J Prev Epidemiol. 2022;7(x):e26182 Original Article

doi 10.34172/jpe.2022.26182 Journal of Preventive Epidemiology http jprevepi.com

Clinical characteristics and cardiovascular risk factors associated with clinical outcome in hospitalized patients with COVID-19

Gholamreza Masoumi[1], Mojtaba Mansouri[2*], Masoud Shahbazi[1], Parastoo Golshiri[1], Keivan Mohammadi[3], Neda Rahimirigi[4]

[1]Department of Anesthesiology and Critical Care, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Department of Community Medicine and Family Physician, Isfahan University of Medical Sciences, Isfahan, Iran
[3]Department of Cardiology, Isfahan University of Medical Sciences, Isfahan, Iran
[4]Isfahan University of Medical Sciences, Isfahan, Iran

Correspondence to:
Mojtaba Mansouri, Email: hart.researchgroup@gmail.com

Received: 9 March 2022
Accepted: 30 April 2022
ePublished: 9 May 2022

Keywords: Cardiovascular disorder, Coronavirus disease, Echocardiographic findings, Mortality

Abstract

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a new coronavirus, was originally recognized as a pandemic by the WHO on early, a new coronavirus, was originally recognized as a pandemic by the WHO on early 2020, and has infected over 243 million people worldwide, killing about five million people between then and October 2021.
Objectives: We investigated the relationship between clinical characteristics, cardiovascular risk factors and echocardiographic findings and in-hospital outcomes of patients who were admitted for COVID-19.
Patients and Methods: A retrospective review of 216 hospitalized patients with COVID-19 who were admitted to Chamran hospital from March 2019 to April 2021 was conducted. Patients' characteristics cardiovascular risk factors, echocardiographic findings, clinical outcomes (discharge (complete recovery/partial recovery) and in-hospital mortality) were recorded. To analyze risk factors associated with outcomes in patients with COVID-19, univariate and multivariate ordinal logistic regression models were conducted.
Results: The most common underlying diseases in patients were hypertension (HTN) (57.9%) and diabetes mellitus (DM) (37.9%), respectively. Cognitive disorders (20.8%) and mitral regurgitation (MR) were the most complication and echocardiographic finding of the patients. In our study, six variables were found to be associated with patient's outcomes, including age, body mass index (BMI), DM, chronic pulmonary diseases, number of hospitalization days and number of an intensive care unit (ICU) admission days.
Conclusion: Our analysis suggests that age, male gender, BMI, number of hospitalization days and ICU admission, chronic pulmonary disease and diabetes are associated with a higher risk of in-hospital mortality and worst prognosis in patients infected by SARS-CoV-2.

Citation: Masoumi G, Mansouri M, Shahbazi M, Golshiri P, Mohammadi K, Rahimirigi N. Clinical characteristics and cardiovascular risk factors associated with clinical outcome in hospitalized patients with COVID-19. J Prev Epidemiol. 2022;7(x):exx. doi: 10.34172/jpe.2022.26182.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a new coronavirus, was originally recognized as a pandemic by the WHO on early 2020, and has infected over 243 million people worldwide, killing about five million people between then and October 2021 (1). The virus's high infectivity, capacity to spread even while asymptomatic, low-virulence, and short incubation time have resulted in fast transmission of the virus across geographic boundaries, resulting in a pandemic. In summary, the coronavirus disease 2019 (COVID-19) pandemic has had two primary effects on human health. For instance, it has resulted in a considerable reduction in the number of people visiting care facilities for a variety of diseases, ranging from mental disorders, to pediatric emergency situations, to cardiovascular diseases (CVDs) (2).

Key point

In a retrospective review of 216 hospitalized patients with COVID-19, we found age, male gender, DM, BMI, number of hospitalization days and an ICU admission and chronic pulmonary disease are associated with a poor prognosis and higher risk of in-hospital mortality in patients infected by SARS-CoV-2.

