A single-centered, retrospective cohort study of critically ill COVID-19 patients: Is the heart at risk?

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ABSTRACT

OBJECTIVE
The Philippines has the highest COVID-19 mortality rate by country (per million) in South East Asia. We aim to explore predictors of mortality among critically ill COVID-19 patients.

METHODS
This single-centered, retrospective cohort study included consecutive patients with confirmed COVID-19 infection and acute respiratory distress syndrome requiring mechanical ventilation and intensive care unit (ICU) admission at The Medical City hospital from March 6 to March 31, 2020. Clinical data were obtained from medical records review and compared between survivors and non-survivors.

RESULTS
Among 30 patients (mean age 65±3 years, interquartile range 32-86; 63% male), hypertension (67%), diabetes mellitus (45%), hyperlipidemia (40%) and smoking history (30%) were common. Those with echocardiogram showed no left ventricular dysfunction except 1 (preexisting heart failure), despite elevated troponin and NT-pro BNP. All had sepsis; 87% had septic shock. Twenty two (73%) died, 6 (20%) discharged improved, 1 (3%) transferred to another hospital (outcome unknown), and 1 (3%) still admitted. Mean duration from ICU admission to death was 13 days for non-survivors. Use of norepinephrine plus vasopressin and unfractionated heparin (UFH) for thromboprophylaxis were significantly higher among non-survivors versus survivors. There was a nonsignificant trend towards a higher mean troponin and NT-proBNP among non-survivors versus survivors.

CONCLUSION
We report that use of norepinephrine plus vasopressin and UFH for thromboprophylaxis were predictors of mortality among critically ill COVID-19 patients. Mean survival time of non-survivors is likely to be 13 days after ICU admission. Elevated troponin and NT-proBNP were not associated with increased mortality.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), unknown before the outbreak began in Wuhan, China, in December 2019.[1] The first case of COVID-19 in Manila, Philippines was reported on January 30, 2020. On March 7, the first local transmission of COVID-19 was confirmed.[1-2] In the South East Asia region, the Philippines continues to have the highest mortality rate by country (per million) and ranks first in the total number of confirmed COVID-19 cases despite early border closure and community quarantine.[3]

While in the majority of COVID-19 infections, clinical symptoms may be mild, nearly 20% of patients develop severe to critical illness.[4-6] Among all patients, a range of 3% to 17% developed acute respiratory distress syndrome (ARDS) compared to a range of 20% to 42% for hospitalized patients and 67% to 85% for patients admitted to the intensive care unit (ICU).[7-12] Patients admitted to the ICU have a reported mortality from 39% to 72% depending on the study.[9,11,13-14] Cardiovascular complications, including myocardial injury and myocarditis, acute myocardial infarction, heart failure, dysrhythmias and venous thromboembolic events can be a significant contributor to the mortality associated with COVID-19. [4,9-10,13,15]

To our knowledge, no previous study has been done locally to explore predictors for in-hospital mortality in COVID-19 patients. Understanding the clinical course and awareness of cardiovascular complications may help guide clinical decision making in ICU care and treatment.

METHODS

STUDY DESIGN AND POPULATION
This single-centered, retrospective cohort study included 30 consecutive patients with critical COVID-19 illness admitted to the ICU at The Medical City, a tertiary care hospital (Metro Manila, Philippines) from March 6 to March 31, 2020. COVID-19 was confirmed by a positive result on reverse transcriptase polymerase chain assay of a nasopharyngeal swab or endotracheal aspirate obtained in accordance with Centers for Disease Control and Prevention (CDC) guidelines.[16] ARDS was defined according to the Berlin Definition.[17] Critical COVID-19 illness has been previously defined.[4,18]

DATA COLLECTION
Institutional Review Board approval and waiver of informed consent were granted. Data on demographics, baseline clinical characteristics, initial laboratory and imaging findings, ICU therapies and outcomes were obtained by chart review from electronic medical records using a standardized case report form. Anonymized data were entered into a database designed

for the study. We looked at mortality or hospital discharge after ICU admission. ICU therapies and outcomes were followed until time of death or hospital discharge. Sepsis and septic shock were defined according to the Surviving Sepsis Guidelines.[19]

STATISTICAL ANALYSIS

Our study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[20] Data were summarized using descriptive statistics. Continuous variables were described as mean ± standard deviation (SD) and other measures of central tendency; likewise comparisons were determined using Student's *t* test as appropriate, or Fisher exact test for categorical variables on survivors and non-survivors. Univariate and multivariate logistic regression were performed to explore the association of clinical variables and risk of mortality. Statistical significance was set at a p-value <0.05. Analysis was performed with Stata version 13 (StataCorp).

