60-day survival of critically ill COVID-19 first comers

Corinna N. Lang (✉ corinna.nadine.lang@uniklinik-freiburg.de)
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

V. Zotzmann
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

B. Schmid
  Department of Emergency Medicine, University Hospital of Freiburg, Faculty of Medicine, University of
Freiburg, Freiburg, Germany

M. Berchtold-Herz
  Heart Center Freiburg University, Department of Cardiovascular Surgery, Faculty of Medicine, University
of Freiburg, Freiburg, Germany

S. Utzolino
  Department of General and Visceral Surgery, Medical Center, University of Freiburg, Freiburg, Germany

P.M. Biever
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

T. Pottgießer
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

D. Duerschmied
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

C. Bode
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

T. Wengenmayer
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

D.L. Staudacher
  Heart Center Freiburg University, Department of Cardiology and Angiology I, Faculty of Medicine,
University of Freiburg, Freiburg, Germany

Research Article

Abstract

Background: Germany reported sufficient intensive care unit (ICU) resources throughout the first wave of coronavirus disease 2019 (COVID-19). The treatment of critically ill COVID-19 patients without rationing may improve the outcome. We therefore analyzed resources allocated to critically ill COVID-19 patients and their outcomes.

Methods: Retrospectively, we enrolled SARS-CoV2 PCR positive patients with respiratory failure from 03/08/2020 to 04/08/2020 and followed until 05/28/2020 in the university hospital of Freiburg, Germany.

Results: Thirty-four COVID-19 patients were admitted to the ICU in the defined interval with medium age of 67±13 (31-86) years. 6/34 (17.6%) were female. All patients suffered from moderate or severe acute respiratory distress syndrome (ARDS), 91.2% of the patients were intubated and 23.5% required extracorporeal membrane oxygenation (ECMO). Proning was performed in 67.6%, renal replacement therapy (RRT) was required in 35.3%. 96% required more than 20 nursing hours per day. Mean ICU stay was 21±19 (1-81) days. 60-day survival of critically ill COVID-19 patients was 50.0% (17/34). Causes of death were multi-organ failure (52.9%), refractory ARDS (17.6%) and intracerebral hemorrhage (17.6%).

Conclusions: Treatment of critically ill COVID-19 patients is protracted and resource intense. In a context without resources shortage, 50% of critically ill COVID-19 survived up to 60 days.

Background

Severe acute respiratory coronavirus 2 (SARS-CoV-2) pandemic encountered southwestern Germany in March 2020, causing relevant case numbers of the virus-related pneumonia (COVID-19). Clinical courses of critically ill patients with COVID-19 were characterized in international cohorts with mortality rates between 50 and 88% (including ongoing treatment cohorts).(1–3) The overall case fatality rates vary internationally (1-12%). Recently, reported case fatality rates in Germany remain lower than in neighboring countries. There are no convincing explanations for this phenomenon, whereas only limited data is available for critically ill patients in Europe and their outcomes.(3,4)

Patients with severe pulmonary failure and adult respiratory distress syndrome (ARDS) are reported to require multiple organ replacement therapies, some of which have to be applied at the same time. As recently reported, severity of COVID-19 cases immensely increases the strain on staff and resources.(1)

This retrospective study analyzes the first cohort of patients on three intensive care units at a third-level treatment center in Freiburg, Germany. During the observation period the center never faced a shortage of human or technical resources for the treatment of those patients with ARDS caused by COVID-19. The

present study focuses on the necessary resources for the treatment, the complications, and hospital survival.

Methods

We enrolled critically ill patients in case of PCR-confirmed SARS-CoV-2 infection and intensive care unit (ICU) admission due to pulmonary failure caused by COVID-19 from 03/08/2020 (date of ICU admission of our first case) to 04/08/2020.

