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Outcomes of patients with COVID-19 in the intensive care unit in Mexico: A multicenter observational study

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ABSTRACT

Background: As of June 15, 2020, a cumulative total of 7,823,289 confirmed cases of COVID-19 have been reported across 216 countries and territories worldwide. However, there is little information on the clinical characteristics and outcomes of critically ill patients with severe COVID-19 who were admitted to intensive care units (ICUs) in Latin America. The present study evaluated the clinical characteristics and outcomes of critically ill patients with severe COVID-19 who were admitted to ICUs in Mexico.

Methods: This was a multicenter observational study that included 164 critically ill patients with laboratory-confirmed COVID-19 who were admitted to 10 ICUs in Mexico, from April 1 to April 30, 2020. Demographic data, comorbid conditions, clinical presentation, treatment, and outcomes were collected and analyzed. The date of final follow-up was June 4, 2020.

Results: A total of 164 patients with severe COVID-19 were included in this study. The mean age of patients was 57.3 years (SD 13.7), 114 (69.5%) were men, and 6.0% were healthcare workers. Comorbid conditions were common in patients with critical COVID-19: 38.4% of patients had hypertension and 32.3% had diabetes. Compared to survivors, nonsurvivors were older and more likely to have diabetes, hypertension or other conditions. Patients presented to the hospital a median of 7 days (IQR 4.5−9) after symptom onset. The most common presenting symptoms were shortness of breath, fever, dry cough, and myalgias. One hundred percent of patients received invasive mechanical ventilation for a median time of 11 days (IQR 6−14). A total of 139 of 164 patients (89.4%) received vasopressors, and 24 patients (14.6%) received renal replacement therapy during hospitalization. Eighty-five (51.8%) patients died at or before 30 days, with a median survival of 25 days. Age (OR, 1.05; 95% CI, 1.02−1.08; $p<0.001$) and C-reactive protein levels upon ICU admission (1.008; 95% CI, 1.003−1.012; $p<0.001$) were associated with a higher risk of in-hospital death. ICU length of stay was associated with reduced in-hospital mortality risk (OR, 0.89; 95% CI, 0.84−0.94; $p<0.001$).

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Conclusions: This observational study of critically ill patients with laboratory-confirmed COVID-19 who were admitted to the ICU in Mexico demonstrated that age and C-reactive protein level upon ICU admission were associated with in-hospital mortality, and the overall hospital mortality rate was high.
Trial registration: ClinicalTrials.gov, NCT04336345.

Introduction

As of June 15, 2020, a cumulative total of 7,823,289 confirmed cases of coronavirus disease 2019 (COVID-19) have been reported across 216 countries and territories worldwide.[1] A total of 150,262 confirmed cases of COVID-19 and 17,580 deaths have been reported in Mexico.[2] Approximately 3% (4,555/150,262) of these patients presented rapidly progressive respiratory failure and required endotracheal intubation and invasive mechanical ventilation.[2] The COVID-19 pandemic continues to pose a major public health threat to Latin American countries, including Mexico. Although scientific knowledge of COVID-19 increases daily, limited information is available on the presenting characteristics and outcomes of Latin American patients requiring admission to intensive care units (ICUs). Therefore, the present study evaluated the clinical characteristics and outcomes of critically ill patients with critical COVID-19 who were admitted to ICUs in Mexico.

Methods

Study design and participants

This study examined 10 hospitals located in Mexico (Appendix). Institutional review board approval was obtained from the participating hospitals in accordance with local ethical regulations. This multi-center observational study is registered at ClinicalTrials.gov (https://clinicaltrials.gov/ct2/show/NCT04336345). Each center collected data on all adult patients (age 18 years and older) who were admitted to the ICU between April 1 and April 30, 2020. All patients included in the study had SARS-CoV-2 infection, which was confirmed by positive polymerase chain reaction testing of nasopharyngeal specimens. Patients who died within 24 h after ICU admission were excluded. The primary outcome parameter was in-hospital mortality (i.e., mortality 30 days following hospital admission).