RESULTS

BASELINE CLINICAL CHARACTERISTICS

Baseline clinical characteristics of the 30 patients are shown in **Table 1**. The mean age was 65±3 years (interquartile range 32 to 86); 63% were male. The most common comorbidities were hypertension (67%), diabetes mellitus (45%), and hyperlipidemia (40%). Ten (30%) were current or ex-smokers. Among those with hypertension (n=20), more than half were taking at least 2 anti-hypertensive agents, 80% were renin-angiotensin-aldosterone system (RAAS) blockers. Half of patients were overweight. The most common symptom on admission to the hospital was dyspnea (63%). The mean duration of symptoms prior to admission was 7±1 days. Seventeen (57%) had documented fever and 16 (53%) had elevated respiratory rate upon examination.

LABORATORY AND IMAGING

Baseline laboratory data and imaging findings are shown in **Table 2**. Not all patients had complete laboratory and imaging data. Lymphopenia was seen in 13 (43%). Ferritin was elevated in majority of patients. Procalcitonin was elevated in half of patients. C-reactive protein, fibrinogen and D-dimer were likewise elevated. Chest radiograph showed pulmonary infiltrates in all patients, with concomitant consolidation in 23%. Eight (27%) patients had chest computed tomography (CT), all with ground glass opacities and 62% with consolidation. There was a disproportionately elevated troponin and N-Terminal proB-type Natriuretic Peptide (NT-proBNP) levels. Echocardiogram obtained in 18 (60%) patients showed normal left ventricular size and systolic function in all except 1 (with preexisting heart failure).

ICU THERAPIES

ICU therapies and complications are shown in Table 3. All patients required invasive mechanical ventilation; 17 (57%) were intubated within 24 hours of admission. Twelve (40%) patients were placed on prone position for at least 16 hours; up to 48 hours in 6 (50%) patients. Four (13%) received neuromuscular blockade.

Eighteen (60%) received azithromycin. Fifteen (50%) received tocilizumab. Twenty-four (80%) received either hydrocholoroquine or chloroquine (only 10 patients completed 10 days). Thirteen (43%) received antiviral therapy. Seventeen

Table 1. Baseline Clinical Characteristics

Variable	Overall (N = 30)
Age, years	65 ± 3.0
Male	19 (63%)
Body mass index, kg/m^2	26.63 ± 1.0
Normal	10 (33%)
Underweight	2 (7%)
Overweight	15 (50%)
Obese	3 (10%)
Co-morbidities	
Hypertension	20 (67%)
Diabetes mellitus	13 (45%)
Hyperlipidemia	12 (40%)
Heart failure	1 (3%)
Atrial fibrillation	1 (3%)
Coronary artery disease	1 (3%)
Prior myocarditis	1 (3%)
Prior stroke	1 (3%)
Peripheral arterial disease	1 (3%)
Chronic obstructive pulmonary disease	3 (10%)
Asthma	1 (6%)
Chronic kidney disease	1 (3%)
Cancer*	2 (7%)
Current or former tobacco smoker	10 (33%)
Medications Prior to Admission	
Angiotensin-converting enzyme inhibitor	1 (3%)
Angiotensin II receptor blocker	15 (50%)
Calcium channel blockers	12 (40%)
≥2 Antihypertensive medications	12 (60%)
Oral hypoglycemic agent	8 (27%)
Insulin	1 (3%)
Statins	12 (40%)
Antiplatelet	7 (24%)
Symptoms on Admission	
Dyspnea	19 (63%)
Fever	17 (57%)
Cough	17 (57%)
Body malaise	17 (57%)
Loss of appetite	5 (17%)
Diarrhea	5 (17%)
Sore throat	3 (10%)
Fatigue	1 (3%)
Duration of symptoms prior to admission, days	7.03 ± 0.7
Vitals on Admission	
Temperature >38 degrees Celsius	17 (57%)
Respiratory rate >24 breaths per minute	16 (53%)
Systolic blood pressure, mmHg	127 ± 4.8
Diastolic blood pressure, mmHg	69.76 ± 2.4
Hypotension (blood pressure <90/60mmHg)	3 (10%)
Heart Rate (HR), beats per minute (bpm)	96 ± 3.9
Tachycardia (HR >90bpm)	13 (43%)