The most prevalent clinical manifestation of COVID-19 is respiratory involvement, which can range from a mild flu-like sickness to potentially fatal acute respiratory distress syndrome or fulminant pneumonia. History of cardiovascular risk factors and CVD, like any other respiratory tract infection, increase susceptibility to COVID-19 (3). COVID-19 has been linked to a variety of cardiovascular involvement, including acute myocardial infarction, thromboembolic events,

myocarditis, takotsubo cardiomyopathy, acute left and right ventricular failure (occurring as a result of increased right ventricular afterload caused by pulmonary emboli or lung involvement) and cardiogenic shock (4). Due to these involvements, the use of transthoracic echocardiography (TTE) in patients with severe COVID-19 on mechanical ventilation or circulatory support has increased. Despite the fact that cardiac biomarkers such as high-sensitivity cardiac troponin (hs-cTnI) are emerging as good predictors of prognosis in these patients, evidence on echocardiographic abnormalities in these individuals is scarce. Studies estimated that about 20%–51% of patients with COVID-19 whom admitted to the health care units, are found to have at least one comorbidity (5). According to some studies, comorbidities like diabetes mellitus (DM), hypertension (HTN), chronic lung disease, chronic kidney disease (CKD), and other chronic diseases are linked to a higher risk of severe complications and death (6).

Objectives

The aim of this study is to evaluation the relation of cardiovascular risk factors and echocardiographic findings with outcome and mortality in patients admitted due to COVID-19 in a tertiary center in Iran.

Patients and Methods

Study design

This cross-sectional study was conducted at Chamran hospital, Isfahan, Iran, a major tertiary cardiology center in the period of March 2019 to April 2021. We included all consecutive patients who were hospitalized due to diagnosis of COVID-19 disease based on having at least one positive polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swabs or a chest CT scan indicating of COVID-19 disease. If more than 10% of the required data is not available in the patient's documents, the patient excluded from the study. Patients' demographic data such as age, gender, occupation, level of education and city of residence were documented.

Patient's medical comorbidities such as HTN, DM, chronic lung disease, hypothyroidism, hyperthyroidism, hyperlipidemia and medications that are taken before COVID-19 were recorded (focusing on the use of ACEI drugs, antibiotics, antiplatelets, antihypertensive drugs, H2 blockers, and anti-inflammatories). DM and HTN was define as a history of DM or taking anti-diabetic drugs and systolic blood pressure of ≥140 mm Hg, or a diastolic blood pressure of ≥90 mm Hg, or taking anti-hypertensive drugs, respectively.

Echocardiography was performed at the beginning of admission and based on the patients hemodynamic, and symptoms may be redone during the time of hospitalization or at the time of discharge. Echocardiographic findings (assessed in accordance with previous guidelines) (7,8) such as and ejection fraction (EF), pericardial effusion, valvular heart disease and pulmonary artery pressure were recorded. In some cases, for better evaluation, transesophageal echocardiography (TEE) was conducted too.

High-level supplement oxygen or mechanical ventilation was conducted for patients with acute respiratory failure [partial pressure arterial oxygen (PaO_2 <70%)] and all patients required invasive mechanical ventilation (IMV) were transferred to intensive care unit (ICU). During hospitalization, echocardiographic findings (TTE or TEE), complication (such as pneumothorax, hemothorax, cognitive disorders, coronary dissection), type of anesthesia [general anesthesia (GA) or sedation], usage of intra-aortic balloon pump (IABP) or ECMO (extracorporeal membrane oxygenation) (V-V and A-V mode), length of stay in ward or ICU and outcome (discharged complete or partial recovered and mortality in hospital) were recorded.

Patients might be discharged if the body temperature turned to <37.3°C for more than two days, respiratory symptoms and lung involvement decreased significantly, and two consecutive negative reverse transcription polymerase chain reaction (RT-qPCR) of SARS-CoV-2 tests were obtained.

Data analysis

The Statistical Package for the Social Sciences (SPSS) version 25 was used for statistical analysis. Continuous variables were described using mean ± standard deviation (SD) or median and interquartile range and categorical variables using numbers and percentage (%). The significance level was chosen to be 0.05. The chi-square/Fisher's exact test and independent sample *t* test/Mann-Whitney U test was conducted for comparing categorical and parametric variables, respectively to analyze risk factors associated with outcomes in patients with COVID-19, univariate and multivariate ordinal logistic regression models were used. A *P* value of less than 0.05 was considered significant.

