



Dementia Clinical Care in Relation to COVID-19

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Keywords COVID-19 · Dementia · Alzheimer's disease · Frailty · Long-term care

Abstract

Purpose of Review This review discusses the complex relationship between COVID-19 and dementia and how the pandemic has affected the management of patients with dementia. This population resulted particularly susceptible to SARS-CoV-2 infection and its effects and also to the negative effects of the measures taken worldwide to control the spread of the virus.

Recent Findings Patients with dementia were at increased risk for COVID-19 compared to patients without dementia, and diagnosis of dementia represents an independent risk factor for hospitalization in COVID-19 patients. Mortality due to SARS-CoV2 infection in

subjects with dementia is 2–5 times higher than in the general population. Cognitive impairment and delirium have been described in COVID-19 survivors. SARS-CoV2 pandemic exacerbates the vulnerability of dementia patients and their caregivers, due to the morbidity and mortality from COVID-19, the indirect effects of the pandemic on the social supports, and the effects on healthcare system on which they depend.

Summary The COVID-19 pandemic requires people with dementia to move from traditional models of health care to innovative models for home care, to support caregivers' burden, and to improve long term care.

Introduction

The current severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic represents a global public health threat. Although the ongoing vaccination campaigns are reducing the spread of the disease among the population and its lethality, we are facing medium and long-term consequences of the pandemic [1]. The frail elderly has been the most affected, either by greater severity and lethality of the disease and for its the negative effects on the quality of their life and that of their families [2••].

During the current pandemic, patients affected by dementia have sustained the greatest burden of suffering in comparison with the remainder of the population, their vulnerability has been exacerbated, and

they experienced the highest morbidity and mortality [3]. On the other hand, dementia-like cognitive impairment has been an increasingly reported complication of coronavirus disease 2019 (COVID-19) [4]. Furthermore, dementia patients have been particularly susceptible to the negative effects of social and family measures to control the spread of the virus and to the changes in the organization of the social and health system to respond to the pandemic emergency [5].

The relationship between COVID-19 and dementia is complex and in part yet to be fully understood; the various aspects of this relationship will be discussed, aiming at offering new and effective models of care for people with dementia.

COVID-19 and Dementia: a Bidirectional Relationship

Ageing, frailty, and comorbidity, which are known risk factors for the development of dementia, have also been associated with both SARS-CoV-2 infection and its adverse outcomes [6, 7].

Patients with dementia have a 2 to 5 times greater risk of experiencing COVID-19 than patients without dementia. Prevalence of dementia in COVID-19 patients is 9% (15 times than in general population), and diagnosis of dementia represents an independent risk factor for hospitalization in COVID-19 patients [8, 9].

Data shows that patients with dementia have worse clinical outcomes from any form of infection, and in general during any acute illness, sarcopenia, malnutrition, immunosuppression, and a large number of comorbidities are commonly associated with dementia and play a key role in determining poorer outcomes of acute diseases of various types [10].

During the ongoing SARS-CoV-2 pandemic, studies have shown that mortality due to SARS-CoV2 infection in persons with dementia is 2–5 times higher than in the general population and that this association remains

significant even when adjusted for age and comorbidity [11, 12]. A retrospective cohort study showed that the mortality rate of dementia patients was higher than that of patients affected by other neurological conditions [13].

Neurological complications, such as neuropsychiatric symptoms, cognitive impairments, delirium, behaviours alteration, anxiety, and depression, have been described in approximately 25% of COVID-19 patients in the acute phase of the disease [14]. Longitudinal studies revealed that COVID-19 survivors showed mental health disorders and neurocognitive disorders and included cognitive impairment as long-term sequelae of infection [15].

The impact on cognitive functioning was present in patients with a history of dementia as well as in those with no prior cognitive impairment. In a recent 3-month prospective study, patients with COVID-19 demonstrated impaired cognitive performance, specifically in the executive and visuospatial domains compared to controls and changes in the thalamus, posterior thalamic radiations, and sagittal stratum on brain MRI [16].

