

Clinical Features and Outcomes of 105 Hospitalized patients with COVID-19 in Seattle, Washington

Frederick S. Buckner MD*¹, Denise J. McCulloch MD MPH*¹, Vidya Atluri MD PhD¹, Michela Blain MD¹, Sarah A. McGuffin MD MSc¹, Arun K. Nalla PhD², Meei-Li Huang PhD², Alex L. Greninger MD², Keith R. Jerome MD PhD^{2,3}, Seth A. Cohen MD¹, Santiago Neme MD¹, Margaret L. Green MD¹, Helen Y. Chu MD MPH¹, and H. Nina Kim MD MSc¹

*Contributed equally

¹ Department of Medicine, University of Washington, Seattle, WA

² Department of Laboratory Medicine, University of Washington, Seattle, WA

³ Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center

Corresponding Author: Frederick S. Buckner, University of Washington, 750 Republican St, Box 358061, Seattle WA, 98109, fbuckner@uw.edu

Key Points: In this case series of 105 consecutively hospitalized COVID-19 patients, the median age was 69 years and 55% had three or more comorbidities. Severe disease occurred in 49% of patients and overall mortality was 33%.

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ABSTRACT

Background: Washington State served as the initial epicenter of the SARS-CoV-2 pandemic in the United States. An understanding of the risk factors and clinical outcomes of hospitalized patients with COVID-19 may provide guidance for management.

Methods: All laboratory-confirmed COVID-19 cases in adults admitted to an academic medical center in Seattle, WA between March 2 and March 26, 2020 were included. We evaluated individuals with and without severe disease, defined as admission to the intensive care unit or death.

Results: One-hundred-five COVID-19 patients were hospitalized. Thirty-five percent were admitted from a senior home or skilled nursing facility. The median age was 69 years and half were women. Three or more comorbidities were present in 55% of patients, with hypertension (59%), obesity (47%), cardiovascular disease (38%) and diabetes (33%) being the most prevalent. Most (63%) had symptoms for 5 days or longer prior to admission. Only 39% had fever in the first 24 hours, whereas 41% had hypoxia at admission. Seventy-three percent of patients had lymphopenia. Of 50 samples available for additional testing, no viral coinfections were identified. Severe disease occurred in 49%. Eighteen percent of patients were placed on mechanical ventilation and the overall mortality rate was 33%.

Conclusions: During the early days of the COVID-19 epidemic in Washington State, the disease had its

greatest impact on elderly patients with medical comorbidities. We observed high rates of severe disease and mortality in our hospitalized patients.

Keywords: COVID-19, SARS-CoV-2, outcomes, hospitalized, comorbidities

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INTRODUCTION

Infections with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first occurred in late 2019 in Hubei Province, China, and has since disseminated worldwide [1, 2]. The first confirmed case in the United States was a returning traveler from Wuhan, China, who presented to medical attention on January 19, 2020, in Snohomish County, Washington [3]. In February, a cluster of COVID-19 cases was identified at a nursing home in Kirkland, Washington, resulting in the first reported death in the US on February 29 [4, 5]. Since that time, the disease has occurred widely in the greater Seattle area and cases have been reported in all 50 states [6].

The epidemiology and clinical features of hospitalized COVID-19 patients have been described in China, South Korea, and Singapore [1, 7-10]. The prominent clinical manifestations have included fever, cough, dyspnea, fatigue, myalgia, and radiographic evidence of pneumonia. Shock, acute respiratory distress syndrome (ARDS), acute cardiac injury, acute kidney injury, and deaths were reported in severe cases [1, 5, 9, 11]. Early reports indicated that the infection occurs in clusters within groups in close contact, and that severe disease was more common in the elderly, men, and those with comorbidities [9]. The epidemiologic and clinical features of COVID-19 disease in the United States are beginning to be elucidated, specifically in critically ill patients [5]. Additional information is needed to help clinicians understand the characteristics of this disease. In this case series, we examine the epidemiology, clinical features, and outcomes of 105 hospitalized patients from three university-affiliated hospitals in Seattle, Washington. The characteristics associated with severe versus non-severe clinical courses are described.

METHODS

Study design and participants

We conducted a retrospective chart review examining the clinical characteristics of adult patients with laboratory-confirmed SARS-CoV-2 infection. Patients were included if they were admitted to one of three University of Washington (UW) affiliated hospitals in Seattle between March 2 and March 26, 2020.

