

1 **Full Title:** Management and Outcomes of Critically-III Patients with COVID-19 Pneumonia at a
2 Safety-net Hospital in San Francisco, a Region with Early Public Health Interventions: A Case
3 Series

4 **Short Title:** Critically-III Patients with COVID-19 Pneumonia in a Region with Early Public
5 Health Interventions

6

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32 **Abstract:**

33 Background: Following early implementation of public health measures, San Francisco has
34 experienced a slow rise and a low peak level of coronavirus disease 2019 (COVID-19) cases
35 and deaths.

36

37 Methods and Findings: We included all patients with COVID-19 pneumonia admitted to the
38 intensive care unit (ICU) at the safety net hospital for San Francisco through April 8, 2020. Each
39 patient had ≥ 15 days of follow-up. Among 26 patients, the median age was 54 years
40 (interquartile range, 43 to 62), 65% were men, and 77% were Latinx. Mechanical ventilation was
41 initiated for 11 (42%) patients within 24 hours of ICU admission and 20 patients (77%) overall.
42 The median duration of mechanical ventilation was 13.5 days (interquartile range, 5 to 20).
43 Patients were managed with lung protective ventilation (tidal volume ≤ 8 ml/kg of ideal body
44 weight and plateau pressure ≤ 30 cmH₂O on 98% and 78% of ventilator days, respectively).
45 Prone positioning was used for 13 of 20 (65%) ventilated patients for a median of 5 days
46 (interquartile range, 2 to 10). Seventeen (65%) patients were discharged home, 1 (4%) was
47 discharged to nursing home, 3 (12%) were discharged from the ICU, and 2 (8%) remain
48 intubated in the ICU at the time of this report. Three (12%) patients have died.

49

50 Conclusions: Good outcomes were achieved in critically ill patients with COVID-19 by using
51 standard therapies for acute respiratory distress syndrome (ARDS) such as lung protective
52 ventilation and prone positioning. Ensuring hospitals can deliver sustained high-quality and
53 evidence-based critical care to patients with ARDS should remain a priority.

54

55 **Introduction:**

56 Coronavirus infectious disease 2019 (COVID-19) caused by the severe acute respiratory
57 syndrome coronavirus-2 (SARS-CoV-2) is now the leading cause of death in the United States.¹
58 The number of reported cases and deaths varies markedly in part due to regional variation in
59 public health responses to the pandemic.²⁻⁵

60
61 Initial reports of outcomes among adults with COVID-19 requiring intensive care unit (ICU)
62 admission showed high overall mortality (62% in China, 26% in Italy, 50% in the United
63 Kingdom, and 50-67% in the US) and mortality exceeding 80% among patients requiring
64 invasive mechanical ventilation.⁶⁻⁹ Mortality has been variable in subsequent reports but
65 exceeds 50% in nearly half of published studies.^{4,7,10-12} Many of these reports are from settings
66 that experienced surges of patients that overwhelmed hospital capacity and presented a
67 challenge to delivering standard ICU care.

68
69 San Francisco was among the first cities in the country to implement strong physical distancing
70 measures. The Mayor declared a state of emergency on February 25 and a regional shelter-in-
71 place order was issued on March 16.^{13,14} The ordinances occurred 28 days and 8 days,
72 respectively, before the first death from COVID-19 was reported in San Francisco on March 24.
73 These actions enabled healthcare systems to mobilize resources for COVID-19 admissions and
74 likely flattened the epidemic curve at a low peak level (1,312 cases of COVID-19 and 21 deaths
75 in San Francisco as of April 23).¹⁵

76
77 Here, we report the first detailed ICU case series from a healthcare system in the United States
78 with sufficient lead time and capacity to increase staffing of ICU care teams, establish dedicated
79 COVID-19 ICUs, and procure supplies and equipment. The objective is to describe the
80 demographics, clinical characteristics, ICU management and outcomes of critically ill patients

81 with COVID-19 pneumonia at Zuckerberg San Francisco General Hospital and Trauma Center
82 (ZSFG).

83

84 **Methods:**

85 STUDY SETTING

86 ZSFG is a 284-bed hospital (58 ICU beds) operated by the San Francisco Department of Public
87 Health and staffed by physicians from the University of California San Francisco. It is the
88 primary provider of safety-net health care and 80% of its patient population receives publicly
89 funded health insurance or is uninsured. San Francisco is the second most densely populated
90 city in the United States and the hospital's catchment includes a population of 881,549 within
91 46.7 square miles.

92

93 To date, COVID-19 ICU admissions have been clustered in two 10-bed ICUs. In addition to
94 regular staffing of medical and surgical ICUs, COVID-19 ICUs were staffed by dedicated
95 physician teams (one intensivist, one critical care fellow, and two internal medicine or
96 anesthesia residents per 10 patients), 1:1 nursing with an extra nurse supporting care for every
97 two mechanically ventilated patients, one respiratory therapist (RT) for up to 4 mechanically
98 ventilated patients with an extra RT available on each unit for additional support, and a
99 dedicated ICU pharmacist. Five ICU staff members including at least one RT and two COVID-19
100 ICU nurses supported prone positioning. A dedicated COVID-19 anesthesia team (one
101 attending physician and one advanced practice provider or resident physician) was available 24
102 hours a day for intubation bundled with placement of vascular access. During the study period,
103 the hospital did not experience shortages in critical equipment or most drugs, and at peak ICU
104 census, 43% of available ventilators were in use. Adequate personal protective equipment and
105 infection control measures were in place (only one clinical staff member has tested positive for
106 SARS-CoV-2 to date).