Results

A total of 216 patients with COVID-19 who were admitted to Chamran hospital during March 2019 to April 2021 were included. 147 (68.1%) patients were male. The mean ± SD of the variables in our patients was, age; 63.7±15.1 years, body mass index (BMI); 25.2±4.1 kg/m^2, total length of hospital stays; 7.6±4.2 days (range :1-39 days), duration of stay in ICU; 6.3± 2.4 days (range; 1 to 32 days) and duration of ventilator connection in ICU patients: 5.6±2.3 days (range; 1 to 26 days). Demographic characteristics of participants were summarized in Table 1. The most common underlying disease in patients were HTN (57.9%) and DM (37.9%), respectively (Table 2). Cognitive disorders (20.8%) and mitral regurgitation (MR) were the most complication and echocardiographic finding of the patients. Table 3 summarizes frequency of complications, echocardiographic findings, types of anesthesia and IABP during the hospitalization. Extracorporeal membrane

Table 1. Demographic characteristics of participants

		Number (N=216)	%
Gender	Male	147	68.1
	Female	69	31.9
Education status	Illiterate	42	19.4
	Undergraduate	32	14.8
	Diploma and postgraduate	82	38
	Higher	60	27.8
Job	Housewife	44	20.4
	Employee/worker	82	38
	Physician	2	0.9
	Unemployed	42	19.4
	Retired	46	21.3

Table 2. Distribution of underlying disease and medication usage frequency

Variable	No. (%) (N=216)	Taking medication related to the disease
		No. (%) (N=216)
Ischemic heart disease	74 (34.3)	70 (32.4)
Chronic lung disease	41 (19)	36 (16.7)
Diabetes mellitus	80 (37)	72 (33.3)
Thyroid disorders	28 (13)	31 (14.4)
Hyperlipidemia	78 (36.1)	72 (33.3)
Hypertension	125 (57.9)	114 (52.8)

Table 3. Frequency distribution of complications, echocardiographic findings, type of anesthesia and drug use

		No. (%) (N=216)
Complications	Pneumothorax	12 (5.6)
	Hemothorax	10 (4.6)
	Pseudoaneurysm	15 (6.9)
	Coronary dissection	15 (6.9)
	Post-operative bleeding	12 (5.6)
	Cognitive disorders	45 (20.8)
Echocardiographic findings	AS	27 (12.5)
	AI	39 (18.1)
	MS	13 (6)
	MR	58 (26.9)
	TR	28 (13)
	Pericardial effusion	25 (11.6)
Type of anesthesia	GA	39 (18.1)
	Sedation	132
IABP		18
Consumed anesthetic drug	Nesdonal	13
	Etomidate	20
	Propofol	119
	Narcotics	91

IABP: Intra-aortic balloon pump, AS: Aortic stenosis, AI: aortic insufficiency, MS: Mitral stenosis, MR: Mitral regurgitation, TR: tricuspid regurgitation

oxygenation was performed in three patients. Two patients underwent V-V ECHMO whom died after five and two days. One patient underwent V-A ECHMO whom died after one day. Among all patients, 155 (71.7%) patients discharged complete recovered, 9 (4.2%) patients were discharged partially recovered, and 49 (22.7%) patients died in-hospital.

All patients were divided into three groups base on their prognosis, discharged with complete recovery, discharged with partial recovery and in-hospital mortality. Ordinal logistic regression model was conducted for evaluation of the effect of potential predictors of COVID-19 outcome (Table 4). Around six variables were found to be associated with patient's outcomes, including age, BMI, DM, chronic pulmonary diseases, number of hospitalization days and number of ICU admission days. The results of multivariate model revealed that odds ratio of outcomes for number of ICU admission days was 0.12(95% CI: 0.06, 0.25; *P* value < 0.001), for patients with DM = 0.52(95% CI: 0.27,1.01), for chronic lung disease = 0.55(95% CI: 0.26,1.17), for BMI = 0.74(95% CI: 0.39,1.41), and for male gender=1.509 (95% CI: 0.77, 3.30). This study showed patients' adherence to medications (HTN, DM, thyroid and dyslipidemia) had not correlation with patient's outcome (*P* value for all of them<0.05).