The hospitals included UW Medical Center (comprised of two campuses: Montlake, a 570-bed tertiary/quaternary care facility and Northwest, a 281-bed community-based care facility) and Harborview Medical Center (HMC), a 413-bed level one trauma center.

Data sources and collection

Demographic data, encounter dates and laboratory measurements were extracted electronically from the UW clinical data warehouse for confirmed cases. The medications, vital signs, radiology studies and clinical events were reviewed by physicians in the Division of Infectious Diseases and entered into a standardized data collection instrument using REDCap (Research Electronic Data Capture) [12].

Study Outcomes

The primary outcome was severe COVID-19, defined as a composite endpoint of admission to an intensive care unit (ICU) or death [13]. Each death was reviewed by two physicians independently to determine whether it was related to COVID-19. Secondary outcomes included shock and acute respiratory distress syndrome (ARDS), which were also adjudicated by two physicians independently. These outcomes were evaluated until May 8, 2020, 43 days from the date the last patient was admitted.

Study Definitions

Fever was defined as a recorded temperature of 38.0°C or higher. Hypoxia was defined as an oxygen saturation less than 90% on ambient air, or requirement of supplemental O₂ [14]. Acute kidney injury (AKI) was defined as an increase in creatinine of 0.3 mg/dL from baseline, or 1.5 times the patient's baseline creatinine [15]. Leukopenia was defined as white blood cell count less than 4x10⁹/L, and lymphopenia was defined as a lymphocyte count less than 1.5x10⁹/L. Cardiac injury was defined as a maximum troponin value of 0.1 ng/mL or higher during hospitalization. Patients were denoted as having ARDS if the physician indicated this in their clinical notes, or, in the absence of this documentation, if the patient had new respiratory failure, bilateral lung opacities on chest imaging, and a PaO₂:FIO₂ ratio ≤ 300 [16]. Shock was defined as hypotension requiring vasopressors. Patients were considered to have received antibiotics during their admission if these were given for more than 48 hours. Patients were considered to have received corticosteroids during their admission if they were newly started on systemic corticosteroids.

Laboratory testing

Nasopharyngeal samples were tested for SARS-CoV-2 by real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) developed by the University of Washington Virology laboratory [17]. Indeterminate results were confirmed at the Washington State Department of Health (WA DOH) laboratory or the Centers for Disease Control and Prevention (CDC). If a patient had an indeterminate result from the UW Virology Lab and a positive result from the WA DOH or CDC laboratory, this subject was considered positive. If available, residual clinical samples were subsequently tested by quantitative real-time RT-PCR for 12 additional respiratory viruses, including influenza A and B, respiratory syncytial virus, adenovirus, human metapneumovirus, parainfluenza viruses 1-4, rhinovirus, bocavirus and seasonal coronaviruses [18]. Semiquantitative viral load was defined as the cycle threshold (Ct) of the initial sample tested.

Statistical Analysis

Continuous variables were displayed as median values with simple or interquartile ranges as appropriate. Categorical variables were summarized as counts of all patients or a subset of evaluated patients with percentages. All analyses were conducted using Stata 14.2 (StataCorp).

Study oversight

This study was approved by the University of Washington Institutional Review Board (STUDY00006181). Informed consent was waived for retrospective review of patient charts.

RESULTS

One-hundred-five patients with confirmed SARS-CoV-2 infection were hospitalized between March 2 and March 26, 2020, with a median follow-up of 9 days (range 1-53). The demographic and clinical characteristics are shown in Table 1. The median age was 69 (range 23-97), half were women and 71% were white. Thirty-five percent of patients lived in a skilled nursing facility or senior living. Most patients (93%) had at least one comorbidity; 55% had three or more chronic medical problems. The most common comorbidities were hypertension (59%), obesity (47%), cardiovascular disease (38%) and diabetes (33%).

The majority of patients (63%) presented with symptoms lasting more than 5 days (Table 2). The most common presenting symptoms were cough (72%), dyspnea (53%), and fatigue (49%). Twenty-three percent of patients reported diarrhea and 22% either nausea or vomiting. Nasal symptoms (congestion/rhinorrhea) and sore throat occurred in 14% and 7%, respectively. The initial chest x-ray was abnormal in 86% of cases. A minority of patients (39%) had a fever on admission or within the first 24 hours. Hypoxia was observed in 41% at the time of admission. Blood laboratories at admission showed leukopenia in 15% and lymphopenia in 73% of patients (Table 3).