107

108 STUDY POPULATION AND DATA COLLECTION

109 All adults (18 years of age or older) admitted to the ICU with respiratory failure between
110 March 24 and April 8 and confirmed to have COVID-19 by an internally-validated reverse
111 transcription polymerase chain reaction assay were included. The UCSF Committee on Human
112 Research approved the study and waived the requirement for informed consent (researchers
113 analyzed only de-identified, anonymized data).

114
115 Data from the electronic medical record were extracted using a form in Research Electronic
116 Data Capture software (REDCap).^{16,17} We obtained demographic data, information on clinical
117 symptoms or signs at presentation, results of laboratory and radiologic studies, co-existing
118 conditions, daily ICU management data, and patient outcomes.

119

120 STUDY DEFINITIONS

121 Daily ventilator parameters, use and duration of mechanical ventilation, prone positioning and
122 neuromuscular blockade were collected through maximum 28 days of follow up. Patient
123 outcome data including hospitalization status were updated through May 10. Acute respiratory
124 distress syndrome (ARDS) was defined using the Berlin criteria.¹⁸

125

126 STATISTICAL ANALYSIS

127 Descriptive statistics were used to summarize the data; results are reported as medians and
128 interquartile ranges or means and standard deviations, as appropriate. Categorical variables
129 were summarized as counts and percentages. Median and individual values for selected
130 ventilator parameters were plotted for each day of mechanical ventilation through 14 days of
131 follow up. Analysis was performed with Stata 15.1 software (StataCorp).¹⁹

132

133 **Results:**

134 PATIENT DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

135 The median age of the study population was 54 years (interquartile range, 43 to 62), 35% were
 136 women, 77% identified as Latinx, and 12% had marginal housing (**Table 1**). The median BMI
 137 was 31.4 (interquartile range, 27.8 to 35.3), 20 (77%) had a documented comorbidity prior to
 138 hospitalization, and 12 (46%) had at least two comorbidities. The most prevalent comorbidities
 139 were diabetes mellitus (n = 15, 58%) with a median hemoglobin A1c of 9.4 (interquartile range,
 140 8.0 to 11.8) and hypertension (n = 14, 54%).

Table 1. Characteristics of Patients at Baseline and at ICU Admission.^a

Baseline Characteristics	Patients (N=26)
Age – median (IQR)	54 (43–62)
Female – no. (%)	9 (35)
Race – no. (%)	
Asian	3 (12)
African-American	2 (8)
White	5 (19)
Other/multiple races	12 (46)
Unknown	4 (15)
Hispanic/Latinx ethnicity – no. (%)	20 (77)
Homeless or marginally housed ^b – no. (%)	3 (12)
BMI ^c – median (IQR)	31.4 (27.8–35.3)
Current or former smoker	6 (23)
Diabetes mellitus (DM) – no. (%)	15 (58)
Hypertension – no. (%)	14 (54)
Chronic lung disease – no. (%)	5 (19)
Other pre-existing disorder – no. (%)	
Chronic kidney disease	3 (12)
Liver disease	3 (12)
Immunocompromised ^d	1 (4)
Disease Severity and Support Required at ICU Admission	
APACHE II score – median (IQR)	15 (11–19)
Highest level of respiratory support within 24 hours of ICU admission – no. (%)	
Low and medium flow oxygen	5 (19)
High flow nasal cannula	11 (42)
Mechanical ventilation	10 (38)
Vasopressors used within 24 hours of ICU admission – no. (%)	15 (58)
1 vasopressor	11 (42)
≥2 vasopressors	4 (15)
Paralyzed within 24h of ICU admission – no. (%)	4 (15)
Prone positioning within 24h of ICU admission – no. (%)	7 (27)
Selected Routine Labs on ICU Admission	
White blood cell count, median (IQR) – x10 ⁹ /L	9.9 (7.3–12.3)
Lymphocyte Count <1 x10 ⁹ /L – no. (%)	16 (62)
Platelet count, median (IQR) – x10 ⁹ /L	240 (195–279)

Aspartate aminotransferase >0.8 ukat/L – no. (%)	12(46)
Alanine aminotransferase >0.67 ukat/L – no. (%)	12(46)
Creatinine, median (IQR) – umol/L	77.8 (55.7–99.9)
>114.9 umol/L – no. (%)	3 (12)
Troponin ≥0.47 ug/L – no./total no. (%)	4/24 (17)
International Normalized Ratio (INR) ≥1.2 – no./total no. (%)	2/25 (8)

Inflammatory Markers^e

D-dimer, median (IQR) – nmol/L	4 (2.7–15.8)
Lactate Dehydrogenase (LDH), median (IQR) – ukat/L	7.2 (5.9–8.9)
Ferritin, median (IQR) – ug/L	936 (454–1606)
C-reactive protein (high sensitivity), median (IQR) – mg/L	200 (140–200)
Procalcitonin, median (IQR) – ng/L	0.33 (0.19–0.84)

Radiographic Data

Bilateral infiltrates on chest radiography – no./total no. (%)	24/26 (92)
Bilateral ground glass opacities on chest computed tomography – no./total no. (%)	8/9 (89)

141 APACHE, Acute Physiology and Chronic Health Evaluation; BMI, body-mass index; IQR, interquartile
142 range.

143 ^a Percentages may not total 100 due to rounding.

144 ^b Marginal housing refers to homelessness or residence in a shelter or housing unit that is inadequate for
145 reasons such as security of tenure, overcrowding, or access to basic facilities.