ARDS treatment

The ARDS treatment followed current guidelines and house-intern standard operating procedures for lung-protective ventilation, prone positioning and supportive therapies.(5) In case of hypoxia or hypercapnia in patients with lung-protective ventilation, ECMO was evaluated by an interdisciplinary team of at least one ECMO specialist, a registered nurses and a perfusionist following local standards.

Inclusion criteria

According to the local pandemic plan, COVID-19 patients were treated at different intensive care units (medical, and surgical). Patients were admitted to out hospital from the emergency room (ER), regular hospital wards, or from first and secondary treatment centers. Our center serves as a reference and referral center for ARDS and ECMO offering a 24/7 ECMO retrieval service. All patients with proven SARS-CoV2 infection and severe respiratory failure requiring ICU therapy were included in the present study. The PCR tests were carried out from nasopharyngeal swabs or tracheal secretion. Patients with high clinical probability of COVID-19 but negative virology testing were excluded.

Endpoint definition:

ARDS was classified according to the Berlin classification (6), Kidney injury according to the RIFLE definition. All patients dismissed home were considered 60-day survivors in regards to this study. The cause of death was determined by clinical judgment of at least two intensivists part of this research project.

Data management

The data collection was carried out till 05/28/2020. We extracted patient related data from our hospital data systems and documentation from transferring hospitals. The local ethics committee approved the study protocol (Ethik-Kommission der Albert-Ludwigs-Universität Freiburg file number 234/20). Hospital survival was defined as discharge from the ICU on a step-down unit / regular ward or hospital discharge. Non-survivors and ICU-survivors were compared with chi-square test and univariate ANOVA. Patients with ongoing therapies were excluded from testing differences. We performed analyses with SPSS, version 26 (IBM, NYC, USA) and Prism, version 8 (GraphPad, San Diego, USA) and a p-value of <0.05 was considered statistically significant

Results

Baseline characteristics and comorbidities

During the observation period, 34 COVID-19 patients with pulmonary failure were admitted and treated on the ICU. Medium age was 67±13 years, 6 (17.6%) were female.

The medical history of the patients comprised overweight (76.5%), hypertension (52.9%), diabetes (25.3%) and cardiac diseases (23.5% coronary artery disease, 17.6% valve operation or chronic heart failure heart). The number of patients with chronic respiratory precondition was low (Table 1).

Simplified Acute Physiology Score (SAPS) II score was significantly higher in non-survivors compared to survivors (50±7 vs. 42±14; p=0.037). No other significant differences in comorbidities were found.

Assessment of symptoms, vitals on admission, virologic findings, microbiological findings, the laboratory measures and imaging are presented in the supplemental material (Table S1).

ICU resources and management

Length of ICU treatment in non-survivors was 17±7 (2-72) days, patients discharged from ICU were treated 25±22 (1-81) days (Table 2). The dates of arrival, cumulative therapies and outcomes of individual patients are displayed in figure 1.

Half of our patients suffered from moderate, half of severe ARDS. Intubation was performed in 91.2% of the cases, prior to the intubation in 10 patients (29.4%) nasal high flow (NHF) and / or non-invasive ventilation (NIV) was applied.

Three patients (8.8%) were exclusively managed with NHF / NIV. On average, patients were on invasive mechanical ventilation (IMV) for 19±21 (0-79) days. Positive end-expiratory pressure (PEEP) levels were high during the three first treatment days on average 12.5±3 (7-18) mbar. Spontaneous breathing on the ventilator was performed in 73.5% in the first 24 hours. Weaning from the respirator was successfully completed in 12 cases before ICU discharge, 5 patients went to a weaning unit.

Veno-venous extracorporeal membrane oxygenation (ECMO) therapy was installed in 8/34 (23.5%) patients for 20±23 (2-75) days. Three patients were weaned from ECMO therapy. 2 patients died of refractory ARDS and 2 because of intracerebral hemorrhage during ECMO, one patient died with abdominal sepsis and bleeding during ECMO therapy.

