS complications,” “neurology,” “dementia,” “mild cognitive impairment,” “Alzheimer’s disease,” “vascular dementia,” “dementia with Lewy bodies,” “frontotemporal dementia,” and “dementia care.” The case reports, clinical trials, cohort, and review studies were reviewed, and we did not exclude articles considering the expert viewpoints and letters to the editor. A total of 92 publications were obtained and thoroughly reviewed.

THE CNS COMPLICATIONS AND POSSIBLE MECHANISMS OF COVID-19

Coronaviruses, which are enveloped viruses with a single-strand, positive-sense RNA genome, are named due to their spikes on the membrane surface, which resemble a ‘crown’ of a medieval European emperor.⁸ The first human coronavirus was isolated from a nasal secretion in 1965 and was revealed to primarily involve the upper respiratory and gastrointestinal tracts.⁸

Due to genomic and receptor-binding structural similarities to the SARS-CoV, SARS-CoV-2 was considered to have the same mechanism of host cell entrance, i.e., the angiotensin-converting enzyme 2 (ACE2) receptor.⁹ SARS-CoV binding to the ACE2 receptor is a critical

step in the initiation of clinical manifestations in COVID-19 patients.¹⁰ ACE2 is a cardio-cerebral vascular protection factor that regulates blood pressure through inhibition of the angiotensin-renin-aldosterone pathways. ACE2 facilitates the conversion of angiotensin II to angiotensin and is widely distributed in nose, lungs, liver, kidneys, capillary endothelium, and brain in normal human physiology.¹¹⁻¹³

Current research has provided evidence that SARS-CoV-2 causes various neurological complications, including anosmia, delirium, acute cerebrovascular disease, paralysis, and meningo-encephalitis. Furthermore, some experts have suggested that SARS-CoV-2 can cause neurodegeneration in COVID-19 patients.¹³ Mao et al.¹⁴ reported that 36.4% of COVID-19 patients, out of 214 confirmed COVID-19 cases, were documented to have various neurological manifestations. The following three mechanisms governing COVID-19-mediated CNS damage have been proposed: 1) direct invasion, 2) immune and inflammatory reaction, and 3) hypoxic brain damage.

Direct pathway to brain

So far, cases with viral encephalitis confirmed with SARS-CoV-2 in the cerebrospinal fluid claim that COVID-19 can attack the CNS.^{7,15} There are two possible ways that SARS-CoV-2 can directly invade the brain. First, SARS-CoV-2 can enter through the blood stream. High levels of cytokines including interleukin (IL)-1, IL-16, and tumor necrosis factor alpha (TNF- α) in the cerebral vessels can damage the blood-brain barrier (BBB). The meninges are rich in blood vessels and contain high levels of ACE2,¹⁶ and BBB breakdown permits the pathogen into brain meninges and parenchyma resulting in seizures and meningo-encephalitis.¹³ The second suggested mechanism is via neuronal routes from the peripheral to CNS.¹⁷ Anosmia and ageusia are common among patients with COVID-19, yet the possibility for a central etiology remains unclear because the symptoms generally improve within weeks.¹⁸⁻²⁰ However, current research report anosmia alone or in combination of parageusia among COVID-19 patients while they showed no significant nasal congestion or rhinorrhea as influenza or rhinovirus.^{18,19,21-23} Also, the murine model studies demonstrate that coronavirus enters the olfactory bulb after exposure by the nasal route and then it can invade the CNS, supporting olfactory transmission of SARS-CoV-2.^{24,25}

Indirect pathway by immune and inflammatory reaction

By binding respiratory epithelial cells, SARS-CoV-2 activates the cytokines and hypercoagulation pathways in the blood, increasing levels of inflammatory markers such as C-reactive protein, ferritin, IL-1, IL-6, TNF- α , and D-dimer.²⁶ Elderly individuals have increased existing baseline of inflammation²⁷ and may suffer more severe complication and higher mortality as a result of inflammatory reaction. This cytokine storm also triggers embolic cerebrovascular accidents,¹⁴ and Li et al.²⁸ claims that hypercoagulable status of COVID-19 patients can lead to blood clots in both cerebral arteries and cerebral veins causing stroke and cerebral venous thrombosis.

Although further research is needed to clarify the exact mechanism of binding of SARS-CoV-2 to ACE2 resulting cytokine storm and the secondary hypercoagulation, there are abundant cases reporting acute stroke in COVID-19 patients.^{14,28-31} Li et al.²⁸ in the study suggests that early treatment to inhibit anti-inflammatory pathway can reduce the risk of acute cerebrovascular disease.³¹

Hypoxic brain damage by COVID-19

Severe cases of COVID-19 may involve acute respiratory failure, sepsis, and multi-organ failure necessitating mechanical ventilation in intensive care unit (ICU). Hypoxia occurs when oxygen supply to the brain is interrupted, and it can lead to confusion, disorientation, delirium and loss of consciousness.³² Solomon and colleagues report the neuropathological findings from autopsies of 18 COVID-19 patients who died in a single teaching hospital between April 14 and April 29, 2020. They examined histopathological examination of brain specimens obtained from 18 patients who died 0 to 32 days after the onset of symptoms of COVID-19. All cases were confirmed COVID-19 by nasopharyngeal swab samples for SARS-CoV-2 on qualitative reverse transcription polymerase chain reaction assays, and histopathological examination of brain specimens and immunohistochemical viral analysis were done. Intriguingly, all patients in the study showed only hypoxic changes and did not show other specific brain changes including encephalitis or viral invasion.³³ This valuable research on the neuropathological findings of COVID-19 decedents demonstrates no evidence of direct invasion of SARS-CoV-2 and supports hypoxic brain damage by COVID-19. However, lack of examination including brain magnetic resonance imaging (MRI) and cerebrospinal fluid, and ambiguity of statements that all patients had a confusional state or decreased arousal from sedation for ventilation make it hard to conclude whether the patients had neurologic signs of CNS involvement.

Another interesting research investigated by Coolen et al.³⁴ was about postmortem brain MRI of 62 patients who died from COVID-19. Only decedents with SARS-CoV-2 positive on nasopharyngeal swab specimen and with typical COVID-19 chest computed tomography scan findings were selected and then brain MRI was performed within 24 hours after death to investigate structural brain abnormalities associated with COVID-19.³⁴ As a result, subcortical hemorrhages in 2 decedents and edematous changes evocative of posterior reversible encephalopathy syndrome in one decedent were detected supporting BBB breakdown via SARS-CoV-2. Asymmetric olfactory bulbs were found in 4 decedents (21%) without olfactory tract nor brainstem abnormalities. Although more data will be needed due to small number of patients excluding those without lung-related evidence, this survey is meaningful in that it shows the opposite results of the neuro-invasion hypothesis through olfactory pathways.

Both papers demonstrate acute stage of CNS complication, and the abnormal misfolding and aggregation of proteins in patients who recovered from acute SARS-CoV-2 infection may lead to long-term brain degeneration.³⁵ Helms and colleagues reported that a third of the COVID-19 patients discharged from ICU were observed to have a dysexecutive syndrome.³⁶ Fotuhi claims that recovered patients from an acute SARS-CoV-2 infection may experience poor memory, attention, or slow processing speed so that it would be helpful to undergo inspection by a neurologist or neurocognitive testing 6–8 months after their hospital discharge if they feel any cognitive problem. As such, patients with low scores in certain cognitive areas should be treated with brain rehabilitation early, which may reduce their risk for future age-related cognitive decline.¹³ Ogier also suggests follow-up screening with cognitive evaluation, brain imaging (MRI, positron emission tomography), and auditory brainstem responses would help to detect brain dysfunction of COVID-19 patients.¹² Overall, long-term follow-up study for those survivors may reveal new neurologic consequences of COVID-19 such as cognitive decline, accelerated aging, and dementia in the future.

IMPACT OF COVID-19 ON PATIENTS WITH COGNITIVE IMPAIRMENT

Dementia patients are especially vulnerable to COVID-19 infection due to their disease state, age,³⁷ and comorbid diseases.³⁸ Furthermore, COVID-19 positive dementia patients may manifest their neurological complications as behavioral and neuropsychological problems. Here, we review the underlying issues that make dementia patients especially vulnerable amid the COVID-19 pandemic.

