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COVID-19 Pandemic: Understanding Patterns and Outcomes in Critically Ill Patients

George Williams, MD, FASA, FCCM, FCCP
Ashish K. Khanna, MD, FCCP, FCCM

What a difference two months make! As a medical community and a society, we have collectively witnessed a significant evolution of knowledge commensurate to the discovery and widespread dissemination of a new disease. Asymptomatic transmission is now accepted as reality with a clear mechanism (*N Engl J Med* April 24, 2020). Testing is more widely available, yet in many forms with varying degrees of accuracy. Hydroxychloroquine is not the magic bullet that we hoped for. In fact, evidence is mounting that the indiscriminate and irrational use of this drug may contribute to an increased number of cardiac events.

For example, a recent report from patients treated in New York showed that the risk of in-hospital cardiac arrests doubles with the use of hydroxychloroquine and azithromycin in combination compared to no use of these agents (*JAMA* May11, 2020). This, combined with no outcome benefit with these drugs, has resulted in a

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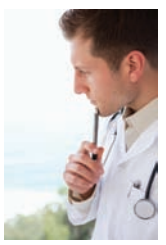
What Should a Graduating Resident Look for in Future Practice?

Richard P. Dutton, MD, MBA, FASA
Robert Koehler



Following 12 years of continuous training in college, medical school, and residency, the shift from training to practice is a momentous event in the career of an anesthesiologist. Deciding where to go and which group to join will influence the rest of one's professional life. What factors should guide this decision?

We looked at this from the perspective of a soon-to-graduate resident and a senior anesthesiologist with wide experience in the profession. Between us, we've tried to anticipate the key questions that should guide the choice of a first practice out of residency. We offer

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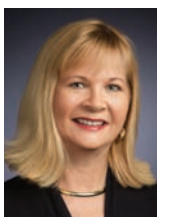
ANESTHESIOLOGY 2020 Goes 100% Virtual

Mary Dale Peterson, MD, MSHCA, FACHE, FASA

Imagine attending the largest annual anesthesiology educational event in the world from the comfort of your home or while you are on call, waiting for a case.

From your laptop or mobile device, envision entering a virtual convention center, complete with signage and a virtual help desk to greet you and answer questions. From there, you will attend lectures, ask questions of the speaker in real time, take part in breakout sessions, and access content you missed later at your convenience.

Welcome to ANESTHESIOLOGY 2020, where the latest virtual conference technology will transform this year's meeting into an entirely online event for the first time. It will be an amazing experience that maintains the quality and variety of education sessions you've come to expect from your annual meeting while also offering opportunities each day to connect



with other participants, educators, and industry representatives.

Drawing 12,000 to 14,000 attendees from 80 countries most years, the ANESTHESIOLOGY annual meeting has always been the largest educational and scientific meeting in the specialty. Given the current phased reopening in Washington, DC, however – with groups of 250 or more prohibited from meeting in October, and mounting scientific evidence about the timing of a cure or vaccine for COVID-19 – it became apparent that holding an in-person meeting of this magnitude would not be possible.

Fortunately, we had time on our side. Since our annual meeting isn't until October,

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COVID-19 and Critical Care

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rapid practice change in most parts of the world. This is a prime depiction of the dynamic nature of the evolution of evidence with the pandemic – what is evidence and best practice today may not be the same a month later.

Pattern with clinical presentation

COVID-19 has posed unique challenges to the care of patients in the critical care, perioperative, inpatient, and community settings (*Anesth Analg* May 7, 2020). The population of patients cared for in the ICU has a diverse set of needs that commonly pertain to several key areas, including mechanical ventilation, renal replacement therapy, hemodynamic stability, and coagulopathy, among others.

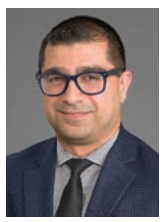
There now appears to be a pattern emerging with the clinical presentation of COVID-19 infection, with a period of convalescence prior to requiring hospitalization due to increased work of breathing or other symptoms. Once a significant oxygen requirement is noted, prone positioning has been found to be extremely important in the care of these patients. Historically, the critical care world generally considered prone positioning to be a way to reduce mortality in mechanically ventilated patients with ARDS, but we have seen over time that prone positioning is helpful long before intubation in COVID-19 and can stave off many of the more challenging aspects of care when patients require respiratory support.