Continuous variables are expressed as mean ± SD; categorical variables are expressed as number of patients (percentage)
* Prior treatment for prostate cancer (n=1) and breast cancer (n=1)

Table 2. Baseline Laboratory Data and Imaging Findings

Variable*	**Overall** (N = 30)
Hemoglobin, g/L	128.73± 2.7
White blood count, x 10^9/L	10.16± 1.5
Normal Range	17 (57%)
>10 x 10^9/L	10 (33%)
<4 x 10^9/L	3 (10%)
Neutrophils	0.78± 0.02
>0.8 10^9/L	26 (87%)
Lymphocytes x10^9/L	0.14± 0.02
<0.8 10^9/L	13 (43%)
Platelet count	228.7± 17.4
Creatinine, mg/dL	1.08± 0.1
Hemoglobin A1c, %	7.675± 0.5
Lactate (N=25) mmol/L	1.328± 0.1
Lactate Dehydrogenase (N=26), U/L	528.15± 35.3
Procalcitonin (N=28), ng/mL	1.16± 0.3
>/= 0.5	14 (50%)
Ferritin (N=27), ng/mL	1428.11± 216.6
>464	23 (85%)
C-Reactive Protein (N=21), mg/L	220.84± 36.3
>3	21 (100%)
D-Dimer (N=8), ug/ml	2.75 ± 0.5
>0.5	7 (88%)
Fibrinogen (N=6), mg/dl	642.33± 92.6
>350	6 (100%)
High-sensitivity cardiac troponin I (N=20), pg/mL	483.39± 288.1
NT-ProBNP pg/mL (N=20)	5798.45± 2418.3
Echocardiography (N=18)	
Left Ventricular Ejection Fraction (LVEF)	
LVEF >50%	17 (94%)
LVEF <50%	1 (6%)
Electrocardiogram on admission	
Sinus rhythm	29 (96%)
Atrial fibrillation	1 (3%)
Corrected QT (QTc), msec	448.9± 7.0
Chest radiography	
Infiltrates only	19 (63%)
Infiltrates + Pleural effusion	4 (13%)
Infiltrates + Consolidation	7 (23%)
Chest computed tomography (N=8)	
Ground Glass	2 (25%)
Ground Glass + Pleural effusion	1 (13%)
Ground Glass + Pleural effusion + Consolidation	1 (13%)
Ground Glass + Consolidation	4 (50%)
Positive Cultures	
Blood (n=30)	12/30 (40%)
Endotracheal aspirate/sputum (N=22)	17/22 (77%)
Urine (n=8)	7/8 (88%)
Organisms Identified on Cultures (N=60)	
Candida albicans[$]	17/60 (28%)
Acinetobacter baumannii[$$]	4/60 (7%)
Klebsiella pneumoniae[$$$]	6/60 (10%)

Continuous variables are expressed as mean ± SD; categorical variables are expressed as number of patients (percentage)
* Not all patients had complete laboratory and imaging data
[$] Identified from blood (5/30), endotracheal aspirate/sputum (9/22), urine (6/8) cultures
[$$] Identified from blood (1/30) and endotracheal/sputum aspirate (3/22) cultures
[$$$] Identified from blood (2/30) endotracheal culture(6/22)

(47%) received steroids. Four (13%) received intravenous immunoglobulin. Twenty nine (97%) received venous thromboembolism (VTE) prophylaxis with either low molecular weight heparin or unfractionated heparin (UFH), depending on renal function.

Sepsis was seen in all patients and 87% had septic shock. All patients received antibiotics. The predominant organisms identified on cultures were Candida albicans, Klebsiella pneumoniae and Acinetobacter baumanii (**Table 2**). Bleeding requiring transfusion was seen in 7 (23%) patients. Fourteen (47%) patients required renal replacement therapy.