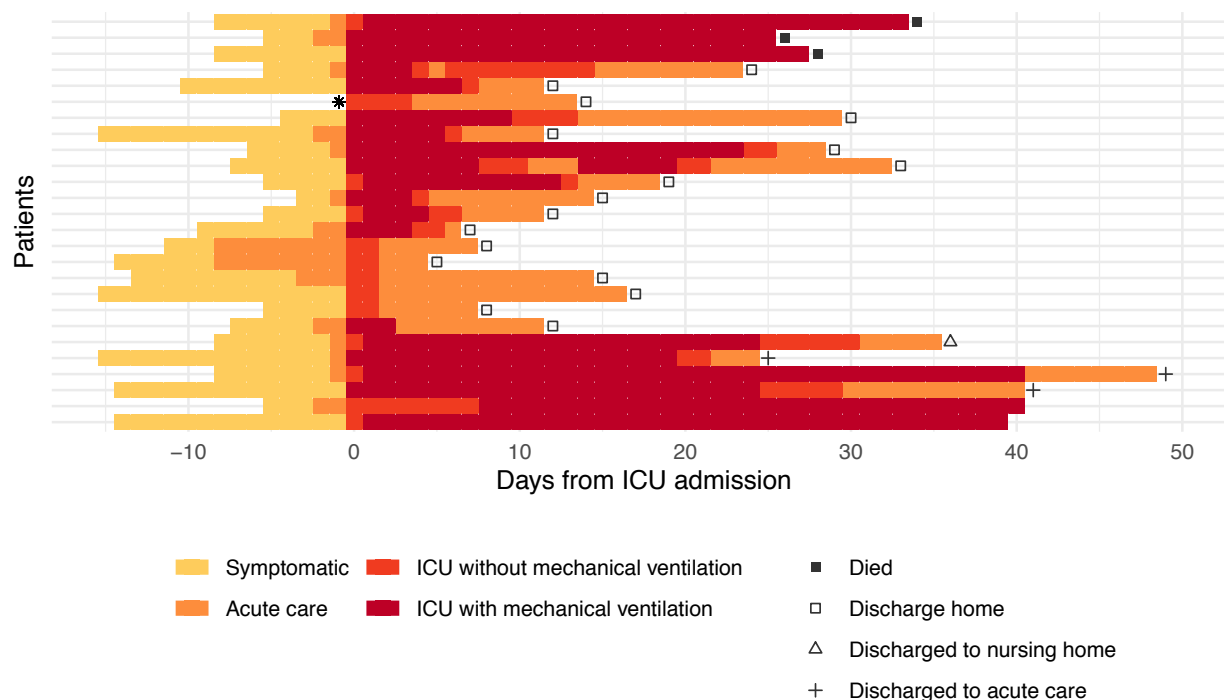
146 ^c Calculated using the weight in kilograms divided by the square of the height in meters

147 ^d Immunocompromised status: patient with Crohn's disease on 6-mercaptopurine.

148 ^e Abnormal elevations in inflammatory markers defined as the following: D-dimer ≥2.7 nmol/L, LDH >3.2
149 ukat/L, Ferritin >322 ug/L, CRP ≥8.1 mg/L, and Procalcitonin ≥0.5 ng/L.

150

151 Patients experienced symptoms for a median of 8 days (interquartile range, 5 to 13) prior to ICU
152 admission (**Figure 1**). Eleven (42%) patients were directly admitted to the ICU of whom 4
153 required immediate mechanical ventilation, and 7 were placed on high flow nasal cannula. Of 15
154 patients transferred to the ICU from an acute care bed, 11 (73%) were intubated within 24 hours
155 of transfer. The median APACHE II score was 15 (interquartile range, 11 to 19) at the time of
156 ICU admission (**Table 1**).²⁰ Twenty (77%) patients met the Berlin criteria for ARDS with 19
157 categorized as having moderate to severe disease based on the ratio of the partial pressure of
158 arterial oxygen to the fraction of inspired oxygen [$PaO_2:FiO_2$] <200.



*Symptom onset date not known

159

160 **Figure 1. Patient Clinical Course.**

161 Clinical course is depicted from symptom onset as reported by the patient on admission through
162 termination of data collection on May 10, 2020. Patients had symptoms for a median duration of
163 8 days (IQR 5-13) before intensive care unit (ICU) admission. Fifteen (58%) patients were
164 hospitalized for a median duration of 2 days (IQR 1-2) before requiring ICU level care and 11
165 (42%) were admitted directly to the ICU. Twenty (77%) patients required mechanical ventilation
166 for a median duration of 13.5 days (IQR 5-20). As of May 10, 2020, 17 (65%) patients had been
167 discharged home, 1 (4%) had been discharged to a skilled nursing facility, 3 (12%) had been
168 transferred from ICU to acute care, and 2 (8%) remained on mechanical ventilation. Three
169 patients (12%) had died. Unless otherwise shown, the ICU admission is ongoing.

170

171 LABORATORY, RADIOLOGIC, AND MICROBIOLOGIC FINDINGS

172 The white blood cell count (WBC) was normal for most patients (median $9.9 \times 10^9/L$; interquartile
173 range, 7.3 to 12.3), though leukocytosis ($WBC >12 \times 10^9/L$) and lymphopenia ($<1 \times 10^9/L$) were
174 present in 31% and 62% of patients, respectively (**Table 1**). Transaminitis was present in 46%
175 of patients. Most patients had elevated blood inflammatory markers, including D-dimer (74%),
176 lactate dehydrogenase (95%), ferritin (92%), and C-reactive protein (100%).