Discussion

In patients with COVID-19, it is essential to consider and assess the disease's severity early and precisely (9). The aim of this study was to explore critical predictive risk factors that can help us establish the severity and outcome in admitted COVID-19 patients based on echocardiographic, underlying disease and in-hospital clinical data.

Our study showed that, the most common underlying disease in patients were HTN (57.9%) and DM (37.9%), respectively. Additionally, cognitive disorders (20.8%) and MR were the most complication and echocardiographic finding of the patients. Sedation was the most type of anesthesia and propofol was the most used anesthetic agent in our patients. Patients with DM, male gender, higher BMI, chronic lung disease, higher numbers of hospitalization and ICU admission days had more poor outcomes.

Different studies have linked variations in COVID-19 outcome to male gender, which is consistent with our findings (10,11). Angiotensin-converting enzyme 2 (ACE2) expression was observed to be more prevalent in Asian men in one study utilizing single-cell sequencing (12). Females acquire stronger innate and adaptive immune responses than men throughout time, and they are less vulnerable to viral infections (13). These two factors might be the basis for poor prognosis of COVID-19 in males compared to females.

Xu et al assessed 400 patients hospitalized with COVID-19 and demonstrated that age >40 years old, HTN, cTnI >0.04 ng/mL, interval between illness onset and diagnosis and admission were independent significant predictors of illness severity and outcome (14). Obesity is connected to a higher prevalence of cardiometabolic illnesses such HTN, dyslipidemia, and DM, all of which are linked to worse outcomes (15). Our analysis revealed a

Table 4. Results of univariate ordinal logistic model using three levels of outcome as response

Variable	B	SE	Wald	*P* value	95% CI	
					Lower bound	Upper bound
Age (y)	0.016	0.018	0.835	0.361	-0.019	0.051
BMI (kg/m²)	-0.107	0.054	3.911	0.048	-0.213	-0.001
Number of hospitalization days	0.225	0.071	10.067	0.002	0.086	0.364
Number ICU days	-0.212	0.058	13.587	0.000	-0.325	-0.099
Male gender	-1.073	0.504	4.531	0.033	-2.060	-0.085
Disease: Pulmonary (ref=not have)	-15.091	0.527	818.93	0.000	-16.124	-14.057
Disease: hypertension (ref=not have)	-0.007	0.436	0	0.988	-0.861	0.848
Disease: Thyroid (ref=not have)	0.233	0.637	0	0.715	-1.016	1.482
Disease: IHD (ref=not have)	0.090	0.439	0.134	0.838	-0.771	0.951
Disease: HLP (ref=not have)	-0.146	0.420	0.042	0.729	-0.969	0.677
Disease: DM (ref=not have)	1.145	0.397	0.120	0.004	0.367	1.923
AS (ref=No)	1.069	0.616	8.313	0.083	-0.138	2.277
AI (ref=No)	0.430	0.495	3.014	0.385	-0.540	1.400
MS (ref=No)	0.779	0.759	0.755	0.305	-0.709	2.267
MR (ref=No)	0.448	0.431	1.054	0.299	-0.397	1.294
TR (ref=No)	0.061	0.602	1.080	0.920	-1.120	1.241
IABP (ref=No)	1.176	0.723	0.230	0.104	-0.242	2.593

SE, standard error; BMI: body mass index, IABP: Intra-aortic balloon pump, AS: Aortic stenosis, AI: aortic insufficiency, MS: Mitral stenosis, MR: Mitral regurgitation, TR: tricuspid regurgitation, DM: diabetes mellitus, IHD: Ischemic heart disease.

linear association between BMI and poor outcome, which was consist with other studies (16,17). However, our results are inconsistent with the study by Kanf et al, which showed non-linear (U shaped) association (18). Zhang et al concluded that obesity is a significant risk factor for death in hospitalized COVID-19 patients (19).