Risk factors of dementia vulnerable to COVID-19

Dementia is typically diagnosed in older people, a population that is particularly vulnerable during the COVID-19 pandemic. Wu et al.⁷ reported that COVID-19 patients over 59 years of age suffered 5 times worse outcomes than younger patients. Moreover, increases in morbidity range from 14.8% in China to as high as 58.9% in Italy among those 80 years or older.³⁹⁻⁴¹

In older individuals, comorbidities, such as hypertension, diabetes, obesity, and heart disease, are more likely to promote a cytokine storm resulting in life-threatening respiratory failure and multi-organ damage.^{38,42-44} Also, respiratory distress is common among most late-stage Alzheimer's disease (AD) patients.⁴⁵ Bauer claims that individuals with dementia are more likely to have cardiovascular disease, diabetes, and pneumonia compared to individuals of the same age without dementia.⁴⁶

Neuroinflammation is a pronounced feature of neurodegeneration and a critical role in the AD pathology.²⁷ David Melzer and colleagues suggests that risks of severe COVID-19 infection are related with the AD susceptibility gene, apolipoprotein E (ApoE). The ApoE e4 genotype not only increases risk of dementia and AD, but also exacerbates microglia-mediated neuroinflammation by inducing immune responses to amyloid pathogenesis and neurodegeneration.^{47,48} According to the data of participants (n = 451,367, 90% of sample) collected in the United Kingdom Biobank, ApoE e4e4 homozygotes were 2.3 to 4.0-fold more prone to COVID-19 test positives (odds ratio [OR], 2.31; 95% confidence interval [CI], 1.65–3.24).⁴⁹ Although the exact mechanisms still need to be studied, this may relate to co-expression of ApoE e4 and ACE2 within type II alveolar epithelial cells in the lung. Thus, dementia patients can be more vulnerable to COVID-19 infection.

Difficulties of dementia amid COVID-19 pandemic

Dementia is a neurodegenerative disorder marked by memory or cognitive issues, behavioral disorders, and difficulty performing daily activities. AD is the most common form of dementia in the world, corresponding to about 60%–70% of cases.⁵⁰ The second most common cause of dementia is vascular dementia (VD), which accounts for about 20% of cases worldwide, followed by dementia with Lewy bodies (15%),⁵¹ and frontotemporal dementia (FTD, 5%).⁵² Patients with AD, or other types of dementia, initially present with mild cognitive decline, termed mild cognitive impairment (MCI), as their daily life and activities are not significantly affected. As dementia progresses, cognitive impairment increases, and patients need more help to complete daily tasks and activities. Since each cognitive disorder presents with overlapping, but often varying, characteristic symptoms, patients with concomitant dementia and COVID-19 may suffer from a diverse array of difficulties. Herein, we discuss the impact of the COVID-19 outbreak on cognitive disorders in an attempt to gain insight for more detailed patient support.

MCI

Most individuals with MCI can manage their daily activities independently; however, they may show impaired adaptation and response to changes in society relative to the general population. As MCI patients stay at home during the COVID-19 pandemic, lack of exercise and social connection, which are paramount to non-pharmacological treatment in MCI patients, may accelerate their cognitive and psychological decline. Moreover, stress, which can be caused by changes in exterior circumstances, i.e. a pandemic, can have detrimental effects on people with MCI.⁵³ Rogers's systemic review identified 72 independent studies that provided data on both the acute and post-illness neuropsychiatric features of COVID-19 infection including depression, anxiety, fatigue, and stress⁵⁴; however, a more comprehensive study is needed to focus on people with MCI or dementia.

AD

As AD progresses, patients progressively display long term memory loss and gradually show a deterioration of language abilities and reduced awareness of time and place, ultimately inhibiting their abilities to carry out daily activities without help. Consequently, AD patients may have difficulty understanding and complying with new policies that are implemented in response to COVID-19, such as wearing masks and keeping physical distance due to their memory impairment. As such, more advanced AD patients will not be able to understand and adjust to the current pandemic situation. Clair et al. investigated the effects of confinement during the COVID-19 crisis on neuropsychiatric symptoms in patients with AD using the Neuropsychiatric Inventory-Questionnaire. Neuropsychiatric symptoms in AD include depression, anxiety, apathy, verbal and physical agitation, and hallucinations. The patients with severe AD show higher tendencies toward confusion and disorientation, and, consequently, these patients were correlated with a higher incidence of neuropsychiatric symptoms. However, reduced social contact and physical activity during isolation may have also induced these changes.⁵⁵ Also, AD patients are more vulnerable to infection because it is difficult to restrict physical contact with others in situations that require physical care.

VD

Cognitive decline associated with VD, which occurs after a vascular brain injury, can vary depending on the brain region affected. VD patients often present with memory loss, similar to AD⁵⁶; VD patients with frontal lobe cerebrovascular damage can present symptoms similar to FTD. Various brain dysfunctions including memory, behavioral, and neuropsychiatric symptoms make the VD patients more susceptible to COVID-19 infection. In addition, patients with VD tend to have motor or sensory neurological deficits, as well as cognitive problems, that arise from previous cerebrovascular diseases. Importantly, consistent, regular exercise and occupational therapy are important for VD patients; however, these therapy programs have been dramatically reduced or even terminated during the COVID-19 pandemic. Thus, the loss of these programs can have dire consequences for VD patients.

Dementia with Lewy bodies

Diffuse Lewy body (DLB) dementia is a disease characterized by the deposition and aggregation of alpha-synuclein, termed Lewy bodies in the brain, that shares symptoms with both AD and parkinsonism. DLB patients often present with delirium-like fluctuating symptoms that include visual hallucination.^{57,58} Furthermore, they often show hypersensitivity to antipsychotics, which may inhibit effective treatment. Specifically, DLB patients initially show signs of delirium or neuropsychiatric symptoms and are subsequently prescribed antipsychotic medications; moreover, the prevalence of hypersensitivity to

antipsychotics in DLB patients is relatively high, from 30 to 50%, and leads to increased cognitive decline, drowsiness, agitation, delirium, or worsening of parkinsonism.⁵⁹ For DLB patients who show signs of parkinsonism, gait difficulty and postural instability increase the risk of falling, thereby restricting daily activities. As such, these require extensive help from other people, which may not be feasible in circumstances where there is a lack of community health services and caregivers, such as during the COVID-19 pandemic.

FTD

FTD is caused by progressive nerve cell loss in the frontotemporal lobes of the brain. FTD patients are diagnosed around 45 to 65 years of age, which is relatively young compared to AD. There are two types of FTD, which are known as behavior variant FTD and primary progressive aphasia. Early FTD patients more prominently display behavioral and language problems rather than memory issues; however, memory loss becomes prominent in advanced stages.⁶⁰ Due to cognitive decline, FTD patients may have difficulties in understanding the necessity for self-quarantining due to a lack of awareness of the criticality of the COVID-19 pandemic. More importantly, they may not accept unfamiliar social guidelines, such as wearing face masks and social distancing. Also, being relatively younger than those with other forms of dementia, FTD patients are more likely to be physically fit, thereby increasing risks associated with violent behavior, impulsivity, disinhibition, and dysexecutive impairment. Furthermore, FTD patients may be resistant to altering daily activities they can no longer perform due to their compulsive and obsessive behaviors. Consequently, these situations may make FTD patients more susceptible to exposure and transmission of COVID-19.

Dire effects of COVID-19 on dementia care

The living environments of patients with dementia can have a tremendous impact on their susceptibility to massive infection. As the disease progresses, they require a considerable amount of support for daily living. As such, dementia patients may either live with their families or reside in communal care homes; these congregated living situations may expose them at high risk of infection.⁶¹ Ergo, up to 80% of the COVID-19 deaths are long-term care residents or workers, and over one-third of COVID-19-related mortalities in the United States are those afflicted with AD.⁶² Additionally, over 600 nursing home residents from a total capacity of 6400 beds died between March 7 and 27, 2020 in Bergamo, Italy,⁶³ and approximately 5,000 older people died in nursing homes in Madrid, Spain. As quarantine measures, nursing home residents have remained in isolation and visitors are temporarily prohibited.⁶⁴ However, employee-mediated transmission at nursing homes remains inevitable, as they are required to commute to and from the facilities.⁶¹ As these effects are seen worldwide, urgent health care policy changes are needed to avoid repeating these failures. Nursing homes should not be hopeless places where elderly people wait to die but should be a supportive place and vibrant atmosphere for them to live out their remaining years.