The mechanisms underlying cognitive impairment in COVID-19 are not yet fully understood. Different mechanisms are thought to be implicated in the pathophysiology of brain damage during SARS-Cov2 infection, in particular neuroinflammation and brain microvascular damage; the hypothesis of a direct brain and neuronal damage from SARS-CoV-2 infection has less evidence [19].

The cognitive decline observed during SARS-CoV2 infection may be caused by direct damage to brain structures, particularly the hippocampus, or be the consequence of a post-intensive care syndrome [17].

The likelihood that COVID-19 represents a risk factor for the development of dementia is a hypothesis of growing interest [18••]. COVID-19 and Alzheimer's disease (AD) have in common the involvement of angiotensin converting enzyme 2 (ACE2) receptors, pro-inflammatory markers such as interleukin-1 (IL-1), IL-6, and APOE4 allele [20]. Individuals with the AD risk allele APOE E4/E4 displayed reduced expression of antiviral defence genes compared to APOE E3/E3 individuals [4]. Recent data showed that apoE4 genotype is associated with raised levels of lipoprotein (a), increasing the risk of severe COVID-19 due to an increased risk of thromboses and other cardiovascular complications [21].

COVID-19 in Dementia Patients

Dementia is a relevant risk for COVID-19 development and influences the clinical presentation, course, and management of affected individuals.

Caring for patients with dementia during the current pandemic is a complex task, involving the management of patients in different settings [22•].

Caring for a Person with Dementia at Home

Because of the various stay-at-home directives issued by various governments, many people with dementia and their caregivers have experienced the current

pandemic in their homes, leading to feelings of loneliness and abandonment, loss of daily habits, and struggle to access normal medical care [23, 24].

Moreover, dementia patients have limited ability to understand the risks of infection, they may not be able to follow the strict procedures of infection control, and it is also difficult to put people with dementia under medical surveillance or quarantine because they may have behavioural problems including wandering or spitting [25].

In this setting of confinement and affective deprivation, changes in neuropsychiatric symptoms were observed in patients with dementia. According to a survey conducted in Italy on 4900 caregivers of patients affected by dementia, over 60% of patients presented a worsening of behavioural and psychological disorders. Anxiety, depression, hallucination, sleep disorders, wandering, and eating disorders were described both as worsening of pre-existing symptoms and as new disorders [26]. Moreover, a survey showed that two-thirds of caregivers experienced stress-related symptoms, and the level of stress experienced by the caregiver was correlated with the severity of the patient's symptoms [27].

Hospitalization for COVID-19 of a Person with Dementia

Demented patients affected by COVID-19 show a higher risk of developing a severe infection, leading to an increased risk of hospitalization and mortality [8].

A retrospective analysis conducted on a large database in the USA shows that patients with dementia present an increased risk of developing COVID-19 compared to patients without dementia: the study shows a strongest correlation with vascular dementia (OR: 3.17; 95% CI: 2.97–3.37), followed by presenile dementia (OR: 2.62; 95% CI: 2.28–3.00), AD (OR: 1.86; 95% CI: 1.77–1.96), and post-traumatic dementia (OR: 1.67; 95% CI, 1.51–1.86) [28]. Moreover, in the cohort of patients with dementia and COVID-19, the risk of hospitalization in a 6-month period was two times higher compared to patients with COVID-19 but no dementia and four times higher compared to patients with dementia but no COVID-19 [28]. These findings are consistent with the hypothesis that dementia and COVID-19 present a synergic effect on the risk of 6-month hospitalization.

A meta-analysis on 24 studies including a population of 46,391 patients showed that dementia is associated with a higher probability of developing severe COVID-19 (RR 2.63; 95% CI 1.41–4.90) and a higher mortality (RR 2.62; 95% CI 2.04–3.36) [29].