Of 39 patients who had SARS-CoV-2 samples available for semi-quantitative testing, the median Ct was 26.5 (range 12.4-35.4) with no difference between severe and non-severe cases. Fifty samples were available for viral coinfection testing. No coinfections with influenza A or B, respiratory syncytial virus, adenovirus, human metapneumovirus, parainfluenza viruses, rhinovirus, or bocavirus were identified. There were no co-infections with coronaviruses 229E, NL63, OC43, or HKU1.

Angiotensin converting enzyme inhibitors or angiotensin receptor blockers were used in 33% of patients (Table 4) while aspirin or non-steroidal anti-inflammatory drugs were used in 35%. The proportion of all patients on corticosteroids was 10% or other immunosuppressants was 11%.

During hospitalization, 42% of patients were treated with hydroxychloroquine (Table 4). In nearly all cases it was dosed at 400 mg PO BID x 1 day, then 200 mg PO BID x 4 days, according to a published study.¹⁰ Remdesivir was provided to 4 patients on a compassionate use protocol. Subsequently, a clinical trial was initiated, and 21 patients were randomized to receive remdesivir or placebo. No other antiviral drugs were administered to treat COVID-19 infection. Half of patients received antibiotics for at least 48 hours during their hospitalization. Only a small fraction (3%) of all patients received corticosteroids at doses that were greater than baseline doses.

With respect to non-pharmacological interventions, 76% of all patients required supplemental oxygen either by nasal cannula (37%), high-flow (23%), or mechanical ventilation (18%). Two were placed on extracorporeal membrane oxygenation (ECMO). Three patients (3%) were newly started on renal replacement therapy.

Thirty-one (30%) patients developed acute kidney injury, which tended to be present on admission (Figure 1). Shock occurred in 17 (16%) patients and occurred on median hospital day 1 (range, 0-10). Acute respiratory distress syndrome was seen in 28 (27%), and 19 (18%) underwent mechanical ventilation, with intubation occurring on median hospital day 1 (range 0-5). Nineteen percent of patients who had a troponin sent (13 of 67) had evidence of cardiac injury. Fifty-one patients (49%)

had severe illness, and 35 patients (33%) died. Among those who died, all deaths were confirmed to be COVID-19-related and death occurred on median hospital day 7 (range 0-20). At the end of our chart review, sixty-six patients survived to discharge (63%), with discharge occurring on median hospital day 9 (range 1-53), and 4 patients remained hospitalized

DISCUSSION

This is among the first case series of COVID-19 patients hospitalized in the United States. At three academic hospitals in Seattle, 105 patients with SARS-CoV-2 infection were admitted between March 2 and March 26, 2020. Fifty-one patients (49%) had severe illness and 35 patients (33%) died. This is a relatively high mortality rate compared to reports from China and Singapore, where mortality rates in hospitalized patients were 1.4% [9], 4.3% [7], and 0% [8]. This is likely due to the more advanced age (median 69 years) of our cohort compared with these previous case series, which reported average ages of 47 [9], 56 [7], and 47 [8]. Additionally, the burden of comorbidities in our population was extremely high, with 93% of patients having at least one comorbidity, also higher than the previously reported rate of comorbidity of 46.4% [7] and 32% [1].

Patients living in nursing or senior living homes comprised 35% of the patients, reflecting the increased risk of living in congregated settings. Aside from one homeless patient, the remaining 65% of patients were domiciled at private residences prior to hospitalization, indicating that the infection was already distributed throughout the community. Travel was not an important risk, indicating that infections were unlikely to be imported. Only 16% participants reported a known contact, indicating ongoing community transmission in the several weeks between the first case and this time period [19].