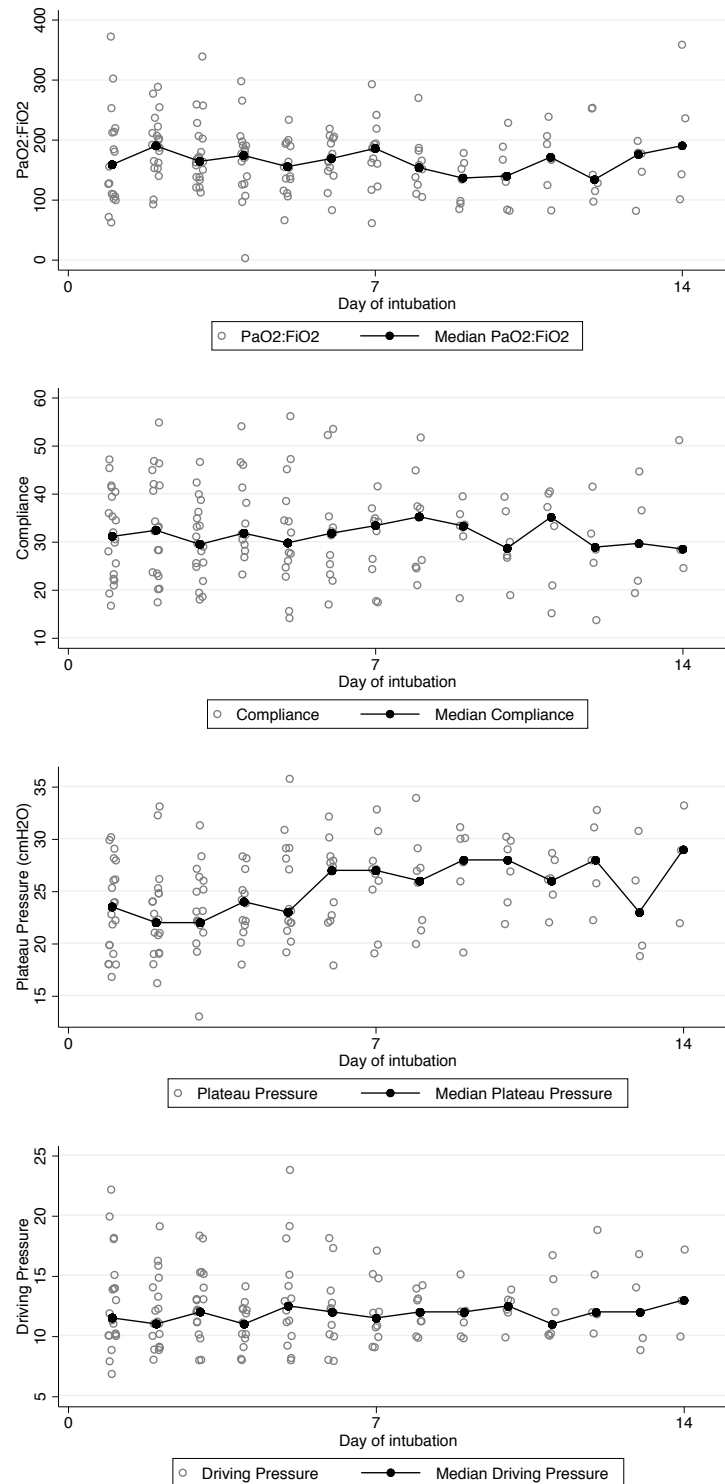
177

178 Chest radiographs obtained before ICU admission demonstrated bilateral infiltrates in 24 (92%),
179 unilateral infiltrates in 1 (4%), and no infiltrates in 1 (4%) (**Table 1**). Chest computed
180 tomography revealed bilateral ground glass opacities in 8 (89%) of 9 studies. At the time of ICU
181 admission, there were no viral co-infections among 23 patients tested and no culture-confirmed
182 bacterial co-infections.

183

184 CLINICAL COURSE AND TREATMENT

185 Six (23%) patients received supplemental oxygen via high flow nasal cannula and 20 (77%)
186 required mechanical ventilation during their ICU course (**Figure 1**). Adherence to lung protective
187 ventilation strategies for patients with ARDS was excellent. The median tidal volume delivered
188 was 6.0 ml/kg of ideal body weight (IBW) (interquartile range, 5.6 to 6.8) and remained ≤ 6 ml/kg
189 IBW on 72% of ventilator days and ≤ 8 ml/kg IBW on 98% of ventilator days. The median plateau
190 pressure on admission was 25 cmH₂O (interquartile range, 22 to 28) and was ≤ 30 cmH₂O on
191 78% of ventilator days. Among those receiving mechanical ventilation, daily ventilator
192 parameters showed marked patient-to-patient variation (**Figure 2**). The median severity of
193 ARDS was moderate at the onset of mechanical ventilation (PaO₂:FiO₂ 159, interquartile range,
194 104 to 217). The median lung compliance was low at the onset of mechanical ventilation (31
195 mL/cmH₂O, interquartile range, 23 to 39, normal is 50-100 mL/cmH₂O) and stayed low over 14
196 days of follow-up. The median plateau pressure was ≤ 25 cmH₂O on each of the first five days of
197 mechanical ventilation and increased to 25 to 30 cmH₂O thereafter. Five patients (25%) had
198 driving pressures ≥ 14 cmH₂O on the first day of mechanical ventilation and 65% of intubated
199 patients had a driving pressure ≥ 14 cmH₂O on at least one day during follow-up.

