Increased Prevalence of Dementia and Neurological Diseases in SARS-CoV-2 Infection Survivors

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Acute Ischemic Stroke and Coronavirus Disease 2019: An Analysis of 27,676 Patients

- 8,163 patients with confirmed COVID-19 among 27,676 patients in the Cerner de-identified COVID-19 dataset.

- 103 (1.3%) patients developed acute ischemic stroke among 8,163 patients with COVID-19.

- 199 (1.0%) patients developed acute ischemic stroke among 19,513 patents in whom COVID-19 was excluded.

- Of the 103 patients with confirmed COVID-19 and acute ischemic stroke, 94 received their COVID-19 diagnosis during the same encounter that they had acute ischemic stroke.

Qureshi AI. Stroke. 2021;52:905–912
Survivors of SARS-CoV-2 infection

- New focus on long-term disability among approximately 513 million survivors worldwide.

Global Situation

519,105,112 confirmed cases

6,266,32 deaths

Source: World Health Organization
How many survivors of SARS-CoV-2 infection are present in USA

- 20 million
- 40 million
- 80 million
- 160 million
Survivors of SARS-CoV-2 infection

- New focus on long-term disability among approximately 80 million survivors in USA.
# Cognitive Impairment Among Survivors of SARS-CoV-2 infection

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients</th>
<th>Definition of cognitive impairment</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hellmuth et al.</td>
<td>100 non-hospitalized</td>
<td>Detailed neuropsychological testing which revealed mild disorganization and inefficient, error-prone task execution.</td>
<td>20 (20%)</td>
</tr>
<tr>
<td>Taquet et al.</td>
<td>236,379 hospitalized</td>
<td>Dementia by ICD-10 codes</td>
<td>6229 (2.6%)</td>
</tr>
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</table>

Cognitive Impairment Among Survivors of SARS-CoV-2 infection

What kind of cognitive deficits do survivors of SARS-CoV-2 infection have:

- Mild cognitive deficits that may or may not be detected by MMSE or MoCA
- Severe cognitive deficits
- Dementia that impairs multiple cognitive and functional domains

- 2 and 3
- 1, 2, and 3
Cognitive Impairment Among Survivors of SARS-CoV-2 infection

- The prevalence and risk of dementia in survivors of SARS-CoV-2 infection has multiple implications for screening, post recovery care and resources, care-giver burden, and financial and productivity loss.

- The impact on public health may be much larger than the acute manifestations of SARS-CoV-2 infection due to lifelong burden of dementia.

Re: Qureshi AI, Baskett WL, Huang W, Naqvi SH, Shyu CR. Open Forum Infectious Diseases. 2022 Apr;9(4):ofac115
Cognitive Impairment Among Survivors of SARS-CoV-2 infection

- The prevalence and risk of dementia in survivors of SARS-CoV-2 infection has multiple implications for screening, post recovery care and resources, care-giver burden, and financial and productivity loss.

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Re: Qureshi AI, Baskett WI, Huang W, Naqvi SH, Shyu CR. Open Forum Infectious Diseases. 2022 Apr;9(4):ofac115
New Onset Dementia Among Survivors of Bacterial Pneumonia

117,12 patients with bacteria pneumonia

No dementia

117,120 patients without bacteria pneumonia

459 (3.6%)

1358 (1.2%)

Up to 17 years

2 years Reference encounter Ascertainment of dementia

New Onset Dementia Among Survivors of Bacterial Pneumonia

No dementia

117,12 patients with bacteria pneumonia

117,120 patients without bacteria pneumonia

2 years Reference encounter Ascertainment of dementia

New Onset Dementia Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection

- Cerner Real-World Data extracted from the electronic medical records of health care facilities.

- The Cerner Real-World Data is available through Cerner Corporation. The Cerner Real World Data Q3 2021 through July 2021 collected from 110 contributing Cerner Real-World Data health systems.
New Onset Dementia Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection

10,403 patients with SARS-CoV-2 infection

No dementia

10,403 patients without SARS-CoV-2 infection

Dementia ICD-10-CM primary diagnosis codes F01.5, F02.8, F03.9, G30, G31, G32

Re: Qureshi AI, Baskett WL, Huang W, Naqvi SH, Shyu CR. Open Forum Infectious Diseases. 2022 Apr;9(4):ofac115
New Onset Dementia Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection

10,403 patients without SARS-CoV-2 infection

No dementia

10,403 patients with SARS-CoV-2 infection

Dementia

ICD-10-CM primary diagnosis codes
F01.5, F02.8, F03.9, G30, G31, G32

2 years Reference encounter 30 days Ascertainment of dementia

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10,403 patients with SARS-CoV-2 infection

No dementia

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312 (3%; 95% CI 2.7%-3.4%)
Median 182 days (interquartile range Q1=113 days, Q3=277 days)

263 (2.5%, 95% CI, 2.2-2.9%)

2 years Reference encounter 30 days Ascertainment of dementia

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Approximately 1 million people have other pneumonia with 25,000 getting dementia

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2 years Reference encounter 30 days Ascertainment of dementia

Re: American Thoracic Society 2019
New Onset Dementia Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection

10,403 patients with SARS-CoV-2 infection

10,403 patients without SARS-CoV-2 infection

Approximately 1 million people have other pneumonia with 25,000 getting new dementia
Approximately 5 million additional SARS-CoV-2 related pneumonias with 150,000 getting new dementia

2 years | Reference encounter | 30 days | Ascertainment of dementia

Re: American Thoracic Society 2019
New Onset Dementia Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection (by age groups)
## New Onset Dementia Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection (multivariate analyses)

<table>
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<th>Predictors</th>
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Abbreviations used: SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; OR: odds ratio; CI: confidence interval.

