

Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy

Giacomo Grasselli, MD; Alberto Zangrillo, MD; Alberto Zanella, MD; Massimo Antonelli, MD; Luca Cabrini, MD; Antonio Castelli, MD; Danilo Cereda, MD; Antonio Coluccello, MD; Giuseppe Foti, MD; Roberto Fumagalli, MD; Giorgio Iotti, MD; Nicola Latronico, MD; Luca Lorini, MD; Stefano Merler, MS; Giuseppe Natalini, MD; Alessandra Piatti, MD; Marco Vito Ranieri, MD; Anna Mara Scandroglio, MD; Enrico Storti, MD; Maurizio Cecconi, MD; Antonio Pesenti, MD; for the COVID-19 Lombardy ICU Network

IMPORTANCE In December 2019, a novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) emerged in China and has spread globally, creating a pandemic. Information about the clinical characteristics of infected patients who require intensive care is limited.

OBJECTIVE To characterize patients with coronavirus disease 2019 (COVID-19) requiring treatment in an intensive care unit (ICU) in the Lombardy region of Italy.

DESIGN, SETTING, AND PARTICIPANTS Retrospective case series of 1591 consecutive patients with laboratory-confirmed COVID-19 referred for ICU admission to the coordinator center (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy) of the COVID-19 Lombardy ICU Network and treated at one of the ICUs of the 72 hospitals in this network between February 20 and March 18, 2020. Date of final follow-up was March 25, 2020.

EXPOSURES SARS-CoV-2 infection confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swabs.

MAIN OUTCOMES AND MEASURES Demographic and clinical data were collected, including data on clinical management, respiratory failure, and patient mortality. Data were recorded by the coordinator center on an electronic worksheet during telephone calls by the staff of the COVID-19 Lombardy ICU Network.

RESULTS Of the 1591 patients included in the study, the median (IQR) age was 63 (56-70) years and 1304 (82%) were male. Of the 1043 patients with available data, 709 (68%) had at least 1 comorbidity and 509 (49%) had hypertension. Among 1300 patients with available respiratory support data, 1287 (99% [95% CI, 98%-99%]) needed respiratory support, including 1150 (88% [95% CI, 87%-90%]) who received mechanical ventilation and 137 (11% [95% CI, 9%-12%]) who received noninvasive ventilation. The median positive end-expiratory pressure (PEEP) was 14 (IQR, 12-16) cm H₂O, and F_{IO₂} was greater than 50% in 89% of patients. The median P_{aO₂}/F_{IO₂} was 160 (IQR, 114-220). The median PEEP level was not different between younger patients (n = 503 aged ≤63 years) and older patients (n = 514 aged ≥64 years) (14 [IQR, 12-15] vs 14 [IQR, 12-16] cm H₂O, respectively; median difference, 0 [95% CI, 0-0]; P = .94). Median F_{IO₂} was lower in younger patients: 60% (IQR, 50%-80%) vs 70% (IQR, 50%-80%) (median difference, -10% [95% CI, -14% to 6%]; P = .006), and median P_{aO₂}/F_{IO₂} was higher in younger patients: 163.5 (IQR, 120-230) vs 156 (IQR, 110-205) (median difference, 7 [95% CI, -8 to 22]; P = .02). Patients with hypertension (n = 509) were older than those without hypertension (n = 526) (median [IQR] age, 66 years [60-72] vs 62 years [54-68]; P < .001) and had lower P_{aO₂}/F_{IO₂} (median [IQR], 146 [105-214] vs 173 [120-222]; median difference, -27 [95% CI, -42 to -12]; P = .005). Among the 1581 patients with ICU disposition data available as of March 25, 2020, 920 patients (58% [95% CI, 56%-61%]) were still in the ICU, 256 (16% [95% CI, 14%-18%]) were discharged from the ICU, and 405 (26% [95% CI, 23%-28%]) had died in the ICU. Older patients (n = 786; age ≥64 years) had higher mortality than younger patients (n = 795; age ≤63 years) (36% vs 15%; difference, 21% [95% CI, 17%-26%]; P < .001).

CONCLUSIONS AND RELEVANCE In this case series of critically ill patients with laboratory-confirmed COVID-19 admitted to ICUs in Lombardy, Italy, the majority were older men, a large proportion required mechanical ventilation and high levels of PEEP, and ICU mortality was 26%.

JAMA. 2020;323(16):1574-1581. doi:10.1001/jama.2020.5394
Published online April 6, 2020.

Viewpoint page 1545 and Editorial page 1559

Video

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The COVID-19 Lombardy ICU Network members appear at the end of the article.

Corresponding Author: Maurizio Cecconi, MD, Department of Anaesthesia and Intensive Care Medicine, Humanitas Clinical and Research Centre-IRCCS, Via Manzoni 56, 20089, Rozzano, Milan, Italy (maurizio.cecconi@hunimed.eu).

On March 11, 2020, the World Health Organization (WHO) declared the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak a pandemic due to the constantly increasing number of cases outside China.¹ Patients with SARS-CoV-2 infection can develop coronavirus disease 2019 (COVID-19), which has resulted in high rates of hospitalization and intensive care unit (ICU) admission.²

On February 20, 2020, the first patient diagnosed with COVID-19 in Italy developed respiratory failure and was admitted to one of the ICUs of Lombardy, a region of northern Italy. Since then, the increasing number of cases recorded in Lombardy, and subsequently throughout the country, led Italy to be the second most affected country in the world, after the US, as of March 27, 2020.³ Local health and government officials in Lombardy responded to the outbreak by creating a network of ICUs (COVID-19 Lombardy ICU Network) coordinated by Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan. This network has managed an exponential surge of patients requiring ICU admission for respiratory support.²

Up through March 18, 2020, a total of 17 713 people had tested positive for the new SARS-CoV-2 coronavirus in Lombardy and 1593 (9%) had been admitted to the ICU. Information on the incidence and clinical characteristics of critically ill patients diagnosed with COVID-19 is still limited. Among hospitalized patients with COVID-19 in China, the percentage of patients who required ICU care has varied from 5% to 32%.^{4,5}

The availability of ICU beds and the provision of intensive care varies among countries.⁶ Knowledge of the baseline characteristics and outcomes of critically ill patients is crucial for health and government officials engaged in planning efforts to address local outbreaks. This case series describes the clinical characteristics of patients with laboratory-confirmed COVID-19 admitted to ICUs of the COVID-19 Lombardy ICU Network in northern Italy.

Methods

This retrospective observational study was performed at the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, which was the regional coordinating center for the COVID-19 Lombardy ICU Network. All consecutive patients with laboratory-confirmed SARS-CoV-2 infection, referred to Ospedale Maggiore Policlinico, and subsequently admitted to one of the ICUs among 72 hospitals in the network between February 20 and March 18, 2020, were enrolled. The institutional ethics board of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, approved this study and due to the nature of retrospective chart review, waived the need for informed consent from individual patients.

