



PERSPECTIVE PIECE

COVID-19 and Hospital-Acquired Delirium

Pooja Nair¹, Aileen Nguyen¹, Nishita Nigam² and Abraham Kanal^{2*}

¹Internal Medicine, St. Mary's Medical Center, San Francisco, California, USA

²Internal Medicine, University of California, San Francisco, California, USA

*Corresponding author: Abraham Kanal, Internal Medicine, University of California, San Francisco, California, USA



Abstract

Delirium is a frequently encountered condition in hospital medicine and can be associated with extended hospitalizations as well as higher rates of morbidity and mortality, with significant impact on the elderly population. The COVID-19 pandemic is expected to increase the burden of delirium amongst hospitalized patients.

Thus far, evidence-based interventions that have been shown to be effective in preventing and reducing the morbidity associated with this condition include early screening and diagnosis, use of technology to reduce social isolation, avoidance of deliriogenic medications, and a multidisciplinary approach to prevent long-term complications.

In this perspective piece, we aim to highlight the risk factors for delirium in patients with COVID-19 and propose key interventions that can be implemented to prevent a delirium epidemic in the midst of this pandemic. This is an issue that can significantly impact the geriatric population and we aim to raise awareness amongst healthcare professionals to enable early intervention.

Introduction

Global transmission of Coronavirus Disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been rapid and remains a significant burden around the globe. In the US, one third of infections and roughly half of hospitalizations occur in adults aged 65 and older [1]. These individuals are at significant risk for delirium, an acute confusional state with an altered level of consciousness. Prior to the pandemic, it was estimated that one third of hospitalized patients greater than 70 years of age experienced delirium during hospital admission [2], a diagnosis which portends increased risk for in-hospital complications, longer lengths of stay and mortality [3]. While SARS-CoV-2 infection is associated with a wide

range of neurologic manifestations including delirium, the systematic adjustments to patient care in response to COVID-19 pandemic present an array of insults which increase the risk for delirium among all hospitalized older adults. Now more than ever, it is crucial that members of the hospital healthcare team adopt an evidence-based, deliberate practice to identify individuals at risk for delirium, prevent its onset and appropriately treat those affected. We have outlined five possible strategies below (Table 1).

Risk Factors of Delirium in COVID-19

Among hospitalized patients there are multifactorial etiologies for delirium, including both predisposing factors (e.g. advanced age, dementia, visual impairment and immobility) and precipitating factors (e.g. surgery, pain, electrolyte abnormalities, infection, psychoactive medications and poor sleep) [2]. Those admitted to the ICU are at further risk of delirium, in-part due to increased noise, bright lighting and continuous alarms [4].

In the era of COVID-19, hospitalized elderly patients who are already at risk of developing delirium are even more vulnerable. Widely implemented hospital visitor restrictions mean that hospitalized older adults are more likely to be isolated from familiar contacts. Of those infected with SARS-CoV-2, airborne isolation and personal protective equipment (PPE), shortages may likely result in less contact with health care providers, as well. Patients infected with COVID-19 may receive medications with deliriogenic potential (e.g. hydroxychloroquine, prednisone) or experience neurologic manifestations of COVID-19 [5]. A recent observational study by Khan, et al. found that 73.6% of ICU patients with COVID-19 developed delirium that persisted for at least

Table 1: Five interventions to identify, prevent and treat delirium during the COVID-19 pandemic.

1. Recognize and label patients who are at increased risk of delirium early in the admission process.
2. Identify delirium early through a high index of suspicion and standardized delirium screening for at-risk individuals.
3. Avoid deliriogenic medications and address medication interactions thoroughly.
4. Utilize adapted modes of communication (e.g video conferencing) to enhance contact between patients and families.
5. Treat delirium using guideline-based recommendations and prioritize non-pharmacological interventions to minimize morbidity and mortality.

one week [6]. Masks and other PPE may pose challenges for communication with and orientation of those with pre-existing sensory deficits.

Differentiating between Delirium and Neuropsychiatric Manifestations of COVID-19

Neuropsychiatric manifestations of COVID-19 have been reported in up to one third of patients, and include headache, anosmia, paresthesias and altered mental status [7]. Multiple theories have been proposed, including direct viral-mediated neuroinvasion and immune- or inflammatory-mediated altered cognition [7]. In certain case reports, these symptoms have occurred independently of the hallmark respiratory symptoms associated with COVID-19 [8]. At present, it remains difficult to distinguish these etiologies for neuropsychiatric symptoms in patients with COVID-19, and further studies are warranted.

