VIEWPOINT

Recovery From Severe COVID-19
Leveraging the Lessons of Survival From Sepsis

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Supplemental content

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As of July 30, 2020, more than 17 million people worldwide have been diagnosed with coronavirus disease 2019 (COVID-19), and more than 665 000 have died. In many countries, the rate of diagnosis continues to increase; for example, more than 50 000 new cases per day were reported in the US during the last week of July.

Patients with severe disease, which affects up to 20% of those hospitalized with COVID-19, develop viral sepsis and acute respiratory distress syndrome (ARDS). While there has been substantial focus on the potentially unique manifestations of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), many of the acute manifestations and outcomes of severe COVID-19 are similar to those of sepsis caused by other pathogens.

Approximately 80% of patients hospitalized with COVID-19, and 60% of those admitted to intensive care units (ICUs), survive. However, similar to the experiences of other sepsis survivors,[1] many COVID-19 survivors are likely to experience long-lasting morbidity.

What Is Expected About Recovery From COVID-19?

Since SARS-CoV-2 was just discovered in January 2020, little published data are available on long-term outcomes and recovery after severe COVID-19. Yet studies in related patient populations, such as those affected with other coronaviruses, all-cause sepsis, or general critical illness, are helpful when considering the likely outcomes of COVID-19 survivors. Studies in these populations document multifaceted problems stemming from sepsis and critical illness, which are collectively described as "post–intensive care syndrome"[2] or "post-sepsis syndrome."

A meta-analysis of 28 studies, which included 2820 patients, examined long-term outcomes after severe disease caused by other coronaviruses (SARS and MERS) and reported high rates of posttraumatic stress disorder (38%), depression (33%), and anxiety (30%) at 6 months following illness, as well as pulmonary dysfunction, reduced exercise tolerance, and reduced health-related quality of life.[3] Cognitive impairment, a key feature of post-sepsis syndrome, was not studied in these investigations, but a prospective cohort study of 516 older adults who survived all-cause sepsis found that it was associated with a nearly 3-fold increase in the odds of moderate to severe cognitive impairment (increasing from 6.1% before sepsis to 16.7% after) and the development of 1 or 2 new functional limitations, such as inability to bathe, toilet, or dress independently.[4]

Sepsis survivors are also vulnerable to further health deterioration. As many as 40% of patients discharged after hospitalization with sepsis are rehospitalized within 90 days, most commonly for recurrent infection or exacerbation of chronic health conditions.[5] These long-term sequelae often profoundly alter patients' lives. In a meta-analysis of 51 studies (7267 patients) who survived critical illness, only 33%, 55%, and 56% of previously employed patients returned to work by 3, 6, and 12 months, respectively, following critical illness.[6]

While cognitive, physical, psychological, and medical impairments are common after sepsis, the clinical presentation varies considerably. Some patients, for example, develop predominantly cognitive symptoms (memory deficits, difficulty concentrating), whereas others experience predominantly physical limitations (exercise intolerance, fatigue, dysphagia) or psychological sequelae (anxiety, depression, nightmares). Additionally, these adverse outcomes may not be limited to those who experience critical illness. Studies of all-cause pneumonia found that mild cognitive impairment and dementia were common in survivors, regardless of pneumonia severity. Similarly, a study of 143 COVID-19 survivors, 13% of whom were admitted to an ICU, found that nearly 90% were experiencing persistent symptoms (with fatigue, dyspnea, and joint pain the most common) 2 months after onset of COVID-19.[7]

Will Recovery From COVID-19 Be Unique?

It is unknown whether recovery from COVID-19 will be different from recovery after sepsis due to other infections. Given that the acute manifestations of severe COVID-19 are similar in many ways to those of sepsis in general, survivors of severe COVID-19 are anticipated to experience similar challenges as other sepsis survivors. Nevertheless, COVID-19 may cause some specific sequelae that result from unique aspects of the pathophysiology of SARS-CoV-2 infection.

The prevalence and severity of post–intensive care syndrome among COVID-19 survivors may also be greater than in general sepsis cohorts because the pandemic has impeded normal care practices. ICU protocols can improve outcomes by prioritizing sedation minimization, daily breathing trials, early mobility, and other evidence-based practices, but these time- and coordination-intensive practices may not occur in overwhelmed ICUs, especially if isolation procedures and other COVID-19–related concerns interfere with usual care. As a result, patients with severe COVID-19 may receive deeper sedation, fewer breathing trials, and more limited mobility than other patients with sepsis, all of which could contribute to a worse recovery.

