Predictors of Mortality in Hospitalized Patients with COVID-19; A Retrospective Analysis

Authors: Farah Harmouch, MD, Kashyap Shah DO, Harsh Goel, MD; St Luke's University Health Network – Department of Medicine

Introduction

As of March 11, 2020, coronavirus disease 2019 (COVID-19), caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a world-wide pandemic by the World Health Organization (WHO). The virus has been noted to have a wide spectrum of clinical manifestations. Infected individuals may be asymptomatic; some require hospitalization while others require ICU support for acute respiratory distress syndrome and/or multiple organ dysfunction syndromes. We present a retrospective analysis aimed at identifying baseline demographic/clinical co-morbidities and biochemical/inflammatory markers at presentation associated with mortality in patients with hospitalized COVID-19 patients.

Methods

ICD-10 codes were used to collect data in a retrospective chart review to identify patients who tested positive for SARS-CoV-2 via PCR and were hospitalized in our health network. Patients who remained hospitalized at the time of data collection were excluded from our study. We collected data on patient demographics, medical comorbidities, and laboratory assays performed at the time of admission or within 24-hours of admission, whichever occurred first. Primary outcome of interest was mortality, i.e. death occurring while hospitalized. Between groups defined by survival, continuous variables were compared using the Student's t-test for normally distributed variables or Mann Whitney U-test for non-normally distributed variables. Categorical variables were compared among survivors and non-survivors using Chi-squared or Fisher's exact test, as appropriate. Univariate analysis was performed to identify individual factors associated with mortality. Factors significant at a p≤ 0.05 were included in multivariate logistic regression to find independent predictors of mortality. For the sake of parsimony, we excluded highly collinear variables, even if significant on univariate analysis. All statistical analyses were performed using SPSS Version 26 (IBM Corp, Armonk, NY).

Variable	Survivors (n=479)	Non-survivors (n=81)	Univariate regression OR (95%CI)
Age	61 (51-72)	78 (69-85) ***	1.065 (1.046-1.084)
Male (%)	278 (58)	42 (51.9)	1.284 (0.801-2.059)
Race			
Caucasian	192 (40.1)	45 (55.6) **	NA
Non-caucasian	287 (59.9)	36 (44.4) **	0.535 (0.333-0.860) **
BMI (kg/m^2)	30.7 (26.9-36.3)	29.6 (24.9-34.8)	0.981 (0.951-1.013)
Morbid Obesity	102 (21.6)	18 (22.2)	1.036 (0.587-1.829)
Smoking	149 (32.6)	32 (42.7)	1.538 (0.935-2.530)
Diabetes mellitus	171 (35.7)	27 (33.3)	0.901 (0.547-1.482)
Hypertension	230 (48)	53 (65.4) **	2.049 (1.253-3.351) **
Congestive heart failure	35 (7.3)	19 (23.5) ***	3.888 (2.094-7.216) ***
CKD≥3	77 (16.1)	34 (42) ***	3.777 (2.281-6.253) ***
Hemodialysis	9 (1.9)	6 (7.4) *	4.178 (1.445-12.075) **
Vascular disease	24 (5)	12 (14.8) **	3.297 (1.577-6.895) **
Chronic Pulmonary disease	35 (7.3)	12 (14.8) *	2.206 (1.092-4.456) *
Asthma	50 (10.4)	6 (7.4)	0.686 (0.284-1.658)
Biochemical variables			
WCC≥10 x10^9/L	76/478 (15.9%)	18/80 (22.5%)	1.536 (0.860-2.741)
ANC≥8 x 10^9/L	76/428 (17.8%)	15/75 (20.0%)	1.158 (0.624-2.148)
ALC≤1 x10^9/L	241/428 (56.3%)	52/75 (69.3%) *	1.754 (1.036-2.970) *
Sodium ≥145 mmol/L	4/478 (0.8%)	6/80 (7.5%) ***	1.055 (1.001-1.112) ***
Creatinine≥1.5 mg/dl	90/478 (18.8%)	35/80 (43.8%) ***	3.353 (2.038-5.516) ***
ALT≤15 U/L	22/470 (4.7%)	9/78 (11.5%) *	2.656 (1.175-6.006) *
AST≥45 U/L	240/470 (51.1%)	44/79 (55.7%)	1.205 (0.746-1.946)
ALP≥120 U/L	54/470 (11.5%)	10/79 (12.7%)	1.116 (0.543-2.297)
Total bilirubin≥1.2 mg/dl	30/470 (6.4)	6/79 (7.6)	1.205 (0.485-2.997)
Tn≥0.05 ng/ml	62/411 (15.1%)	35/68 (51.5%) ***	5.970 (3.455-10.316) ***
BNP≥500 pg/ml	105/317 (33.1%)	31/53 (58.5%) ***	2.845 (1.570-5.155) ***
LDH≥250 U/L	272/320 (85.0%)	48/56 (85.7%)	1.059 (0.472-2.378)
Ferritin≥500 ng/ml	118/391 (30.2%)	22/65 (33.8%)	1.677 (0.947-2.969)
ESR≥50 mm/hr	142/229 (62.0%)	32/42 (76.2%)	1.961 (0.918-4.186)
CRP≥25 mg/L	339/386 (87.8%)	57/59 (96.6%) *	3.951 (0.934-16.721)
DDR≥1 mcg/ml	201/356 (56.5%)	48/61 (78.7%) **	2.847 (1.490-5.441) **
Procalcitonin≥0.5 ng/ml	69/449 (15.4%)	25/77 (32.5%) ***	2.648 (1.541-4.551) ***
IL6≥12.2 pg/ml	104/119 (87.4%)	13/14 (92.9%)	1.875 (0.229-15.385)