Early Screening and Diagnosis for At-Risk Patients

Ideally, identification of at-risk individuals should take place in the emergency department, as patients are especially prone to developing delirium during transitions between providers and locations. The Journal of Geriatric Emergency Medicine developed a supplement which highlights delirium as a medical emergency to be prevented or identified early in the hospital course [9]. Early recognition of these patients means that enhanced delirium precautions may be implemented immediately upon their arrival to the medical ward. Numerous delirium risk prediction models have been developed for inpatient adults, most of which include advanced age, pre-existing cognitive and functional impairment, sensory impairment and severe illness [10]. Models such as these should be applied broadly to all admitted patients, whose scores should be included amongst other vital information in handoffs between providers. This will assist in diagnosing delirium, especially the hypoxic variant, may require a high-index of suspicion. The Confusion Assessment Module (CAM) is a validated, widely-used tool which can be utilized to make the diagnosis of delirium in suspected individuals.

Preventing and Treating Delirium

Decades of research have identified evidence-based interventions which are effective in both preventing and treating delirium, and are exclusively non-pharmacologic. At present, there is no convincing evidence for bene-

fit in the use of any pharmacologic therapy in either the prevention or treatment of delirium [3]. Care bundles such as HELP (Hospital Elder Life Program) have been shown to significantly reduce the incidence of delirium through a multifaceted, non-pharmacologic approach, and these materials have been made readily available on the program website [2]. These include promoting family presence and regular mobility, minimizing pain and noise, as well as optimizing regular sleep-wake cycles and bowel/bladder habits [2]. Unfortunately, many of these bundled protocols are difficult or impossible to apply to patients in isolation. For these patients, providers must make a deliberate effort to overcome these barriers in delirium prevention and treatment. LaHue, et al. published a list of recommendations adapted to the COVID-19 patient population [11]. Notable suggestions include daily tele-conferencing between patients and their family, enhancing mobilization with instructional handouts, and continuing current ICU best-practices such as spontaneous awakening trials despite the challenges posed by pronation and isolation. The Hospital Elder Life Program has similarly produced materials to enhance communication and engagement with isolated, hospitalized, older adults infected with SARS-CoV-2. Some authors have suggested that a more aggressive pharmacologic approach should be taken for COVID-19 patients with hyperactive delirium, foregoing the slow titration of antipsychotics typically used for pharmacological delirium treatment [12]. The evidence for such an approach is limited, and the potential benefit from mitigated self-harm must always be carefully balanced with the well-established risk of pharmacologic intervention.

Use of Technology to Promote Communication

In addition to diligent application of existing delirium interventions, we believe that there is an increasing need for institutions and providers to take a proactive approach in finding creative methods to identify, prevent and treat delirium during the COVID-19 pandemic. Many institutions have adopted methods to enhance availability of video-conferencing technology for their isolated patients, allowing for regular communication between patients, families and providers. When combined with remote interpreter services, this technology may have the added benefit of overcoming the language barriers in patients with limited English proficiency. Prior studies have explored the use of video conferencing to connect institutionalized, older adults with their loved

ones, and special attention should be paid to overcome an expected degree of difficulty in adopting new technologies amongst this population [13]. Studies have also shown that music and nightly ear-plugs reduce delirium, anxiety and pain amongst hospitalized patients [14].

Avoidance of Deliriogenic Medications

Use of deliriogenic medications such as hydroxychloroquine (HCQ) and corticosteroids for COVID-19 must be carefully considered in patients at risk for delirium. If they are used, patients should be regularly screened for the development of neuropsychiatric effects. Of note, antivirals like remdesivir and protease inhibitors are associated with hepatotoxicity and may have downstream effects on the metabolism of other psychotropic agents such as valproic acid [15]. Similarly, in mechanically ventilated patients who require prone positioning, cautious use of sedatives and neuromuscular blockade is crucial in preventing increased rates of ICU delirium [16].

Preventing Long-Term Complications

Delirium has been found to precipitate mental health disorders such as depression and anxiety, as well as long-term cognitive impairments [17,18]. The BRAIN-ICU study found that a longer duration of delirium was associated with increased cognitive impairments, independent of sedative use, pre-existing cognitive impairment or co-existing conditions [19]. A systematic review of patients who recovered from SARS and Middle East Respiratory Syndrome (MERS) revealed a high incidence of depression, fatigue and post-traumatic stress disorder [20]. Hospital providers should partner with patient's families and primary care teams to ensure patients are monitored for such neuropsychiatric sequelae after discharge. Evidence from systematic reviews suggests that early application of physical and psychological rehabilitation interventions are of utmost importance to counter the ramifications of an intensive care stay [19].

Conclusion

The COVID-19 pandemic is likely to result in an increased burden of delirium amongst hospitalized patients, with an outsized impact on those with SARS-CoV-2 infection. Older adults are at significant risk for hospitalization, morbidity and mortality due to COVID-19, and are similarly vulnerable to the short- and long-term sequelae of delirium associated with hospitalization. It is more prudent than ever for healthcare providers to apply established protocols and implement new, creative technologies to screen for, prevent and treat hospital-acquired delirium during the COVID-19 pandemic.