Once infected by COVID-19, elderly dementia patients will most likely experience neuropsychological problems such as delirium.⁶⁵ Infected patients are subsequently transferred to an ICU, or any isolated facility, and surrounded by unfamiliar medical workers with face shields and strange equipment. A study by Helms reported the presence of agitation in 69% (40/58) of COVID-19 patients with acute respiratory distress syndrome (n = 58, median age 63 years) admitted to an ICU.³⁶ Moreover, two-thirds of these agitated patients (26/40) showed confused mentality. Many of these patients develop restlessness, anxiety, and agitation, and their attempts to get out of bed can result in the need for physical restraint and/or pharmacological sedation.

Finally, the medical community must consider the impact of COVID-19-related social restrictions and containment policies on dementia patients. To prevent the COVID-19 transmission, many countries adopted drastic measures such as strict quarantines, prohibiting social gatherings, and even lock-down. As a result, reduced physical activities, lack of social engagements with families and friends, and cancelled day care center programs may worsen the cognitive, physical, and neuropsychological condition of the patients with dementia.⁶⁶ Being confined at home may increase levels of stress, anxiety, and a feeling of loneliness and depression. This is critical for dementia patients, as stress is known to be detrimental to patients with cognitive impairments.⁵³ In addition to the patients, we must also focus on the well-being of families and caregivers who may be suffering from reduced public health care support or home care services during the COVID-19 outbreak.

STRATEGY FOR MANAGING DEMENTIA DURING THE COVID-19 PANDEMICS

As COVID-19 continues to evolve in many countries, contagious virus and social quarantine measures cause deleterious impact on elderly dementia people and their families or healthcare workers. Thus, we propose multiple strategies to promote healthy living for people suffering from dementia and their caregivers. Below, we discuss the following four strategies aimed at improving dementia patient care during the COVID-19 pandemic: 1) general preventive measures of COVID-19 infection, 2) strategies for dementia care at home and nursing facilities according to activities of daily living (ADL) and dementia subtypes, 3) strategies for ICU care after COVID-19 diagnosis, and 4) measures and suggestions for public health care system and governmental response to COVID-19.

General preventive measures of COVID-19 infection

COVID-19 is transmitted person to person through direct contact, respiratory droplets and aerosolized viral particles.⁵⁷ There are still debates whether the virus transmits via droplet or aerosol, beyond the matter, wearing face mask is highly recommended considering the potential for asymptomatic or pre-symptomatic transmission. Also, we unconsciously touch our eyes, nose, and mouth frequent times a day, and furthermore, the spread of coronavirus can occur through unexpected paths, such as elevator buttons or air conditioner. Hand washing, alcohol gel sanitizer, masks, and even goggles can effectively prevent infections caused by touching. Various measures, from reducing outdoor activity to social distancing, have been implemented to curb the viral spread. Additional strategies for decreasing coronavirus transmission include regular house cleaning, frequent air ventilation through open windows, and disinfecting tableware or other items of frequent use via ultraviolet light. Also, regular exercise, healthy eating, stress reduction, and regular sleep are other effective ways to stay healthy during the COVID-19 pandemic.⁶⁷ General preventive strategies of COVID-19 infection are summarized in **Table 1**.

Table 1. General preventive measures of COVID-19 infection

General preventive measures of COVID-19 infection
• Hand washing, alcohol gel sanitizer, masks, and even goggles can help to prevent infections
• Avoid crowded places where physical distancing cannot be maintained
• Do regular house cleaning and frequent air ventilation through a window
• Disinfect tableware or items of frequent use via UV light

COVID-19 = coronavirus disease 2019, UV = ultraviolet.

Strategies for dementia care at home and nursing facilities according to ADL and characteristics of dementia

MCI and early dementia

For patients with MCI and early dementia that live at home independently, we have provided the following detailed recommendations. These recommendations have been categorized for patients, caregivers including family members, and medical experts including physicians and health care staff.

1) For patients

- Try to maintain in healthy condition; healthy diet, home-based exercise, meditation, and cognitive training⁶⁸⁻⁷¹
- Plan your daily chores and activities according to the day of the week^{69,72}
- Plan the delivery of food, medicine, and other daily necessities including masks, soaps, and hand sanitizers⁷²
- Use reminder memos or sticker signs to remember personal hygiene against infection; mask, hand wash, hand sanitizer^{69,72}
- Have a regular sleeping schedule⁷²
- Try to avoid excessive day time sleep⁶⁹
- Avoid excessive TV watching or video viewing
- Do outdoor activity with personal protective equipment (PPE) at less crowded times and places
- Keep physical distancing, but stay emotionally connected with your family and friends
- Make a list of contacts of family, friends, neighbors, and your general physicians to contact you when needed^{67,71,73}
- Save numbers of dementia helplines or hotlines in your cell phone⁷¹
- Check if an internet connection is available at home
- Learn how to telecommunicate using a cell phone or a computer⁷⁴
- Care for a plant or pet with affection and attention^{68,70}
- Think positively and limit watching negative COVID-19-related news^{69,72}

2) For families and caregivers

- Pay more attention to patients' physical and mental health⁷⁵
- Frequent and regular telecommunication with the patient to promote feelings of compassion and bonding^{67,72}
- If you detect any symptomatic changes from the patient, do not hesitate to seek medical attention
- Help the patient install and learn how to use the internet if he/she is not familiar with it⁶⁶
- Currently, many cognitive disorder associations distribute free, online home-based exercise and cognition training programs. Help the patient get familiarized with these web-based programs
- Make sure to communicate with the patient in a positive way, especially when discussing the news

3) For physicians and health-care staffs

- Maintain proper hygiene and always wear PPE to avoid cross infection⁷⁶
- Perform regular health check-ups on dementia patients at home via cell phone or computer
- Inform guidelines for hygiene measures and self-help guidance to decrease stress such as meditation or relaxation exercise via electronic media⁶⁴

- Educate patients how to use social media with intuitive and easy training program⁷²
- Provide web-based peer group social meeting, cognitive therapy games and programs⁷²
- Provide person to person contact to promote health,⁶⁴ such as smaller group activities that can keep a minimum distance between the participants
- Provide tele-counselling for neuropsychological symptoms and mental/emotional support, especially for patients who have experienced loss of friends or family due to COVID-19⁶⁴
- Offer hotlines for those who develop symptoms that suggest acute illness^{68,69,72}

Moderate to severe symptoms of dementia

As the disease progresses, dementia patients experience a decline in overall cognitive function and the majority of them enter nursing homes. In this case, keeping physical distance is extremely difficult because they are dependent on others even for basic living care. Thus, caution and stringent measures against COVID-19 are required for those in nursing homes or retirement facilities where massive infection and mortality can occur.⁶² Medical workers and caregivers at nursing facilities should pay more attention to using hand sanitizers that contain ethanol, hydrogen peroxide, or sodium hypochlorite before caring for the next patient, changing commonable supplies to individual use, disinfecting public places regularly, ventilating rooms frequently, and arranging separate mealtimes in small groups to promote physical distancing are recommended. Also, nursing homes need to ensure adequate stores of PPE for caregivers, and, additionally, caregivers should be checked for body temperature and any symptoms related to COVID-19 before entering the facilities.⁷⁶ Testing for suspected COVID-19 exposure should be carried out promptly. “At high risk” workers, e.g., workers who have relatives with COVID-19 symptoms or who have had close contact history with confirmed COVID-19 patients, must be excluded from front line care. Also, regular testing for COVID-19 among the staff is necessary to identify asymptomatic infections.