Additionally, since COVID-19-induced lung disease frequently presents with normal lung compliance, a patient may not be tachypneic and have a relatively low work of breathing even when oxygenation is poor when compared to other forms of acute respiratory failure more traditionally seen in the acute care setting. These "happy hypoxic" folks are therefore tricky to manage, and it takes skill and clinical prowess on the part of the intensivist to know when to intervene with endotracheal intubation. An important problem is that mechanical ventilation seems to have an association with worsening clinical condition, beyond what may be obvious. Though in the absence of an appropriate denominator, we may not be in place to put a clear figure on this mortality number on mechanical ventilation at the current time (*Am J Respir Crit Care Med* May 13, 2020). Once these patients are intubated, they frequently need mechanical ventilation for one to three weeks. This clinical picture is sometimes referred to as COVID-19-induced ARDS, or "CARDS," in the literature (*Crit Care Med* May 13, 2020). During this prolonged time on mechanical ventilation, there are opportunities for concomitant infections with traditional nosocomial organisms such as *Pseudomonas aeruginosa* or MRSA. The ongoing care of these patients and prevention of nosocomial complications is a point of emphasis for critical care teams caring for these patients.

In addition, there is a pattern of illness wherein a period of relative stability during the first week or so may be followed by a fairly dramatic spiral into multi-system organ failure, associated with a sharp and disproportionate rise in inflammatory markers such as D-dimer, C-reactive protein, IL-6, ferritin, LDH, and others (*Lancet* March 28, 2020). Some of these are now a therapeutic target for drugs being used or under investigation (*Biomed Pharmacother* May 14, 2020). Organ failure here seems to be a combination of hemodynamic (COVID-induced myocardial injury) and renal shutdown. Hemodynamic failure may be particularly challenging in that it may be a combination of traditional high-output septic shock and COVID-induced myocardial injury generally manifested as cardiogenic shock. The use of appropriate afterload increasing agents, inotropes, newer vasopressors, and the connection with the renin-angiotensin modulating drugs have all been questioned (*Hypertension Research* April 27, 2020; *Crit Care* 2020;24:136).

Respiratory failure that is unresponsive to oxygenation and lung protection via conventional mechanical ventilation, with adjunctive therapy, also brings several patients to the point of using extra corporeal membrane oxygenation (ECMO), usually with a veno-venous cannulation. While this has raised several ethical conundrums, most centers supporting these systems have attempted to formulate guidelines for patient selection that are not far removed from those promulgated by the extra corporeal life support (ELSO) group. The next challenge after prolonged mechanical ventilation with or without ECMO is liberation from these devices, where the need for a tracheostomy, and the ask for performing the procedure safely and in a timely manner, has stressed systems.

George Williams, MD, FASA, FCCM, FCCP
Chair, ASA Committee on Critical Care Medicine, and Associate Professor and Vice Chair for Critical Care Medicine, Department of Anesthesiology, Medical Co-Director, Lyndon B. Johnson General Hospital Surgical ICU, UT Houston Health Sciences Center.



Ashish K. Khanna, MD, FCCP, FCCM
Vice Chair, ASA Committee on Critical Care Medicine, Associate Professor and Section Head for Research, Department of Anesthesiology, Section on Critical Care Medicine, Wake Forest School of Medicine, Wake Forest Baptist Health, Winston-Salem, North Carolina.

COVID-19 and coagulation

COVID-19 also appears to be a disorder of coagulation, and indeed has been described by some as an ongoing endothelial inflammation. Hence, the need for aggressive anticoagulation in this population appears to be clear; however, there is still evolution pertaining to how much anticoagulation is needed and for how long. A low-grade DIC and localized pulmonary thrombotic microangiography results clinically in unrecognized or delayed diagnosed venous or arterial thromboembolic events, sometimes with disastrous consequences. Following D-dimer, platelet count, and aPTT several times a week is a common strategy, with escalation of care when signs of deviation from the norm occur. Concern about causing bleeding has always been a consideration, but unless there is a clinical reason