According to the WHO guidance,⁷ laboratory confirmation for SARS-CoV-2 was defined as a positive result of real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay of nasal and pharyngeal swabs. This guidance was implemented locally with the adjunct of using RT-PCR assay from lower respiratory tract aspirates as well.

Key Points

Question What are the baseline characteristics and outcomes of patients with laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection admitted to intensive care units (ICUs) in Lombardy, Italy?

Findings In this retrospective case series that involved 1591 critically ill patients admitted from February 20 to March 18, 2020, 99% (1287 of 1300 patients) required respiratory support, including endotracheal intubation in 88% and noninvasive ventilation in 11%; ICU mortality was 26%.

Meaning In this case series of critically ill patients admitted to ICUs in Lombardy, Italy, with laboratory-confirmed coronavirus disease 2019 (COVID-19), a high proportion required mechanical ventilation and ICU mortality was 26% as of March 25, 2020.

Data were recorded by staff of the coordinator center on an electronic worksheet during daily telephone calls performed by intensivists of the hospitals of the COVID-19 Lombardy ICU Network.

Data Collection

Clinical data reported in this study were collected by phone within the first 6 to 24 hours following ICU admission. The recorded data included the following: age, sex, medical comorbidities, mode of respiratory support (invasive mechanical ventilation, noninvasive mechanical ventilation, oxygen mask), level of positive end-expiratory pressure (PEEP), fraction of inspired oxygen (F_{IO_2}), arterial partial pressure of oxygen (P_{aO_2}), P_{aO_2}/F_{IO_2} ratio, the use of extracorporeal membrane oxygenation (ECMO), and prone positioning. The number of patients who had died, had been discharged, and were still admitted in the ICU as of March 25, 2020, were recorded, and ICU length of stay also was determined.

Statistical Analysis

No statistical sample size calculation was performed a priori, and sample size was equal to the number of patients treated during the study period. Continuous variables are presented as median and interquartile range (IQR) with 95% CIs. Categorical variables are expressed as number of patients (percentage) with 95% CIs. Differences in distributions of patient characteristics by median age subgroups and by presence/absence of hypertension are reported using differences with 95% CIs. Percentages of available data for the overall population are based on the total number of patients included in the study, distribution of available data over the age subgroups are based on the available data for that variable, and the other percentages are calculated using the number of available data for that subgroup.

Patients were grouped by age and by median age. Age groups were defined as follows: 0 through 20 years; 21 through 40 years; 41 through 50 years; 51 through 60 years; 61 through 70 years; 71 through 80 years; 81 through 90 years; and 91 through 100 years. Younger and older age were classified as age lower than the median age and age equal or higher than the median age.

Table 1. Demographic and Clinical Characteristics of Patients in the First 24 Hours of ICU Admission for COVID-19 in Lombardy, Italy

	Patients by age, y, No. (%)								
	All	0-20	21-40	41-50	51-60	61-70	71-80	81-90	91-100
No. (%)	1591 (100)	4 (<1)	56 (4)	143 (9)	427 (27)	598 (38)	341 (21)	21 (1)	1 (<1)
Age, median (IQR), y	63 (56-70)	16 (14-19)	34 (31-38)	47 (44-49)	56 (54-59)	65 (63-68)	74 (72-76)	83 (81-84)	91
Males	1304 (82)	3 (75)	44 (79)	119 (83)	355 (83)	484 (81)	279 (82)	19 (90)	1 (100)
Females	287 (18)	1 (25)	12 (21)	24 (17)	72 (17)	114 (19)	62 (18)	2 (10)	0
Comorbidities, No. with data	1043	3	35	82	273	380	253	1	1
None	334 (32)	0	23 (66)	50 (61)	107 (39)	107 (28)	47 (19)	0	0
Hypertension	509 (49)	0	4 (11)	21 (26)	121 (44)	195 (51)	156 (62)	12 (75)	0
Cardiovascular disease ^a	223 (21)	0	1 (3)	4 (5)	43 (16)	87 (23)	81 (32)	6 (38)	1 (100)
Hypercholesterolemia	188 (18)	0	1 (3)	1 (1)	30 (11)	92 (24)	59 (23)	5 (31)	0
Diabetes, type 2	180 (17)	0	1 (3)	4 (5)	40 (15)	86 (23)	46 (18)	3 (19)	0
Malignancy ^b	81 (8)	0	0	2 (2)	10 (4)	33 (9)	33 (13)	3 (19)	0
COPD	42 (4)	0	1 (3)	0	8 (3)	12 (3)	20 (8)	1 (6)	0
Chronic kidney disease	36 (3)	0	0	2 (2)	10 (4)	17 (4)	7 (3)	0	0
Chronic liver disease	28 (3)	0	0	2 (2)	8 (3)	13 (3)	5 (2)	0	0
Other ^c	205 (20)	3 (100)	6 (17)	10 (12)	49 (18)	77 (20)	55 (22)	5 (31)	0
Respiratory support, No.	1300	2	46	108	351	487	287	18	1
Invasive mechanical ventilation	1150 (88)	2 (100)	37 (80)	87 (81)	315 (90)	449 (92)	246 (86)	14 (78)	0
Noninvasive ventilation	137 (11)	0	8 (17)	16 (15)	33 (9)	36 (7)	39 (14)	4 (22)	1 (100)
Oxygen mask	13 (1)	0	1 (2)	5 (5)	3 (1)	2 (<1)	2 (1)	0	0
PEEP, cm H ₂ O									
No.	1017	2	33	81	278	377	234	11	1
Median (IQR)	14 (12-16)	9.5 (5-14)	14 (10-15)	14 (12-15)	14 (12-15)	14 (12-16)	14 (12-15)	12 (8-15)	10
F _{IO₂} , %									
No.	999	2	31	81	270	375	228	11	1
Median (IQR)	70 (50-80)	40 (30-50)	60 (50-70)	60 (50-80)	65 (50-80)	70 (55-80)	70 (50-80)	60 (50-90)	60
P _{aO₂} /F _{IO₂} ratio									
No.	781	2	26	58	213	306	169	7	0
Median (IQR)	160 (114-220)	259 (195-323)	201.5 (123-248)	168.5 (112-260)	163 (120-230)	152.5 (110-213)	163 (120-205)	150 (86-250)	NA
Prone position, No./total (%)	240/875 (27)	0/2	3/25 (12)	24/71 (34)	70/247 (28)	90/337 (27)	51/187 (27)	2/6 (33)	NA
ECMO, No./total (%)	5/498 (1)	NA	0/15	0/42	2/149 (1)	3/193 (2)	0/95	0/4	NA

Abbreviations: COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; F_{IO₂}, Fraction of inspired oxygen; ICU, intensive care unit; IQR, interquartile range; NA, not applicable; P_{aO₂}, arterial partial pressure of oxygen; PEEP, positive end-expiratory pressure.
^a Cardiovascular disease includes cardiomyopathy and heart failure.

