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Editorial Anesthetic Considerations for Recovered COVID-19 Patients



THE NOVEL coronavirus disease 2019 (COVID-19) has infected more than 38 million people worldwide and has resulted in more than one million deaths.¹ As of October 14, 2020, there were more than 26 million recovered patients. With more and more patients being considered "COVID-19 recovered," anesthesiologists must be prepared to treat and manage this emerging, poorly understood patient population for elective and emergency surgery. Multiple considerations exist for anesthesiologists, including residual pulmonary dysfunction, lingering sequelae of arterial and venous embolic phenomena with associated anticoagulation, myocardial dysfunction, adrenal insufficiency from corticosteroid courses, neurologic manifestations, and residual neuromuscular weakness in the subset of critically ill patients. An awareness of these issues is paramount for anesthesiologists caring for this growing patient population.

The most common severe manifestation of COVID-19 is respiratory failure caused by acute respiratory distress syndrome. Patients experience a spectrum of severity that includes requiring nasal cannula supplemental oxygen up to and including the need for extracorporeal membrane oxygenation support and even lung transplantation.^{2–4} Preliminary reports of patients recovering from COVID-19 have described residual shortness of breath and deranged pulmonary function tests suggestive of restrictive lung disease.⁵⁻⁷ In the case of patients who continue to be symptomatic and polymerase chain reaction negative, the most reasonable approach would be to delay elective surgery until resolution of symptoms. If surgery is time-sensitive but not an emergency (such as in malignancy), it is reasonable to obtain pulmonary function tests to classify residual lung pathology in order to the guide intraoperative and potential postoperative ventilator management. In the case of an emergency, then surgery must proceed, and characterization and treatment of pulmonary pathology will need to occur intraoperatively. Note that COVID-19 also may include cardiac involvement and that shortness of breath or dyspnea on exertion could be a result of myocardial dysfunction. In patients with restrictive lung disease, ventilation management can be challenging; lower tidal volumes and more modest positive end-expiratory pressure are a reasonable approach in order to avoid overdistention of viable lung tissue. 8

Throughout the spectrum of disease, COVID-19 is known to result in a hypercoagulable state, with a high risk of arterial and venous thromboembolic phenomena.^{9,10} In the largest study to date, hospitalized, non-critically ill patients with COVID-19 were found to have an 11.5% thrombosis rate, whereas intensive care unit patients experienced a 29.4% thrombosis rate.⁹ This is an important consideration in patients presenting for surgery given the potential for difficult vascular access as a result of thrombosis and the attendant effects of outpatient anticoagulation on hemostasis in emergency cases. Finally, in the case of arterial embolic phenomena to vital organs such as the brain, hemorrhagic conversion may be a concern with heparinization for procedures requiring cardio-pulmonary bypass or those involving the administration of tissue plasminogen activator for clot lysis.

Literature on the myocardial effects of COVID-19 is expanding. Magnetic resonance imaging has found abnormalities in hospitalized and healthy recovering patients.^{11,12} In addition, stress cardiomyopathy may be more common during the pandemic, even though a direct pathophysiologic relationship to severe acute respiratory syndrome coronavirus 2 is not causal.¹³ Clinicians should have a high index of suspicion for residual cardiac involvement in hemodynamically compromised patients presenting for surgery if other causes for hypotension are ruled out.

Multiple studies on the use of corticosteroids for COVID-19–associated acute respiratory distress syndrome have suggested a mortality benefit.^{14–16} Doses of corticosteroids ranged from 50 mg of hydrocortisone every six hours to 20 mg dexamethasone per day. Courses were typically a minimum of seven days. In referencing the American Society of Anesthesiologists guideline document, patients undergoing a short course of steroids may in fact not require stress dose steroids.¹⁷ However, these guidelines suggest that a dose of 20 mg of prednisone per day for three or more weeks may be sufficient to cause hypothalamic-pituitary adrenal axis suppression. In the case of the 6 mg or 20 mg daily dosing of dexamethasone, this is roughly 40 mg or 130 mg daily of prednisone, respectively. Although not three weeks in duration, this dosing is significant and may result in adrenal suppression in patients anesthetized for major surgery or those undergoing surgery in extremis. Because of a high likelihood of receiving steroid treatment, clinicians should consider the use of stress dose corticosteroids (100 mg of hydrocortisone followed by 50 mg every six hours) in patients recovered from COVID-19 if other, more common, causes of persistent hypotension are ruled out.¹⁷

Neurologic manifestations related to COVID-19, including stroke, intracranial hemorrhage, and critical illness myopathy related to prolonged intubation and immobility, are important considerations in recovered COVID-19 patients.¹⁸⁻²⁰ In patients presenting for surgery after long intensive care unit stays, avoiding the use of succinylcholine may be prudent to reduce the risk of rhabdomyolysis and hyperkalemia.²¹ As stated earlier, patients with COVID-19 may experience ischemic or hemorrhagic intracranial pathology, with the possibility of additional intracranial bleeding with the administration of anticoagulants. A meticulous review of prior central nervous system imaging should be undertaken before procedures that necessitate anticoagulation or thrombolytic therapy in order to minimize the risk of intracranial hemorrhage. Finally, many patients recovering from COVID-19 may experience post-traumatic stress disorder related to prolonged hospitalization; acknowledging this and discussing what concerns patients may have related to procedures performed by anesthesiologists or proceduralists are crucial to assuage anxiety.