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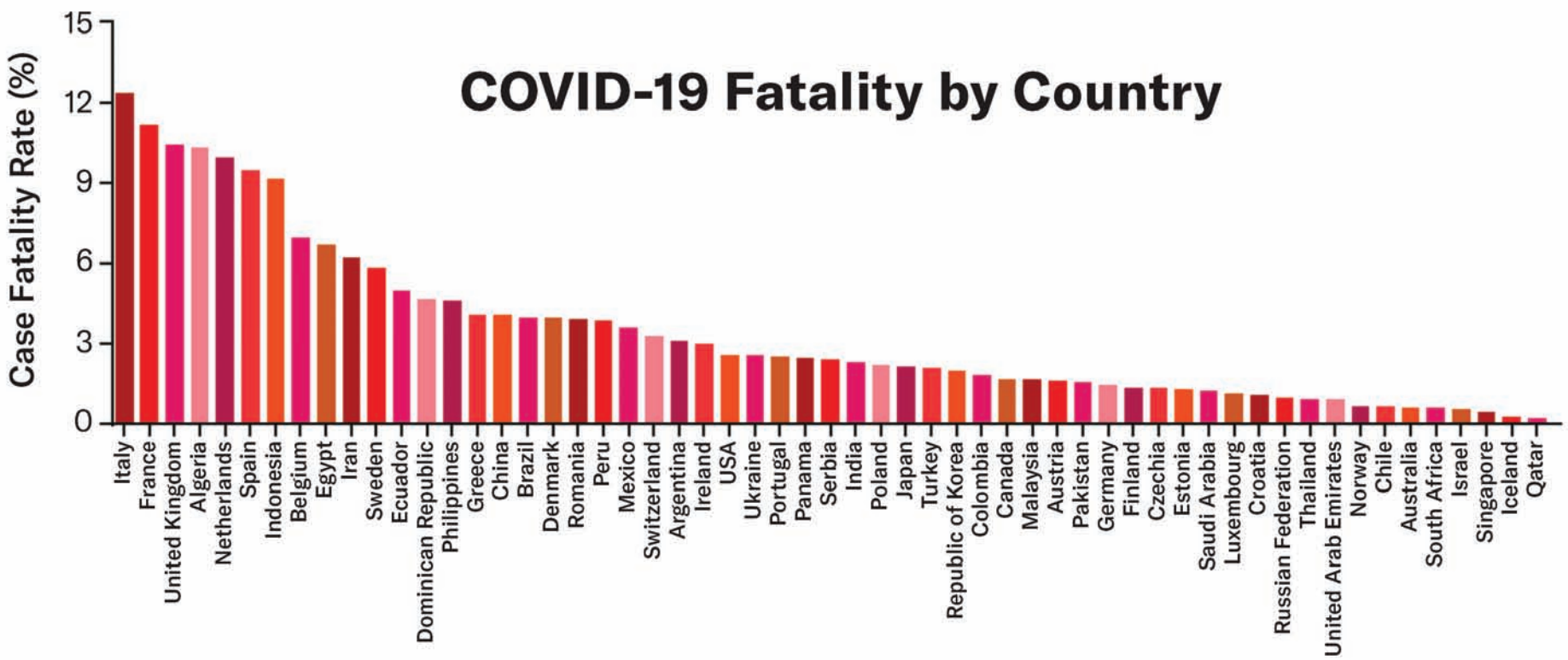

Figure: Image from Research (Wash DC) April 19, 2020

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International Response

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line of defense in emergency care, ORs and in ICUs. Donning PPE, especially for aerosol-generating procedures including endotracheal intubation, endotracheal/oral suction and extubations, became mandatory. Our most experienced anesthesiologists performed the endotracheal intubations. Most of our anesthesiologists preferred preoxygenation, video-laryngoscopy, and rapid-sequence induction during endotracheal intubation. High-efficiency hydrophobic filters are placed between the facemask and breathing circuit or between facemask and the Ambu® bag.

The ICA decided not to conduct its 2nd International Annual Conference in Bangalore in September this year in a conventional manner. In striving to provide the best educational platform, the ICA, in collaboration with Narayana Hrydayalaya, Bangalore, and the University of Minnesota, has released two series of online courses on various aspects of COVID-19, free of cost. These are available on www.medknit.org as of July 1 of this year. ICA is planning to conduct regular webinars involving eminent faculty covering the entire spectrum of anesthesia education.

Japan – Japanese Society of Anesthesiologists (JSA)

Dr. Hiroshi Otake, Chairman of Committee on International Affairs, JSA

The COVID-19 virus in Japan has started to settle down, although 17,000 people were infected as of the end of May. About 650 patients were intubated and 165 patients were on extracorporeal membrane oxygenation (ECMO). In terms of outcome so far, the recovery rate has been prominent. Sixty-six percent of ECMO patients were successfully weaned from ECMO (two-thirds of them were discharged and the rest were still admitted), although 23% died. Sixty-three % of intubated patients without ECMO recovered and 21% died (data from Japan ECMOnet for COVID-19).

The JSA has provided practice recommendations for the safety of anesthesiologists and patients during the COVID-19 crisis. Those recommendations have been renewed on a timely basis as conditions evolved. JSA and the Japanese Society of Intensive Care Medicine have published a combined statement on how they tackled COVID-19 infections by sharing information on the number of patients with intubation or ECMO, providing training on mechanical ventilation, and improving the personal protection equipment supply. JSA also conducted weekly surveys of the number of surgeries restricted by the infection and case reports of anesthesia provided for COVID-19 (including suspected) patients to share management strategies among members.

We continue to support our members and collaborate with global societies to overcome this pandemic.