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Model 1. Baseline demographic characteristics + cardiovascular risk factors + dementia risk factors.

New Onset Dementia Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection (multivariate analyses)

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The odds of new onset dementia were 30% higher among patients with pneumonia associated with SARS-CoV-2 infection compared with other pneumonias.

Model 1. Baseline demographic characteristics + cardiovascular risk factors + dementia risk factors.
Identify the true statements about pneumonia and dementia

- Survivors of bacteria pneumonia have a higher risk of dementia than those without pneumonia.

- Survivors of SARS-CoV-2 related pneumonia have a higher risk of dementia than survivors of other pneumonia.

- Survivors of SARS-CoV-2 related pneumonia have a higher risk of dementia due to higher risk of stroke.
Cognitive Impairment Among Survivors of SARS-CoV-2 infection - Pathophysiology

- Hypoxia/cerebral ischemia
- Meningitis/Encephalitis
- Systemic inflammatory mediators IL-1, IL-6
- Increase in Vagal N activity
- Gaps in blood brain barrier
- Disrupt blood brain barrier
- Activate capillary endothelium
- Neuronal injury
- Astrocyte/microglia activation
- PGE2
Cognitive Impairment Among Survivors of SARS-CoV-2 infection—Pathophysiology

- **SARS-CoV-2 infection**
  - Hypoxia/cerebral ischemia
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    - Increase in Vagal N activity
  - Gaps in blood brain barrier
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      - PGE2
  - Neuronal injury
    - Astrocyte/microglia activation

Virus does not enter brain
Cognitive Impairment Among Survivors of SARS-CoV-2 infection—Pathophysiology

SARS-CoV-2 infection

Hypoxia/cerebral ischemia

Immune activation

Systemic inflammatory mediators IL-1, IL-6

Increase in Vagal N activity

Demyelination Encephalitis

Gaps in blood brain barrier

Disrupt blood brain barrier

Activate capillary endothelium

Neuronal injury

Astrocyte/microglia activation

PGE2
New Cardiovascular Events Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection

- 10,691 patients with SARS-CoV-2 infection
- Ischemic stroke, myocardial infarction, hemorrhagic stroke

- 10,691 patients without SARS-CoV-2 infection

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<tr>
<th>2 years</th>
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<th>30 days</th>
<th>Ascertainment of new cardiovascular events</th>
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</table>

Reference encounter

Ascertainment of new cardiovascular events
New Cardiovascular Events Among Survivors of Pneumonia Associated with Severe Acute Respiratory Syndrome Coronavirus 2 Infection

No difference in rate of new cardiovascular events
Anticoagulants and antiplatelet therapy should not be initiated for the prevention of venous thromboembolism or arterial thrombosis for non-hospitalized patients with SARS-CoV-2 infection, unless the patient has other indications for the therapy or is participating in a clinical trial (strong evidence based on expert opinion).

Leentjens et al.
Routine antithrombotic treatment is not recommended in patients with SARS-CoV-2 infection after discharge based on pathophysiology of SARS-CoV-2 infection related coagulopathy and data from randomized controlled trials.
Cognitive Impairment Among Survivors of SARS-CoV-2 infection—Implications

- Occurrence of new onset dementia may increase the burden of disability among survivors of SARS-CoV-2 infection.

- US President---long-term symptoms of SARS-CoV-2 infection could be considered a disability under federal civil rights laws of Americans With Disabilities Act.

- National Institutes of Health research emphasizes on Long COVID can be debilitating and some people will require assistance with personal care months after the initial infection with 80% reporting difficulty in ability to work and 36% reported negative financial consequences.

- Social Security has released an emergency message giving its employees some guidance on how to handle applications that allege "post-COVID conditions."
Long-COVID or Post-COVID conditions

- Dyspnea or increased respiratory effort
- Fatigue
- Post-exertional malaise and/or poor endurance
- “Brain fog,” or cognitive impairment
- Cough
- Chest pain
- Headache
- Palpitations and/or tachycardia
- Arthralgia
- Myalgia

- Paresthesia
- Abdominal pain
- Diarrhea
- Insomnia and other sleep difficulties
- Fever
- Lightheadedness
- Impaired daily function and mobility
- Rash (e.g., urticaria)
- Mood changes
- Anosmia or dysgeusia
- Menstrual cycle irregularities
### Interim Guidance on Evaluating and Caring for Patients with Post-COVID Conditions

The U.S. Centers for Disease Control and Prevention recommends using the umbrella term “post-COVID conditions” for a wide range of signs and symptoms that occur 4 or more weeks after acute COVID-19 infection.

**Standardized case definitions are still being developed....**
## Long-COVID or Post-COVID conditions

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Cognitive Impairment Among Survivors of SARS-CoV-2 infection—Next Steps

- Screening for cognitive deficits among survivors of SARS-CoV-2 infection. Several screening tests are available for use in survivors of SARS-CoV-2 infection including Saint Louis University Mental Status (SLUMS) Examination, Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE).

**WHO --- WHEN ---HOW --- THAN WHAT…**

- Social Security may have to establish new onset dementia as a "medically determinable impairment," or MDI to determine whether SARS-CoV-2 infection survivors are unable to work for 12 months and thus eligible for benefits.
Zeenat Qureshi Institutes 2022—Thank you

St. Cloud, Minnesota, USA

Donka National Hosp, Conakry, Guinea

Firat University, Elasig, Turkey

Xuan Wu Hosp, Beijing, China