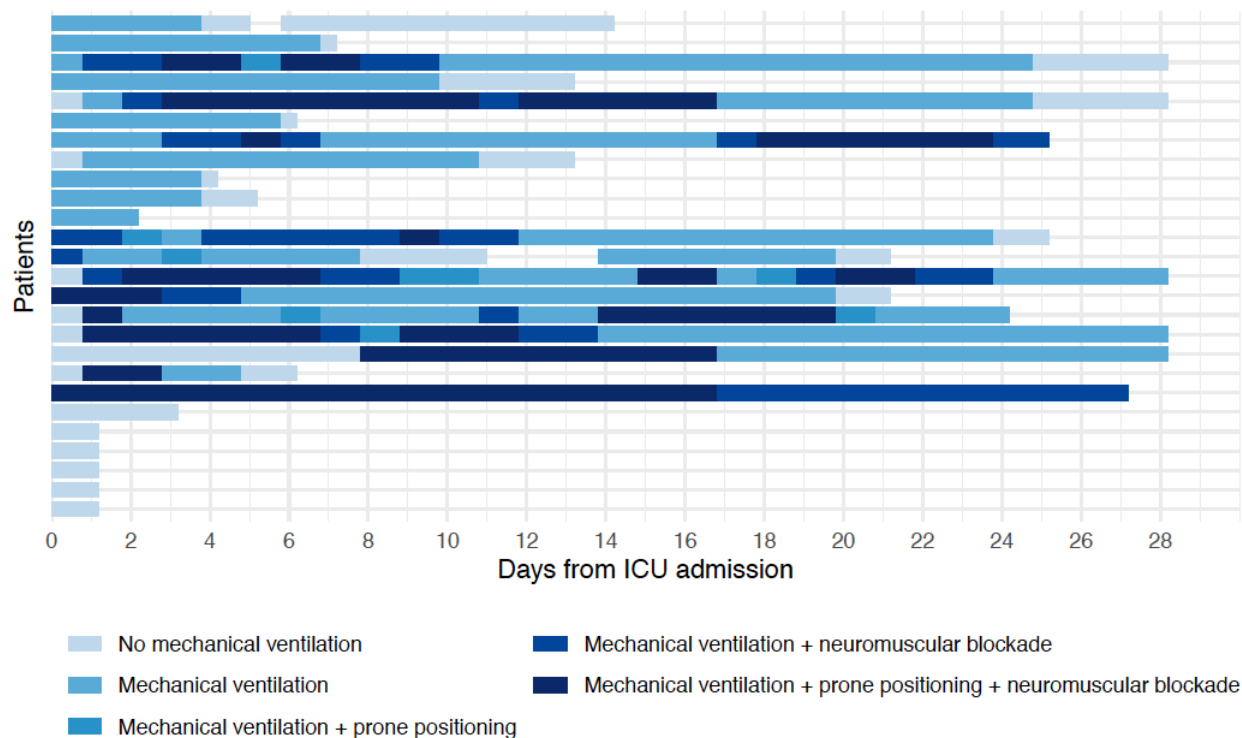


200

201 **Figure 2. Respiratory Metrics Among Mechanically Ventilated Patients.**

202 Each white dot represents the daily value recorded closest to 8 AM for each patient on
203 mechanical ventilation. The black dot represents the median value for all measurements on a
204 given day of ventilation. PaO₂ denotes partial pressure of arterial oxygen and FiO₂ denotes the
205 fraction of inspired oxygen. Compliance is calculated using tidal volume divided by the
206 difference between the plateau and the positive end expiratory pressures. The driving pressure
207 is the difference between the plateau pressure and the positive end expiratory pressure.

208 In addition to lung protective ventilation, ARDS was primarily managed using standard therapies
209 for hypoxemic respiratory failure (**Figure 3**). In particular, 13 of 20 (65%) patients mechanically
210 ventilated were placed in the prone position for 16-20 hours a day for a median duration of 5
211 days (interquartile range, 2 to 10) and a maximum of 17 days (**Table 2**). Prone positioning was
212 initiated early in moderate to severe ARDS.²¹ At the time of initiation, the median PaO₂ was 71
213 mmHg (interquartile range, 63 to 84), median FiO₂ was 0.7 (interquartile range, 0.5 to 0.7) and
214 median PEEP was 12 cmH₂O (interquartile range, 12 to 14). Twelve (46%) patients received
215 neuromuscular blockade for a median duration of 9 days (interquartile range, 6 to 12). Four
216 (15%) patients received inhaled epoprostenol (median 11 days, interquartile range 3 to 12).
217 Mechanically ventilated patients required a high level of sedation (**Table 2**).



218

219 **Figure 3. Ventilation Timeline, 24 March-4 May 2020.**

220 Mechanically ventilated patients were managed using a lung protective ventilation strategy
221 based on the ARDSNet protocol. Daily ventilation status with or without adjunctive treatments
222 for hypoxemic respiratory failure including prone positioning and neuromuscular blockade are
223 shown through May 4. Breaks correspond to days that a patient was not in the ICU.

