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Prognostication and Proactive Planning in COVID-19

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Abstract: Accurate prognostication is challenging in the setting of SARS-CoV-2, the virus responsible for COVID-19, due to rapidly changing data, studies that are not generalizable and lack of morbidity and functional outcomes in survivors. To provide meaningful guidance to patients, existing mortality data must be considered and appropriately applied. While most people infected with SARS-CoV-2 will recover, mortality increases with age and co-morbidity in those who develop severe illness.

Keywords: Prognosis, SARS-CoV-2, COVID-19, Palliative care, Prognostication, Proactive planning

Running Title: Prognostication and Proactive Planning in COVID-19

Introduction
Palliative care clinicians aim to equip patients and families with accurate prognostic information in order to align medical interventions with patient priorities. Accurate prognostication is particularly challenging in the case of SARS-CoV-2, the virus responsible for COVID-19, due to several factors including incomplete and rapidly changing data, challenges in generalizing data between regions, and lack of morbidity and functional outcomes in survivors. The high transmission rate of this virus has led to a worldwide pandemic. This has increased lay discussion about the risk of mortality the virus carries, particularly for older adults and people with co-morbid conditions such as diabetes, coronary artery disease, chronic respiratory disease, cancer or hypertension(1).   As we work to provide accurate and personalized recommendations to our patients, we must closely examine available data and apply to our patient populations.

Severity of Illness
Despite a large number of people being infected, over 3.1 million people worldwide as of April 29[th,] 2020, most of those infected are asymptomatic or have mild symptoms. On April 1st the World Health Organization reported 25% of SARS-CoV-2+ patients in Wuhan, China were asymptomatic and never developed symptoms(2). Many patients who have increased risk of severe disease, including those >65 years old and those with co-morbidities of heart disease, diabetes, lung disease, asthma or obesity, recover. Initial data suggest that only 20% of those with confirmed COVID-19 positive test go onto have severe symptoms(3). However, for those who develop severe illness, mortality increases with age and co-morbidity.

Overall Mortality
  The Case Fatality Rate(CFR), the number of people who die divided by the number of people known to be infected with the virus, is widely variable around the world. With numbers as low as 0.7% in Germany, where testing is prevalent, up to 10.7% in Italy for a global fatality rate of 4.7% as of April 6th, 2020(4). Older adults are disproportionally affected by COVID-19. Data from the Washington Department of Health shows that while one in ten confirmed cases were in adults greater than 80 years of age, this age group accounted for 54% of all deaths(5). This aligns with nationwide CFR that increases with older age, with rates up to 27.3% in those >85 years as reported by the Centers for Disease Control(6). (Figure 1) When widespread testing is more available worldwide, it is expected a more accurate CFR will be lower than currently reported.

Hospitalized Patients
National data on frequency of hospitalization of infected patients is lacking as of this publication due to inconsistent reporting methods. Individual states, however, report similar hospitalization rates via The COVID Tracking Project, revealing rates ranging from 8-24% with higher hospitalization frequency correlating directly with age(7).   Of those who were sick enough to require hospitalization in one hospital in Wuhan, China, 28% (54/191) died(4). Older age, higher Sequential Organ Failure Assessment (SOFA) score and elevated d-dimer at admission were risk factors associated with death. Northwell Health in the New York City area demonstrated similar mortality in their hospital system, with 553 deaths out of 2634 (20.9%) patients hospitalized March 1st through April 4th 2020(8).   However, this data only includes those who were discharged alive or died. Given that the majority of patients (3066 of the 5700 patients) remained hospitalized, the actual mortality rate may be higher or lower than this one time snapshot.

Intensive Care

Of patients who were sick enough to require intensive care in a Wuhan, China hospital, 61.5%(32/52) died in hospital with a median duration of 7 days from admission to ICU until death(9). Patients with acute respiratory distress syndrome(ARDS) and older adults were more likely to die, with a median age of 64.6 years of those who died and a median age of 51.9 years for survivors. Similarly, 67% (14/21) patients in a Washington state hospital, the majority of which came from a nursing home, died following intensive care admission, and 24% remained critically ill at the time of reporting(10). An Italian cohort study demonstrated lower mortality, at 26% (405/1581)(11). However, the true mortality is likely significantly higher given that 58% (920/1581) of patients remained in the intensive care unit at the time of the publication. As noted with previous studies, mortality significantly worsened with increasing age. (Figure 1)

Intubated patients
Patients who require mechanical ventilation demonstrate very high mortality rates, ranging from 81-97%(9,12). It is not yet clear whether mortality in the New York system Northwell Health may be different. In their dataset of 1,151 patients who were mechanically ventilated, 3% were discharged alive, 25% had died, and 72% were still in the ICU(8). Therefore we can estimate the mortality is somewhere between 25% and 97%. The Intensive Care National Audit and Research Center in the United Kingdom documented a lower mortality rate when including non-invasive positive pressure ventilation. In their population, patients who required advanced respiratory support, inclusive of BIPAP, CPAP and mechanical ventilation and extracorporeal respiratory support, 67% were dead at the end of their critical care stay(13). Caution is warranted when looking at these data as they are biased towards reporting patient outcomes of those who died or recovered quickly, and may underreport those with a long duration of mechanical ventilation.

Survival after cardiac resuscitation
A single study has demonstrated poor outcomes for COVID-19+ patients who require in-hospital cardiac resuscitation. Overall 30 day survival for the 136 patients who underwent in-hospital resuscitation in the setting of COVID-19 was only 2.9%(14). Only one of the 136 patients survived with a favorable neurologic status (Cerebral Performance Category (CPC) score of 1 or 2. As a comparison, previous data prior to the COVID-19 pandemic showed that the overall survival to discharge after treated in-hospital cardiac arrest in those without is approximately 18%, with about half of those patients neurologically intact or with only mild neurologic deficits at discharge (CPC of 1)(15).

