

Multidisciplinary Guidance to Manage Comatose Patients with Severe COVID-19

In Spring 2020, New York City (NYC) rapidly became an epicenter of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease 2019 (COVID-19) global pandemic, with a reported 200,547 cases between March 8 and May 31, 2020.¹ Over one fifth of hospitalized patients in NYC were critically ill, many on mechanical ventilation with multi-organ failure requiring prolonged sedation.² The neurology consultation service quickly became an integral part of the care for the many critically ill patients with COVID-19 with impaired consciousness. The mechanism of these disorders of consciousness in patients infected by COVID-19 is poorly understood and may be due to multi-organ failure, hypoxia, systemic inflammation, hypercoagulability, and possible neuro-invasion.³ Uncertainty about the trajectory of this novel disease as well as concerns for health care worker safety created challenges in relying on standard behavioral, electrophysiological, imaging, and laboratory data that guides diagnostic workup and prognostication in patients with disorders of consciousness. To provide a comprehensive weighing of the rapidly evolving body of evidence in an area of great uncertainty, we instituted a multidisciplinary COVID-19 Coma Board modeled after the tumor board concept.⁴

This biweekly, secure web-based multidisciplinary conference first met on May 13, 2020, with participants representing neurocritical care, epilepsy, stroke, neuroradiology, neurovascular, neurohospitalist, neuroinfectious disease, rehabilitation medicine, and pharmacology. Data was presented by the consult team using a standardized data collection format (Table). This study was approved by the institutional review board at Columbia University Irving Medical Center. The requirement for written informed consent was waived because the observational study design involves no more than minimal risk. In our first 8 case discussions, 5 patients were above 60 years old (53%), 3 were women (38%), 4 had episodes of hypoxia (defined as at least one documented arterial blood gas with a PO₂ below 55 mmHg), 1 suffered cardiopulmonary arrest, and

7 developed renal failure. The mean days on mechanical ventilation were 40 (+/- 21 days), of sedation were 33 (+/- 18 days), of treatment with opiates were 39 (+/- 23 days), and 6 received neuromuscular blockade (Supplementary Table S1). At the time of presentation, neurological examination included eye opening (none 1, to pain 3, to voice or spontaneous in 4), pupillary light reflexes were intact in all, and corneal reflexes present in 6. Two patients followed simple verbal commands, whereas the other 6 followed no commands. Five had no motor response, the other 3 each had one with tonic posturing, localization to noxious stimulation, and stimulus-provoked myoclonus. Three patients had positive urine toxicology for benzodiazepines at the time of consultation, 3 had electroencephalograms (EEGs) available (none with seizures or periodic discharges, and all with discontinuous and attenuated background activity). All had computed tomography (CT; N = 7) or magnetic resonance imaging (MRI; N = 2) of the brain available demonstrating 1 patient with diffuse cerebral edema on CT, restricted diffusion and increased T2 signal in the cortex and basal ganglia on MRI, and diffusion restriction in bilateral globus pallidi and cerebral peduncles on MRI. Pharmacological regimens were reviewed and factors contributing to drug accumulation were discussed, including drug duration and half-life, organ dysfunction, drug interactions, body weight, and age.

The COVID-19 Coma Board concluded that major contributing factors of coma included medication effects (N = 6), anoxic injury (N = 1), and urinary tract infection (UTI; N = 1). Further diagnostic testing was recommended, including urine toxicology (N = 3), MRI (1 case of restricted diffusion seen in the globus pallidus with increased T2 signal in the central pons, and a second case with cortical punctate infarcts; additionally, 2 MRIs were available at follow-up meetings of the COVID-19 Coma Board and showed chronic lacunar infarcts in one and diffuse atrophy and chronic microvascular disease in the other), and lumbar puncture (N = 1). At the time of this

TABLE. Structured Information Provided to the COVID-19 Coma Board

Standardized list of medical information obtained and reviewed at the conference
1. Admission date
2. Length of stay of current admission
3. Intubation date
4. Extubation and/or tracheostomy date
5. Paralytics received
6. Sedation medication received
7. Duration (days) hypoxemia
8. Occurrence of cardiac arrest
9. Use of hemodialysis or continuous veno-venous hemofiltration (CVVH)
10. Active infections other than COVID-19 at the time of consultation
11. Serologic markers of renal dysfunction
12. Serologic markers of liver dysfunction
13. Urine toxicology result
14. Neuro imaging (head CT or brain MRI)
Minimal neurological examination by neurology consultation service
1. Level of consciousness
• Arousal: eye opening
• Command following: 1-step, multistep, orientation to self, place, and time
2. Brainstem function: pupillary light reflex, corneal reflex, oculocephalic reflex, respiratory pattern
3. Motor response: to commands, noxious stimuli, tone, reflexes
CT = computed tomography; COVID-19 = coronavirus disease 2019; MRI = magnetic resonance imaging.

report, 4 of the patients had recovered consciousness, 1 remained unconscious, 1 had died, and the other 2 continued to follow simple commands only (1 patient did not have follow-up). Diagnostic findings in patients with persistent coma and death included evidence of punctate restricted diffusion in the cortex and more diffuse restricted diffusion in the basal ganglia, and lymphocytic pleocytosis with elevated protein on cerebrospinal fluid analysis.

The COVID-19 Coma Board provided a comprehensive, multidisciplinary assessment and recommendations of comatose patients with COVID-19 with an uncertain prognosis. The virtual platform enabled subspecialty contribution while maintaining social distancing. Cases demonstrated a high degree of complexity, including multi-organ dysfunction, use of polypharmacy regimens with long half-life sedatives in the setting of national drug shortages, and non-detection of certain sedatives/opioids in routine urine toxicology screens. The board faced pragmatic decisions about diagnostic tests taking into account health care worker safety. This conference facilitated re-integrating educational conferences into the residency program, in particular, providing residents with a platform to share ongoing scientific literature of this novel disease and learn from our multidisciplinary specialists. This format may constitute a blueprint for expert assessments of comatose patients with COVID-19 that could be scalable and applicable to broader health care systems in future pandemic surges.

Long-term recovery increasingly calls into question the self-fulfilling prophecy of early withdrawal of care for patients with acute disorders of consciousness. The science underlying impairment and recovery of consciousness is rapidly accelerating and increasingly complex.⁵ The institution of multidisciplinary Coma Boards may serve unconscious patients with or without COVID-19 well beyond the current pandemic.

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Additional supporting information can be found in the online version of this article.

References

1. Available at: <https://www1.nyc.gov/site/doh/covid/covid-19-data.page>, viewed May 31, 2020
2. Cummings MJ, Baldwin MR, Abrams D, et al. Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. *Lancet* 2020;S0140-6736:31189-2. [https://doi.org/10.1016/S0140-6736\(20\)31189-2](https://doi.org/10.1016/S0140-6736(20)31189-2).
3. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: a literature review. *J Clin Neurosci* 2020;S0967-5868:31078-X. <https://doi.org/10.1016/j.jocn.2020.05.017>.
4. American College of Surgeons. Cancer Program Standards (2016 Edition). Available at: <http://www.facs.org/quality-programs/cancer/coc/standards>. Accessed April 26, 2016.
5. Posner JB, Saper CB, Schiff ND, Claassen J, eds. *Plum and Posner's diagnosis and treatment of stupor and coma*. Oxford, UK: Oxford University Press, 2019.

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