Diabetes mellitus is the second most prevalent comorbidity in COVID-19 hospitalized patients (after HTN), and its frequency rises with age (20). Our research found that diabetic individuals infected with SARS-CoV-2 have poorer prognosis than those without diabetes, regardless of age. Beyond the obvious link between DM and atherosclerosis and CVD, poor glycemic management may have a deleterious impact on the fate of diabetic patients hospitalized due to COVID-19 via a variety of pathways (21). Our study revealed that patients with more days of ICU admission had worst prognosis. The mortality among coronavirus confirmed cases admitted to ICU was found to be 39 percent in a recent study which means, there is one death for every three cases of admission (22). This is consisted with some other studies (20,23). The likely cause for high mortality in ICU may be discussed in terms of a limited number of mechanical ventilators, proper laboratory investigation, integrated patient monitoring, presence of co-morbidities and hospital-acquired infections (24).

Conclusion

Our analysis suggests that age, male gender, BMI, number of hospitalization days and ICU admission, chronic pulmonary disease and diabetes are associated with higher risk of in-hospital mortality and worst prognosis in patients infected by SARS-CoV-2.

Limitations of the study

Our research has a number of limitations. To begin with, the retrospective design of our study may have affected the integrity of the data and lowered its validity; therefore, additional prospective cohort studies should be considered in the future.

Second, the patients in our study are all from Isfahan province, indicating that large-scale nationwide studies are urgently needed to give more accurate and complete data. Third, the progression of sickness in distinct subtypes needed to be examined thoroughly. Clinicians needed a model for predicting illness progression in order to effectively guide treatment.

Authors' contribution

MGh: Principal investigation, Concept, design. MM: Concept and design, Data gathering. ShM: Principal investigation, writing, revision. GP: Data analysis, writing. MK: Revision, data gathering. RN: Revision, Data gathering.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan University of Medical Sciences approved this study. The institutional ethical committee at Isfahan University of Medical Sciences approved all study protocols (IR.MUI.MED.REC.1400.022). Accordingly, written informed consent taken from all participants before any intervention. Besides, ethical issues (including plagiarism, data fabrication and double

publication) have been completely observed by the authors.

Funding/Support
The authors declare that they have no funding/support.

