SARS-CoV-2 in a Southeastern US Hospital System: Interplay of Complications and Code Status Downgrades

Sydney M Schieffer, Scott C Pelland, Colleen Hagopian, and David M Cline

Introduction

The SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) pandemic has challenged health-care systems worldwide. Although research surrounding COVID-19 has primarily focused on management and treatment principles,[1-3] many studies have sought to categorize the nature of the disease and highlight patient factors that may increase mortality from COVID-19.[4-6] Although data exist that outline epidemiological and mortality factors for hospital admissions with COVID-19,[4,7,8] there remains a gap in the full characterization of these patients' admissions. This study explored COVID-19 admissions to extrapolate on the relationships between the high mortality rate of COVID-19 and medical complications that present during patient admissions. The study's objectives were to investigate the severity and impact of patient complications on mortality, and to explore the relationship between these complications, code status downgrades (defined as a de-escalation of code status from full code to either limited intervention or comfort care), and mortality. These factors highlight the impact of COVID-19 on discussions about palliative care and informed code status downgrades.

Key words: COVID-19 complications; COVID-19 mortality; code status downgrade; acute respiratory failure; outcomes research; hospital admission.

The authors are affiliated with the Department of Emergency Medicine, Atrium Health Wake Forest Baptist Medical Center, Winston Salem, North Carolina.

The study received no external funding but was supported internally by the Department of Emergency Medicine at Atrium Health Wake Forest Baptist Medical Center.

The authors have disclosed no conflicts of interest.

Correspondence: David M Cline MD, Department of Emergency Medicine, Atrium Health Wake Forest Baptist Medical Center, 1 Medical Center Blvd, Winston Salem, NC 27157. E-mail: dcline@wakehealth.edu.

DOI: 10.4187/respcare.09748

Methods

A retrospective chart review was conducted of 346 patients who presented to the emergency department or who transferred from outside hospital emergency departments for admission due to symptoms related to COVID-19 at a tertiary medical health-care system in central North Carolina. A custom REDCap (Research Electronic Data Capture system)[9,10] was used to track individual admissions, demographics (sex, age, body mass index), preexisting comorbidities (active cancer, hypertension history, diabetes), hospital course, and eventual disposition. The study was approved under expedited review category 5 by the institutional review board of the study's home institution (approval 00066056).

Patient presentations for COVID-19 hospital admissions were identified from March 22, 2020, to June 30, 2020. Adult and pediatric patients met inclusion criteria if they were admitted for suspected COVID-19-related respiratory illness or if they had a positive COVID-19 status on admission with an illness likely related to COVID-19 infection. Some patients tested positive for COVID-19 on admission for an illness that could reasonably be associated with COVID-19 infection, such as fever, respiratory distress, transient ischemic attack workups, and cholecystitis. These subjects were included after agreement among all the investigators. Some patients (including peripartum and laboring mothers, psychiatric admissions, and those undergoing elective procedure preoperative testing) were incidentally admitted with COVID-19. These patients were excluded because the indication for admission was not related to their positive COVID-19 infection, and they would have been discharged to home if not admitted for their non-COVID-19–related diagnosis.

Statistical Analysis

Data were analyzed by using SAS 9.4 (SAS Institute, Cary, North Carolina). The chi-square test or the Fisher exact test was used to determine the univariate association between categorical variables (complications or life-sustaining interventions) and code status downgrades or mortality. Odds

Table 1. Multivariate Analysis of COVID-19 Complications, Life-Sustaining Interventions, Comorbidities, and the Association With Code Status Downgrade

Parameters	Subjects, *n* (%)	Odds Ratio	95% CI	*P*
Complication				
Respiratory failure	215 (62.1)	4.09	1.45–11.50	.008
Sepsis (with or without shock)	98 (28.3)	1.45	0.45–4.55	.53
Acute kidney injury	95 (27.5)	3.30	1.43–7.60	.005
Required vasopressor	69 (19.9)	2.03	0.32–12.99	.91
Required intubation	66 (19.1)	5.52	0.09–29.41	.058
Hypotension	56 (16.2)	3.56	1.16–10.87	.03
Metabolic acidosis	45 (13.0)	1.02	0.36–2.89	.97
Arrhythmia	40 (11.6)	1.29	0.51–3.27	.59
Liver injury	42 (12.1)	1.06	0.40–2.82	.77
Septic shock	49 (14.2)	3.00	0.89–10.09	.08
Cardiogenic shock	13 (3.8)	2.28	0.51–10.06	.28
Acute pulmonary embolism	12 (5.8)	4.95	1.22–20.63	.02
Acute heart failure	12 (3.5)	4.08	0.99–16.66	.051
Comorbidities				
History of hypertension	208 (60.1)	1.39	0.34–5.15	.63
History of diabetes mellitus	126 (36.4)	1.08	0.04–3.42	.89
Active cancer	16 (4.7)	2.5	0.51–12.6	.25
Advancing age	NA	1.14	1.08–1.20	<.001

NA = not applicable

ratios (OR) and 95% CIs were calculated with a significance set at $P < .05$. Logistic regression was used for multivariate analysis to determine the association of comorbidities, complications, and life-sustaining interventions with a code status downgrade. Logistic regression was also used for multivariate analysis to determine the association of comorbidities, COVID-19–related complications, life-sustaining interventions, and a code status downgrade with mortality. All factors chosen for inclusion in the multivariate models had a univariate association with either a code status downgrade (Table 1) or mortality (Table 2) ($P < .05$).