With respect to comorbidities, hypertension (59%), obesity (47%), cardiovascular disease (38%), diabetes (33%), and chronic kidney disease (26%) were the most notable and tended to be more

prevalent in cases with severe clinical outcomes. It is striking that 55% of the patients had 3 or more comorbidities, underscoring the vulnerability of chronically ill individuals to COVID-19. Similar associations have been observed in influenza: diabetes and cardiovascular disease are known to increase the risk of developing complications from influenza [20], and previous work has shown an association between obesity and poor outcomes in influenza infection [21, 22]. Furthermore, the association between the presence of hypertension, cardiovascular disease, and diabetes with poor outcomes was documented among patients with Middle East respiratory syndrome (MERS) coronavirus infection [23]. Chronic lung disease including COPD (10%) and asthma (10%) were surprisingly uncommon. Only two pregnant patients were observed in this cohort and they recovered without complications. The frequency of obesity, hypertension, and diabetes associated with our hospitalized COVID-19 patients is concerning given the high prevalence of these conditions in the US population.

Of pre-admission medications, statins were the most common (42%) followed by ACE inhibitors or ARBs (33% combined). There is conflicting evidence on the effect of renin-angiotensin-aldosterone system (RAAS) inhibitors on angiotensin-converting enzyme 2 (ACE2) [24]. In animal models, ACE inhibitors and ARBs upregulate surface expressed ACE2, a binding target of SARS-CoV2 [25], which could worsen disease. However, animal studies have shown that these medications decrease severe lung injury in some viral pneumonias [26]. Our study could not determine if these medications were a risk factor for severe disease.

For most patients, COVID-19 was not an abrupt illness leading to sudden hospitalization; the majority (63%) of patients reported symptoms for least 5 days prior to admission. Only a minority of patients (39%) had documented fever in the first 24 hours of hospitalization. Absence of fever in some patients has been previously reported [9]. The absence of fever in the majority of this largely geriatric cohort is an important finding. Clinicians evaluating older patients will need to have a high index of suspicion for COVID-19 in those who present without fever. Cough (72%), dyspnea (53%),

and fatigue (49%) were the most common symptoms reported by patients, consistent with other studies [1, 7]. Gastrointestinal complaints were noted in a minority. Hypoxia and elevated temperatures in the first 24 hours of hospitalization were more frequent in severe COVID-19 but notably, there were few presenting clinical signs or symptoms that distinguished those who would go on to severe disease.

Objective data on the patients demonstrated findings previously reported. Chest imaging was abnormal in the vast majority of patients, consistent with previous reports [7]. A majority of patients (73%) had lymphopenia, which was more commonly observed in severe COVID-19. Transaminases were mildly elevated in 22-33% of patients, but rarely more than twice the upper limit of normal. Viral coinfection was not identified, concordant with previous published studies describing influenza coinfection only in case reports.

Few patients (3%) received corticosteroids, consistent with recent published recommendations [27]. A subset of patients was treated with hydroxychloroquine (40%) or were enrolled in a trial with remdesivir (20%) based on preliminary data suggesting antiviral activity against SARS-CoV2 [28, 29]; whether these provide clinical benefit remains unknown.

A large fraction (76%) of these patients required oxygen supplementation, including 18% who received mechanical ventilation. Hemodynamic shock, which occurred in 16% of patients in this group, has been reported previously [5, 9]. The frequency of acute kidney injury (30%) appears higher than the reports from China of 0.5% to 7% [1, 9] and likely attributable to the advanced age and high comorbidity burden of our cohort, although severe illness was not limited to the elderly patients in this group.

Our study has some limitations. First, as with any observational study derived from routinely collected clinical data, there is the potential for incomplete capture or misclassification of baseline characteristics, particularly for patients who did not receive primary care in our system. Next, this

study was performed early in the COVID-19 outbreak when testing was not widespread and attention was heavily focused on nursing homes. In addition, 4 of these patients remained hospitalized at the time of manuscript submission with partial follow-up. A larger clinical cohort may reveal additional features not readily apparent in our series.

In conclusion, COVID-19 has spread rapidly throughout the United States and most of the world. The early experience in Seattle indicated that patients requiring hospitalization for COVID-19 were generally of advanced age with multiple comorbidities. The high morbidity and mortality we observed underscores the urgency of widespread preventive measures to protect this vulnerable population.

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ARTICLE INFORMATION

Author Contributions: Dr. H.N. Kim had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Concept and design:* F.S. Buckner, H.Y. Chu, D.J. McCulloch, and H.N. Kim. *Acquisition, analysis, or interpretation of data:* V. Atluri, F.S. Buckner, M. Blain, D.J. McCulloch, S.A. McGuffin, A.K. Nalla, and M.L. Huang. *Drafting of the manuscript:* F.S. Buckner, D.J. McCulloch, H.Y. Chu, and H.N. Kim. *Critical Revisions of manuscript for important intellectual content:* K.R. Jerome, A.L. Greninger, M.L. Green, S. Neme, and S.A. Cohen.