COVID-19 in Long-term Care Facilities

The current pandemic had a great impact on long-term care facilities (LTCF) and nursing homes (NH), with numerous and vast outbreaks reported in care facilities all over the world, affecting not only residents but also workers and visitors [30].

COVID-19-related deaths in LTCF residents represented from 30 to 60% of all COVID-19-related deaths worldwide, and the risk of death among LTCF residents increased about 4 times during the pandemic when compared to the previous years [31]. Due to advanced age and comorbidity, residents of long-term care facilities represent a particularly vulnerable population. About 50–75% of NH residents suffer from Alzheimer's disease or other form of dementia, and this represents the most important risk factor for COVID-19 mortality among this population [32].

Delirium in COVID-19 Patients with Dementia

COVID-19 patients with dementia may be hospitalized due to the characteristic symptoms of the infection (pneumonia, fever, respiratory failure). However, deterioration of functional status, behavioural symptoms, and in about two-third of cases, delirium, especially in the hypoactive form, are the most frequent symptoms of COVID-19 among patients affected by dementia [33].

The prevalence of delirium in elderly patients with COVID-19 ranges from 25 to 42%, and in ICU patients is about 70%; in dementia subject, the prevalence is up to 65% [34, 35]. The risk of delirium increases with age and with the severity of cognitive impairment. Delirium is associated with a higher risk of mortality among these patients [36•].

Many studies have investigated the relationship between COVID-19 and delirium, hypothesizing that complications of COVID-19 may exacerbate known risk factors for delirium or that SARS-CoV-2 infection may have a direct effect on the central nervous system [37]. It is important to underline that social distancing and the limitation of interactions with relatives could further contribute to the development of delirium by limiting the support patients receive from their loved ones. Moreover, personal protective equipment (PPE), such as gowns, masks, and face shields, could confound patients with pre-existing sensory or cognitive impairments [38].

According to a multicenter study conducted in Italy older persons, age, dementia, and pre-existing comorbidity were significantly associated with prevalent delirium, and a relevant proportion of patients presented a hypoactive form of delirium [35]. Delirium may be considered a marker of clinical severity in older patients with COVID-19 [39]. Its presence should be investigated in all patients with COVID-19 using a standardized tool, such as the Confusion Assessment Methods and the 4AT test, leading to a timely diagnosis of this condition [40].

Management of delirium in COVID-19 is challenging. Identifying of at risk patients, the definition of the premorbid functional status, drug history, and evaluation of nutritional status are the first steps for delirium prevention and appropriate treatment [41].

Delirium prevention programs are essential, despite the challenges posed by additional measures established in hospitals, such as the restriction of outside visitors, the use of face masks, and other PPE which can disorient and scare patients [36•]. General intervention measures should be put in place whenever possible. Measure such as reorient and reassure patients,

leave glasses and hearing aids in place, promote sleep hygiene, mobilize the patients whenever possible, maintain an adequate level of hydration are all effective preventive measures. Moreover, the presence of pain should be assessed and treated if necessary. Furthermore, drug prescription should be optimizing with particular attention to the anticholinergic burden [42].

The use of non-pharmacological approaches to manage delirium in COVID-19 patients is difficult, but extremely important: avoid unnecessary tubes, catheters, and physical restraints, optimize nutritional and fluid intake, promote families contact using video call, and improve mobility involving physical and occupational therapist [39].

Current recommendations state that drug treatment should only be started in patients with delirium who present agitation, aggression, hallucinations, and delusions which pose a risk of imminent harm to the patient or their carer [43].