Results

The overall mortality rate in this study was 14.2% (49 deaths of 346 subjects). The mortality rate stratified by admission code status was the following: 12.1% in 314 subjects with full code (38 deaths), 33.3% in 30 subjects with limited treatment (10 deaths), and 50% in 2 subjects in comfort care (1 death). The mortality rate for 294 subjects maintained at their admission code status was 3.1%; the mortality rate for 52 subjects with a code status downgrade was 76.9%, ($P < .001$). Of the 49 deaths, the code status at admission was de-escalated in 40 subjects. In the 40 subjects with code status downgrade and who died, the median (interquartile range [IQR]) time from admission to code status downgrade was 10 (15, 6–21) d; the median time between code status downgrade and death was 0.25 (1, 0–1) d.

In contrast, for the 12 subjects with code status downgrade and who survived to discharge, the median (IQR) time from admission to code status downgrade was 9 (11, 1–12) d and the median (IQR) time from code status downgrade to discharge was 8 (9.5, 2–11.5) d. There were 9 subjects who died without a downgrade in code status: 7 subjects who were intubated full code, 1 subject in limited treatment, and 1 subject admitted under comfort care. Fatal cardiac arrests occurred in the 7 subjects who were intubated: 2 with ventricular fibrillation while undergoing dialysis, and 5 with pulseless electrical activity arrests in the setting of hypoxia despite maximal therapy.

The multivariate analysis results to determine an association between the complications or life-sustaining interventions, comorbidities, and a code status downgrade are shown in Table 1. Fifteen percent of the subjects had a code status downgrade during the hospitalization for COVID-19, most commonly from full code status to comfort care. Respiratory failure, acute kidney injury, sepsis, hypotension, and pneumonia were the most common complications seen. The complications or comorbidities that were statistically significant and independently associated with code status downgrade after multivariate analysis included respiratory failure (OR 4.09, 95% CI 1.45−11.50; $P = .008$), acute kidney injury (OR 3.30, 95% CI 1.43−7.60; $P = .005$), hypotension (OR 3.56, 95% CI 1.16−10.87; $P = .03$) acute pulmonary embolism (OR 4.95, 95% CI 1.22−20.63; $P = .02$), and advancing age (OR 1.14, 95% CI 1.08−1.20: $P < .001$).

Table 2. Multivariate Analysis of the Association of Complications, Required Interventions, and Change in Code Status With Mortality

Parameter	Subjects, *n* (%)	Odds Ratio	95% CI	*P*
Complication				
Respiratory failure	215 (62.1)	1.20	0.27–5.46	.81
Sepsis (with or without shock)	98 (28.3)	2.04	0.24–17.2	.51
Acute kidney injury	95 (27.5)	1.02	0.24–4.29	.98
Required vasopressor	69 (19.9)	7.85	0.74–83.78	.09
Required intubation	66 (19.1)	1.65	0.18–14.92	.66
Hypotension	56 (16.2)	7.81	1.01–55.55	.040
Code status change	52 (15.0)	52.55	12.53–220.41	<.001
Metabolic acidosis	45 (13.0)	2.96	0.59–14.60	.18
Arrhythmia	40 (11.6)	2.43	0.49–12.80	.28
Liver injury	42 (12.1)	2.54	0.53–12.16	.24
Septic shock	49 (14.2)	11.52	0.91–145.42	.059
Cardiogenic shock	13 (3.8)	4.39	0.42–46.03	.22
Acute pulmonary embolism	12 (5.8)	4.38	0.42–46.03	.15
Acute heart failure	12 (3.5)	3.98	0.03–43.48	.25
Comorbidities				
History of hypertension	208 (60.1)	2.87	1.30–6.31	.01
History of diabetes mellitus	126 (36.4)	2.83	0.481–16.6	.25
Active cancer	16 (4.7)	8.30	0.878–78.4	.065
Advancing age	NA	1.06	1.01–1.12	.02

NA = not applicable

The results when comorbidities, complications, life-sustaining interventions, and code status downgrade were included in the multivariate procedure to determine an association between those factors and mortality are detailed in Table 2. A code status downgrade had the strongest association with death after controlling for the other factors (OR 52.55, 95% CI 12.53−220.41; $P < .001$). In addition, hypotension (OR 7.81, 95% CI 1.01−55.55; $P = .040$), hypertension history (OR 2.87, 95% CI 1.30−6.312; $P = .01$), and advancing age (OR 1.05 95% CI 1.01−12; $P = .02$) were all independently associated with death.