Next, we need to consider the characteristics of dementia patients since they may have unique difficulties amid the COVID-19 pandemic. As mentioned above, AD patients have memory impairment, which will require a frequent explanation of current COVID-19-related policies and hygiene measures. Since stress accelerates cognitive decline in AD patients,⁷⁴ it is critical to balance exposure to stress-reducing environments, such as planned outdoor activities, while following basic hygiene guidelines. Due to the effects of memory loss in dementia patients, their families and caregivers can be annoyed by their repeated questions and forgetfulness, and easily recognizable visual reminders on personal hygiene can be particularly helpful. Sometimes behavioral and psychological symptoms of dementia (BPSD), which are common in AD and vary in characteristics and severity among patients, can cause greater stress to families and caregivers than the patients themselves.⁷⁷ Tele-counselling hotlines can aid in relieving suffering related to BPSD symptoms. In addition, family members often feel tired and stressed due to long-term care of dementia patients^{55,66}; thus, it is important to share the burden of care with other family members or caregivers. This can be accomplished by making “care and rest” schedules.

For VD patients, the continuation of their daily neurological training, such as speech, occupational, and gait therapy, is critically important. As such, web-based rehabilitation programs and renting portable therapy tools can be helpful for VD patients.

Extensive attention should be given to the prevention of delirium in DLB patients. Neuropsychiatric symptom occurrences can often increase upon hospitalization due to

COVID-19 infection; in these cases, physicians must realize that DLB patients require greater attention and, if prescribed antipsychotics (e.g. quetiapine and risperidone), their hypersensitivity to antipsychotics must be considered. Previous studies suggest that both motor and cognitive training can be helpful in the management of psychiatric symptoms, including agitation and psychosis in DLB patients.⁵⁷ Telecommunication, including phone or video, with physical, speech, and occupational therapists can be a helpful source of guidance for performing at-home therapeutic activities.⁷⁸

Lastly, people with FTD often have trouble adapting their behavior to new circumstances and following COVID-19-related social policies, such as social distancing. Home-based exercise and planned outdoor activities with caregivers are encouraged, with the caveat of avoiding densely populated areas. Confined FTD patients may experience boredom, causing an increase in compulsive and obsessive behaviors (e.g. overeating); therefore, these patients require more organized daily plans that include enjoyable therapeutics. Creating a new routine that aligns with the current circumstances can be also a useful strategy for FTD patients. In addition, prevention of overuse or addiction to TV/video is critically important and can be accomplished by scheduling and limiting daily watching. Counseling for behavioral management of FTD via telephone hotlines²⁷ and providing self-help guidance for reducing stress, such as exercise, relaxation, and meditation, through electronic media can also provide beneficial effects.⁶⁴ Strategies for dementia care at home and nursing facilities are abridged in **Table 2**.

Table 2. Strategies for dementia care at home and nursing facilities according to ADL and characteristics of dementia

Strategies for dementia care at home and nursing facilities according to ADL and characteristics of dementia

1. Mild cognitive impairment and early dementia

1) For patients

- Plan your daily chores and activities according to the day of the week. This will help you prevent disorientation relating to time
- Plan the delivery of food, medicine, and other daily necessities including masks, soaps, and hand sanitizers
- Have a regular sleep schedule
- Try to maintain physical health; healthy diet, home-based exercise, meditation, and cognitive training
- Try to avoid excessive day time sleep
- Regularly clean and ventilate your house
- Raise a plant or pet with affection and attention
- Use memos or sticker signs to remember personal hygiene; mask, hand wash, hand sanitizer
- Do outdoor activity with PPE at less crowded times and places
- Maintain physical distancing, but stay connected with your family and friends
- Make contact lists containing family, friends, neighbors, and your general physician
- Save numbers of dementia helplines or hotlines in your cell phone
- Check if an internet connection is available at home
- Learn how to telecommunicate using a cell phone or a computer
- Avoid excessive TV or video watching
- Think positively and limit watching negative COVID-19-related news

2) For families and caregivers

- Pay more attention to the patient's physical and mental health
- Frequent and regular telecommunication with the patient to promote feelings of compassion and bonding
- If you detect any symptomatic changes from the patient, do not hesitate to seek medical attention
- Help the patient install and learn how to use the internet if he/she is not familiar with it
- Currently, many cognitive disorder associations distribute free, online home-based exercise and cognition training programs. Help the patient get familiarized with these web-based programs
- Make sure to communicate with the patient in a positive way, such as when discussing the news

3) For physicians and health-care staffs

- Maintain proper hygiene and always wear PPE to avoid cross infection
- Regularly check-up on dementia patients at home via cell phone or computer
- Inform guidelines for hygiene measures and self-help guidance to decrease stress such as meditation or relaxation exercise via electronic media

(continued to the next page)

Table 2. (Continued) Strategies for dementia care at home and nursing facilities according to ADL and characteristics of dementia**Strategies for dementia care at home and nursing facilities according to ADL and characteristics of dementia**

- Educate patients on social media use with an intuitive and easy training program
 - Provide web-based peer-group social meetings, as well as cognitive therapy games and programs
 - Provide person to person contact to promote health,⁶⁴ such as smaller group activities that can keep a minimum distance between the participants
 - Provide tele-counseling for neuropsychological symptoms and mental/emotional support, especially for patients who have experienced loss of friends or family due to COVID-19
 - Offer hotlines for those who develop symptoms that suggest acute illness
 - Offer hotlines for those who develop symptoms suspecting acute illness
2. Moderate to severe symptoms of dementia
- Medical workers and caregivers at nursing facilities should pay more attention to use of hand sanitizers that contain ethanol, hydrogen peroxide, or sodium hypochlorite between patients
 - Change commonable supplies to individual use
 - Regularly disinfect public places
 - Ventilate rooms frequently
 - Arrange separate mealtimes in small groups to promote physical distancing
 - Prepare adequate stacks of PPE for caregivers
 - Check body temperature and any symptoms related to COVID-19 before entering the facilities
 - If necessary, promptly test for COVID-19
 - Provide guidelines to “at high risk” workers that exclude from the front line care workers
 - Regularly testing for COVID-19 among staff is necessary to identify asymptomatic infections
3. Strategies with characteristics of dementia
- 1) Alzheimer's disease
- Need to remind repeatedly about current policies and hygiene measures
 - Use easily recognizable visual reminder on personal hygiene
 - Plan outdoor activities that follow hygiene rules
 - Tele-counselling hotline for BPSD symptoms can help families or caregivers deal with and relieve their suffering
 - Share the burden of care by making “care and rest” schedules with other caregivers
- 2) VD
- Maintain everyday training according to the patient's neurological deficits, including speech, occupational, gait therapy
 - Web-based rehabilitation programs and renting portable therapy tools can be helpful
 - Depending on areas of dysfunction, VD patients can apply the strategies of AD or FTD patients
- 3) Dementia with Lewy bodies
- Care should be taken to prevent the occurrence of delirium
 - In cases of hospitalization in the ICU or isolated wards due to COVID-19 infection, DLB patients require greater attention; prescriptions of low dose antipsychotics (e.g. quetiapine and risperidone) is preferred in consideration due to hypersensitivity to antipsychotics
 - At-home therapeutic activities via telecommunication for both motor and cognitive training can be helpful
- 4) FTD
- Home based exercise and planned outdoor activities, avoiding densely populated areas, with caregivers are encouraged
 - Have more organized daily plans that include enjoyable therapeutic activities
 - Create a new routine which fits within the context of the current circumstances
 - Prevent overuse or addiction to TV/video by scheduling and restricting daily use
 - Counselling for behavioural management of FTD via telephone hotlines is helpful
 - Providing self-help guidance for reducing stress through electronic media can result in beneficial effects for FTD patients

ADL = activities of daily living, PPE = personal protective equipment, COVID-19 = coronavirus disease 2019, BPSD = behavioral and psychological symptoms of dementia, VD = vascular dementia, AD = Alzheimer's disease, FTD = frontotemporal dementia, ICU = intensive care unit, DLB = diffuse Lewy body.