Data collection and definitions

The investigators collected data using preprinted (recorded by each center on an electronic worksheet) or electronic case report forms using a secured internet-based website (EasyTrial COVID-19 server: https://covid19.easytrial.net). Two investigators reviewed the data for plausibility and the availability of primary and secondary outcome measures. Any doubts were clarified with the center in question. There was no on-site monitoring. Data collection upon ICU admission included demographic data and comorbid diseases. Clinical and laboratory data for the Acute Physiology and Chronic Health Evaluation (APACHE II),[3] the Sequential Organ Failure Assessment (SOFA)[4] and the Mexican Sequential Organ Failure Assessment (MEXSOFA®)[5] scores were reported as the worst values within 24 h after ICU admission. Demographic, clinical, and laboratory data were collected during the first day of the ICU stay and included the need for invasive mechanical ventilation (IMV), prone position, need for vasopressor therapy, need for renal replacement therapy, length of IMV, length of stay in the hospital before ICU admission, bacterial/fungal coinfection, treatment (renal replacement therapy, vasopressors, antiviral agents, glucocorticoids, tocilizumab, hydroxychloroquine with azithromycin, chloroquine, and any antibiotics), and hospital mortality. Length of ICU stay was measured as the number of days from ICU admission until ICU discharge. The presence of the following comorbid conditions was recorded: systemic hypertension, diabetes mellitus, smoking, solid tumor, chronic obstructive pulmonary disease, and chronic renal failure. The severity of acute respiratory distress syndrome (ARDS) was defined as mild, moderate or severe according to the Berlin definitions.[6] Critical COVID-19 patients were defined as patients who required endotracheal intubation at any time during hospitalization or who experienced life-threatening complications, such as ARDS, shock, and/or organ dysfunction.[7] Clinical laboratory testing was performed in the laboratories of each participating site. Because not all participating centers had the capacity to assess all inflammatory/injury markers, we recorded routine blood test results that were performed as part of the usual clinical care of each patient, which included blood count, serum creatinine, total bilirubin, D-dimer, ferritin and C-reactive protein, where available. We used global reference ranges for the interpretation of laboratory results and the International System of Units to ensure that laboratory values from all local laboratories were converted to the same unit.

Statistical analysis

No statistical sample size calculation was performed a priori, and sample size was equal to the total number of patients with critical COVID-19 who were treated at participating centers during the study period. All patients completed follow-up examinations by June 04, 2020. Continuous variables are expressed as means (SD) and medians (IQR). Categorical variables are expressed as frequencies and percentages. Missing data were not imputed. Student's t-test (for normally distributed data) or the Mann−Whitney U-test (for nonnormally distributed data) were used to compare continuous variables. Data distributions were determined using the Kolmogorov−Smirnov test. The Chi-squared test (for normally distributed data) and Fisher's exact test (for nonnormally distributed data) were used to compare categorical variables. Variables with a $p < 0.05$ in the univariate analysis were entered into the model using a forward stepwise procedure. A variable was entered into the model using a forward stepwise procedure (sequentially entering significant variables) if its associated significance level was $p < 0.05$, and a variable was removed from the model if its associated significance level was $p > 0.100$. The age of the patient, C-reactive protein levels on ICU admission and ICU length of stay were entered in the analysis as continuous measures. The remaining variables (hypertension, diabetes mellitus, expectoration, and tocilizumab treatment) were considered categorical factors and were valued as 0 if absent and as 1 if present. The APACHE II scores were not entered into the multivariable analysis due to their possible collinearity with age because age is included in this scoring system. The length of IMV and hospital length of stay were not entered into the multivariable analysis due to possible collinearity with length of ICU stay. The results are summarized as odds ratios (ORs) and 95% confidence intervals (CIs). Two-tailed p-values < 0.05 were considered statistically significant. The area under the receiver operating characteristic curve was used to evaluate the ability of the model to discriminate between patients who lived and patients who died (discrimination) .[8] Goodness-of-fit (Hosmer-Lemeshow) was calculated to assess the relevance of the logistic regression model.[9] Survival curves were estimated using the Kaplan-Meier method. A two-sided p-value < 0.05 was considered statistically significant.