According to the British Geriatrics Society clinical practice guide for the treatment of delirium and COVID-19, for cases in which rapid control of symptoms is required, such as violence or aggression, the first-line agent recommended is haloperidol (maximum dose 5 mg in 24 h) or quetiapine in patients requiring a sedative antipsychotic [44]. Antipsychotics should be started at low doses on a daytime bases, as needed and based on symptom severity, paying attention to comorbidities and monitoring of ECG alteration [45]. Benzodiazepines are widely prescribed for delirium, even though data supporting this practice are limited [46]. Intramuscular formulation or lorazepam may be used in patients with COVID-19 and severe agitation, especially when antipsychotic drugs are contraindicated [44]. The use of benzodiazepines in combination with antipsychotic could led to greater sedation, increasing the risk of respiratory depression in patients with pneumonia [47].

Compared to benzodiazepines and antipsychotics, melatonin and ramelteon (a melatonin receptor agonist) are a safer option that should be considered for prevention and treatment of sleep-wake rhythm disorders and delirium [48]. The management of delirium needs an individualized approach, including non-pharmacological as well as pharmacological interventions. The evaluation of risk factors, in particular cognitive decline, is strongly recommended in all older persons with COVID-19, and the evaluation of physical health conditions, functional status, sensory impairments, and potential drugs interactions is essential [39].

Dementia Care During the COVID-19 Pandemic

The current pandemic has exacerbated the vulnerability of dementia patients and their caregivers, due both to the morbidity and mortality from COVID-19 and from the indirect effects of the pandemic on their social supports networks and on healthcare system from which they depend [49].

COVID-19 has negatively influenced the clinical management of dementia patients in different ways. The rapid increase in the number of COVID-19 cases during the first months of the pandemic caused a shortage of hospital

beds and a strain on healthcare providers. Moreover, the increased burden on healthcare systems often resulted in a diversion of resources away from patients with chronic diseases [50]. The usual diagnostic workup was disrupted, with the cancellation or delay of non-urgent appointments and an increased use of telemedicine [51].

The postponement of non-pharmacological interventions that depend on direct interaction, such as group exercises and rehabilitation activities, led to cognitive, affective, and physical deterioration [52].

In LTCF, older adults were likely to experience additional distress owing to the reduction of family visits, as well as limitations on recreational activities and interactions with fellow residents [53].

The progressive increase in vaccination rates in at-risk populations dramatically reduced morbidity and mortality from COVID-19 in community-dwelling people and in LTCF residents [54].

Unfortunately, not in all countries, the vaccination of people with dementia has been considered a priority, despite the disproportionate negative impact of COVID-19 on these patients.

A recent statement from Alzheimer Europe recommended governments to:

- Include dementia as a risk factor for severe COVID-19, prioritizing people with dementia for the COVID-19 vaccine, regardless of age, place of residence, or other risk factors for severe COVID-19.
- Prioritize the inoculation of informal caregivers of patents affected by dementia, acknowledging their important contribution during the pandemic to the care, support, and even survival of people with dementia.
- Ensure that reasonable accommodations are made, and support mechanisms are in place when planning the vaccination of people with dementia, such as the possibility to be vaccinated at home and to have decision making support [55].

Home Care

The most important change in the care offered to dementia patients living at home has been the shift from the conventional office visits to virtual visits. The so-called telemedicine has been used before, but during the current pandemic, its use dramatically increased, particularly for older, frail, and demented patients [56].

Studies have shown that management of dementia is possible through virtual tools, and these interventions may increase the psychological well-being of people with dementia and their caregivers [57]. Services that might be offered through a virtual visit include cognitive rehabilitation, physical exercise, speech/swallowing education, walking assessment and training, and education and support for caregivers [58]. Nonetheless, direct patient-doctor contact remains central in the care of patients affected by dementia, and this dimension should be recovered as soon as possible.

Current and potential future applications of technologies such as artificial intelligence and robotics will provide telemedicine with an enormous

potential. These technologies, however, present numerous inherent risks, such as a degree of depersonalization of care and a difficult access to these resources by patients with severe neurocognitive disorders and with vision or hearing impairment. Moreover, the collection and safe storage of the vast amount of data generated by these interactions generate growing concerns [59, 60].