Strategies for ICU care after COVID-19 diagnosis

Once diagnosed with COVID-19, elderly patients with dementia will be admitted to an ICU or isolated medical department. About 84% of observed patients experienced neurological symptoms from ICU admission to discontinuation of neuromuscular blockade.³⁶ Elderly dementia patients have more tendency to have neuropsychiatric symptoms including delirium and agitation, and thus pre-emptive measure and delicate treatment are needed. Since many dementia patients have impaired language and comprehension ability, they may feel extremely anxious and be scared of unfamiliar environments with inadequate communication. This new environment can lead to increased stress and behavioural problems in dementia patients.⁷⁹

Family members of dementia patients must be prepared for a possible COVID-19 diagnosis. Once the patients are confirmed with COVID-19 and sent to the hospital, it may be too late to discuss the issue with them. Family members are recommended to explain the realities of a COVID-19 diagnosis, including hospitalized treatment if COVID-19 is confirmed, and to reassure patients that these actions are for the patient's benefit. Preparations, such as making necessary item lists for admission or packing patient attachment items in advance, can help family members respond appropriately when hospitalization is needed. Also, a care emergency may occur if the primary caregiver becomes ill with COVID-19. In this case, family members should discuss contingency plans.^{50,80}

The prevention and management of delirium require detailed training for ICU physicians and nurses who may care for elderly dementia patients with COVID-19. Once delirium and other neuropsychologic symptoms occur, infection control procedures become extremely difficult. The act of taking off the mask or the attached lines and trying to get out of bed by shouting can make the surrounding patients feel agitated. Medical professionals can reduce ICU-related delirium risks using standard guidelines to assess and manage pain, as well as by avoiding urinary retention and constipation and supplying adequate oxygenation.⁸¹ Common adjustable causes for delirium, such as electrolytes disturbance, hypoxemia, and dehydration, can be easily monitored and promptly managed.

Regular pain assessment through behavioral pain scales, numerical rating scale, or critical care pain observation tool are recommended.⁸² Regular delirium screening via the confusion assessment method for the ICU and intensive care delirium screening checklist can take advantages to manage delirium early. Also, physicians should review past medical history and previous medications of elderly patients. DLB patients can present hypersensitivity to antipsychotics so that antipsychotics (e.g. quetiapine and risperidone) at low dose are recommended.^{59,83} Abrupt cessation of previous medications should be avoided in order to prevent withdrawal symptoms. During management, it is recommended to withdrawal unnecessary psychoactive medications and to prohibit prolonged use of sedatives or stay in ICU.⁸¹

Non-pharmacological interventions are also emphasized by promoting psychological stability with warm attitudes and repeated reminding of current location and date.⁸¹ Using visual picture cards also can help identify and care for their needs. Allowing a small desk clock, calendar, radio, and attachment items of patients can be helpful. In ICU/isolation ward, face-to-face video call can be better promoted to enable frequent communication between patients and their families to mitigate delirium and patients' distress.⁸⁴

As discussed earlier, SARS-CoV-2 infection can provoke neurologic complications including acute stroke or encephalopathy. Therefore, timely referral and engagement of neurologists are necessary if the elderly patients present any suspicious signs of neurological abnormality during COVID-19 management. Strategies for ICU care after COVID-19 diagnosis are briefly described in **Table 3**.

Measures and suggestions for public health care system and government

In some countries, overwhelming numbers of COVID-19 patients have caused shortages of hospital beds and ventilators, and, consequently, elderly patients with dementia have been relegated to the post-care ranking of critical care.^{41,43} This disaster could be repeated if early prevention or control of an outbreak fails. Conversely, we propose that vulnerable parties should be given priority of care to prevent these failures in the future. Dementia patients and health care

Table 3. Strategies for ICU care after COVID-19 diagnosis

Strategies for ICU care after COVID-19 diagnosis

- Family members should prepare for the possibility of COVID-19 diagnosis in advance
- Assuming the patient is infected, it should be helpful to explain and reassure him/her about the physical symptoms prior to inpatient treatment and, further, to explain that these measures are intended for treatment, not for harm
- Preparations such as making a list of necessary items for admission or packing attachment items in advance can help family members respond quickly and appropriately when a new situation occurs
- In case the patient's primary caregiver gets infected, family members need to have contingency plans
- For prevention and management of delirium, reduce ICU delirium risks using standard guidelines to assess and manage pain, avoiding urinary retention and constipation, and supplying adequate oxygenation
- Regular pain assessment and delirium screening is required
- Physicians must review past medical history of elderly patients as DLB patients can present hypersensitivity to antipsychotics, and previous medications in order to avoid withdrawal symptoms
- During management, it is beneficial to withdrawal unnecessary psychoactive medications and to prohibit prolonged use of sedatives or stay in ICU
- The medical staff can promote psychological stability by presenting positive and compassionate attitudes and providing repeated reminders of the current location and date
- Use visual picture cards to identify and care for their needs
- Allowing a small desk clock, calendar, radio, and attachment items of patients can be helpful
- Face-to-face video calls that allow frequent communication between patients and their family members, which may mitigate delirium and patients' distress
- Contact a neurologist for further examination in the event a patient shows any symptoms of acute stroke or encephalopathy

ICU = intensive care unit, COVID-19 = coronavirus disease 2019, DLB = diffuse Lewy body.

workers at group facility should be considered a public health priority and provided with enough preventive measures and supplies.^{85,86} Pre-emptive preventions for elderly dementia patients who are more vulnerable to infection and transmission is necessary for effective infection control, prevention of medical supplies shortages, and reduction of medical costs.

During the COVID-19 outbreak, treatment facilities and daycare centers were closed, and telecommunication became more important as elderly people were isolated due to termination or reduced social health services. To combat this issue, many Dementia Safety Centers in Korea have distributed “memory aid-packages” to quarantined elderly dementia patients. While these packages slightly vary between regions, they contain a variety of helpful items such as guidelines to prevent COVID-19, face masks, exercise tools (e.g. stretching bands), plant raising kits, and learning materials or tools for cognitive activities. Telecommunication and virtual communication with their families and friends are encouraged to maintain social connections.⁷⁹ Web-based home programs for cognition, exercise, and counseling can help to improve dementia patient health. At the same time, dedicated employees have been conducting regular telephone consultations to monitor patient health and provide consultation about COVID-19. Advanced information and communications technologies (ICTs) have driven Korea's successful pre-emptive response that help “flatten the curve” of daily infection (**Fig. 1**). ICTs played a pivotal role in preventing COVID-19 transmission by promptly tracing contacts and providing the latest information on COVID-19.⁸⁷ Moreover, the availability of high-speed internet connections will become very important for rapid responses to pandemics in the future.

However, some experts have outlined some issues with telemedicine, which must be solved before it is universally utilized. Neurological patient exams are typically not feasible without direct contact and many countries do not have the wireless infrastructure to fully adopt telemedicine.⁵⁹ Instead, medical experts can currently ask patients and caregivers to record the patient's cognitive, behavioral, and mental state over the phone, whereby the medical professional can then offer medical consultation. Yet, social engagement is still a critical need for elderly patients with dementia, who typically have difficulties adapting to new technologies. Thus, human contact via home-visiting services and small group

therapies should still be encouraged. For example, Korea's Dementia Safety Center provides guidelines for home visits that provide information to health care workers about following strict personal hygiene measures. Also, the previous study by Lee supports that home-visiting cognitive intervention for the elderly dementia patients can bring positive benefits to improve cognition, emotion, and functional abilities.⁸⁸ Moreover, for dementia patients who stay at home for fear of infection, or who are under quarantine, health care services can be continued via telephone services in the event a “memory aid-package” has been delivered.

Due to the lockdown of facilities, there have been gaps in care, resulting in the need for government aid for a lot of families.⁸⁹ Specifically, many people have had an increased burden of not only homeschooling their children but also watching over elderly parents as well. In addition to neuropsychiatric symptom severity in dementia patients, longer confinement durations have also been correlated with caregiver distress.⁵⁵ Family caregivers of patients with AD are sometimes referred to as “invisible second patients,”⁹⁰ and as a medical community, we need to be aware of their stress as well. Moreover, financial problems, such as sudden job loss due to the economic shutdown, may compound stress among caregivers. Governmental support for families, caregivers, and patients is important. In addition, care networks should be operated at the government level for elderly dementia patients without families.

Governmental policies that govern dementia patients are another key factor in controlling the spread of the virus.⁹¹ For example, a guidebook or message with an on-line link that provides sufficient information in case of COVID-19 infection may help patients and families prepare for these circumstances, thereby reducing anxiety. For patients with cognitive disorders, a guidebook covering the procedures of hospitalization and treatment with easy language and visual pictures could be helpful. Moreover, contact information for urgent medical counseling should be available within any guidebook. Delivery of aid-kits for cognitive and exercise training can also ensure consistency of at-home therapy during the COVID-19 pandemic. Government-level tele-healthcare⁹² and counseling efforts for elderly dementia patients may greatly aid in overcoming the ever-changing landscape of the COVID-19 pandemic. Recommendations for public health care system and government are encapsulated in **Table 4**.