^b Malignancy includes active neoplasia and neoplasia in remission.
^c Other includes anemia, asthma, inflammatory bowel disease, epilepsy, chronic respiratory insufficiency, endocrine disorders, connective tissue diseases, neurologic disorders, chronic pancreatitis, immunocompromise, and organ transplant.

Mann-Whitney rank sum test was used to compare non-parametric continuous variables between median age subgroups and patients with or without hypertension. χ^2 or Fisher exact test was used for categorical variables as appropriate. All statistical tests were 2-tailed, and statistical significance was defined as $P < .05$. Analyses were performed using SAS 9.4. The analyses have not been adjusted for multiple comparisons, and given the possibility of type I error, the findings should be interpreted as exploratory and descriptive.

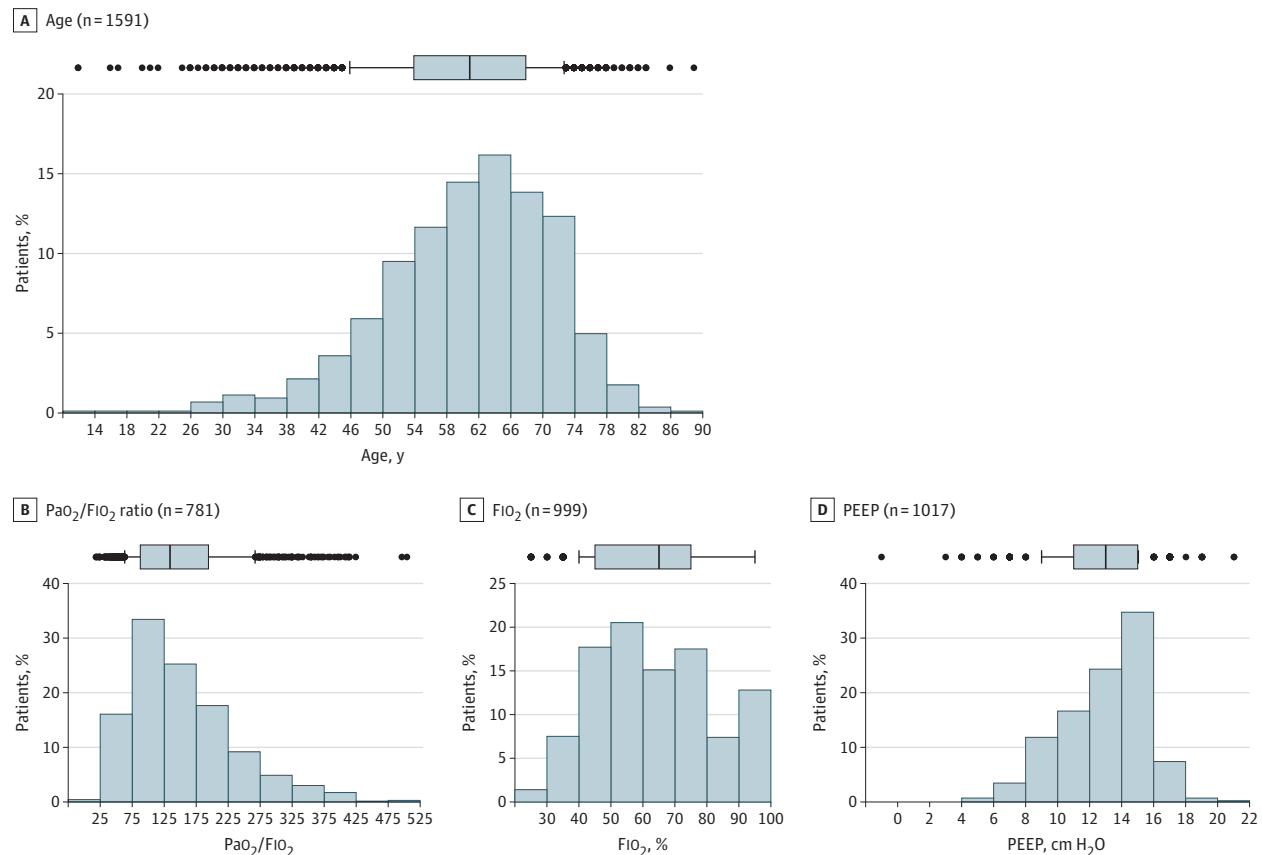
Results

From February 20 to March 18, 2020, a total of 1694 patients with suspected or confirmed COVID-19 were referred to the co-

ordinating center. A total of 77 patients had pending and 24 patients had negative test results for SARS-CoV-2; for 2 patients, data were not available. Thus, data from 1591 critically ill patients with laboratory-confirmed COVID-19 were included in this report.

Table 1 shows the demographic and clinical characteristics of the patients. Overall, 82% (1304 of 1591 patients [95% CI, 79.98%-83.82%]) were male, similarly distributed among all age groups. The median age was 63 years (IQR, 56-70) (range, 14-91 years [95% CI, 63-64]) among 1591 patients. A total of 363 patients (23% [95% CI, 21%-25%]) were aged 71 years and older, and 203 (13% [95% CI, 11%-15%]) were younger than 51 years. In this report, median age was used to stratify patients as younger (age \leq 63 years) or older (age \geq 64 years).

Figure. Distribution of Age and Respiratory Measures on Admission to a COVID-19 Intensive Care Unit



COVID-19 indicates coronavirus disease 2019; PEEP, positive end-expiratory pressure; FiO₂, fraction of inspired oxygen; PaO₂, arterial partial pressure of oxygen. Boxplots show the 25th, 50th, and 75th percentiles (box); 10th and 90th percentiles (whiskers); and outlying points (circles).

Sixty-eight percent (95% CI, 65%-71%) of patients had at least 1 comorbidity. Hypertension was the most common comorbidity, affecting 509 (49% [95% CI, 46%-52%]) of 1043 patients with available data. The second most common comorbidities were cardiovascular disease (223 patients, 21% [95% CI, 19%-24%]) and hypercholesterolemia (188 patients, 18% [95% CI, 16%-20%]). Only 42 patients (4% [95% CI, 3%-5%]) had a history of chronic obstructive pulmonary disease. All the patients older than 80 years had at least 1 comorbidity, and 496 of 650 patients (76% [95% CI, 73%-80%]) older than 60 years had at least 1 comorbidity.