Results

The flow chart of this study is shown in Fig. 1. A total of 164 patients with critical COVID-19 were included. Table 1 reports presenting characteristics, treatment in the ICU and outcomes of patients with critical COVID-19, according to in-hospital death. Mean age was
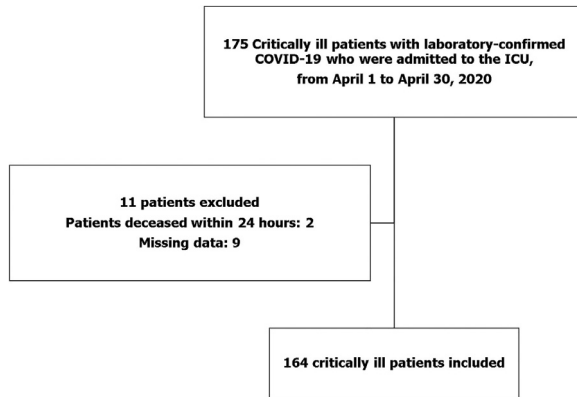

Fig. 1. Flow chart of the study and included patients with critical COVID-2019.

57.3 years (SD 13.7), and 114 patients (69.5%) were men. The mean body mass index was 30.7 kg/m², and 10 patients (6.0%) were healthcare workers. A total of 38.4% of patients had hypertension, and 32.3% had diabetes (Table 1). Demographic variables and comorbidities were compared between survivors and nonsurvivors. Nonsurvivors were older and more likely to have comorbid conditions such as diabetes and hypertension. Patients presented to the hospital a median of 7 days (IQR 4.5−9) after symptom onset. The most common presenting symptoms were shortness of breath, fever, dry cough, and myalgias. A total of 164 (100%) patients received IMV for a median of 11 days (IQR 6−14), 139 (89.4%) patients received vasopressors, and 24 (14.6%) received renal replacement therapy during hospitalization. Seven (4.2%) patients received high-flow nasal cannula oxygen therapy or noninvasive ventilation, and 100% of patients subsequently required IMV. Laboratory findings of critically ill patients infected with SARS-CoV-2 on admission to the ICU are presented in Table 2. Infections were microbiologically confirmed in 26 (15.9%) of 164 patients. Antibiotics were administered empirically to 162 of 164 (98.7%) patients. Antiviral agents were also administered to 86 (52.4%) patients in this study (Table 1). The median length of ICU stay among survivors was 13 days (IQR 10 to 16), and the median length of hospital stay among survivors was 15 days (IQR 12 to 19) (Table 1). Eighty-five (51.8%) patients died at or before 30 days, with a median survival of 25 days (Fig. 2). Age (OR, 1.05; 95% CI,

Table 1
Characteristics, treatment in the intensive care unit and outcomes of patients with critical COVID-19 based on in-hospital death.