CONCLUSION

The neurological complications of SARS-CoV-2 are similar to those attributed to earlier coronavirus epidemics, such as SARS in 2003, and MERS in 2012. However, the COVID-19 pandemic has already exceeded the overall totals of people infected with previous coronaviruses and is still not under control in many countries. Therefore, COVID-19-related neurological complications for dementia patients must be examined. Long term follow-up studies will be needed to understand the effects of COVID-19 on the incidence or prevalence of dementia. Also, well-designed large cohort studies to examine the effectiveness of therapeutic strategies on people with cognitive impairment are necessary in the near future.

This is a narrative review study to present detailed strategies on caring for dementia patients during a pandemic. Moreover, these strategies are based on cognitive impairment severity and features of each dementia type. Measures are discussed from the viewpoint of three groups, dementia patients, their families and guardians, and medical or health care staff. Our study provided information on infection prevention and mitigation of the hardships

Table 4. Measures and suggestions for public health care system and government**Measures and suggestions for public health care system and government**

- Dementia patients and medical staff at group facility should be considered a public health priority and should be provided with enough preventive measures and supplies
- Supply “memory aid-packages,” which are beneficial to home confined elderly dementia patients
- Monitor the health of dementia patients and caregivers during the COVID-19 pandemic via regular telephone consultations
- Telecommunication and virtual communication with patient families and friends are encouraged to maintain social connection
- Web-based home programs for cognition, exercise, and counselling can help improve patient health
- Establishment of high-speed internet connections remains an important factor for the rapid response and control of a pandemic
- Medical experts can offer medical consultation via recorded logs from patients and caregivers outlining the patient's current cognitive, behavioural, and mental state
- Physical contact remains necessary for elderly dementia patients who have difficulties adapting to new technologies
- Human contact via at home-visiting services and small group therapies should be encouraged
- Provide guidelines to health care workers for home visits since they are required to follow strict personal hygiene measures when visiting patient homes
- Health care services should be continued by telephone after the delivery of “memory aid-packages” in cases of dementia patients who stay at home for fear of infection or who are under quarantine
- Governmental support for financial and mental problems among families and caregivers is necessary
- Care networks should be operated at the government level for elderly dementia patients without families
- A guidebook or message with an on-line link that provide sufficient information about COVID-19 infection data can help patients and families to prepare and, thereby, reduce anxiety
- For dementia patients, a guidebook introducing the procedure of hospitalization and treatment with concise and easy language, expressed with visual pictures, and contact information for urgent medical counseling or help is needed
- Delivery of aid-kits to promote cognitive and exercise training can ensure therapy consistency at home
- Government-level efforts including tele-healthcare and counseling for elderly dementia patients can greatly help with overcoming the obstacles associated with the COVID-19 pandemic

COVID-19 = coronavirus disease 2019.

from the management and care of dementia patients during the COVID-19 outbreak. We hope this study can guide health care leaders to formulate new standard guidelines for dementia patient care during the current pandemic, as well as any future pandemics.

REFERENCES

1. World Health Organization. Coronavirus disease (COVID-19) situation reports. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>. Updated 2020. Accessed October 15, 2020.
2. 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(5):e61.
[PUBMED](#) | [CROSSREF](#)
3. CoronaBoard. Billboard of COVID-19. <https://coronaboard.kr/>. Updated 2020. Accessed October 15, 2020.
4. Kwon KT, Ko JH, Shin H, Sung M, Kim JY. Drive-through screening center for COVID-19: a safe and efficient screening system against massive community outbreak. *J Korean Med Sci* 2020;35(11):e123.
[PUBMED](#) | [CROSSREF](#)
5. Her M. How is COVID-19 affecting South Korea? What is our current strategy? *Disaster Med Public Health Prep* 2020:1-3.
[PUBMED](#) | [CROSSREF](#)
6. Kraemer MUG, Yang CH, Gutierrez B, Wu CH, Klein B, Pigott DM, et al. The effect of human mobility and control measures on the COVID-19 epidemic in China. *Science* 2020;368(6490):493-97.
[PUBMED](#) | [CROSSREF](#)
7. Wu Y, Xu X, Chen Z, Duan J, Hashimoto K, Yang L, et al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun* 2020;87(March):18-22.
[PUBMED](#) | [CROSSREF](#)
8. Su S, Wong G, Shi W, Liu J, Lai ACK, Zhou J, et al. Epidemiology, genetic recombination, and pathogenesis of coronaviruses. *Trends Microbiol* 2016;24(6):490-502.
[PUBMED](#) | [CROSSREF](#)
9. 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(10224):565-74.
[PUBMED](#) | [CROSSREF](#)

10. Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nat Rev Microbiol* 2019;17(3):181-92. [PUBMED](#) | [CROSSREF](#)
11. Pleasure SJ, Green AJ, Josephson SA. The spectrum of neurologic disease in the severe acute respiratory syndrome coronavirus 2 pandemic infection. *JAMA Neurol* 2020;77(6):679-80. [PUBMED](#) | [CROSSREF](#)
12. Ogier M, Andéol G, Sagui E, Dal Bo G. How to detect and track chronic neurologic sequelae of COVID-19? Use of auditory brainstem responses and neuroimaging for long-term patient follow-up. *Brain Behav Immun Health* 2020;5:100081. [PUBMED](#) | [CROSSREF](#)
13. Fotuhi M, Mian A, Meysami S, Raji CA. Neurobiology of COVID-19. *J Alzheimers Dis* 2020;76(1):3-19. [PUBMED](#) | [CROSSREF](#)
14. 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(6):683-90. [PUBMED](#) | [CROSSREF](#)
15. Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J, et al. A first case of meningitis/encephalitis associated with SARS-coronavirus-2. *Int J Infect Dis* 2020;94(March):55-8. [PUBMED](#) | [CROSSREF](#)
16. Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infect Dis Poverty* 2020;9(1):45. [PUBMED](#) | [CROSSREF](#)
17. Sepehrinezhad A, Shahbazi A, Negah SS. COVID-19 virus may have neuroinvasive potential and cause neurological complications: a perspective review. *J Neurovirol* 2020;26(3):324-9. [PUBMED](#) | [CROSSREF](#)
18. Xydakis MS, Dehgani-Mobaraki P, Holbrook EH, Geisthoff UW, Bauer C, Hautefort C, et al. Smell and taste dysfunction in patients with COVID-19. *Lancet Infect Dis* 2020;20(9):1015-6. [PUBMED](#) | [CROSSREF](#)
19. Lee Y, Min P, Lee S, Kim SW. Prevalence and duration of acute loss of smell or taste in COVID-19 patients. *J Korean Med Sci* 2020;35(18):e174. [PUBMED](#) | [CROSSREF](#)
20. Lee JM, Lee SJ. Olfactory and gustatory dysfunction in a COVID-19 patient with ankylosing spondylitis treated with etanercept: case report. *J Korean Med Sci* 2020;35(21):e201. [PUBMED](#) | [CROSSREF](#)
21. Vaira LA, Salzano G, Deiana G, De Riu G. Anosmia and ageusia: common findings in COVID-19 patients. *Laryngoscope* 2020;130(7):1787. [PUBMED](#) | [CROSSREF](#)
22. Lechien JR, Chiesa-Estomba CM, De Siati DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *Eur Arch Otorhinolaryngol* 2020;277(8):2251-61. [PUBMED](#) | [CROSSREF](#)
23. Giacomelli A, Pezzati L, Conti F, Bernacchia D, Siano M, Oreni L, et al. Self-reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. *Clin Infect Dis* 2020;71(15):889-90. [PUBMED](#) | [CROSSREF](#)
24. Netland J, Meyerholz DK, Moore S, Cassell M, Perlman S. Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. *J Virol* 2008;82(15):7264-75. [PUBMED](#) | [CROSSREF](#)
25. Dubé M, Le Coupanec A, Wong AHM, Rini JM, Desforges M, Talbot PJ. Axonal transport enables neuron-to-neuron propagation of human coronavirus OC43. *J Virol* 2018;92(17):e00404-18. [PUBMED](#) | [CROSSREF](#)
26. Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. *Lancet Respir Med* 2020;8(6):e46-7. [PUBMED](#) | [CROSSREF](#)
27. Naughton SX, Raval U, Pasinetti GM. Potential novel role of COVID-19 in Alzheimer's disease and preventative mitigation strategies. *J Alzheimers Dis* 2020;76(1):21-5. [PUBMED](#) | [CROSSREF](#)
28. Li Y, Li M, Wang M, Zhou Y, Chang J, Xian Y, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study. *Stroke Vasc Neurol* 2020;5(3):279-84. [PUBMED](#) | [CROSSREF](#)