Among 1300 patients with available respiratory support data, 1287 (99% [95% CI, 98%-99%]) who were admitted to the ICU needed invasive or noninvasive respiratory support. A total of 1150 patients (88% [95% CI, 87%-90%]) required endotracheal intubation and mechanical ventilation, and 137 patients (11% [95% CI, 9%-12%]) were treated with noninvasive ventilation. Invasive mechanical ventilation was used in 565 (88% [95% CI, 85%-90%]) of the 645 younger patients with available data and in 585 (89% [95% CI, 87%-92%]) of the 655 older patients (difference, -2% [95% CI, -5% to 2%]; *P* = .33). Noninvasive ventilation was used in 70 (11% [95% CI, 9%-14%]) of the 645 younger patients with available data and in

67 (10% [95% CI, 8%-13%]) of the 655 older patients (difference, -1% [95% CI, -4% to 3%]; *P* = .71).

The median (IQR) positive end-expiratory pressure (PEEP) was 14 (12-16) cm H₂O (n = 1017). PEEP levels as high as 22 cm H₂O were applied. Among a total of 999 patients with available data, 887 (89% [95% CI, 87%-91%]) required a fraction of inspired oxygen (FiO₂) of at least 50%, and 120 (12% [95% CI, 10%-14%]) required 100% FiO₂. The median PaO₂/FiO₂ ratio was 160 (IQR, 114-220 [95% CI, 152-166]) (n = 781). PEEP level grouped by median age was not significantly different (median, 14 [IQR, 12-15] cm H₂O in the group aged ≤63 years vs 14 cm H₂O [IQR, 12-16] in the group aged ≥64 years; median difference, 0 [95% CI, 0-0]; *P* = .94). FiO₂ was higher in older patients (median, 60% [IQR, 50%-80%] in the group aged ≤63 years vs 70% [IQR, 50%-80%] in the group aged ≥64 years; median difference, -10% [95% CI, -14% to -6%]; *P* = .006). PaO₂/FiO₂ was higher in the younger patients (163.5 [IQR, 120-230] in the group aged ≤63 years vs 156 [IQR, 110-205] in the group aged ≥64 years; median difference, 7 [95% CI, -8 to 22]; *P* = .02).

The **Figure** shows distribution of age, PEEP, FiO₂, and PaO₂/FiO₂. At admission, 240 of 875 patients (27% [95% CI, 25%-31%]) were treated with prone ventilation and 5 of 498

Table 2. Patient Disposition From COVID-Only Intensive Care Units (ICUs), Total and Stratified by History of Hypertension

	Patients by age, y, No. (%)								
	All (N = 1591)	0-20 (n = 4)	21-40 (n = 56)	41-50 (n = 143)	51-60 (n = 427)	61-70 (n = 598)	71-80 (n = 341)	81-90 (n = 21)	91-100 (n = 1)
Overall									
Outcome, No. with data	1581	2	56	142	423	596	340	21	1
Died in ICU	405 (26)	0	4 (7)	16 (11)	63 (15)	174 (29)	136 (40)	11 (52)	1 (100)
Discharged from ICU	256 (16)	0	20 (36)	35 (25)	90 (21)	69 (12)	40 (12)	2 (10)	0
Still in ICU as of 3/25/2020 ^a	920 (58)	2 (100)	32 (57)	91 (64)	270 (64)	353 (59)	164 (48)	8 (38)	0
Patients with hypertension^b									
No.	509	0	4 (<1)	21 (4)	121 (24)	195 (38)	156 (31)	12 (2)	0
Outcome									
Died in ICU	195 (38)	0	0	4 (19)	24 (20)	82 (42)	78 (50)	7 (58)	0
Discharged from ICU	84 (16)	0	1 (25)	8 (38)	26 (21)	25 (13)	23 (15)	1 (8)	0
Still in ICU as of 3/25/2020 ^a	230 (58)	0	3 (75)	9 (43)	71 (59)	88 (45)	55 (35)	4 (33)	0
Patients without hypertension^b									
No.	526	1 (<1)	31 (6)	60 (11)	148 (28)	184 (35)	97 (18)	4 (1)	1 (<1)
Outcome									
Died in ICU	114 (22)	0	3 (10)	3 (5)	21 (14)	43 (23)	40 (41)	3 (75)	1 (100)
Discharged from ICU	128 (24)	0	17 (55)	19 (32)	47 (32)	33 (18)	12 (12)	0	0
Still in ICU as of 3/25/2020 ^a	284 (54)	1 (100)	11 (35)	38 (63)	80 (54)	108 (59)	45 (46)	1 (25)	0

^a Patients were admitted between 2/20/2020 and 3/18/2020, with follow-up through 3/25/2020.

^b Hypertension status for those with outcome data was available for 1035 patients; hypertension status overall was available for 1043 patients.

(1% [95% CI, 0.3%-2%]) required extracorporeal membrane oxygenation (ECMO).

Compared with patients without hypertension (n = 526), patients with hypertension (n = 509) were significantly older (median age, 66 [IQR, 60-72] years vs 62 [IQR, 54-68] years; median difference, 4 [95% CI, 2-6]; $P < .001$) and had higher PEEP levels (median [IQR], 14 [12-16] vs 14 [12-15] cm H₂O; median difference, 0 [95% CI, 0-0]; $P = .003$) and lower PaO₂/FIO₂ (median, 146 [IQR, 105-214] vs 173 [IQR, 120-222]; median difference, -27 [95% CI, -42 to -12]; $P = .005$). However, there was no statistically significant difference in FIO₂ (median, 70 [IQR, 50-80] in the group with hypertension vs 60 [IQR, 50-80] in the group without hypertension; median difference, 10 [95% CI, 6-14]; $P = .05$).

Among the 1581 patients with ICU disposition data available as of March 25, 2020, 920 patients (58% [95% CI, 56%-61%]) were still in the ICU, 256 (16% [95% CI, 14%-18%]) had been discharged from the ICU, and 405 (26% [95% CI, 23%-28%]) had died in the ICU. ICU mortality was higher in those who were older (Table 2). ICU mortality was significantly lower in younger patients (≤ 63 years) compared with older patients (≥ 64 years) (15% vs 36%; difference, -21% [95% CI, -26% to -17%]; $P < .001$). The percentage of patients discharged from the ICU was significantly higher among younger patients compared with older patients (21% vs 11%; difference, 9% [95% CI, 6%-13%]; $P < .001$).