Although active cancer ($n = 16$) had an isolated univariate association with mortality (OR 3.1, 95% CI 1.02−9.31), in the multivariate models, active cancer was not associated with mortality or a code status downgrade. Of 16 subjects with active cancer, 13 were full code and 3 were in limited care at admission. Three of the subjects with full code cancer were intubated, and 1 survived. Ten of the 13 subjects with active cancer and who were not intubated survived, which yielded 5 total deaths in the group or a 31% mortality rate. Four of the 5 subjects with active cancer had a code status downgrade before death, the exception being 1 subject on limited care who arrested while on high-flow nasal canula.

Discussion

There was a significant association between mortality and code status downgrade, with a large OR, a shared decision that, in the setting of acute severe illness, typically represents acceptance of impending death. A code status downgrade reflects a variety of factors related to patient decline and worsening clinical picture, which impacts patient and/or family expectations of a terminal outcome. No subject had his or her code status upgraded to a higher level of care when faced with respiratory failure. However, there were 9 subjects who died while their admission code status was maintained, and 7 of this group remained intubated. In each of these cases, there was a rapid change in clinical condition. In one case, code status was being discussed with the family when the subject suddenly arrested.

In our study of code status downgrade, we found an independent association between code status downgrade with respiratory failure, acute kidney injury, hypotension, acute pulmonary embolism, and advancing age in our population, as determined by multivariable logistic regression. With the exception of active cancer, all the factors listed in Table 1 had an isolated univariate association with code status downgrade, but the association with code status downgrade did not remain when controlling for other factors. Reading the progress notes of the subjects who died revealed a common theme. A patient who is intubated experiences a downturn in stability with hypotension or the onset of a complication such as acute kidney injury, which possibly requires renal replacement therapy in the ICU. The family decides to de-escalate care. The patient is compassionately extubated and dies soon thereafter. The median time of 0.25 d (6 h) between code status downgrade and death, for the subjects with a code status downgrade who died in the hospital, reflects this pattern.

As with any retrospective chart review study, there is an opportunity for documentation error. Incomplete documentation (eg, unknown subject history on arrival) also made demographic and comorbidity analysis difficult. Another limitation of our study was the lack of feedback from the subjects and families with regard to their decision to request or accept a downgrade code status. Future prospective study could record what factors influenced their decisions.

The most consistent factors in this study associated with a code status downgrade were respiratory failure, acute kidney injury, hypotension, acute pulmonary embolism, and advancing age. Code status downgrades, clinical hypotension, hypertension history, and advancing age were also significantly associated with mortality. A code status downgrade preceded death in 40 of the 49 subjects who died. The remaining 9 subjects had rapid demise, due to ventricular fibrillation (2 subjects) or pulseless electrical activity due to hypoxia (5 subjects). The continued importance of goals of care discussions in the assessment of patients who are critically ill and with COVID-19 cannot be understated.

ACKNOWLEDGMENTS

The authors thank Brian Hiestand MD, Andrea Fernandez MD, Samantha Hopp, Oluchi Nwoke MD, Natalia Osipchuk MD, and Philippe Ayers MD, for their help in study coordination and data collection.

REFERENCES

1. Halpin DMG, Criner GJ, Papi A, Singh D, Anzueto A, Martinez FJ, et al. Global Initiative for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease. The 2020 GOLD Science Committee Report on COVID-19 and chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2021;203(1):24-36.
2. Popkin BM, Du S, Green WD, Beck MA, Algaith T, Herbst CH, et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. Obes Rev 2020;21(11): e13128.
3. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA 2020;324(8):782-793.
4. Flythe JE, Assimon MM, Tugman MJ, Chang EH, Gupta S, Shah J, et al; STOP-COVID Investigators. Characteristics and outcomes of individuals with pre-existing kidney disease and COVID-19 admitted to intensive care units in the United States. Am J Kidney Dis 2021;77 (2):190-203.e1.
5. Mackman N, Antoniak S, Wolberg AS, Kasthuri R, Key NS. Coagulation abnormalities and thrombosis in patients infected with SARS-CoV-2 and other pandemic viruses. Arterioscler Thromb Vasc Biol 2020;40(9):2033-2044.
6. Zitelny E, Newman N, Zhao D. STEMI during the COVID-19 pandemic - an evaluation of incidence. Cardiovasc Pathol 2020;48:107232.
7. Ng JH, Hirsch JS, Hazzan A, Wanchoo R, Shah HH, Malieckal DA, et al; Northwell Nephrology COVID-19 Research Consortium. Outcomes among patients hospitalized with COVID-19 and acute kidney injury. Am J Kidney Dis 2021;77(2):204-215.e1.
8. Santus P, Radovanovic D, Saderi L, Marino P, Cogliati C, De Filippis G, et al. Severity of respiratory failure at admission and in-hospital mortality in patients with COVID-19: a prospective observational multicentre study. BMJ Open 2020;10(10):e043651.
9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42(2):377-381.
10. Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019;95:103208.