29. Lodigiani C, Iapichino G, Carenzo L, Cecconi M, Ferrazzi P, Sebastian T, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res* 2020;191:9-14.
[PUBMED](#) | [CROSSREF](#)
30. Oxley TJ, Mocco J, Majidi S, Kellner CP, Shoirah H, Singh IP, et al. Large-vessel stroke as a presenting feature of COVID-19 in the young. *N Engl J Med* 2020;382(20):e60.
[PUBMED](#) | [CROSSREF](#)
31. Zhou B, She J, Wang Y, Ma X. A case of coronavirus disease 2019 with concomitant acute cerebral infarction and deep vein thrombosis. *Front Neurol* 2020;11:296.
[PUBMED](#) | [CROSSREF](#)
32. Row BW. Intermittent hypoxia and cognitive function: implications from chronic animal models. *Adv Exp Med Biol* 2007;618:51-67.
[PUBMED](#) | [CROSSREF](#)
33. Solomon IH, Normandin E, Bhattacharyya S, Mukerji SS, Keller K, Ali AS, et al. Neuropathological features of COVID-19. *N Engl J Med* 2020;383(10):989-92.
[PUBMED](#) | [CROSSREF](#)
34. Coolen T, Lolli V, Sadeghi N, Rovai A, Trotta N, Taccone FS, et al. Early postmortem brain MRI findings in COVID-19 non-survivors. *Neurology* 2020;95(14):e2016-27.
[PUBMED](#) | [CROSSREF](#)
35. Lippi A, Domingues R, Setz C, Outeiro TF, Krisko A. SARS-CoV-2: at the crossroad between aging and neurodegeneration. *Mov Disord* 2020;35(5):716-20.
[PUBMED](#) | [CROSSREF](#)
36. Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020;382(23):2268-70.
[PUBMED](#) | [CROSSREF](#)
37. Ji W, Huh K, Kang M, Hong J, Bae GH, Lee R, et al. Effect of underlying comorbidities on the infection and severity of COVID-19 in Korea: a nationwide case-control study. *J Korean Med Sci* 2020;35(25):e237.
[PUBMED](#) | [CROSSREF](#)
38. Lee JY, Kim HA, Huh K, Hyun M, Rhee JY, Jang S, et al. Risk factors for mortality and respiratory support in elderly patients hospitalized with COVID-19 in Korea. *J Korean Med Sci* 2020;35(23):e223.
[PUBMED](#) | [CROSSREF](#)
39. Bonafè M, Prattichizzo F, Giuliani A, Storci G, Sabbatinelli J, Olivieri F. Inflamm-aging: Why older men are the most susceptible to SARS-CoV-2 complicated outcomes. *Cytokine Growth Factor Rev* 2020;53:33-7.
[PUBMED](#) | [CROSSREF](#)
40. Wang L, He W, Yu X, Hu D, Bao M, Liu H, et al. Coronavirus disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. *J Infect* 2020;80(6):639-45.
[PUBMED](#) | [CROSSREF](#)
41. Rosenbaum L. Facing COVID-19 in Italy - ethics, logistics, and therapeutics on the epidemic's front line. *N Engl J Med* 2020;382(20):1873-5.
[PUBMED](#) | [CROSSREF](#)
42. Atkins JL, Masoli JAH, Delgado J, Pilling LC, Kuo CL, Kuchel GA, et al. Preexisting comorbidities predicting severe COVID-19 in older adults in the UK biobank community cohort. <https://www.medrxiv.org/content/10.1101/2020.05.06.20092700v1.article-info>. Updated 2020. Accessed July 7, 2020.
43. Perrotta F, Corbi G, Mazzeo G, Boccia M, Aronne L, D'Agnano V, et al. COVID-19 and the elderly: insights into pathogenesis and clinical decision-making. *Aging Clin Exp Res* 2020;32(8):1599-1608.
[PUBMED](#) | [CROSSREF](#)
44. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020;323(18):1775-6.
[PUBMED](#)
45. Perry G. Alzheimer's disease patients in the crosshairs of COVID-19. *J Alzheimers Dis* 2020;76(1):1.
[PUBMED](#) | [CROSSREF](#)
46. 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(1):10.
[PUBMED](#) | [CROSSREF](#)
47. Yamazaki Y, Zhao N, Caulfield TR, Liu CC, Bu G. Apolipoprotein E and Alzheimer disease: pathobiology and targeting strategies. *Nat Rev Neurol* 2019;15(9):501-18.
[PUBMED](#) | [CROSSREF](#)
48. Shi Y, Manis M, Long J, Wang K, Sullivan PM, Remolina Serrano J, et al. Microglia drive APOE-dependent neurodegeneration in a tauopathy mouse model. *J Exp Med* 2019;216(11):2546-61.
[PUBMED](#) | [CROSSREF](#)

49. Kuo CL, Pilling LC, Atkins JL, Masoli JAH, Delgado J, Kuchel GA, et al. APOE e4 genotype predicts severe COVID-19 in the UK biobank community cohort. <https://www.medrxiv.org/content/10.1101/2020.05.07.20094409v2>. Updated 2020. Accessed July 7, 2020.
50. World Health Organization. *Risk Communication and Community Engagement Readiness and Response to Coronavirus Disease (COVID-19): Interim Guidance*. Geneva: World Health Organization; 2020.
51. McKeith IG. Dementia with Lewy bodies. *Br J Psychiatry* 2002;180:144-7.
[PUBMED](#) | [CROSSREF](#)
52. Arvanitakis Z. Update on frontotemporal dementia. *Neurologist* 2010;16(1):16-22.
[PUBMED](#) | [CROSSREF](#)
53. Simard M, Hudon C, van Reekum R. Psychological distress and risk for dementia. *Curr Psychiatry Rep* 2009;11(1):41-7.
[PUBMED](#) | [CROSSREF](#)
54. Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry* 2020;7(7):611-27.
[PUBMED](#) | [CROSSREF](#)
55. Boutoleau-Bretonnière C, Pouclet-Courtemanche H, Gillet A, Bernard A, Deruet AL, Gouraud I, et al. The effects of confinement on neuropsychiatric symptoms in Alzheimer's disease during the COVID-19 crisis. *J Alzheimers Dis* 2020;76(1):41-7.
[PUBMED](#) | [CROSSREF](#)
56. Meyer JS, Xu G, Thornby J, Chowdhury MH, Quach M. Is mild cognitive impairment prodromal for vascular dementia like Alzheimer's disease? *Stroke* 2002;33(8):1981-5.
[PUBMED](#) | [CROSSREF](#)
57. McKeith IG, Boeve BF, Dickson DW, Halliday G, Taylor JP, Weintraub D, et al. Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB consortium. *Neurology* 2017;89(1):88-100.
[PUBMED](#) | [CROSSREF](#)
58. Gore RL, Vardy ER, O'Brien JT. Delirium and dementia with Lewy bodies: distinct diagnoses or part of the same spectrum? *J Neurol Neurosurg Psychiatry* 2015;86(1):50-9.
[PUBMED](#) | [CROSSREF](#)
59. Boot BP, McDade EM, McGinnis SM, Boeve BF. Treatment of dementia with Lewy bodies. *Curr Treat Options Neurol* 2013;15(6):738-64.
[PUBMED](#) | [CROSSREF](#)
60. Bang J, Spina S, Miller BL. Frontotemporal dementia. *Lancet* 2015;386(10004):1672-82.
[PUBMED](#) | [CROSSREF](#)
61. Rada AG. COVID-19: the precarious position of Spain's nursing homes. *BMJ* 2020;369:m1554.
[PUBMED](#) | [CROSSREF](#)
62. Yourish K, Lai KKR, Ivory D, Smith M. One-third of all U.S. coronavirus deaths are nursing home residents or workers. <https://www.nytimes.com/interactive/2020/05/09/us/coronavirus-cases-nursing-homes-us.html>. Updated 2020. Accessed May 11, 2020.
63. Trabucchi M, De Leo D. Nursing homes or besieged castles: COVID-19 in northern Italy. *Lancet Psychiatry* 2020;7(5):387-8.
[PUBMED](#) | [CROSSREF](#)
64. Wang H, Li T, Barbarino P, Gauthier S, Brodaty H, Molinuevo JL, et al. Dementia care during COVID-19. *Lancet* 2020;395(10231):1190-1.
[PUBMED](#) | [CROSSREF](#)
65. Morandi A, Lucchi E, Turco R, Morghen S, Guerini F, Santi R, et al. Delirium superimposed on dementia: a quantitative and qualitative evaluation of patient experience. *J Psychosom Res* 2015;79(4):281-7.
[PUBMED](#) | [CROSSREF](#)
66. Brown EE, Kumar S, Rajji TK, Pollock BG, Mulsant BH. Anticipating and mitigating the impact of COVID-19 pandemic on Alzheimer's disease and related dementias. *Am J Geriatr Psychiatry* 2020;28(7):712-21.
[PUBMED](#) | [CROSSREF](#)
67. The Alzheimer's Association. Coronavirus (COVID-19): tips for dementia caregivers. [https://www.alz.org/help-support/caregiving/coronavirus-\(covid-19\)-tips-for-dementia-care](https://www.alz.org/help-support/caregiving/coronavirus-(covid-19)-tips-for-dementia-care). Updated 2020. Accessed June 20, 2020.
68. UK Alzheimer's Society. 5 great ways to keep moving at home - tips for people with dementia. <https://www.alzheimers.org.uk/blog/5-exercise-activities-dementia-coronavirus>. Updated 2020. Accessed June 23, 2020.
69. Alzheimer's Disease International (ADI). ADI offers advice and support during COVID-19. <https://www.alz.co.uk/news/adi-offers-advice-and-support-during-covid-19>. Updated 2020. Accessed June 17, 2020.