Although COVID-19 remains an entity undergoing active research, it is of the utmost importance to recognize that patients recovered or recovering from it represent an even greater unknown. Virtually every anesthesiologist will need to care for this growing population, and thus an understanding of anesthesia-relevant issues is necessary to deliver effective care. Large, ideally prospective, studies are necessary to discover the anesthetic management challenges in these patients. Anesthesiologists must take an active role in the surgical care of the COVID-19 recovered to ensure the best possible outcomes for this complex patient population.

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References

 Johns Hopkins University and Medicine. COVID-19 dashboard by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). Available at: https://coronavirus.jhu.edu/map.html. Accessed October 14, 2020.

- 2 Guan W, Ni Z, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. New Engl J Med 2020;382:1708–20.
- 3 Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in critically ill patients in the Seattle region—case series. New Engl J M ed 2020;382:2012–22.
- 4 Lang C, Jaksch P, Hoda MA, et al. Lung transplantation for COVID-19associated acute respiratory distress syndrome in a PCR-positive patient. Lancet Respir Med 2020;8:1057–60.
- 5 Huang Y, Tan C, Wu J, et al. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. Respir Res 2020;21:163.
- **6** Zhao Y, Shang Y, Song W, et al. Follow-up study of the pulmonary function and related physiological characteristics of COVID-19 survivors three months after recovery. EClinicalMedicine 2020;25:100463.
- 7 Fumagalli A, Misuraca C, Bianchi A, et al. Pulmonary function in patients surviving to COVID-19 pneumonia. Infection 2020. https://doi.org/ 10.1007/s15010-020-01474-9; July 28 [E-pub ahead of print] accessed: October 14, 2020.
- 8 Marchioni A, Tonelli R, Rossi G, et al. Ventilatory support and mechanical properties of the fibrotic lung acting as a "squishy ball. Ann Intensive Care 2020;10:13.
- 9 Bilaloglu S, Aphinyanaphongs Y, Jones S, et al. Thrombosis in hospitalized patients with COVID-19 in a New York City health system. JAMA 2020;324:799–801.
- 10 Yusuff H, Zochios V, Brodie D. Thrombosis and coagulopathy in COVID-19 patients requiring extracorporeal membrane oxygenation. ASAIO J 2020;66:844–6.
- 11 Lala A, Johnson KW, Januzzi JL, et al. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. J Am Coll Cardiol 2020;76:533–46.
- 12 Rajpal S, Tong MS, Borchers J, et al. Cardiovascular magnetic resonance findings in competitive athletes recovering from COVID-19 infection. JAMA Cardiol 2020. https://doi.org/10.1001/jamacardio.2020.4916; Sep 11 [E-pub ahead of print] Accessed: October 14, 2020.
- 13 Jabri A, Kalra A, Kumar A, et al. Incidence of stress cardiomyopathy during the coronavirus disease 2019 pandemic. JAMA Network Open 2020;3: e2014780.
- 14 The RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19 — preliminary report. New Engl J Med 2020. https://doi.org/10.1056/NEJMoa2021436; July 17 [E-pub ahead of print] Accessed: October 14, 2020.
- 15 Tomazini BM, Maia IS, Cavalcanti AB, et al. Effect of dexamethasone on days alive and ventilator-free in patients with moderate or severe acute respiratory distress syndrome and COVID-19: The CoDEX randomized clinical trial. JAMA 2020;324:1307.
- 16 The Writing Committee for the REMAP-CAP Investigators, Angus DC, Derde L, et al. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19: The REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. JAMA 2020;324:1317.
- 17 Liu MM, Reidy AB, Saatee S, Collard CD. Perioperative steroid management. Anesthesiology 2017;127:166–72.
- 18 Carroll E, Lewis A. Catastrophic intracranial hemorrhage in two critically ill patients with COVID-19. Neurocrit Care 2020. https://doi.org/10.1007/ s12028-020-00993-5; May 26 [E-pub ahead of print] Accessed: October 14, 2020.
- 19 Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. New Engl J Med 2020;382:2268–70.
- 20 Bagnato S, Boccagni C, Marino G, et al. Critical illness myopathy after COVID-19. Int J Infect Dis 2020;99:276–8.
- 21 Martyn JAJ, Richtsfeld M, Warner DO. Succinylcholine-induced hyperkalemia in acquired pathologic states. Anesthesiology 2006;104: 158–69.