As of March 25, 2020, the median (IQR) length of stay in the ICU was 9 (6-13 [95% CI, 9-9]) days (n = 1591). Among patients still in the ICU (n = 920), the median (IQR) length of stay was 10 days (8-14 [95% CI, 10-11]); among patients discharged from the ICU (n = 256), the median length of stay was 8 days (5-12 [95% CI, 8-9]); and among patients who died

in the ICU (n = 405), the median length of stay was 7 (5-11 [95% CI, 7-8]) days.

The prevalence of hypertension was higher among patients who died in the ICU (63%, 195 of 309 patients) compared with those discharged from the ICU (40%, 84 of 212 patients) (difference, 23% [95% CI, 15%-32%]; $P < .001$) (Table 2).

Discussion

In this case series of critically ill patients admitted to ICUs in Lombardy, Italy, with laboratory-confirmed COVID-19 from February 20 to March 18, 2020, the majority were older men, a large proportion required mechanical ventilation and high levels of PEEP, and ICU mortality was 26%.

The majority of patients in this case series were admitted to the ICU because of acute hypoxemic respiratory failure that required respiratory support. Endotracheal intubation and invasive mechanical ventilation were needed in 88% of the patients, whereas only 11% could be managed with non-invasive ventilation. The need for invasive mechanical ventilation in this patient population was higher than that recently reported for other ICU patients: 71% (Washington State, US),⁸ 47% (Wuhan, China),⁹ 42% (Wuhan, China)¹⁰ and 30% (Wuhan, China; of note, half of these were treated with ECMO).⁵ The need for invasive mechanical ventilation in this critically ill Italian patient population was also higher compared with data reported by 2 Chinese studies from Wuhan, including all adult inpatients with laboratory-confirmed COVID-19 and patients hospitalized with severe disease (with rates of 17%¹¹ and 15%,⁴ respectively).

Conversely, in previously cited reports, noninvasive ventilation has been used much more frequently both inside and outside the ICU. For the ICU population, the use of noninvasive ventilation was reported as 19% (Washington State, US),⁸ 42% (Wuhan, China),⁹ 56% (Wuhan, China),¹⁰ and 62% (Wuhan, China; of note, this value included patients receiving high-flow nasal cannula).⁵ In previous reports, noninvasive ventilation was used in 14% of adult inpatients with laboratory-confirmed COVID-19¹¹ and 32% of hospitalized patients with severe laboratory-confirmed COVID-19.⁴

The higher rate of intubation in the current case series could be due to the severity of hypoxia (the median PaO_2/FiO_2 was 160), thus requiring high levels of PEEP. However, in one of the recent reports, the PaO_2/FiO_2 ratio upon ICU admission was even lower (136).⁹ Another potential explanation is that the majority of the patients requiring noninvasive ventilation in northern Italy were able to be managed outside the ICU and were thus not included in this report. Data regarding use of respiratory support were missing for some patients ($n = 291$, or 18.3%), which may also have influenced the rates of respiratory support reported in this study.

The population in this study consisted mostly of men (82%, which is higher than previously reported) and older individuals.^{4,9,10} The median age of the patients admitted to the ICU was 63 (IQR, 56-70) years old, which is the same as the median age of all the positive Italian cases with COVID-19¹² suggesting that, to date, older age alone is not a risk factor for admission to the ICU.

In this cohort of patients, 68% had at least 1 comorbidity, in line with that reported by Wang et al (72.2%),⁹ but much higher than in other reports.^{4,5} Similar to other previous reports,^{4,9} hypertension was the most common comorbidity, followed by cardiovascular disorders, hypercholesterolemia, and diabetes. Among older patients, comorbidities were common but a relatively small percentage of patients had pulmonary disease.

Previous reports described different mortality rates among patients requiring ICU admission, from 16%⁹ to 38%,⁵ 62%,¹⁰ 67%,⁸ and 78%.¹¹ In this study, at 5 weeks after the first admission in ICU, the majority of the patients (58%) were still in the ICU, 16% of the patients had been discharged from the ICU, and 26% had died in the ICU. The death rate was higher among those who were older. However, these outcome data should be interpreted with caution because most patients were still hospitalized in the ICU and the minimum follow-up was 7 days; in particular, the mortality rate could eventually be higher.

To the best of our knowledge, this is the largest case series of patients with COVID-19 and severe illness who required admission to the ICU. Available data indicate consid-

erable variability among different countries in both the proportion of severe cases of COVID-19 among those testing positive and in the proportion of severe cases of COVID-19 among those hospitalized with the disease. Among western countries, Italy seems to have a higher rate of severely ill patients and thus it is particularly relevant to report the demographic and clinical characteristics of this population upon admission to the ICU. The majority of the patients had moderate to severe respiratory failure and required invasive mechanical ventilation and high levels of PEEP.

These data could reflect a different organization of health care systems in the world. In Italy, for instance, noninvasive ventilation is delivered both in ICUs and in other hospital wards. The amount of intensive care support that has been provided by intensivists outside of previously existing ICUs and newly created ICUs was not quantified. While the final figures are not yet available, the number of level 2 ICU beds (providing high-flow oxygen, continuous positive airway pressure, or noninvasive ventilation) is estimated to be high with a large number of beds created to increase capacity to deal with severely ill patients during the COVID-19 outbreak. These data will be collected soon to provide a complete description of the critically ill patients with COVID-19.

These data also suggest that the need for organ support and intensive care, regardless of the reason, in the COVID-19 outbreak is substantial, with 9% of all positive cases being probably a conservative estimate. The volume of critically ill patients with COVID-19 infection that ICUs might be required to manage may be substantial, and adequate ICU capacity to deal with severe respiratory failure should be planned.

Limitations

This study has several limitations. First, this was a retrospective study, and data were acquired via telephone. Second, the critical nature of the Lombardy situation did not allow the coordinator to obtain more detailed information, such as baseline medication use. Third, the follow-up time is still relatively short compared with the course of the disease, and the reported mortality data and length of stay data reported in this study could change. Fourth, there were relatively large amounts of missing data for some outcomes.

Conclusions

In this case series of critically ill patients with laboratory-confirmed COVID-19 admitted to ICUs in Lombardy, Italy, the majority were older men, a large proportion required mechanical ventilation and high levels of PEEP, and ICU mortality was 26%.

ARTICLE INFORMATION

Accepted for Publication: March 28, 2020.