Proning was performed in 67.6%. If proning was not indicated, alternative strategies were incomplete prone positioning (135°), pilot´s seat positioning or the use of a rotational bed. Thus, 88.2% of our patients underwent daily therapeutic positioning maneuvers.

Acute kidney injury was noticed in 85.3% of the patients, renal replacement therapy (RRT) was required in 35.3% of all cases. Due to vasoplegic or cardiogenic shock, non-survivors significantly more often

required vasopressor therapy (17/17 vs. 11/17; p=0.007) and transfusions (12/17 vs. 5/17; p=0.016).

The initial antiviral treatment followed house-intern expert consensus and was a combination of hydrochloroquine and lopinavir/ritonavir (70.6%) and later on a hydrochloroquine only treatment (23.5%). Five patients received tocilizumab (14.7%). Additional information is presented in the supplements (Table S2).

Resource intense multi-organ replacement ICU treatment was measured in nursing hours using Inpuls®-categories in 25 patients. A time investment of > 20 hours per day was necessary in 96.0% of our patients and required a 1:1 nurse-patient ratio. Additional information is presented in the supplements. The cumulative therapies are displayed in figure 2.

Outcomes and complications

At the end of the follow up, exactly half of our patients were dead, the other half was discharged from ICU, including 5 transferals to weaning units (4 in-house transferals). More than half of the survivors were able to be discharged home (58.8%), 2 went on a rehabilitation therapy without oxygen supply. On average the survival since admission was 60±8 days (51-81 days).

The clinical course was complicated by pneumothorax or pneumomediastinum in 6 (17.6%) cases. Furthermore, 5 (14.7%) patients exhibited non-fatal pulmonary embolism / thrombosis in segmental and sub-segmental lung arteries. Superinfections during treatment in 18 (52.9%) cases were dominated by *Serratia marcescens* (33.3%). *Aspergillus fumigatus* superinfection was detected in 2 (11.1%) patients (Table 3). Intracerebral hemorrhage was significantly more often recorded in non-survivors (p=0.015).

Nine (52.9%) patients died because of untreatable multi-organ failure as the main cause of death in the cohort. Three (21.4%) patients died because of refractory ARDS. Notably, 3/17 (17.6%) patients died of fatal intracerebral hemorrhage. Because of SARS-CoV-2 PCR positivity organ donation was impossible in these patients. Two (11.8%) patients did not continue therapy because of "do not resuscitate" (DNR) orders and received palliative treatment. No medical autopsies were carried out in this cohort (Table 3).

Discussion

We present a 60-day follow-up of our first critically ill COVID-19 patients due to pulmonary failure in southwestern Germany. The age and common comorbidities were similar to international cohorts.(1–3,7) In our cohort, 60-day survival was 50.0%. Importantly, the majority of our survivors were able to return into their former lives.

This is similar to the case-fatality rate of 49.0% reported for "critical cases" in a large Wuhan registry (8) and much lower than suggested by early reports in the COVID-19 pandemic for patients with severe pulmonary failure.(2,3) Importantly, we present data with a long follow-up. In other registries a very small number of patients actually could return to normal life.(2,3) Therefore, we can report a sounder estimate of prognosis of COVID-19 patients.

As Germany did not experience a shortage of ICU resources, it is not surprising that in our cohort, ICU therapy lasted longer than reported in other registries.(1,9) Also, more resources were allocated to patients in this registry including multiple organ replacement therapies – ECMO therapies (1) and renal replacement therapy was required more often than reported in other cohorts from Wuhan or New York.(1–3) Another German registry similar rates of ECMO and renal replacement therapy.(3) We are the first to report an estimate on the enormous amounts of nursing hours required for treating these patients.