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Table 1. Demographics and Baseline Characteristics of Patients Infected with SARS-CoV2

	All patients (N=105)	Not Severe (n=54)	Severe (n=51)
Age, years	69 (23-97)	67 (25-96)	70 (23-97)
>60 years	70 (67)	38 (70)	32 (63)
Sex			
Male	53 (50)	23 (43)	30 (59)
Female	52 (50)	31 (57)	21 (41)
Race			
White	75 (71)	41 (76)	34 (67)
Black	6 (6)	4 (7)	2 (4)
Asian/Pacific Islander	18 (17)	7 (13)	11 (21)
Unknown or other	6 (6)	2 (4)	4 (8)
Hispanic ethnicity	18 (17)	10 (19)	8 (16)
Smoking (ever)	22/86 (26)	12/45 (27)	10/41 (24)
Alcohol (any)	26/87 (30)	14/45 (31)	12/42 (29)
Comorbidity			
Hypertension	62 (59)	32 (59)	30 (59)
Obesity, BMI >30 kg/m ²	44/93 (47)	21/50 (42)	23/43 (53)
Cardiovascular ^a disease	40 (38)	22 (42)	18 (35)
Diabetes	35 (33)	17 (31)	18 (35)
Chronic kidney disease	27 (26)	12 (22)	15 (29)
Heart failure	20 (19)	13 (24)	7 (14)
Cancer	16 (15)	5 (9)	11 (22)
Asthma	10 (10)	7 (13)	3 (6)
Obstructive sleep apnea	12 (11)	5 (9)	7 (14)
COPD	11 (10)	4 (7)	7 (14)
Autoimmune disease	9 (9)	5 (10)	4 (8)
Transplant (solid organ)	4 (4)	3 (6)	1 (2)
HIV infection	1 (1)	0	1 (2)
Pregnancy	2 (2)	2 (4)	0
Comorbidity burden			

None	7 (7)	3 (5)	4 (8)
1-2	40 (38)	23 (43)	17 (33)
3 or more	58 (55)	28 (52)	30 (59)
Residence			
Homeless	1 (1)	1 (2)	0
Senior living	10 (10)	7 (13)	3 (6)
Skilled nursing facility	26 (25)	10 (19)	16 (31)
Home	67 (64)	35 (66)	32 (63)
Epidemiologic risk factor			
None	50 (48)	27 (50)	23 (45)
Travel	2 (2)	0	2 (4)
Known contact	17 (16)	10 (19)	7 (16)
Nursing/care facility	35 (33)	17 (31)	18 (35)

^aIncludes cerebrovascular disease. Values are noted as median (range), n of all patients (%) or a proportion of subset, n/N (%).

Table 2. Clinical Signs and Symptoms on Presentation

	All patients (N=105)	Not Severe (n=54)	Severe (n=51)
Vitals			
First temperature	36.9 (35.3-39.8)	36.8 (36.1-39.3)	37 (35.3-39.8)
T >38.0 C x 1 st 24 hours	37 (39)	13 (25)	24 (55)
Heart rate >100 bpm	39 (37)	19 (35)	20 (39)
Systolic pressure, mmHg	129 (70-188)	130 (93-188)	125 (70-173)
Respiratory rate	20 (14-48)	19 (14-32)	22 (14-48)
Hypoxia ^a	43 (41)	10 (19)	33 (65)
Symptoms			
Symptoms x >5 days	54/86 (63)	31/43 (72)	23/43 (53)
Cough	76 (72)	41 (76)	35 (69)
Dyspnea	56 (53)	24 (44)	32 (63)
Fatigue	51 (49)	29 (54)	22 (43)
Fever/Chills	49 (47)	25 (46)	24 (47)
Anorexia	33 (31)	18 (33)	15 (29)
Sputum production	19 (18)	8 (15)	11 (22)
Diarrhea	24 (23)	12 (22)	12 (24)
Myalgia/arthralgia	25 (24)	15 (28)	10 (20)
Nausea/vomiting	23 (22)	14 (26)	9 (18)
Chest pain	15 (14)	9 (17)	6 (12)
Congestion/rhinorrhea	15 (14)	9 (17)	6 (12)
Headache	8 (8)	4 (7)	4 (8)
Sore throat	7 (7)	5 (9)	2 (4)
Imaging			
Abnormal CXR	78/91 (86)	36/45 (80)	42/46 (91)
Abnormal Chest CT	18/19 (95)	7/8 (88)	11/11 (100)

Values are noted as median (range), n of all patients (%) or a proportion of subset, n/N (%).