Characteristic	All Patients (n = 164)	Alive (n = 79)	Dead (n = 85)	p-value
Age, years, mean ± SD	57.3 ± 13.7	49.4 ± 13.1	57.0 ± 13.3	<0.001
Sex, male, n (%)	114 (69.5)	55 (69.6)	59 (69.4)	0.977
Body mass index, kg/m² mean ± SD	30.7 ± 5.5	30.2 ± 4.9	31.2 ± 6.0	0.272
APACHE II, mean ± SD	12.7 ± 5.5	11.8 ± 5.0	13.6 ± 5.9	0.039
SOFA score, median (IQR)	6 (4−8)	6 (4−8)	6 (4−8)	0.676
MEXSOFA® score, mean ±SD	6.0 ± 2.3	5.8 ± 2.4	6.1 ± 2.1	0.440
Comorbid conditions, n (%)				
Systemic hypertension	63 (38.4)	22 (27.8)	41 (48.2)	0.010
Diabetes mellitus	53 (32.3)	16 (20.2)	37 (69.8)	0.001
Smoking	24 (14.3)	13 (16.4)	11 (12.9)	0.659
Solid tumors	10 (6.0)	6 (8.6)	4 (4.7)	0.524
Chronic obstructive pulmonary disease	4 (2.4)	1 (1.2)	3 (3.5)	0.621
Chronic renal failure	6 (3.6)	4 (5)	2 (2.3)	0.430
Signs and symptoms, n (%)				
Shortness of breath	152 (92.6)	70 (88.6)	82 (96.4)	0.053
Fever	138 (84.1)	67 (84.8)	71 (83.5)	0.822
Dry cough	131 (79.8)	60 (75.9)	71 (83.5)	0.226
Myalgia	84 (51.2)	44 (55.6)	40 (47.0)	0.269
Expectoration	32 (19.5)	9 (11.3)	23 (27.0)	0.011
Rhinorrhea	31 (18.9)	15 (18.9)	16 (18.8)	0.979
Diarrhea	29 (17.6)	10 (12.6)	19 (22.3)	0.104
Duration of symptoms before hospital admission, days, median (IQR)	7 (4.5−9)	7 (4−9)	7 (5−9)	0.526
ARDS mild to moderate, n (%)	93 (56.7)	48 (60.7)	45 (52.9)	0.313
ARDS severe, n (%)	71 (43.3)	31 (39.2)	40 (47.1)	
Treatment, n (%)				
High flow nasal cannula	5 (3.0)	4 (5.0)	1 (1.1)	0.197
Non-invasive mechanical ventilation	2 (1.2)	2 (2.5)	0 (0)	0.271
Invasive mechanical ventilation	164 (100)	79 (100)	85 (100)	NA
Prone position	93 (56.7)	43 (54.4)	50 (58.8)	0.570
Renal replacement therapy	24 (14.6)	11 (13.9)	13 (15.3)	0.804
Vasopressors	139 (89.4)	69 (87.3)	70 (82.3)	0.374
Antiviral agents	86 (52.4)	38 (48.1)	48 (56.4)	0.284
Glucocorticoids	66 (40.2)	27 (34.1)	39 (45.8)	0.127
Tocilizumab	42 (25.6)	28 (35.4)	14 (16.4)	0.005
Hydroxychloroquine with azithromycin	54 (32.9)	30 (37.9)	24 (28.2)	0.185
Chloroquine	48 (28.0)	27 (34.1)	19 (22.3)	0.092
Any antibiotics	162 (98.7)	79 (100)	83 (97.6)	0.498
Outcomes				
Mechanical ventilation, days, median (IQR)	11 (6−14)	12 (7.5−15)	8 (5−13)	0.003
ICU length of stay, days, median (IQR)	12 (7−15)	13 (10−16)	8 (5−13)	<0.001
Hospital length of stay, days, median (IQR)	13 (8−18)	15 (12−19)	10 (7−14)	<0.001

SD: standard deviation; APACHE: Acute Physiology and Chronic Health Evaluation; SOFA: Sequential Organ Failure Assessment, MEXSOFA®: Mexican Sequential Organ Failure Assessment; IQR: interquartile range, ARDS: Acute respiratory distress syndrome, ICU: intensive care unit.

Table 2
Laboratory findings on intensive care unit admission of patients with critical COVID-19 based on in-hospital death.