Conflicts of Interest

Authors have no conflicts of interest to disclose.

References

1. CDC COVID-19 Response Team (2020) Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) -United States, February 12-March 16, 2020. *MMWR Morb Mortal Wkly Rep* 69: 343-346.
2. Tammy T Hsieh, Jirong Yue, Esther Oh, Margaret Puelle, Sarah Dowal, et al. (2015) Effectiveness of multicomponent non pharmacological delirium interventions: A meta-analysis. *JAMA Intern Med* 175: 512-520.
3. Inouye S, Westendorp R, Saczynski J (2014) Delirium in elderly people. *Lancet* 383: 911-922.
4. Karin J Neufeld, Jirong Yue, Thomas N Robinson, Sharon K Inouye, Dale M Needham (2016) Antipsychotic medication for prevention and treatment of delirium in hospitalized adults: A systematic review and meta-analysis. *J Am Geriatr Soc* 64: 705-714.
5. Ling Mao, Huijuan Jin, Mengdie Wang, Yu Hu, Shengcai Chen, et al. (2020) Neurologic Manifestations of Hospitalized Patients with Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol* 77: 1-9.
6. Sikandar H Khan, Heidi Lindroth, Anthony J Perkins, Yasser Jamil, Sophia Wang, et al. (2020) Delirium Incidence, Duration and Severity in Critically Ill Patients with COVID-19. *MedRxiv*.
7. Scott R Beach, Nathan C Praschan, Charlotte Hogan, Samuel Dotson, Flannery Merideth, et al. (2020) Delirium in COVID-19: A case series and exploration of potential mechanisms for central nervous system involvement. *Gen Hosp Psychiatry* 65: 47-53.
8. Walid A Alkeridy, Ibrahim Almaghlouth, Rashed Alrashed, Khalid Alayed, Khalifa Binkhamis, et al. (2020) A Unique Presentation of Delirium in a Patient with Otherwise Asymptomatic COVID-19. *J Am Geriatr Soc* 68: 1382-1384.
9. Michael L Malone, Teresita M Hogan, Adam Perry, Kevin Biese, Alice Bonner, et al. (2020) COVID-19 in Older Adults: Key Points for Emergency Department Providers. *Journal of Geriatric Emergency Medicine* 1: 1-11.
10. Heidi Lindroth, Lisa Bratzke, Suzanne Purvis, Roger Brown, Mark Coburn, et al. (2018) Systematic review of prediction models for delirium in the older adult inpatient. *BMJ Open* 8: e019223.
11. Sara C LaHue, Todd C James, John C Newman, Armond M Esmaili, Cora H Ormseth, et al. (2020) Delirium Prevention in the Age of COVID-19. *J Am Geriatr Soc* 68: 947-949.
12. Barton J Sanders, Melissa Bakar, Sonal Mehta, M Carrington Reid, Eugenia L Siegler, et al. (2020) Hyperactive Delirium Requires More Aggressive Management in Patients with COVID-19: Temporarily Rethinking "Low and Slow". *J Pain Symptom Manage* 60: e31-e32.
13. Wendy Moyle, Cindy Jones, Jenny Murfield, Fangli Liu (2020) For Me at 90, It's Going to Be Difficult: Feasibility of using iPad video-conferencing with older adults in long-term aged care. *Aging Ment Health* 24: 349-352.
14. Network for Investigation of Delirium: Unifying Scientists (2020) Preventing Delirium During COVID-19 with Evidence-Based Tools 2020.
15. Melanie Bilbul, Patricia Papparone, Anna M Kim, Shrutti Mutalik, Carrie L Ernst (2020) Psychopharmacology of COVID-19. *Psychosomatics*.
16. Katarzyna Kotfis, Shawniqua Williams Roberson, Jo Ellen Wilson, Wojciech Dabrowski, Brenda T Pun, et al. (2020)

- COVID-19: ICU delirium management during SARS-CoV-2 pandemic. *Crit Care* 24: 176.
17. Davydow DS (2009) Symptoms of depression and anxiety after delirium. *Psychosomatics* 50: 309-316.
 18. PP Pandharipande, TD Girard, JC Jackson, A Morandi, JL Thompson, et al. (2013) Long-Term Cognitive Impairment after Critical Illness. *N Engl J Med* 369: 1306-1316.
 19. Stam H, Stucki G, Bickenbach J (2020) Covid-19 and post intensive care syndrome: A call for action. *J Rehabil Med* 52: jrm00044.
 20. Rogers J, Chesney E, Oliver D, Pollak T, McGuire P, et al. (2020) Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: A systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry* 7: 611-627.