^a Defined as O2 saturation of <90% on ambient air or requiring supplemental O2.

Table 3. Laboratory Measurements on Presentation

	All patients (n=105)	Not Severe (n=54)	Severe (n=51)
White blood cell count, x 10 ⁹ /L	6.4 (4.6-8.8)	5.3 (4.3-7.3)	7.3 (5.8-13.3)
<4	15 (15)	10 (18)	5 (10)
4-10	68 (66)	41 (76)	27 (55)
≥10	20 (19)	3 (6)	17 (35)
Lymphocyte count, x 10 ⁹ /L	1.1 (0.6-1.5)	1.2 (0.8-1.6)	0.9 (0.5-1.4)
<1.5	74 (73)	36 (69)	38 (78)
Neutrophil count, x 10 ⁹ /L	4.3 (3.0-6.3)	3.8 (2.8-5.1)	5.4 (3.3-8.4)
Hemoglobin, g/dL	12 (10.8-13.2)	12.1 (11.3-13.4)	11.7 (10.2-12.6)
Platelet count, x 10 ⁹ /L	210 (147-260)	207 (158-237)	211 (128-279)
<150	27 (26)	11 (20)	16 (33)
Prothrombin time, s (n=70)	14.1 (13.4-15.8)	14 (13.2-16.3)	14.2 (13.5-15.6)
Partial thromboplastin time, s (n=53)	35 (30-40)	36 (31-40)	33.5 (30-41)
Alanine aminotransferase, U/L (n=94)	25 (17-39)	22 (13-31)	30 (19-55)
>40	21/94 (22)	6/47 (13)	15/47 (32)
Aspartate aminotransferase, U/L (n=94)	32 (22-48)	27 (20-37)	39 (25-60)
>40	31/94 (33)	9/47 (19)	22/47 (47)
Total bilirubin, mg/dL (n= 94)	0.5 (0.4-0.8)	0.5 (0.4-0.7)	0.5 (0.3-0.9)
Blood urea nitrogen, mg/dL	21 (13-32)	16 (12-23)	26 (21-37)
Creatinine (serum), mg/dL	0.84 (0.66-1.32)	0.83 (0.61-1.06)	0.88 (0.69-1.45)

All values are noted as median (interquartile range, IQR), n of all patients (%) or a proportion of subset, n/N (%).

Table 4. Medications, Interventions and Complications

	Total (n=105)
Medications on admission	
Statin	44 (42)
Aspirin/NSAID	37 (35)
ARB	16 (15)
ACE inhibitor	19 (18)
Immunosuppressant(s)	12 (11)
Corticosteroid	10 (10)
Medications during hospital course	
Antibiotics	51 (50)
Hydroxychloroquine	44 (42)
Remdesivir vs placebo (trial)	21 (20)
Remdesivir (compassionate use)	4 (4)
Corticosteroids	3 (3)
Interventions	
Highest level of Oxygen support	
None	22 (21)
O2 by nasal cannula	39 (37)
High-flow O2 or non-rebreather	24 (23)
Non-invasive (BiPAP)	1 (1)
Mechanical ventilation	17 (16)
ECMO	2 (2)
Hemodialysis/SLED/CRRT (newly initiated)	3 (3)
Complications	
Shock	17 (16)
ARDS	28 (27)
Cardiac injury	13/67 (19)
Acute kidney injury	31 (30)
Death	35 (33)

Values represent all patients, N (%) or a proportion of subset, n/N (%).

Figure Title and Legend

Figure 1: Time to onset of COVID-19 complications.

Legend: Points represent individual patients; bars represent the median with interquartile ranges; number of observations are noted above the x-axis. Abbreviations: acute kidney injury (AKI) and intensive care unit admission (ICU).

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Figure 1