Laboratory values	All Patients ($n = 164$)	Alive ($n = 79$)	Dead ($n = 85$)	p-value
Hemoglobin, g/dL, mean ± SD	13.5 ± 2.17	13.3 ± 2.1	13.7 ± 2.2	0.251
White blood cells count, 10^9/L, median (IQR)	10.5 (7.4−13.0)	11 (8.1−12.8)	10 (7.3−13.5)	0.407
Neutrophils, 10^9/L, mean ± SD	9.1 ± 4.9	9.3 ± 5.1	8.9 ± 4.8	0.626
Lymphocytes, 10^9/L, median (IQR)	0.8 (0.5−1.1)	0.8 (0.5−1.1)	0.8 (0.5−1.1)	0.880
Platelets, 10^9/L, mean ± SD	252 ± 95.3	246 ± 101	259 ± 89.4	0.374
Serum creatinine, mg/dL, median (IQR)	1.05 (0.81−1.56)	1.16 (0.81−1.72)	0.95 (0.76−1.39)	0.172
Total bilirubin, mg/dL, median (IQR)	0.65 (0.42−0.88)	0.61 (0.40−0.81)	0.69 (0.49−0.98)	0.089
D-dimer, μg/ml, median (IQR)	1.15 (0.68−2.53)	1.16 (0.73−2.84)	1.16 (0.68−2.1)	0.420
Ferritin level, ng/ml, median (IQR)	944 (565−1375)	888 (520−1119)	997 (620−1531)	0.054
C-reactive protein, mg/dL, median (IQR)	31 (17.9−131.4)	25 (12.7−32)	54 (27.8−213)	<0.001

SD: standard deviation, IQR: interquartile range.

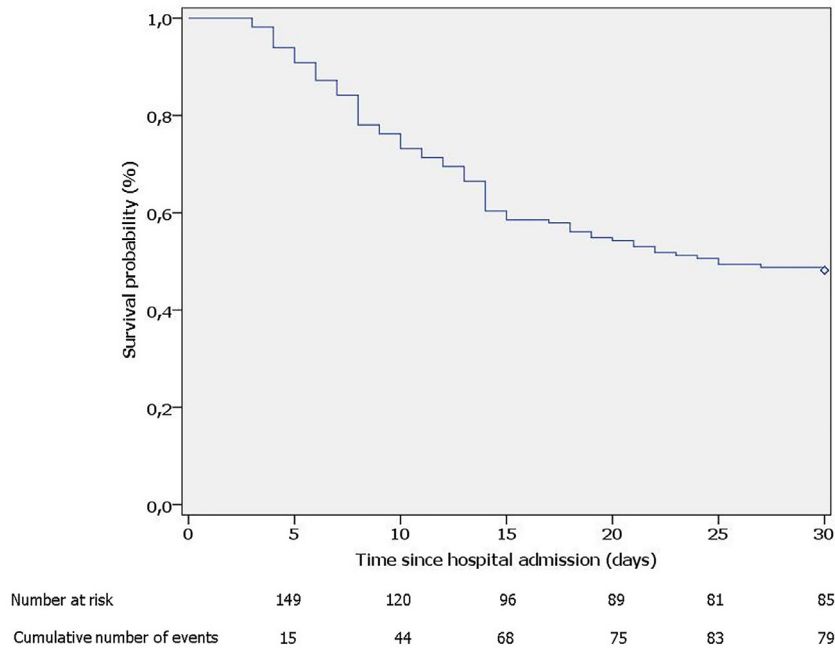| Number at risk	149	120	96	89	81	85
Cumulative number of events	15	44	68	75	83	79

Fig. 2. Survival of critically ill patients with COVID-19.

1.02−1.08, p<0.001) and C-reactive protein levels upon ICU admission (OR, 1.008; 95% CI, 1.003−1.012, p<0.001) were associated with an increased risk for in-hospital death. ICU length of stay was associated with reduced in-hospital mortality risk (OR, 0.89; 95% CI, 0.84−0.94, p<0.001) [goodness of fit, (Hosmer-Lemeshow), $\chi2$=4.806, p = 0.778, AUC: 0.79 (95% confidence interval: 0.73−0.86), p<0.001] (Table 3).