Clinicians should consider offering a combination of traditional, in-person visits with telemedicine services, tailored on the preferences and needs of the patient [61].

Caregiving

Caregivers of patients affected by dementia often experience stress and anxiety, and these conditions have a severe impact on their quality of life, on their ability to manage problems arising from the disease and, ultimately, on the quality of life of the patients themselves. As already described, during the current pandemic, psychological disturbances have increased among caregivers.

In a study conducted in 87 Italian dementia centres, about 90% of caregivers reported at least one symptom of stress, and nearly 30% reported four or more symptoms. The most prevalent symptoms were concerns for the consequences of a possible infection on the patient's health (75%) and anxiety (46%), and the main risk factors for stress were identified as a conflicting relationship with the patient and discontinuity in assistance [62].

The pandemic placed additional burdens on caregivers, both in caring for their relatives and in managing their own mental health. Some caregivers described a feeling of abandoned by the institutions and by the patient's doctors. Moreover, they felt burdened by the responsibilities of managing situations normally handled with the help of other family members, family associations, and staff of formal care [63].

Moreover, patients with moderate to severe dementia could not understand the changes in their routine (social distancing, less regular visits of relatives, use of masks) causing anxiety, agitation, and delusions.

The opportunity to discuss the current pandemic with a patient affected by dementia depends on the stage of cognitive impairment. Caregivers should judge how this information could impact the patient's mood and behaviour. If the patient can understand least some information and instructions on how protect him or her, then a conversation about the pandemic could be helpful. If there are reasons to believe that the patient could be frightened by the prospect of a potentially severe disease, the conversation could be futile and possibly even harmful.

Caregivers must have support through formal services and informal organizations to oppose the sense of abandonment, without increasing concern about the patient's risk of contracting COVID-19. There is the need for the planning of interventions targeted at the prevention of caregiver stress and relief of caregiver burden in quarantine and lockdown situations, with specific counselling services, and the reorganization of usual social care services and avoiding the interruptions in medical assistance (using telemedicine services) [63].

Long-term Care

COVID-19 disproportionately affected residents in LTCF and in NH due to the high prevalence of frailty, chronic conditions, disability, and dementia among these patients [64]. These conditions are known risk factors for both the development and severity of the infection, resulting in high rates of infections and mortality. During the first months of the pandemic other reasons concurred.

Other reasons concurred to the rapid spread of the disease among residents and workers of LTCF: the shortage of nursing staff, the crowding of residents rooms, the closed environment, and the sharing of common spaces between health personnel and residents. In addition, many nursing homes experienced inadequate testing capacity and shortages of PPE [65].

Residents with dementia presented an increased risk of severe disease due to the presence on behavioural disturbances (wandering, agitation) resulting in difficulties in maintaining isolation and the need for high-contact care [66].

Vaccination of residents and workers, along with other infection control measures, determined a dramatic decrease in the risk of COVID-19 infection in LTCF and NH, with a reduction of cases, hospitalization, and mortality rates [67].

According to a Report from Centers for Disease Control and Prevention (CDC), issued on April 2021, in 78 nursing facilities 71% of cases of SARS-CoV-2 infection occurred among unvaccinated residents, 23% among partially vaccinated and only 4% in fully vaccinated residents [68]. The majority of vaccinated residents who developed breakthrough infections were asymptomatic or presented mild symptoms; only 2 residents were hospitalized and only 1 died [68].

The vaccination rate of LTCF personnel varies widely among the US and Europe, due to different regulations. In the USA, vaccinations are not mandatory, and only some long-term care operators are demanding their healthcare professional (HCP) to be vaccinated.

According to a CDC report from August 2021, in US Nursing Homes 82.4% of the residents and only 60% of the HCP are vaccinated [69]. In Italy, the vaccination is mandatory for all HCP, and the percentage of not vaccinated is about 6% (with significant regional differences, from 0.2 to 12%) (according to data of Ministry of Health, Italian Government, updated to July 2021).