Pediatric Patients
In a United States(US) study of COVID-19 cases from 50 states and 4 territories reported on April 2nd, 2020, 1.7% were persons aged <18 years despite this age group accounting for 22% of the US population(16, 17). A portion of this population required hospitalization, estimated at 5.7%–20% while 0.58%–2.0% required ICU admission. This is consistent with previous reports that COVID-19 illness often has a mild course among younger patients(18). Although symptoms of COVID-19 were typically less severe than those of adult patients, young children, particularly infants, were vulnerable to infection in this study, consistent with data from the Chinese Center for Disease Control(18). Patients aged 15-17 years were the most common age group to be infected, accounting for 1/3 of the cases, but hospitalization was most common in patients aged <1 year. One out of 728 children confirmed to have COVID-19 died in the China study, a 14 year old boy(18). Three out of 2572 children died in the US study(16).

Proactive Planning

In this dynamic medical environment, it is incumbent on palliative care, primary care, emergency and critical care clinicians to incorporate existing data with prior knowledge to inform accurate prognostication and alignment of care with patient goals. The above studies, in combination with existing knowledge about the impact of performance status, pneumonia severity, comorbidities and age can be utilized to develop a prediction of the odds of morbidity and mortality for patients seeking guidance. As in non-COVID times, our aim is to understand the priorities of our patients, including their minimal acceptable state of being. Only then can then we utilize current and past findings to help them understand the likelihood they will maintain an acceptable state should they get infected with SARS-CoV-2 and require hospitalization or intensive care.

Conclusion

While most patients infected with SARS-CoV-2 will recover, those who get severe illness and require hospitalization, intensive care, intubation and cardiac resuscitation have escalating levels of mortality. Evolving data should be viewed as preliminary and used to supplement existing constructs.

Figure 1 United States Case Fatality Rate February 12th-March 16th 2020

Figure 2 Patient Disposition from COVID-Only Intensive Care Units in Lombardy Italy

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1. Ashour, H.M., et al., *Insights into the Recent 2019 Novel Coronavirus (SARS-CoV-2) in Light of Past Human Coronavirus Outbreaks.* Pathogens, 2020. **9**(3).
2. World Health Orgnization Press Conference Retrieved from: https://www.who.int/docs/default-source/coronaviruse/transcripts/who-audio-emergencies-coronavirus-press-conference-full-01apr2020-final.pdf?sfvrsn=573dc140_2
3. Xu, Z., et al., *Full spectrum of COVID-19 severity still being depicted.* Lancet, 2020. **395**(10228): p. 947-948.
4. Omer, S.B., P. Malani, and C. Del Rio, *The COVID-19 Pandemic in the US: A Clinical Update.* JAMA, 2020.
4. Zhou, F., et al., *Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study.* Lancet, 2020. **395**(10229): p. 1054-1062.
5. Department of Health, State of Washington website Retrieved: https://www.doh.wa.gov/Emergencies/Coronavirus
6. Centers for Disease Control Morbidity & Mortality Weekly Report March 27th 2020 Retrieved: https://www.cdc.gov/mmwr/index.html April 18th, 2020
7. The COVID Tracking Project Retrieved: https://covidtracking.com/data April 18th, 2020
8. Richardson, S., et al., *Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area.* JAMA, 2020.
9. Yang, X., et al., *Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study.* Lancet Respir Med, 2020.
10. Arentz, M., et al., *Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State.* JAMA, 2020.

11.   Grasselli, G., et al., *Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy.* JAMA, 2020.

12.   Weiss, P. and D.R. Murdoch, *Clinical course and mortality risk of severe COVID-19.* Lancet, 2020. **395**(10229): p. 1014-1015.

13.   Intensive Care National Audit & Research Center April 24th report https://www.icnarc.org/Our-Audit/Audits/Cmp/Reports

14.   Shao, F., et al., *In-hospital cardiac arrest outcomes among patients with COVID-19 pneumonia in Wuhan, China.* Resuscitation, 2020.

15.   Ebell, M.H., et al., *Development and validation of the Good Outcome Following Attempted Resuscitation (GO-FAR) score to predict neurologically intact survival after in-hospital cardiopulmonary resuscitation.* JAMA Intern Med, 2013. **173**(20): p. 1872-8.

16.   Coronavirus Disease 2019 in Children- United States, February 12-April 2, 2020. MorbMortal Wkly Rep 2020:69:422-426

17.   Bridged race population estimates. Atlanta, GA: US Department of Health and Human Services, CDC; 2020. https://wonder.cdc.gov/bridged-race-population.html

18.   Yuanyuan D. et al Epidemiology of COVID-19 Among Children in China Pediatrics April 2020, e20200702; DOI: https://doi.org/10.1542/peds.2020-0702

Age group (no. of cases)	%*		
	Hospitalization	ICU admission	Case-fatality
0–19 (123)	1.6–2.5	0	0
20–44 (705)	14.3–20.8	2.0–4.2	0.1–0.2
45–54 (429)	21.2–28.3	5.4–10.4	0.5–0.8
55–64 (429)	20.5–30.1	4.7–11.2	1.4–2.6
65–74 (409)	28.6–43.5	8.1–18.8	2.7–4.9
75–84 (210)	30.5–58.7	10.5–31.0	4.3–10.5
≥85 (144)	31.3–70.3	6.3–29.0	10.4–27.3
Total (2,449)	20.7–31.4	4.9–11.5	1.8–3.4

Patient Disposition From COVID-Only Intensive Care Units (ICUs), Lombardy Region, Italy

■ Discharged from ICU   ■ Stil in ICU as of 3/25/2020   ■ Died in ICU