224

Table 2. ICU Management and Outcomes.^a

Treatment of Hypoxemic Respiratory Failure	Patients (N=26)
Mechanical ventilation – no. (%)	20 (77)
Median duration of mechanical ventilation (IQR) – days	13.5 (5–20)
Prone positioning – no./total no. (%)	13/20 (65)
Median duration of prone positioning (IQR) – days	5 (2–10)
Neuromuscular blockade Infusion - no./total no. (%)	12/20 (60)
Median duration of neuromuscular blockade infusion (IQR) - days	8.5 (6.5–12)
Inhaled epoprostenol – no./total no. (%)	4/20 (20)
Median duration of inhaled epoprostenol (IQR) – days	11 (3–12)
Referred for ECMO consideration – no./total no. (%)	4/20 (20)
Transferred for ECMO – no./total no. (%)	2/20 (10)
Drug Therapies^b	
Remdesivir placebo-controlled trial – no. (%)	12 (46)
Mesenchymal stem cells placebo-controlled trial – no. (%)	5 (19)
Hydroxychloroquine – no. (%)	13 (50)
Median duration of hydroxychloroquine (IQR) – days	2 (1–5)
Azithromycin – no. (%)	20 (77)
Median duration of azithromycin (IQR) – days	4 (2.5–5)
Systemic steroids – no. (%)	
Given for ARDS	0 (0)
Given for other indications	3 (12)
Sedatives and Analgesic Infusions	
Propofol - no. (%)	20 (77)
Median of maximum dose (IQR) mcg/kg/min	80 (80–80)
Median duration of infusion (IQR) – days	8 (3–12)
Midazolam – no. (%)	11 (42)
Median of maximum dose (IQR) mg/hr	5 (4–8)
Median duration of infusion (IQR) – days	9 (3–11)
Dexmedetomidine – no. (%)	14 (54)
Median of maximum dose (IQR) mcg/kg/hr	1.1 (0.7–1.5)
Median duration of infusion (IQR) – days	2 (1–4)
Fentanyl – no. (%)	20 (77)
Median of maximum dose (IQR) mcg/hr	250 (150–350)
Median duration of infusion (IQR) – days	8 (4–14)
Hydromorphone – no. (%)	3 (12)
Range of Maximum Infusion – mg/hr	4–6
Range of duration of infusion – days	1–19
Other Therapies	
Mediation duration of vasopressor use (IQR) – days	6 (4–13.5)
Continuous renal replacement therapy – no. (%)	5 (19)
Outcomes	
Hospitalization status – no. (%)	
Discharged to home	17 (65)
Discharged to skilled nursing facility	1 (4)
Discharged to acute care	3 (12)
Still in ICU – mechanically ventilated	2 (8)
Died	3 (12)

Median length of stay (IQR) – days	
Hospital	15 (12–25)
ICU	9 (3–24)
Other adverse outcomes – no. (%)	
Re-intubated within 48 hours – no./total no. (%)	1/20 (5)
Re-admitted to ICU after discharge	2 (8)
Treated for ventilator-associated pneumonia – no./total no. (%)	6/20 (30)
Catheter-associated urinary tract infections	1 (4)
Confirmed central line infection	0 (0)

225 IQR, interquartile range; ARDS, acute respiratory distress syndrome; ECMO, extracorporeal membrane
226 oxygenation.

227 ^a Percentages may not total 100 due to rounding.

228 ^b Two mutually exclusive clinical trials were enrolling patients during the study period. Twelve patients
229 (46%) were enrolled in a trial testing Remdesivir vs. placebo (NCT04257656) for Covid-19 disease, and 5
230 (19%) were enrolled in a trial testing human Mesenchymal Stromal Stem Cells vs. placebo
231 (NCT03818854) for severe ARDS.

232
233 Twenty (77%) patients required vasopressor support for a median duration of 6 days
234 (interquartile range, 4 to 13.5), and 5 (19%) patients needed continuous renal replacement
235 therapy (CRRT). No patients received systemic steroids or other immunosuppressive
236 medications for treatment of COVID-19. Three patients received systemic steroids for other
237 indications (one each for refractory septic shock, stridor, and bronchospasm with underlying
238 obstructive lung disease). Nine patients received therapeutic anticoagulation: 2 for confirmed
239 venous thromboembolic disease, 1 to prevent clotting of the CRRT circuit, and 6 for empiric
240 treatment of pulmonary embolism. Anti-coagulation was discontinued in 5 of 6 patients treated
241 empirically after negative imaging studies, and the sixth patient was not stable enough to obtain
242 imaging. Other treatments are summarized in **Table 2**.

243

244 OUTCOMES

245 Patients were followed for at least 21 hospital days. As of May 10, among the 26 patients, 17
246 (65%) were discharged home, 1 (4%) was discharged to a skilled nursing facility, 3 (12%) were
247 discharged to an acute care bed, and 2 (8%) were still in the ICU requiring mechanical
248 ventilation (**Table 2**). Three (12%) patients have died.

249

250 The median length of hospital admission was 15 days (interquartile range, 12 to 25), and the
251 median length of ICU admission was 9 days (interquartile range, 3 to 24). Twenty (77%)
252 patients were mechanically ventilated for a median of 13.5 days (interquartile range, 5 to 20).
253 Length of stay and length of mechanical ventilation are likely to be underestimated as 5 patients
254 remain in the hospital (including 2 still in the ICU). Four patients were referred and two were
255 transferred to an extracorporeal membrane oxygenation (ECMO) center. Other adverse ICU
256 outcomes included re-intubation within 48 hours for 1 patient and readmission to the ICU for 2
257 patients. Six (30%) mechanically ventilated patients were treated for ventilator-associated
258 pneumonia (VAP). One patient developed a catheter-associated urinary tract infection, but no
259 patients developed central-line associated infections.