Table 1: Baseline clinical characteristics, overall and by mortality. Continuous variables are presented as median (25th-75th percentile), and categorical variables as n (%). Significance of difference between subgroups (survivors versus non-survivors) *p≤0.05, **p≤0.01, ***p≤0.001

	B	S.E.	Wald	df	p value	OR	95% CI for OR Lower	95% CI for OR Upper
AGE	.056	.014	15.010	1	.000	1.057	1.028	1.088
CKD3(1)	.750	.401	3.494	1	.062	2.118	.964	4.651
high_Tn(1)	1.002	.397	6.379	1	.012	2.723	1.252	5.926

Table 2: Clinical and biochemical variables found to be significant on univariate regression were entered into stepwise backward multiple logistic regression conditional upon likelihood-ratio probability.

Results

560 patients were included in our study – median age was 63 and 57.1% were males. 81 patients (15.5%) did not survive. Non-survivors were noted to be older in age (median age 78 versus 61 in survivors) and more commonly had hypertension (HTN), congestive heart failure (CHF), and chronic kidney disease (CKD) ≥ 3 (Table 1). On univariate analysis, age, HTN, CHF, CKD ≥ 3, hemodialysis, vascular disease, and pulmonary disease predicted mortality (Table 1). Among biochemical markers, absolute lymphocyte count (ALC) < 1,000/µ, sodium levels, elevated creatinine, cardiac troponin, and brain natriuretic peptide (BNP), predicted mortality (Table 1). Among inflammatory markers, only procalcitonin and d-dimer were associated with mortality. All significant predictors in table 1 were included in multivariate logistic regression except BNP (due to significant collinearity with cardiac troponin as well as CHF) and serum creatinine (due to significant collinearity with CKD). Results of multivariate regression are summarized in table 2.

Discussion

We present a retrospective analysis of a large cohort of hospitalized COVID-19 patients in a large tertiary-care US hospital, indeed one of the largest cohorts at the time of writing. Though we found a large number of baseline comorbid illnesses, as well as serum markers associated with mortality among these patients, age and elevated troponin emerged as the only independent predictors of mortality. CKD stage 3 or higher was borderline significant. Of note, none of the inflammatory markers, though frequently checked in these patients, predicted mortality. Though having a relatively large sample size, we had significant missing data for some biochemical variables, leading to a smaller sample for multivariate analysis than the overall sample. Moreover, our search for medical co-morbidities was performed using ICD-10 codes, rather than hand searching the charts, hence being dependent on quality of documentation, and a potential source of error. However, we believe that such errors should be uncommon and equally distributed among the comparison groups.