Discussion

To our knowledge, this study is the first report of patients with critical COVID-19 from Latin America. Most patients with critical COVID-19 admitted to the 10 ICUs in Mexico were men over 57 years of age with hypertension and diabetes, and 6% were health-care workers. As mentioned in previous studies, greater than 60% of patients with critical COVID-18 were men.[10,11] The mean age of patients admitted to the ICU was 57 years old, which is less than the median age reported in other studies.[10,13] Patients with hypertension and diabetes exhibited significantly decreased survival, but neither of these comorbidities was an independent factor associated with mortality. One hundred percent of patients received IMV, and nearly 90% received vasopressors. Compared to other reports,[10, 11,12] this study corroborates the very high incidence of multiple organ failure in patients with severe COVID-19, as shown by the proportion of

Table 3
Variables predictive of in-hospital mortality according to univariate and multivariate analyses.

Variables	Univariate				Multivariate			
	OR	95% CI		P value	OR	95% CI		P value
Age	1.04	1.01	1.07	0.001	1.05	1.02	1.08	<0.001
Systemic hypertension	2.41	1.26	4.62	0.008				
Diabetes mellitus	3.03	1.51	6.09	0.002				
Expectoration	2.88	1.24	6.70	0.014				
Tocilizumab treatment	0.35	0.17	0.74	0.006				
Length of intensive care unit stay	0.90	0.85	0.95	<0.001	0.89	0.84	0.94	<0.001
C-reactive protein	1.008	1.004	1.01	<0.001	1.008	1.003	1.01	<0.001

patients requiring IMV (164 [100%]), vasopressors (139 [89.4%]) and renal replacement therapy (24 [14.6%]).

C-reactive protein is an acute inflammatory factor that increases up to 1000-fold at sites of infection or inflammation.[14] Elevated levels of C-reactive protein may be linked to the overproduction of inflammatory cytokines in patients with critical COVID−19.[15] Higher levels of C-reactive protein might be a predictive marker in determining which patients with mild COVID-19 will progress to critical disease.[16] Patients with critical COVID-19 who died in the hospital exhibited significantly higher C-reactive protein concentrations than survivors in our study. This result suggests that the C-reactive protein levels upon admission to the ICU may be useful for predicting the prognosis of patients with critical COVID-19. Previous studies reported mortality rates that ranged from 35.2% to 72% in these patients.[10,12,13,17] In a cohort of 52 critically ill patients with confirmed SARS-CoV-2 infection from a single center in Wuhan, China, 32 (61.5%) patients died at 28 days.[17] A total of 405 (26%) of 1581 patients and 784 (35.4%) of 2215 patients who were critically ill with laboratory-confirmed COVID-19 also died at 28 days in a cohort from Lombardy Region, Italy[10] and a US cohort,[13] respectively. The mortality in our report was higher than that reported in critically ill patients with COVID-19 in Italy[10] but lower than in other studies.[18,19] Our data confirm high hospital mortality rates in patients with critical COVID-19.

The present study has several limitations. First, the small sample size may limit the generalizability of our findings. Second, the observational nature of the study is a limitation. Finally, we had no specific information on long-term outcomes or quality of life in survivors. Further research is needed to extend our results in larger cohorts.

Conclusions

The present observational study of critically ill patients with laboratory-confirmed COVID-19 admitted to ICUs in Mexico demonstrated that age and CRP levels upon ICU admission were associated with in-hospital mortality, and the associated hospital mortality rate was high.

Author contributions

Dr Ñamendys-Silva had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Ñamendys-Silva, Dominguez-Cherit
Acquisition of data: All authors
Statistical analysis: Ñamendys-Silva.
Drafting of the manuscript: Ñamendys-Silva, Alvarado-Ávila, Dominguez-Cherit, Rivero-Sigarroa
Critical revision of the manuscript for important intellectual content: All authors.