PREDICTORS OF MORTALITY

There were 22 (73%) who died, 6 (20%) discharged improved, 1 (3%) transferred to another hospital (outcome unknown), and 1 (3%) still admitted in the hospital at the time this study was written (**Table 3**). Comparison of clinical characteristics and outcomes are shown in **Table 4**. Norepinephrine plus vasopressin and UFH therapies were significantly higher among non-survivors versus survivors. The mean number of days admitted at the hospital was significantly higher among survivors versus non-survivors (excluding 1 patient still admitted). Although not significant, there was a trend towards a higher mean troponin and NT-proBNP among non-survivors versus survivors. There was also a nonsignificant trend towards a shorter mean duration of symptoms prior to consult among survivors versus non-survivors.

On univariate analysis (**Table 5**), norepinephrine plus vasopressin and UFH therapies were associated with increased mortality. Mean duration from ICU admission to death was 13 days for non-survivors. We found that troponin and NT-proBNP were not associated with increased mortality. On multivariate analysis (**Table 6**), we did not expect to find significant interactions with mortality given with our small sample size.

DISCUSSION

We report 30 confirmed COVID-19 patients with ARDS who required mechanical ventilation and ICU care during the first month of the outbreak in Metro Manila. Mortality was 73%, higher compared to previous studies on critically ill COVID-19 patients. We found the mean survival time of non-survivors is likely to be 13 days after ICU admission. In the study by Yang et al, 71% required mechanical ventilation, mortality was 61.5% and median duration from ICU admission to death was 7 (IQR 3-11) days. Bhatraju et al reported that 75% required mechanical ventilation and mortality was 50%. In the largest cohort of COVID-19 patients from China,[4] 5% were identified as critical with a case fatality rate of 49%.

We found the use of norepinephrine plus vasopressin was associated with increased mortality. In our cohort, all patients developed sepsis and majority developed shock that required vasopressor support. Similar to Bhatraju et al, we did not find evidence of left ventricular dysfunction (except in 1 with preexisting heart failure) in those who had an echocardiogram. In the study by Zhou et al, sepsis was the most common complication; septic shock was seen in 20% of patients, all of whom died.[13] Yang et al and Bhatraju et al reported vasopressor use in 35% and 71% of patients, respectively.

Table 3. ICU Therapies and Complications

	N (%)
ICU Therapies	
Mechanical Ventilation	30 (100%)
On admission	6 (20%)
Within 24 hours	11(37%)
>24 hours	13 (43%)
Unfractionated Heparin	29 (97%)
Low Molecular Weight Heparin	14 (47%)
Novel Oral Anticoagulants	1 (3%)
Lopinavir + Ritonavir	9 (30%)
Oseltamivir	4 (13%)
Hydrochloroquine	10 (33%)
Chloroquine	14 (47%)
Tocilizumab	15 (50%)
Intravenous Immunoglobulins	4 (13%)
Azithromycin	18 (60%)
Antibiotics	30 (100%)
Steroids	14 (47%)
Vasopressors	
Norepinephrine	26 (87%)
Vasopressin	17 (57%)
Epinephrine	2 (7%)
Dobutamine	1 (3%)
Dopamine	1 (3%)
Neuromuscular blockade	4 (13%)
Continuous Renal Replacement Therapy	14 (47%)
Prone position	12 (40%)
16 hours	2 (17%)
24 Hours	4 (33%)
48 hours	6 (50%)
Complications	
Sepsis	30 (100%)
Septic Shock	26 (87%)
Bacteremia	12 (40%)
Arrhythmias	
Ventricular Tachycardia	3 (10%)
Atrial Fibrillation	7 (23%)
Unstable Bradycardia	4 (13%)
Bleeding	
Upper Gastrointestinal	8 (27%)
IJ site bleeding	1 (3%)
Transfusion Requiring	7 (23%)
Outcomes	
Died in hospital	22 (73%)
Discharged from Hospital	6 (20%)
Still admitted	1 (3%)
Transferred	1 (3%)