70. Understand Together Campaign. At home activities: meaningful activities for PWD, families and carers. <https://www.understandtogether.ie/Training-resources/Helpful-Resources/Publications/At%20Home%20Activities.pdf>. Updated 2020. Accessed June 12, 2020.
71. Alzheimer Scotland. Coronavirus: guidance for people with dementia and carers. <https://www.alzscot.org/sites/default/files/2020-03/Coronavirus%20tips.pdf>. Updated 2020. Accessed March 22, 2020.
72. IDEAL. How to stay well during the COVID-19 pandemic: 5 key messages for people living with dementia. http://www.idealproject.org.uk/media/universityofexeter/schoolofpsychology/ideal/covid-19/Dementia_leaflet_Coronavirus.pdf. Updated 2020. Accessed April 24, 2020.
73. The Alzheimer Society of Ireland. Tips for vulnerable people living alone/self-isolating. <https://alzheimer.ie/wp-content/uploads/2020/03/Tips-for-vulnerable-adultsv4.pdf>. Updated 2020. Accessed March 13, 2020.
74. Korczyn AD. Dementia in the COVID-19 period. *J Alzheimers Dis* 2020;75(4):1071-2.
[PUBMED](#) | [CROSSREF](#)
75. Jung SJ, Jun JY. Mental health and psychological intervention amid COVID-19 outbreak: perspectives from South Korea. *Yonsei Med J* 2020;61(4):271-2.
[PUBMED](#) | [CROSSREF](#)
76. Jin H, Hong C, Chen S, Zhou Y, Wang Y, Mao L, et al. Consensus for prevention and management of coronavirus disease 2019 (COVID-19) for neurologists. *Stroke Vasc Neurol* 2020;5(2):146-51.
[PUBMED](#) | [CROSSREF](#)
77. Tible OP, Riese F, Savaskan E, von Gunten A. Best practice in the management of behavioural and psychological symptoms of dementia. *Ther Adv Neurol Disorder* 2017;10(8):297-309.
[PUBMED](#) | [CROSSREF](#)
78. Bloem BR, Dorsey ER, Okun MS. The coronavirus disease 2019 crisis as catalyst for telemedicine for chronic neurological disorders. *JAMA Neurol* 2020;77(8):927-8.
[PUBMED](#) | [CROSSREF](#)
79. Gerlach LB, Kales HC. Managing behavioral and psychological symptoms of dementia. *Psychiatr Clin North Am* 2018;41(1):127-39.
[PUBMED](#) | [CROSSREF](#)
80. US Centers for Disease Control and Prevention. CDC's recommendations for the next 30 days of mitigation strategies for Seattle-King, Pierce, and Snohomish Counties based on current situation with widespread COVID-19 transmission and affected health care facilities. https://www.cdc.gov/coronavirus/2019-ncov/downloads/Seattle_Community_Mitigation.pdf. Updated 2020. Accessed March 26, 2020.
81. Andrews LJ, Benken ST. COVID-19: ICU delirium management during SARS-CoV-2 pandemic-pharmacological considerations. *Crit Care* 2020;24(1):375.
[PUBMED](#) | [CROSSREF](#)
82. Suzuki T. Does the combination use of two pain assessment tools have a synergistic effect? *J Intensive Care* 2017;5:1.
[PUBMED](#) | [CROSSREF](#)
83. Pyun JM, Park YH, Yang J, Ryoo N, Kim S. Hypersensitivity to atypical antipsychotics in dementia with Lewy bodies: is it common or rare? *Parkinsonism Relat Disord* 2020;76:44-5.
[PUBMED](#) | [CROSSREF](#)
84. Udeh C, Udeh B, Rahman N, Canfield C, Campbell J, Hata JS. Telemedicine/virtual ICU: where are we and where are we going? *Methodist DeBakey Cardiovasc J* 2018;14(2):126-33.
[PUBMED](#)
85. Adams JG, Walls RM. Supporting the health care workforce during the COVID-19 global epidemic. *JAMA* 2020;323(15):1439-40.
[PUBMED](#) | [CROSSREF](#)
86. World Health Organization. Infection prevention and control guidance for long-term care facilities in the context of COVID-19: interim guidance. <https://apps.who.int/iris/handle/10665/331508>. Updated 2020. Accessed August 10, 2020.
87. The Government of the Republic of Korea. Flattening the curve on COVID-19: how Korea responded to a pandemic using ICT. http://overseas.mofa.go.kr/gr-en/brd/m_6940/view.do?seq=761548&srchFr=&srchTo=&srchWord=&srchTp=&multi_itm_seq=0&itm_seq_1=0&itm_seq_2=0&company_cd=&company_nm=&page=1. Updated 2020. Accessed April 27, 2020.
88. Lee J, Lee AY, Daejeon Metropolitan Dementia Center. Home-visiting cognitive intervention for the community-dwelling elderly living alone. *Dement Neurocogn Disord* 2020;19(2):65-73.
[PUBMED](#) | [CROSSREF](#)
89. Chan EY, Gobat N, Kim JH, Newnham EA, Huang Z, Hung H, et al. Informal home care providers: the forgotten health-care workers during the COVID-19 pandemic. *Lancet* 2020;395(10242):1957-9.
[PUBMED](#) | [CROSSREF](#)

90. Brodaty H, Donkin M. Family caregivers of people with dementia. *Dialogues Clin Neurosci* 2009;11(2):217-28.
[PUBMED](#)
91. Yum HK. Suggestions to prepare for the second epidemic of COVID-19 in Korea. *J Korean Med Sci* 2020;35(19):e191.
[PUBMED](#) | [CROSSREF](#)
92. Benaque A, Gurruchaga MJ, Abdelnour C, Hernández I, Cañabate P, Alegret M, et al. Dementia care in times of COVID-19: experience at Fundació ACE in Barcelona, Spain. *J Alzheimers Dis* 2020;76(1):33-40.
[PUBMED](#) | [CROSSREF](#)