260

261 **Discussion:**

262 We report for the first time the results of a case series of critically ill patients with COVID-19
263 from a region with early public health interventions to slow the spread of SARS-CoV-2 and
264 adequate time and resources to prepare for COVID-19 ICU admissions. We had five weeks to
265 prepare from the time the Mayor declared a state of emergency to our first ICU patient with
266 COVID-19. Although we experienced a higher patient volume than normal, our hospital did not
267 experience any significant shortages of staff, pharmaceuticals, or equipment needed to provide
268 standard ICU management of ARDS. Findings from this case series differ from other published
269 data in two important ways: (1) mortality among critically ill patients with COVID-19, including
270 those mechanically ventilated, has been low, and (2) the lung compliance observed in patients
271 with COVID-19 pneumonia and ARDS has been similar to reported values in patients with
272 ARDS from other causes. Overall, our findings reinforce the importance of public health
273 measures such as physical distancing to enable hospitals to deliver standard care to critically ill
274 patients with respiratory failure from COVID-19 pneumonia.

275

276 There are several potential explanations for the lower mortality observed in our cohort
277 compared with previous case series. Patients in this cohort were younger than in previously
278 published case series and were admitted from the community rather than skilled nursing
279 facilities. However, approximately three-quarters had a comorbidity previously associated with
280 worse outcomes in COVID-19 pneumonia and nearly half had two such comorbidities. Our
281 patients were also comparable to other cohorts by standard assessment of severity of illness
282 including length of stay, vasopressor use, need for continuous renal replacement therapy, and
283 APACHE II score.⁹ Despite adherence to lung protective ventilation, a substantial fraction of
284 patients had high driving pressures, a metric associated with mortality in ARDS.²² These data, in
285 combination with the use of advanced management for hypoxemic respiratory failure and CRRT
286 in a substantial proportion of patients, argue against the possibility that our low observed
287 mortality reflects a less severely ill population.

288
289 Patient care at our institution was focused on proven therapies for ARDS including lung
290 protective ventilation, a fluid conservative strategy, and the use of prone positioning and
291 neuromuscular blockade for moderate to severe disease.^{21,23-30} Adherence to lung protective
292 ventilation for ARDS is known to be generally poor and has not been reported in prior case
293 series of COVID-19 related ARDS.³¹ However, one can infer that in healthcare systems under
294 stress, barriers to implementing these protocols would be even more difficult to overcome. We
295 presume a key driver of good outcomes in this cohort was also our ability to mobilize sufficient
296 critical care trained physician and non-physician staff. Our data suggest that among severely ill
297 patients admitted to the ICU with COVID-19 pneumonia, good outcomes can be achieved so
298 long as healthcare systems are not overwhelmed and are able to deliver evidence-based
299 treatments for ARDS and hypoxemic respiratory failure for prolonged periods. However, clinical
300 trials of experimental treatments to reduce the need for ICU admission, duration of ICU
301 admission and long-term outcomes remain critically important.

302

303 Our data suggest that the pulmonary physiology of COVID-19 pneumonia is variable with a
304 range of compliance values similar to ARDS cohorts before the COVID-19 pandemic.^{22,32,33}
305 While the median values of compliance and tidal compliance may be marginally higher than
306 what is reported in studies of ARDS from other causes, we did not observe a preponderance of
307 a high compliance phenotype of COVID-19 ARDS that has been reported elsewhere.³⁴⁻³⁶ We
308 managed our ventilators with standard ARDSNet protocols and did not alter our supportive care
309 strategies for patients with ARDS from COVID-19.

310
311 Our study has several limitations. First, this is a small cohort of patients from a single center
312 with censoring of outcome data for 8 patients who remain intubated without adjudication of
313 ultimate disposition. Mortality may be underestimated but would still be at most 40% in
314 ventilated patients, similar to what has been reported for moderate to severe ARDS.³¹ Second,
315 our COVID-19 ICU staffing model and resource mobilization was possible due to monetary
316 support from emergency funds and may not be generalizable in particular to private or non-
317 academically affiliated healthcare systems. Last, our study was not designed to evaluate
318 reasons for the high proportion of Latinx patients in our cohort (77%) compared to the usual
319 patients who receive care in our hospital (25%), an important disparity that requires further
320 study.

321
322 Our early experience of the COVID-19 pandemic substantively adds to what is known about
323 outcomes in critically ill patients with COVID-19 pneumonia and does not resemble the
324 experience reported in many other settings. Majority of patients (81%) have been discharged
325 from the ICU, including 65% who have been discharged home. Early efforts to develop
326 coordinated local and regional response plans with contingency planning for personnel,
327 equipment, and pharmaceutical shortages are vital to prepare for later phases of this pandemic
328 with anticipated ebbs and flows in patient volume. While awaiting the results of clinical trials and
329 ultimately an effective vaccine, our findings highlight the ongoing importance of public health

330 measures to minimize peak hospital case load during outbreaks and thereby enable ICUs to
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332