Categorical variables are expressed as number of patients (percentage)
*Sepsis and septic shock were defined according to the Surviving Sepsis Guidelines

In our cohort, those with procalcitonin and CRP had elevated levels in 50% and 100%, respectively. Candida albicans, Klebsiella pneumoniae and Acinetobacter baumanii were the predominant organisms identified on cultures. Our findings suggest that the observed shock may be due to bacterial/fungal co-infection. Rawson et al reviewed current literature surrounding bacterial/fungal co-infection in patients with coronavirus infection. Of 9 studies reporting bacterial co-infection in COVID-19 cases, 62/806 (8%) cases of bacterial/fungal co-infection were reported; 72% of COVID-19 cases received antibacterial therapy.[21] The pathogenesis of sepsis, as well as bacterial/fungal co-infection and use of broad-spectrum empirical antibiotics in COVID-19 needs further investigation.

Although no screening was performed, VTE was not observed in our cohort. Nearly all patients were given anticoagulation for VTE prophylaxis. Interestingly, we found that UFH for VTE prophylaxis was associated with increased mortality. The mechanism of this increased mortality is uncertain, as we did not see a significant increase in bleeding, including major bleeding requiring blood transfusion. In a study by Maatman et al, 31 (28%) of 109 COVID-19 patients admitted in the ICU developed VTE despite almost all being on heparin thromboprophylaxis. There was no difference in mortality among patients who developed VTE compared to those without VTE.[22]

Cardiac injury and heart failure have been reported among patients hospitalized with COVID-19.[13,23-24] In a meta-analysis by Santoso et al, cardiac injury was associated with mortality, need for ICU care and severity of disease in patients with COVID-19.[25] In one report of 4 fatal COVID-19 cases,[26] only focal mild fibrosis and mild myocardial hypertrophy were seen on postmortem needle core biopsy of the heart, changes likely related to their underlying diseases. In another report of 1 COVID-19 patient with cardiogenic shock, viral particles were seen on endomyocardial biopsy, likely due to a viremic phase or macrophage migration from the lungs.[27]

The mechanisms of cardiac injury is still not clear, and data on the incidence of heart failure is limited. In the sex-, age-, and comorbid illness-matched case control study of Du et al, they found CD3+CD8+ T cells ≤75 cell/μL and cardiac troponin I ≥0.05 ng/mL were predictors for high mortality of COVID-19 pneumonia patients with similar age and underlying diseases.[28] They note that the elevation of cardiac troponin I in COVID-19 patients was just indicative of myocardial injury that was probably secondary to severe hypoxemia. We found, in contrast to previous studies, a nonsignificant trend towards a higher mean troponin and NT-proBNP levels among non-survivors versus survivors. In our cohort, all patients had ARDS requiring mechanical ventilation. In addition, there was no predominance of cardiovascular disease and in those with echocardiogram, all (except one with preexisting heart failure), had normal systolic function on echocardiogram. Severe hypoxemia from ARDS may have contributed to the elevated troponin and NT-proBNP.

Except for the use of UFH and norepinephrine plus vasopressin support, we did not see a difference in mortality for the different ICU therapies, including antimalarials and prone position. Prone position, done in almost half our patients, had no benefit and even showed a trend for higher mortality among those proned for up to 48 hours. This may be explained by the dissociation between relatively preserved lung mechanics and the severity of hypoxemia, resulting in an atypical form of the syndrome despite fulfilling criteria for ARDS.[29]