Korea – Korean Society of Anesthesiologists (KSA)

Dr. Justin Sangwook Ko, Director of International Affairs of KSA

South Korea continues to earn high praise for its proactive and transparent efforts to battle coronavirus and set a standard for other countries to follow. The Korean medical community provides the most up-to-date information and safety guidelines for caring for COVID-19 patients. The KSA is also committed to standing in the forefront of providing safe anesthetic care to patients while ensuring the safety of health care workers. KSA is reaching out to our members through various routes such as webinars, telecommunication conferences, and guideline publications. Notably, KSA published the following two guidelines for COVID-19 in our official journal, the *Korean Journal of Anesthesiology*: 1) "Recommendations for anesthesia in patients suspected of COVID-19 coronavirus infection" (*Korean J Anesthesiol* 2020;73:89-91) and 2) "Guidelines for control and prevention of COVID-19 in surgical and anesthetic settings" (*Korean J Anesthesiol* May 2020). KSA's mission is to contribute to providing the best health care through best practices in anesthesiology, pain medicine, and critical care. The KSA is striving to achieve this mission during the COVID-19 pandemic crisis.

KSA is strongly committed to hosting its 97th Annual Scientific Meeting (KoreAnesthesia 2020) on November 5-7, 2020 at Paradise City, Incheon, Korea. However, its format will be different from years past since the safety of attendees will be our upmost priority. KSA is working hard to organize KoreAnesthesia 2020 to maintain its international format, modified to meet the needs of all members. Please stay tuned for more updated information at koreanesthesia.org. ■

COVID-19 and Critical Care

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to be concerned, anticoagulation is generally pursued. Early non-randomized data suggests improved outcomes in those with more aggressive anticoagulation regimens (*J Thromb Haemost* 2020;18:1094-99).

The overall goals on coagulation remain a moving target, and we hope that improved scientific investigation will help standardize care and at some stage help develop guidelines to recommend appropriate therapy.

Chronic co-morbidities

Chronic co-morbidities can have a negative effect on the outcomes of COVID-19 patients, with hypertension, cardiovascular disease, chronic kidney disease, and diabetes being associated with increased mortality (Research (Wash DC) April 19, 2020). Knowing that older individuals carry most of these comorbid conditions, initial data from China labelled COVID-19 as a disease with poor prognosis in that age group. However, the U.S. experience has been different, and most data here shows that the young are not entirely spared. The mortality rate of COVID-19 appears to vary widely based on the country (see figure, page 8). Results such as these should be interpreted with some skepticism; to accurately determine the case fatality rate, full knowledge of the infection rate must be obtained. As testing is not universally available for the entire community, a true incidence is not known; therefore, a true case fatality rate cannot be calculated. It is likely that the case fatality rate in the U.S. is lower, but this is not certain. Patients who require operative intervention and who are simultaneously infected with COVID-19 have generally been found to have high mortality rates, sometimes in excess of 25% (*Surg Infect* (Larchmt) May 13, 2020). This makes the pre-operative testing very important in achieving safe anesthesia care as elective cases resume in the U.S.

Valuable tools

A first step in understanding this illness is the need for better real-time data dashboards. One such effort is the Society of Critical Care Medicine's (SCCM's) Viral Infection and Respiratory Illness Universal Study (VIRUS) registry, with the aim of a real-time COVID-19 registry of current ICU and hospital care patterns to allow evaluation of safety and observational effectiveness of COVID-19 practices. This effort has resulted in a live dashboard that may be accessed at sccmcovid19.org.

Similarly, the ELSO group has established a very useful ECMO registry. These tools will be essential as we attempt to develop mortality and morbidity prediction models in the near future. One such model has already been developed using data from China, but given the tremendous variability observed between different countries with regard to the nature and outcomes of this illness, it is likely that more country-specific tools will be needed (*JAMA Intern Med* May 12, 2020).

In addition, data that focused on socio-economic and geographic determinants of disease outcomes – air-travel, population density, nursing home numbers, and racial ethnic numbers – need to be factored into future predictive models.

COVID-19 stretched us thin and exposed gaps in our health care model. Fortunately, we as a community of anesthesiologists rose to the occasion and led from the front within and outside the OR and ICU. With the utilization of resources such as the COVID Activated Emergency Scaling of Anesthesiology Responsibilities (CAESAR) ICU initiative, this can be done (*Anesth Analg* May 7, 2020). This free tool has now been downloaded more than 100,000 times by teams around the world (www.asahq.org/in-the-spotlight/coronavirus-covid-19-information/caesar).

As time progresses, our medical community should be prepared to have an ongoing new normal in the ICU and OR. There will be a need to determine strategies for long-term management of patients who had severe COVID-19 infection. Since more than 40% of ICU patients have ongoing medical needs and 20% have multiple hospital re-admissions, we should be prepared for a similar natural history in the COVID-19 population. Such patients could frequently present to the OR for repeated surgeries related to their medical co-morbidities; anesthesiologists would again be called upon to provide safe and innovative care for COVID-19 patients. ■

> **"COVID-19 stretched us thin and exposed gaps in our health care model. Fortunately, we as a community of anesthesiologists rose to the occasion and led from the front within and outside the OR and ICU ."**

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