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339 **References:**

- 340 1. National Vital Statistics System. Provisional Death Counts for Coronavirus Disease
341 (COVID-19). Centers for Disease Control and Prevention, 2020. (Accessed 23 April, 2020, at
342 <https://www.cdc.gov/nchs/nvss/vsrr/covid19/index.htm>.)
- 343 2. CDC Covid Response Team. Geographic Differences in COVID-19 Cases, Deaths, and
344 Incidence - United States, February 12-April 7, 2020. *MMWR Morb Mortal Wkly Rep*
345 2020;69:465-71.
- 346 3. Liang WH, Guan WJ, Li CC, et al. Clinical characteristics and outcomes of hospitalised
347 patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): A
348 Nationwide Analysis of China. *Eur Respir J* 2020.
- 349 4. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics,
350 Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New
351 York City Area. *JAMA* 2020.
- 352 5. Prem K, Liu Y, Russell TW, et al. The effect of control strategies to reduce social mixing
353 on outcomes of the COVID-19 epidemic in Wuhan, China: a modelling study. *The Lancet Public*
354 *health* 2020.
- 355 6. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. COVID-19 in Critically Ill Patients in the
356 Seattle Region - Case Series. *N Engl J Med* 2020.
- 357 7. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with
358 SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational
359 study. *The Lancet Respiratory medicine* 2020.
- 360 8. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591
361 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA*
362 2020.
- 363 9. ICNARC report on COVID-19 in critical care. London, UK: Intensive Care National Audit
364 & Research Centre; 2020.
- 365 10. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients
366 with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020;395:1054-62.
- 367 11. Myers LC, Parodi SM, Escobar GJ, Liu VX. Characteristics of hospitalized adults with
368 COVID-19 in an integrated health care system in California. *Journal of the American Medical*
369 *Association* 2020:E1-E3.
- 370 12. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients
371 With COVID-19 in Washington State. *JAMA* 2020.
- 372 13. Declaration of local health emergency regarding novel coronavirus disease 2019
373 (COVID-19). City and County of San Francisco, 2020. at
374 <https://www.sfdph.org/dph/alerts/files/HealthOfficerLocalEmergencyDeclaration-03062020.pdf>.)
- 375 14. Order of the Health Officer No. C19-07. San Francisco, CA: City and County of San
376 Francisco; 2020.
- 377 15. Tracking COVID-19 in San Francisco. San Francisco Department of Public Health, 2020.
378 (Accessed 21 April 2020, at [https://data.sfgov.org/stories/s/fjki-2fab-tracking-COVID-19-in-san-](https://data.sfgov.org/stories/s/fjki-2fab-tracking-COVID-19-in-san-francisco)
379 [francisco](https://data.sfgov.org/stories/s/fjki-2fab-tracking-COVID-19-in-san-francisco).)
- 380 16. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic
381 data capture (REDCap)--a metadata-driven methodology and workflow process for providing
382 translational research informatics support. *J Biomed Inform* 2009;42:377-81.
- 383 17. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international
384 community of software platform partners. *J Biomed Inform* 2019;95:103208.
- 385 18. Force ADT, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the
386 Berlin Definition. *JAMA* 2012;307:2526-33.
- 387 19. StataCorp. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC;
388 2017.
- 389 20. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease
390 classification system. *Crit Care Med* 1985;13:818-29.

- 391 21. Guerin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory
392 distress syndrome. *N Engl J Med* 2013;368:2159-68.
- 393 22. Amato MB, Meade MO, Slutsky AS, et al. Driving pressure and survival in the acute
394 respiratory distress syndrome. *N Engl J Med* 2015;372:747-55.
- 395 23. Matthay MA, Aldrich JM, Gotts JE. Treatment for severe acute respiratory distress
396 syndrome from COVID-19. *The Lancet Respiratory medicine* 2020.
- 397 24. Matthay MA, Zemans RL, Zimmerman GA, et al. Acute respiratory distress syndrome.
398 *Nat Rev Dis Primers* 2019;5:18.
- 399 25. Rice TW, Janz DR. In Defense of Evidence-Based Medicine for the Treatment of
400 COVID-19 ARDS. *Ann Am Thorac Soc* 2020.
- 401 26. Acute Respiratory Distress Syndrome N, Brower RG, Matthay MA, et al. Ventilation with
402 lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the
403 acute respiratory distress syndrome. *N Engl J Med* 2000;342:1301-8.
- 404 27. National Heart L, Blood Institute Acute Respiratory Distress Syndrome Clinical Trials N,
405 Wiedemann HP, et al. Comparison of two fluid-management strategies in acute lung injury. *N*
406 *Engl J Med* 2006;354:2564-75.
- 407 28. Sud S, Friedrich JO, Adhikari NK, et al. Effect of prone positioning during mechanical
408 ventilation on mortality among patients with acute respiratory distress syndrome: a systematic
409 review and meta-analysis. *CMAJ* 2014;186:E381-90.
- 410 29. Papazian L, Forel JM, Gacouin A, et al. Neuromuscular blockers in early acute
411 respiratory distress syndrome. *N Engl J Med* 2010;363:1107-16.
- 412 30. Moss M, Ulysse CA, Angus DC, National Heart L, Blood Institute PCTN. Early
413 Neuromuscular Blockade in the Acute Respiratory Distress Syndrome. Reply. *N Engl J Med*
414 2019;381:787-8.
- 415 31. Bellani G, Laffey JG, Pham T, et al. Epidemiology, Patterns of Care, and Mortality for
416 Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries.
417 *JAMA* 2016;315:788-800.
- 418 32. Nuckton TJ, Alonso JA, Kallet RH, et al. Pulmonary dead-space fraction as a risk factor
419 for death in the acute respiratory distress syndrome. *N Engl J Med* 2002;346:1281-6.
- 420 33. Seeley E, McAuley DF, Eisner M, Miletin M, Matthay MA, Kallet RH. Predictors of
421 mortality in acute lung injury during the era of lung protective ventilation. *Thorax* 2008;63:994-8.
- 422 34. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory
423 treatments for different phenotypes? *Intensive Care Med* 2020.
- 424 35. Gattinoni L, Chiumello D, Rossi S. COVID-19 pneumonia: ARDS or not? *Crit Care*
425 2020;24:154.
- 426 36. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 Does
427 Not Lead to a "Typical" Acute Respiratory Distress Syndrome. *Am J Respir Crit Care Med* 2020.
428