Table 4. Comparison of Clinical Characteristics and Outcomes

Variables*	Non-Survivors N=22	Survivors N=8	*P* value
Demographics			
Age (mean)	67	60	0.263
Males	13	6	0.672
BMI (mean)	27	27	0.960
Hypertension	14	6	0.682
Diabetes mellitus	11	2	0.283
Smoking history	5	3	0.658
Number of days in the hospital[$]	22 (12.9)	7 (31)	0.001
Onset of Symptoms (Days)	22 (7.4)	8 (6)	0.397
Laboratories			
WBC Count	22 (11.01)	8 (7.82)	0.347
>10 x 10^9/L	9	1	0.330
Neutrophil count >0.8 x10^9/L	21 (0.79)	8 (0.77)	0.656
Lymphocyte count <0.8 x 10^9/L	21 (0.13)	8 (0.15)	0.629
HBa1c	11 (8.15)	5 (6.62)	0.159
Procalcitonin	20 (1.18)	8 (1.09)	0.888
CRP	14 (231.89)	7 (198.76)	0.678
Ferritin	19 (1479)	8 (1305)	0.722
Lactate	19 (1.43)	6 (1)	0.131
D Dimer	5 (3.36)	3 (1.73)	0.125
Troponin	14 (654)	6 (85)	0.379
NT-Pro-BNP	14 (6898)	6 (3232)	0.502
Chest Xray			
Infiltrates + Consolidation	6	1	0.833
Chest CT			
Ground Glass + Consolidation	3	1	0.286
Corrected QT Interval, *msec*	22 (452.5)	8 (438.87)	0.399
Echocardiography			
Left Ventricular Ejection Fraction	13 (57.64)	5 (57.96)	0.953
ICU Therapies•			
Anticoagulation			
Unfractionated Heparin	22	7	0.012
Low Molecular Weight Heparin	9	5	0.417
Lopinavir + Ritonavir	8	1	0.374
Oseltamivir	2	2	0.284
Tociluzimab	11	4	**
Anti-malarial			
Hydrochloroquine	6	4	0.384
Chloroquine	11	3	0.689
Days on Chloroquine	10 (7.1)	3 (7.33)	0.926
Days on Hydrochloroquine	6 (6.5)	2 (8.5)	0.570
Azithromycin	12	5	0.407
Antibiotics	22	8	♠
Steroids	9	5	0.645
Vasoactive Agents			
Vasopressin + Norepinephrine	16	1	0.009
Norepinephrine	19	7	**
Neuromuscular blockade	5	0	0.290
Continuous renal replacement therapy	14	1	0.215
Proning	9	3	0.136
16 Hours	2	0	
24 Hours	2	3	
48 Hours	5	0	

Some limitations should be recognized. First, because we focused on COVID-19 patients with critical illness, our sample size was small. Second, since this was an observational study, not all patients had complete baseline laboratory and imaging tests performed. Finally, our cohort may have an underestimated mortality. At the time our study was written, 1 patient remained admitted at the hospital and 1 patient transferred to another hospital with unknown outcome data.

The clinical course and outcomes of critically ill COVID-19 patients during the first month of the outbreak in Metro Manila are similar to reports from other countries. The mortality of our cohort was high at 73%. We report the use of norepinephrine plus vasopressin and UFH for VTE prophylaxis were predictors of increased mortality among critically ill COVID-19 patients. Mean survival time of non-survivors is likely to be 13 days after ICU admission. We report that elevated troponin and NT-proBNP were not associated with increased mortality. Our findings suggest that those patients who eventually died had greater hemodynamic instability and thus required more vasopressor support. We can conclude that critically ill COVID-19 patients who require inotropic support are at increased risk of death. Although we believe our findings may help guide clinical decision making in COVID-19 patients requiring ICU care, caution must be applied when interpreting results presented here in view of our small cohort.

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None

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KEYWORDS

COVID-19, Critically Ill, Predictors of Mortality

REFERENCES

1. Coronavirus disease (COVID-19) in the Philippines. World Health Organization *https://www.who.int/philippines*
2. Department of Health, Republic of the Philippines. *www.doh.gov.ph/covid-19/case-tracker*
3. Center for Strategic and International Studies, Southeast Asia Covid-19 tracker, 2020. *https://www.csis.org*
4. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) out- break in China: summary of

Table 4. Comparison of Clinical Characteristics and Outcomes

Variables*	Non-Survivors N=22	Survivors N=8	*P* value
Complications•			
Sepsis	22	8	0.757
Septic shock	19	7	0.284
Arrhythmia			
Ventricular tachycardia	3	0	0.50
Bleeding requiring transfusion	4	4	0.158

* values are reported as number of patients (mean)
$ data did not include 1 patient still admitted
•missing data for 1 patient who was transferred to another hospital
** *p* value is 1.000
▲ *p* value cannot be determined

Table 5. Predictors of Mortality (Univariate Analysis)