However, vaccinations alone are not sufficient to prevent outbreaks of infection in NH settings [67]. Hence, other preventive measure should be maintained, such mandatory use of face mask masks for visitors and HCP, symptoms screening and testing to identify outbreaks.

Besides, protocols for the management of residents after an exposure to COVID-19 should be adopted in every LTCF. Periodic testing for SARS-CoV-2, in unvaccinated, asymptomatic HCP, should be adopted in addition to symptoms screening.

Residents who develop COVID-19 must be evaluated to determine the severity of disease and the need for hospitalization; many patients with COVID-19 will not require hospitalization and can be managed in the NH setting, to reduce complication such as delirium, particularly in demented patients.

One of the most relevant aspects in the management of NH is the need to reorganize visits of relatives and other socialization activities. Protocols are now in place and NH are gradually and under strict rules, reopening their doors to external visitors. The same is true for physical and occupational therapy and socialization activities.

Conclusion

Caring for people with dementia in the time of SARS-CoV-2 pandemic is a challenge, due to the greater susceptibility of this population to this disease, and their vulnerability to the negative effects of the restriction imposed to control the spread of the virus [70]. Healthcare systems should cope with the worsening of neuropsychological and behavioural symptoms and the increase in caregivers' burden, for example, enacting specific programme of care and support of patients and carers, through telemedicine when deemed appropriate.

The current pandemic requires people with dementia to move from traditional models of health care to innovative models for solving problems (see Table 1).

Table 1 General principles of care for older people with dementia during SARS-CoV-2 pandemic

Home care

- Implementation of telemedicine and telehealth services
- Periodical assessment of cognitive status and behavioural symptoms
- Evaluation of caregivers' stress
- Early commitment of social services
- Education for patients and caregivers about COVID-19 prevention
- Screening for COVID-19 symptoms (typical and atypical, such as delirium)
- Vaccination against SARS-CoV-2 for patients with dementia and formal and informal caregivers

Acute care

- Screening for delirium risk
- Assessing cognitive status, functional status and behavioural symptoms
- Avoiding precipitating factors for delirium
- Providing early mobilisation
- Adapting visitor restriction policies for frail and demented elderly

Long-term care

- Screening for delirium risk
- Reorganization of socializing activities
- Allow visits for relatives in relation to their vaccination status
- Definition of a care plan in relation to general condition and stage of dementia
- Discussion of advanced directives and activation of palliative care when appropriate
- Vaccination against SARS-CoV2 of all residents, health care personnel and possibly visitors

The pandemic has determined the onset of many ethical issues, which became significant in people with dementia, such as end-of-life decisions and palliative care, the consent to care and to vaccination, the restrictions of relations with family members for the respect of safety rules, the behavioural symptoms control and the use of physical and pharmacological restraints, and the respect of dignity of the person and of their privacy [71].

Further research on the relationship between COVID-19 and dementia is needed in order to (1) identify the mechanisms underlying brain involvement during SARS-CoV-2 infection; (2) determine the reasons for the increased susceptibility to SARS-CoV-2 among dementia patients; (3) define the pathogenesis of delirium during the infection and develop protective and therapeutic strategies; (4) examine the correlation between COVID-19 and behavioural and cognitive function, and the risk of dementia onset; (5) develop home care services tailored for dementia patients; and (6) rethink long-term care services trying to balance the safety needs with the quality of life of the patients.

Author Contribution

AB and RR write the review; LB, FG, FC, and MT contribute to the revision and discussion.

Compliance with Ethical Standards

Conflict of Interest

Angelo Bianchetti declares that he has no conflict of interest. Renzo Rozzini declares that he has no conflict of interest. Luca Bianchetti declares that he has no conflict of interest. Flaminia Coccia declares that she has no conflict of interest. Fabio Guerini declares that he has no conflict of interest. Marco Trabucchi declares that he has no conflict of interest.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

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