Published Online: April 6, 2020.
doi:10.1001/jama.2020.5394

Author Affiliations: Dipartimento di Anestesia, Rianimazione ed Emergenza-Urgenza, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy (Grasselli, Zanella, Pesenti); Department

of Pathophysiology and Transplantation, University of Milan, Milan, Italy (Grasselli, Zanella, Pesenti); Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy (Zangrillo, Scandroglio); Vita-Salute San Raffaele University Milan, Italy (Zangrillo); Department of Anesthesiology, Intensive Care and Emergency Medicine, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy (Antonelli); Università

Cattolica del Sacro Cuore, Rome, Italy (Antonelli); Università degli Studi dell'Insubria and Azienda Ospedaliera Ospedale di Circolo e Fondazione Macchi, Varese, Italy (Cabrini, Piatti); Department of Anesthesiology and Intensive Care, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Polo Universitario, University of Milan, Milan, Italy (Castelli); DG Welfare, Lombardy Region, Milan, Italy (Cereda); Department of Anesthesiology and

Intensive Care, ASST Cremona - Ospedale di Cremona, Cremona, Italy (Coluccello); School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy (Foti, Fumagalli); Department of Anesthesia and Intensive Care Medicine, ASST Monza, Monza, Italy (Foti); Department of Anaesthesia and Intensive Care Unit, IRCCS San Matteo Hospital and University of Pavia, Pavia, Italy (Iotti); Department of Anaesthesiology, Intensive Care and Perioperative Medicine, Spedali Civili University Hospital, Brescia, Italy (Latronico); Department of Medical and Surgical Specialties, Radiological Sciences, and Public Health, University of Brescia, Brescia, Italy (Latronico); Department of Anaesthesia and Intensive Care, ASST Papa Giovanni XXIII, Bergamo, Italy (Lorini); Bruno Kessler Foundation, Trento, Italy (Merler); Department of Anesthesia and Intensive Care, Fondazione Poliambulanza Hospital, Brescia, Italy (Natalini); Anesthesia and Intensive Care Medicine, Policlinico di Sant'Orsola, Alma Mater Studiorum University of Bologna, Bologna, Italy (Ranieri); Dipartimento Emergenza Urgenza, UOC Anestesia e Rianimazione, ASST, Lodi, Italy (Storti); Department of Anaesthesia and Intensive Care Medicine, Humanitas Clinical and Research Centre-IRCCS, Rozzano, Milan, Italy (Ceconi); Humanitas University, Milan, Italy (Ceconi).

Author Contributions: Dr Zanella had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Drs Grasselli and Zangrillo equally contributed to this work.

Concept and design: Ceconi, Grasselli, Zangrillo, Zanella, Foti, Ranieri, Storti, Pesenti.

Acquisition, analysis, or interpretation of data: Ceconi, Grasselli, Zanella, Antonelli, Cabrini, Castelli, Cereda, Colucello, Foti, Fumagalli, Iotti, Latronico, Lorini, Merler, Natalini, Piatti, Ranieri, Scandroglio, Storti, Pesenti.

Drafting of the manuscript: Ceconi, Grasselli, Zanella, Castelli, Cereda, Fumagalli, Lorini, Piatti, Ranieri, Storti.

Critical revision of the manuscript for important intellectual content: Ceconi, Grasselli, Zangrillo, Zanella, Antonelli, Cabrini, Colucello, Foti, Iotti, Latronico, Merler, Natalini, Ranieri, Scandroglio, Storti, Pesenti.

Statistical analysis: Zanella, Cereda.

Administrative, technical, or material support: Zangrillo, Lorini.

Supervision: Ceconi, Grasselli, Antonelli, Cabrini, Colucello, Foti, Latronico, Ranieri, Storti, Pesenti.

Conflict of Interest Disclosures: Dr Ceconi reported personal fees from Edwards Lifesciences, from Directed Systems, and from Cheetah Medical outside the submitted work. Dr Grasselli reported personal fees and nonfinancial support from Getinge and from Biotest, personal fees from Thermofisher, grants and personal fees from Fisher&Paykel, and personal fees from Draeger Medical outside the submitted work. Dr Iotti reported personal fees from Hamilton Medical, from Getinge Italia, from Eurosets, from Intersurgical, and from Burke & Burke outside the submitted work. Dr Pesenti reported personal fees from Maquet, from Novalung/Xenios, from Baxter, and from Boehringer Ingelheim outside the submitted work. No other disclosures were reported.

Funding/Support: This study was supported in part by institutional funding (Ricerca corrente

2020) of the Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.

Role of the Funder/Sponsor: The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

COVID-19 Lombardy ICU Network: Adriana Nailescu, MD, ASST Lodi-Ospedale Maggiore di Lodi, Lodi (Italy); Alberto Corona, MD, Ospedale di Valle Camonica Esine, ASST Vallecamonica, Brescia (Italy); Alberto Zangrillo, MD, IRCCS San Raffaele Scientific Institute, Milan, Italy and Vita-Salute San Raffaele University Milan, Italy; Alessandro Protti, MD, Humanitas Research Hospital, Milan, Italy; Andrea Albertin, MD, "San Giuseppe" Hospital, Multimedica Group, Milan (Italy); Andrea Forastieri Molinari, MD, ASST Lecco - Ospedale di Lecco, Lecco (Italy); Andrea Lombardo, MD, ASST Lariana - Ospedale Sant'Anna, Como (Italy); Angelo Pezzi, MD, ASST Nord Milano - Ospedale Edoardo Bassini, Cinisello Balsamo (Italy); Annalisa Benini, MD, ASST Monza - Ospedale San Gerardo, Monza (Italy); Anna Mara Scandroglio, MD, IRCCS San Raffaele Scientific Institute, Milan, Italy; Annalisa Malara, MD, ASST Lodi - Ospedale Maggiore di Lodi, Lodi (Italy); Antonio Castelli, MD, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, University of Milan, Milan (Italy); Antonio Coluccello, MD, ASST Cremona - Ospedale di Cremona, Cremona (Italy); Antonio Micucci, MD, Hospital "Sant'Antonio Abate" of Cantù, ASST Lariana, Como; Antonio Pesenti, MD, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli studi di Milano, Milano, Italy; Antonello Sala, MD, ASST Vimercate - Ospedale di Vimercate, Vimercate (Italy); Armando Alborghetti, MD, Policlinico San Pietro - Ponte San Pietro (Italy); Benvenuto Antonini, MD, ASST Garda - Ospedale di Manerbio, Manerbio (Italy); Carlo Capra, MD, ASST Laghi, Ospedale di Circolo e Fondazione Macchi; Carmine Troiano, MD, ASST Crema - Ospedale Maggiore di Crema, Crema (Italy); Claudio Roscitano, MD, Humanitas Gavazzeni, Bergamo (Italy); Danilo Radrizzani, MD, ASST Ovest Milanese - Ospedale Nuovo di Legnano, Legnano (Italy); Davide Chiumello, MD, ASST Santi Paolo e Carlo - Ospedale San Paolo, Milan (Italy); Davide Coppini, MD, ASST Garda - Ospedale Civile di "La Memoria", Gavardo (Italy); Davide Guzzon, MD, ASST Lecco - Ospedale di Merate, Merate (Italy); Elena Costantini, MD, Humanitas Research Hospital, Milan; Elena Malpetti, MD, Fondazione Poliambulanza Istituto Ospedaliero, Brescia (Italy); Elena Zoia, Children's Hospital Vittore Buzzi, ASST FBF Sacco, Milan (Italy); Emanuele Catena, MD, ASST Fatebenefratelli - Ospedale Sacco, Milan (Italy); Emiliano Agosteo, MD, Clinica "San Carlo" Paderno Dugnano, Milano (Italy); Enrico Barbara, MD, Humanitas Mater Domini Hospital, Castellanza, Varese, Italy; Enrico Beretta, MD, ATS Montagna - Ospedale "Eugenio Morelli" di Sondalo, Sondalo (Italy); Enrico Boselli, MD, ASST Rhodense - Presidio ospedaliero Garbagnate Milanese (Italy); Enrico Storti, MD, ASST Lodi - Ospedale Maggiore di Lodi, odi (Italy); Fabiola Harizay, MD, ASST Cremona - Ospedale di Cremona, Cremona (Italy); Federica Della Mura, MD, ASST Melegnano - Ospedale di Vizzolo Predabissi, Melegnano (Italy); Ferdinando Luca Lorini, ASST Papa Giovanni XXIII, Bergamo, Italy; Francesco Donato Sigurtà, MD, Istituto di Cura "Città di Pavia", Pavia (Italy); Francesco Marino, MD,