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Declarations of Competing Interest

The authors state that there are no conflicts of interest related to this study.

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Group Information: The Mexico COVID-19 Critical Care Collaborative Group investigators are listed in the Supplement. Supplementary material associated with this article may be found in the online version.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.hrtlng.2020.10.013.

References

1. Coronavirus Disease (COVID-19): Situation Report-147. Geneva: World Health Organization (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200615-covid-19-sitrep-147.pdf?sfvrsn=2497a605_4).
2. Conferencia 15 De Junio: Comunicado Técnico Diario. Mexico: Secretaría de Salud Federal (https://coronavirus.gob.mx/2020/06/15/conferencia-15-de-junio/).
3. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818–829.
4. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the working group on sepsis-related problems of the European society of intensive care medicine. Intensive Care Med.. 1996;22(7):707–710.
5. Namendys-Silva SA, Silva-Medina MA, Vásquez-Barahona GM, et al. Application of a modified sequential organ failure assessment score to critically ill patients. Braz J Med Biol Res. 2013;46(2):186–193.
6. Definition Task Force ARDS, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin definition. JAMA. 2012;307(23):2526–2533.
7. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) China, 2020. China CDC Weekly. Accessed August 24, 2020. http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51.
8. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology. 1982;143(1):29–36.
9. Hosmer DW, Taber S, Lemeshow S. The importance of assessing the fit of logistic regression models: a case study. Am J Public Health. 1991;81(12):1630–1635.
10. Grasselli G, Zangrillo A, Zanella A, et al. Baseline characteristics and outcomes of 1591 patients infected with SARS-CoV-2 admitted to ICUs of the Lombardy region, Italy [published online ahead of print, 2020 Apr 6]. JAMA. 2020;323(16):1574–1581.
11. Gupta S, Hayek SS, Wang W, et al. Factors Associated With Death in Critically Ill Patients With Coronavirus Disease 2019 in the US. JAMA Intern Med. 2020;15. https://doi.org/10.1001/jamainternmed.2020.3596. Published online July.
12. Xu J, Yang X, Yang L, et al. Clinical course and predictors of 60-day mortality in 239 critically ill patients with COVID-19: a multicenter retrospective study from Wuhan, China. Crit Care. 2020;24(1):394. https://doi.org/10.1186/s13054-020-03098-9. Published 2020 Jul 6.
13. Grasselli G, Greco M, Zanella A, et al. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA Intern Med. 2020. https://doi.org/10.1001/jamainternmed.2020.3539. Published online July 15.
14. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Front Immunol. 2018;9:754. https://doi.org/10.3389/fimmu.2018.00754. Published 2018 Apr 13.
15. Ali N. Elevated level of C-reactive protein may be an early marker to predict risk for severity of COVID-19 [published online ahead of print, 2020 May 30]. J Med Virol. 2020. https://doi.org/10.1002/jmv.26097. 10.1002/jmv.26097.
16. Wang G, Wu C, Zhang Q, et al. C-reactive protein level may predict the risk of COVID-19 aggravation. Open Forum Infect Dis. 2020;7(5). https://doi.org/10.1093/ofid/ofaa153. ofaa153. Published 2020 Apr 29.
17. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study [published correction appears in Lancet Respir Med. 2020 Apr;8(4): e26] Lancet Respir Med. 2020;8(5):475–481. https://doi.org/10.1016/S2213-2600(20)30079-5.
18. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study [published correction appears in Lancet. 2020 Mar 28;395(10229):1038] [published correction appears in Lancet. 2020 Mar 28;395(10229):1038]. Lancet. 2020;395 (10229):1054–1062. https://doi.org/10.1016/S0140-6736(20)30566-3.
19. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State [published online ahead of print, 2020 Mar 19]. JAMA. 2020;323(16):1612–1614. https://doi.org/10.1001/jama.2020.4326.