Variables*	Non-Survivors N=22	Survivors N=8	*Odds Ratio (95% CI)*	*P* value
Demographics				
Diabetes mellitus	11	2	3	0.233
Laboratories				
HBa1c	11 (8.15)	5 (6.62)	2.17	0.193
Lactate	19 (1.43)	6 (1)	16.3	0.106
D Dimer	5 (3.36)	3 (1.73)	2.9	0.146
Troponin I	14 (654)	6 (85)	1.00 (0.99-1.01)	0.335
BNP	14 (6898)	6 (3232)	1.00 (0.99-1.0002)	0.393
Days in hospital	22 (12.9)	7 (31)	0.9 (0.83-0.97)	0.011
Anticoagulation (UFH)	22	7	10.2 (1.54-67.21)	0.016
Vasopressin + Norepinephrine	16	1	3.4 (1.01-5.91)	0.006

Table 6. Predictors of Mortality (Multivariate Analysis)

Variables*	*Odds Ratio (95% CI)*	*P* value
Demographics		
Age	0.94 (0.65-1.36)	0.771
Diabetes mellitus	6.81 (0.002-22288.78)	0.642
Laboratories		
HBa1c	0.14 (0.00006-302.81)	0.618
Lactate	627 (9.15-4.30)	0.484
Troponin I	1.01 (0.96-1.06)	0.601

a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020;323:1239–1242.
5. Richardson S, Hirsch J. Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020;323:2052-2059.
6. Richardson S, Hirsch J. Narasimhan M, et al. Clarification of mortality rate and data in abstract, results, and table 2. *JAMA* 2020;323:2098.
7. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708-1720.
8. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507-513.
9. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497-506.
10. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA.* 2020;23:1061-1069.
11. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA* Intern Med 2020;[Epub ahead of print]
12. 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. *Lancet Respir Med* 2020;8:475-481.
13. 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;395:1054–1062
14. Bhatraju P, Ghassemieh B, Nichols M, et al. Covid-19 in critically ill patients in the Seattle region – case series. *N Engl J Med* 2020;382:2012-2022.
15. Long B, Brady W. Gottlieh M, et al. Cardiovascular complications in COVID-19. *Am J Emerg Med.* 2020;[Epub ahead of print]
16. Interim guidelines for collecting, handling, and testing clinical specimens from persons for coronavirus disease 2019 (COVID-19). Centers for Disease Control and Prevention 2020. *https://www.cdc.gov*
17. Ranieri VM, Rubenfeld G, Thompson BT, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA* 2012;307:2526-2533.
18. Chinese clinical guidance for COVID-19 pneumonia diagnosis and treatment (7th edition). *http://kjfy.meetingchina.org/msite/news/show/cn/3337.html*
19. Rhodes A, Evans L, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Critical Care Medicine* 2017;45:486-552.
20. Von Elm E, Altman DG, Egger M, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;370:1453–1457.
21. Rawson TM, Moore LSP, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: A rapid review to support COVID-19 antimicrobial prescribing. *Clinical Infectious Diseases* 2020;[Epub ahead of print]
22. Maatman T, Jalali F, Feizpour C, et al. Routine Venous Thromboembolism Prophylaxis May Be Inadequate in the Hypercoagulable State of Severe Coronavirus Disease 2019. *Critical Care Medicine* 2020;[Epub ahead of print]
23. Shi S, Qin M, Shen B et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMAA Cardiol* 2020;[Epub ahead of print]
24. Chen T, Wu D, Chen H et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* 2020;368:[Epub ahead of print]
25. Santoso A, Pranata R, Wibowo A, et al. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: A meta-analysis. *Am J Em Med* 2020; April 14th https://doi.org/10.1016/j.ajem.2020.04.052.
26. Tian S, Xiong Y, Liu H et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies. *Modern Pathology* 2020;33:1007-1014.
27. Tavazzi G, Pellegrini C, Maurelli M et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. *European Journal of Heart Failure* 2020;[Epub ahead of print]
28. Du, Rong-Hui et al. Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study. *Eur Respir J.* 2020; doi: 10.1183/13993003.00524-2020
29. Gattinoni L, Coppola S, Cressoni M, et al. COVID-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome. American Journal of Respiratory and Critical Care Medicine 2020;201:1299-1300.