What Are Best Practices to Promote Recovery?

Despite limited data specific to recovery from COVID-19, the practices that are recommended to enhance recovery from sepsis are applicable to patients recovering from severe COVID-19 (eTable in the Supplement).[1] Patients with viral sepsis from COVID-19 should receive these recommended practices, including anticipatory guidance regarding potential new problems, screening for new impairments at hospital discharge and early out-

patient follow-up, anticipation and mitigation of risk for common and preventable health deterioration, medication optimization, and referral or instructions for a structured exercise program. Patients have an increased risk of mortality for at least 2 years after sepsis, and in patients with declining health leading to hospitalization for COVID-19, it is important to consider transitioning to a palliative focus of care.

These recommended practices are associated with better clinical outcomes. In a cohort of 189 sepsis survivors from 10 US hospitals, 65% had screening for new functional or mental health impairments, 62% had medications optimized, 58% had care alignment processes documented (eg, goals of care discussion, palliative care referral), and 46% were monitored for common and preventable causes of health deterioration.[8] Receipt of these practices was associated with lower odds of rehospitalization or death, but only 20% of patients received all 4 recommended practices within 90 days of sepsis hospitalization,[8] suggesting the need to develop better implementation strategies for these recommended practices.

How Can Health Care Systems Facilitate Best Practices for Recovery?

Even before the COVID-19 pandemic, there was a need to develop better systems by which to promote recovery and adaptation to new disability after sepsis. The 2017 World Health Organization resolution on sepsis identified support of sepsis survivors as a key priority in addressing the worldwide burden of sepsis. COVID-19 now underscores the urgency of this clinical problem and represents an important opportunity to develop and test new programs that support sepsis survivors.

In the US, more than one-third of older sepsis survivors are admitted to post–acute care facilities following hospital discharge for ongoing skilled nursing care and rehabilitation, such as physical, occupational, and speech therapy. However, numerous outbreaks of SARS-CoV-2 infection have occurred in skilled nursing facilities. Patients and families may therefore be reluctant to accept placement at a post–acute care facility, and even if willing, facility availability may be limited due to closures, downsizing, or additional placement requirements to mitigate spread of COVID-19 (eg, serial negative SARS-CoV-2 test results). As a result, a greater proportion of patients may be discharged home, placing additional responsibility on informal caregivers and outpatient clinicians.

The only clinical trial to date on recovery from sepsis randomized 291 patients to a multicomponent primary care management intervention vs usual care and was conducted prior to COVID-19.[9] The intervention included education for patients and clinicians about sepsis and its common sequelae; case management by nurses with ICU experience, focusing on symptom monitoring; and decision support by physicians trained in both primary and critical care. There was no significant difference in mental health–related quality of life at 6 months (the primary outcome), but the intervention group experienced improvements in several secondary outcomes related to physical function and disability.

Another clinical trial examining a sepsis transition and recovery program (NCT03865602) began enrollment prior to the pandemic and will randomize 708 sepsis survivors to usual care vs the intervention, in which a centrally located nurse navigator uses telephone counseling and electronic health record–based support to facilitate best practices for post-sepsis care (eTable in the Supplement).

Concurrent with the conduct of randomized clinical trials, health care systems around the world have leveraged post-ICU clinics and peer support programs to address the multifaceted needs of sepsis survivors. In addition to supporting patients and families, these programs provide a central environment within which to study sepsis survivorship and test the comparative effectiveness of different strategies intended to promote recovery and adaptation. The Critical and Acute Illness Recovery Organization (CAIRO) is a collaborative of such programs working to identify and disseminate best practices for recovery.

In a qualitative study of clinicians from 21 sites, lack of funding and difficulty accessing in-person clinics were key barriers to the development of critical illness recovery programs, whereas alignment with organizational priorities was a key facilitator.[10] The pandemic has already resulted in a rapid expansion of telehealth capability and acceptance, which should be leveraged to increase accessibility to recovery programs. COVID-19 has also raised public awareness of sepsis survivorship issues, which may lead funders, insurers, and health care systems to prioritize investments in recovery programs. Importantly, these investments could help not only survivors of severe COVID-19 but also the approximately 15 million patients who survive non–COVID-19 sepsis each year.

ARTICLE INFORMATION

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