Clinical Institute Betato Matteo, Vigevano, Pavia (Italy); Francesco Mojoli, Department of Intensive Medicine, I.R.C.C.S. San Matteo Hospital; Department of Clinical surgical, Pediatric and Diagnostic Sciences, University of Pavia, Italy; Frank Rasulo, MD, ASST Spedali Civili, Brescia (Italy); Giacomo Grasselli, MD, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli studi di Milano, Milano, Italy; Giampaolo Casella, Grande Ospedale Metropolitano Niguarda, Milan, Italy; Gianluca De Filippi, MD, ASST Rhodense - Presidio ospedaliero Garbagnate Milanese (Italy); Gianpaolo Castelli, MD, ASST Mantova - Ospedale Carlo Poma, Mantova (Italy); Giorgio Aldegheri, MD, IRCCS Multimedica, Sesto San Giovanni (Italy); Giorgio Gallio, MD, ASST Vimercate - Ospedale di Vimercate, Vimercate (Italy); Giorgio Iotti, MD, Fondazione IRCCS Policlinico San Matteo, Pavia (Italy); Giovanni Albano, MD, Humanitas Gavazzeni, Bergamo (Italy); Giovanni Landoni, MD, IRCCS Ospedale San Raffaele Scientific Institute, Milan (Italy); Giovanni Marino, MD, ASST Melegnano - Ospedale di Vizzolo Predabissi, Melegnano (Italy); Giovanni Vitale, MD, Policlinico San Marco, Zingonia (Italy); Giovanni Battista Perego, MD, Istituto Auxologico "San Luca", Milano (Italy); Giulia Evasi, MD, ASST Lecco - Ospedale di Lecco, Lecco (Italy); Giuseppe Citerio, MD, Hospital of Desio, ASST Monza, Monza (Italy); Giuseppe Foti, MD, ASST Monza - Ospedale San Gerardo, Monza (Italy); Giuseppe Natalini, MD, Fondazione Poliambulanza Istituto Ospedaliero, Brescia (Italy); Giuseppe Sala, MD, Istituto Clinico Città Studi, Milano (Italy); Guido Merli, MD, ASST Crema - Ospedale Maggiore di Crema, Crema (Italy); Ilaria Sforzini, MD, ASST Pavia - Ospedale Civile di Voghera, Voghera (Italy); Leonardo Bianciardi, MD, Hospital of Pieve di Coriano, ASST Mantova, Mantova (Italy); Livio Carnevale, MD, ASST Pavia - Ospedale di Vigevano, Vigevano (Italy); Lorenzo Grazioli, MD, ASST Papa Giovanni XXIII, Bergamo (Italy); Luca Cabrini, MD, Ospedale di Circolo e Fondazione Macchi, Varese (Italy); Luca Guatterri, MD, Ospedale "Sacra Famiglia" Fatebenefratelli, Erba (Italy); Luca Salvi, Centro Cardiologico Monzino, Milan (Italy); Marco Dei Poli, MD, IRCCS Policlinico San Donato, Milan (Italy); Marco Galletti, MD, Ospedale Valduce, Como (Italy); Marco Gemma, MD, Fatebenefratelli Hospital, ASST Fatebenefratelli Sacco; Marco Ranucci, MD, IRCCS Policlinico San Donato, Milan (Italy); Mario Riccio, MD, Istituti Ospitalieri di Cremona - C.no Ospedale Oglio Po, Casalmaggiore (Italy); Massimo Borelli, MD, Ospedale Treviglio - Caravaggio, Treviglio (Italy); Massimo Zambon, MD, ASST Melegnano-Martesana, Presidio di Cernusco sul Naviglio (Italy); Matteo Subert, MD, Hospital of Melzo, ASST Melegnano Martesana, Milan (Italy); Maurizio Ceconi, MD, Humanitas Research Hospital, Milan (Italy); Maurizio Giovanni Mazzoni, MD, Humanitas Gavazzeni, Bergamo (Italy); Maurizio Raimondi, MD, ASST Pavia - Ospedale Civile di Voghera, Voghera (Italy); Mauro Panigada, MD, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy; Mirko Belliato, Department of Intensive Medicine, I.R.C.C.S. San Matteo Hospital; Department of Clinical surgical, Pediatric and Diagnostic Sciences, University of Pavia, Italy; Nicola Bronzini, MD, Clinical Institute "Sant'Anna", Brescia; Nicola Latronico, MD, ASST Spedali Civili, Brescia (Italy); Nicola Petrucci, MD, ASST Garda - Ospedale di Desenzano d/G, Desenzano del Garda (Italy); Nicolangela Belgiorino,