References

1. COVID W. Dashboard. Geneva: World Health Organization 2020.
2. Ferrero F, Ossorio MF, Torres FA, Debaisi G. Impact of the COVID-19 pandemic in the paediatric emergency department attendances in Argentina. Arch Dis Child. 2021;106:e5. doi: 10.1136/archdischild-2020-319833
3. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, et al. Cardiovascular Considerations for Patients, Health Care Workers, and Health Systems During the COVID-19 Pandemic. J Am Coll Cardiol. 2020;75:2352-71. doi: 10.1016/j.jacc.2020.03.031
4. Hu H, Ma F, Wei X, Fang Y. Coronavirus fulminant myocarditis treated with glucocorticoid and human immunoglobulin. Eur Heart J. 2021;42:206. doi: 10.1093/eurheartj/ehaa190
5. Mohammadi K, Tabatabaee A, Akbari M. Kinin–kallikrein system; a possible pathway responsible for COVID-19. Immunopathol Persa. 2021;7:e11. doi: 10.34172/ipp.2021.11
6. Hussain S, Baxi H, Chand Jamali M, Nisar N, Hussain MS. Burden of diabetes mellitus and its impact on COVID-19 patients: A meta-analysis of real-world evidence. Diabetes Metab Syndr. 2020;14:1595-602. doi: 10.1016/j.dsx.2020.08.014
7. Bajgain KT, Badal S, Bajgain BB, Santana MJ. Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. Am J Infect Control. 2021;49:238-246. doi: 10.1016/j.ajic.2020.06.213.
8. Hindocha R, Garry D, Short N, Ingram TE, Steeds RP, Colebourn CL, et al. A minimum dataset for a Level 1 echocardiogram: a guideline protocol from the British Society of Echocardiography. Echo Research and Practice. 2020;7:G51-G8.doi: 10.1530/ERP-19-0060.
9. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. 2015;16:233-71. doi: 10.1093/ehjci/jev014.
10. Ma X, Ng M, Xu S, Xu Z, Qiu H, Liu Y, et al. Development and validation of prognosis model of mortality risk in patients with COVID-19. Epidemiol Infect. 2020;148:e168. doi: 10.1017/S0950268820001727.
11. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382:1708-20. doi: 10.1056/NEJMoa2002032
12. Zhang SY, Lian JS, Hu JH, Zhang XL, Lu YF, Cai H, et al. Clinical characteristics of different subtypes and risk factors for the severity of illness in patients with COVID-19 in Zhejiang, China. Infect Dis Poverty. 2020;9:85.doi: 10.1186/s40249-020-00710-6
13. Cai H. Sex difference and smoking predisposition in patients with COVID-19. Lancet Respir Med. 2020;8:e20.doi: 10.1016/S2213-2600(20)30117-X
14. Jaillon S, Berthenet K, Garlanda C. Sexual Dimorphism in Innate Immunity. Clin Rev Allergy Immunol. 2019;56:308-21. doi: 10.1007/s12016-017-8648-x.
15. Xu K, Zhou M, Yang D, Ling Y, Liu K, Bai T, et al. Application of ordinal logistic regression analysis to identify the determinants of illness severity of COVID-19 in China. Epidemiol Infect. 2020;148:e146. doi: 10.1017/S0950268820001533.
16. Ren L, Yu S, Xu W, Overton JL, Chiamvimonvat N, Thai PN. Lack of association of antihypertensive drugs with the risk and severity of COVID-19: A meta-analysis. J Cardiol. 2021;77:482-91.doi: 10.1016/j.jjcc.2020.10.015.
17. Saito T, Yamaguchi T, Kuroda S, Kitai T, Yonetsu T, Kohsaka S, et al. Impact of body mass index on the outcome of Japanese patients with cardiovascular diseases and/or risk factors hospitalized with COVID-19 infection. J Cardiol. 2022;79:476-481. doi: 10.1016/j.jjcc.2021.09.013.
18. Hendren NS, de Lemos JA, Ayers C, Das SR, Rao A, Carter S, et al. Association of Body Mass Index and Age With Morbidity and Mortality in Patients Hospitalized With COVID-19: Results From the American Heart Association COVID-19 Cardiovascular Disease Registry. Circulation. 2021 Jan 12;143:135-144. doi: 10.1161/CIRCULATIONAHA.120.051936.
19. Kang IS, Kong KA. Body mass index and severity/fatality from coronavirus disease 2019: A nationwide epidemiological study in Korea. PLoS One. 2021;16:e0253640. doi: 10.1371/journal.pone.0253640.
20. Zhang F, Xiong Y, Wei Y, Hu Y, Wang F, Li G, et al. Obesity predisposes to the risk of higher mortality in young COVID-19 patients. J Med Virol. 2020;92:2536-42. doi: 10.1002/jmv.26039
21. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ. 2020;368:m1091. doi: 10.1136/bmj.m1091.
22. Giugliano D, Maiorino MI, Bellastella G, Chiodini P, Esposito K. Glycemic Control, Preexisting Cardiovascular Disease, and Risk of Major Cardiovascular Events in Patients with Type 2 Diabetes Mellitus: Systematic Review With Meta-Analysis of Cardiovascular Outcome Trials and Intensive Glucose Control Trials. J Am Heart Assoc. 2019;8:e012356. doi: 10.1161/JAHA.119.012356
23. Abate SM, Ahmed Ali S, Mantfardo B, Basu BJPo. Rate of Intensive Care Unit admission and outcomes among patients with coronavirus: A systematic review and Meta-analysis. PloS one. 2020;15:e0235653. doi: 10.1371/journal.pone.0235653
24. Arabi YM, Murthy S, Webb SJIcm. COVID-19: a novel coronavirus and a novel challenge for critical care. Intensive care medicine. 2020;46:833-6. doi: 10.1007/s00134-020-05955-1.
25. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323:1061-9. doi: 10.1001/jama.2020.1585.