MD, Istituto Clinico San Rocco, Ome (Italy); Paola Tagliabue, MD, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy; Paolo Cortellazzi, MD, Ospedale Città di Sesto San Giovanni, ASST Nord Milano, Milan (Italy); Paolo Gnesin, MD, ASST Franciacorta - Presidio Ospedaliero Mellino Mellini, Chiari (Italy); Paolo Grosso, MD, Policlinico di Monza, Monza (Italy); Paolo Gritti, MD, ASST Papa Giovanni XXIII, Bergamo (Italy); Paolo Perazzo, MD, IRCCS Orthopedic Institute Galeazzi, Scientific Direction, Milan (Italy); Paolo Severgnini, MD, ASST 7 Laghi, Ospedale di Circolo e Fondazione Macchi; Patrizia Ruggieri, MD, ASST Cremona - Ospedale di Cremona, Cremona (Italy); Pietro Sebastiano, MD, Istituto Clinico Città di Brescia - Istituti Ospedalieri Bresciani, Gruppo San Donato, Brescia (Italy); Remo Daniel Covello, ASST Valle Olona - Ospedale di Busto Arsizio, Busto Arsizio (Italy); Raquel Fernandez-Olmos, MD, Fondazione Poliambulanza Istituto Ospedaliero, Brescia (Italy); Roberto Fumagalli, MD, ASST Grande Ospedale Metropolitano Niguarda, Milan (Italy); Roberto Keim, MD, ASST Bergamo est - Ospedale "Bolognini", Seriate (Italy); Roberto Rona, MD, ASST Monza - Ospedale San Gerardo, Monza (Italy); Roberto Valsecchi, MD, General Hospital "Moriggia Pelascini" Gravedona, Como (Italy); Sergio Cattaneo, MD, ASST Spedali Civili, Brescia (Italy); Sergio Colombo, MD, IRCCS Ospedale San Raffaele Scientific Institute, Milan (Italy); Silvia Cirri, MD, Istituto Clinico Sant'Ambrogio, Milano (Italy); Stefano Bonazzi, MD, Hospital "M.O. Locatelli", Piario, ASST Bergamo Est, Bergamo (Italy); Stefano Greco, MD, ASST Valle Olona - Ospedale di Saronno, Saronno (Italy); Stefano Muttini, MD, ASST Santi Paolo e Carlo - Ospedale San Carlo, Milan (Italy); Thomas Langer, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy and School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy; Valentina Alaimo, MD, ASST Mantova - Ospedale Carlo Poma, Mantova (Italy); Uberto Viola, MD, Ospedale "San Pellegrino", Gruppo Mantova Salus, Mantova (Italy).

Additional Contributions: We thank Eleonora Carlesso, MS (Università degli Studi di Milan), for data management and statistical analysis, Serena Brusatori, MD (Università degli Studi di Milan) and Paolo Cadringer, MS (former Ospedale Maggiore Policlinico), for support in data management. We thank Chiara Paleari, MD (Università degli Studi di Milan), and Emanuela Cattaneo, MD (Università degli Studi di Milan), and Giuliana Fusetti, MA (Ospedale Maggiore Policlinico), and Luigia Scudeller, MD (Ospedale Maggiore Policlinico) for help in preparing the documents for the ethics committee. We thank Marina Leonardelli (Ospedale Maggiore Policlinico) and Patrizia Minunno (Ospedale Maggiore Policlinico) for administrative support.

We thank all the staff of the COVID-19 Lombardy ICU Network coordination: Anna Ribboni, retired MD, Lorenzo Chiaravalli, MD (former Ospedale San Gerardo, Monza), Barbara Marcora, retired MD, Barbara Antonelli, MD (Ospedale Maggiore Policlinico), Michele Battistin, MS (Ospedale Maggiore Policlinico), Lucio Caccamo, MD (Ospedale Maggiore Policlinico), Daniele Dondossola, MD (Ospedale Maggiore Policlinico), Luisa Napolitano, MD (Ospedale Maggiore Policlinico), Francesca Rossi, MD (Ospedale Maggiore Policlinico), Caterina Accardo, MD (Università degli Studi di Milan), Chiara Anzanello, MD (Università degli Studi di Milan), Elena Cadone Ughi, MD (Università degli Studi di Milan), Davide Calabretta, MD (Università degli Studi di Milan), Sebastiano Colombo, MD (Università degli Studi di Milan), Marianna Di Feliciantonio, MD (Università degli Studi di Milan), Gaetano Florio, MD (Università degli Studi di Milan), Giorgio Giudici, MD (Università degli Studi di Milan), Amedeo Guzzardella, MD (Università degli Studi di Milan), Alessia Kersik, MD (Università degli Studi di Milan), Chiara Minaudo, MD (Università degli Studi di Milan), Matilde Moro (Università degli Studi di Milan), Carolina Negro, MD (Università degli Studi di Milan), Carolina Perali, MD (Università degli Studi di Milan), Martina Ratti, MD (Università degli Studi di Milan), Serena Todaro (Università degli Studi di Milan), Alberto Tredese, MD (Università degli Studi di Milan), Clarissa Uslenghi (Università degli Studi di Milan), Valentina Vago (Università degli Studi di Milan), and Bianca Della Santa, MD (Humanitas University, Milan), Arianna Pieroni, MD (Humanitas University, Milan), Francesca Terenzi, MD (Humanitas University, Milan). We thank Marco Salmoiraghi, MD (DG Welfare, Regione Lombardia) and Aida Andreassi, MD (DG Welfare, Regione Lombardia) and all the staff of the DG Welfare, Regione Lombardia for logistical and organizational support. We thank all the health care staff of the COVID-19 Lombardy ICU Network. These individuals were not compensated for their role in the study.

REFERENCES

1. WHO Director-General's opening remarks at the media briefing on COVID-19: 11 March 2020. Published March 11, 2020. Accessed March 30, 2020. <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19--11-march-2020>
2. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an

emergency response. *JAMA*. Published online March 13, 2020. doi:10.1001/jama.2020.4031

3. Coronavirus COVID-19 global cases by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins. Updated March 30, 2020. Accessed March 30, 2020. <https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6>
4. Guan WJ, Ni ZY, Hu Y, et al; China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. Published online February 28, 2020. doi:10.1056/NEJMoa2002032
5. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497-506. doi:10.1016/S0140-6736(20)30183-5
6. Rhodes A, Ferdinande P, Flaatten H, Guidet B, Metnitz PG, Moreno RP. The variability of critical care bed numbers in Europe. *Intensive Care Med*. 2012;38(10):1647-1653. doi:10.1007/s00134-012-2627-8
7. WHO. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance, 25 January 2020. Published January 25, 2020. Accessed March 30, 2020. <https://apps.who.int/iris/handle/10665/330854>
8. Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA*. Published online March 19, 2020. doi:10.1001/jama.2020.4326
9. 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;323(11):1061-1069. doi:10.1001/jama.2020.1585
10. 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;S2213-2600(20)30079-5. Published online February 24, 2020. doi:10.1016/S2213-2600(20)30079-5
11. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062. doi:10.1016/S0140-6736(20)30566-3
12. Istituto Superiore di Sanità [Higher Institute of Health]. Integrated surveillance of COVID-19 in Italy. Published March 22, 2020. Accessed March 30, 2020. https://www.epicentro.iss.it/coronavirus/bollettino/Infografica_22marzo%20ENG.pdf