As for cause of death, only 17.6% died from refractory respiratory failure. Data of 92 COVID-19 associated deaths states ARDS as the main complication followed by myocardial injury, liver and kidney injury and multiple organ failure.(10) In pandemic conditions, resource shortages might necessitate rapid decisions regarding futility compared to normal conditions. Survival rate in the present study is lower than described for a general ARDS population (60-day survival 68% (11)). When considering, that ARDS mortality is lower in tertiary hospitals than in hospitals of first and second treatment level (12), the high mortality found in this registry might suggest a significant case-fatality rate of COIVD-19 patients requiring ICU therapy. According to the SAPS II score, our cohort had a relatively high predicted risk of death (over 40%), which is higher than in cohorts characterized beforehand. Also, many patients treated on our ICU were transferred for severe pulmonary failure and ECMO evaluation. Therefore, considering the small patient numbers and the lack of a control group, we cannot compare mortality of COVID-19 patents with ARDS to other ARDS patients.

As stated by Klok et al. the incidence of thrombotic complications is up to 31% in COVID-19 patients on the ICU.(4) The notable rate of 14.7% non-fatal pulmonary artery thrombosis is in line with their findings. Further studies concentrated on autopsies and confirmed a high rate of thrombembolic events.(13) At the moment the underlying mechanism for the coagulopathy leading to pulmonary artery thrombosis and cerebral bleeding, which were leading causes of the complications in this cohort, is unknown. Nevertheless, the coagulopathic state in COVID-19 does not only seem to lead to thrombotic events as documented, but also to a relevant rate of bleedings. In the cohort five intracerebral hemorrhages occurred, three being fatal.

<u>Limitations:</u>

First, the case number is limited and the data has to be verified by larger cohorts and longer follow-up intervals. Second, the cohort is a selected one as the university hospital of Freiburg is a tertiary center. The center has a large number of patient allocations from primary or secondary treatment centers because of evaluation of ECMO therapy or limited resources in the other centers.

Conclusions

Caring for critically ill COVID-19 patients requires an immense amount of organ replacement therapies, nursing hours and ICU days. The 60-days survival is 50% in a German tertiary treatment center despite full resources. High mortality in COVID-19 might be disease-specific rather than caused by resource shortage.

List Of Abbreviations

ARDS, severe acute respiratory distress syndrome

BMI, body mass index

COVID-19, coronavirus disease 2019

DNR order, do not resuscitate order

ER, emergency room

ECMO, extracorporeal membrane oxygenation

ICU, intensive care unit

Inpuls®, Intensivpflege- und Leistungserfassungssystem (Inpuls®, Heidelberg, Germany)

IMV, invasive mechanical ventilation

NHF, nasal high flow

NIV, non-invasive ventilation

NYC, New York City

P insp, inspiratory pressure

P peak, measured peak pressure

RRT, renal replacement therapy

SAPS II score, simplified acute physiology score14

SARS-CoV-2, severe acute respiratory coronavirus 2

PEEP, positive end-expiratory pressure

TISS Score, therapeutic intervention scoring system 15

Declarations

Ethics approval and consent to participate: The local ethics committee approved the study protocol; verbal or written consent was deemed unnecessary (Ethik-Kommission der Albert-Ludwigs-Universität Freiburg im Breisgau 234/20).

References

1. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, u. a. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020;8(5):475–81.

2. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, u. a. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 22. April 2020;

3. Dreher M, Kersten A, Bickenbach J, Balfanz P, Hartmann B, Cornelissen C, u. a. The Characteristics of 50 Hospitalized COVID-19 Patients With and Without ARDS. Dtsch Ärztebl Int. März 2020;117(10):271–8.

4. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers D, Kant KM, u. a. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: An updated analysis. Thromb Res. 30. April 2020;

5. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, u. a. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). Intensive Care Med. 2020;46(5):854–87.

6. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, u. a. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 20. Juni 2012;307(23):2526–33.

7. Arentz M, Yim E, Klaff L, Lokhandwala S, Riedo FX, Chong M, u. a. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. JAMA. 28. April 2020;323(16):1612–4.

8. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 7. April 2020;323(13):1239–42.

9. Bhatraju PK, Ghassemieh BJ, Nichols M, Kim R, Jerome KR, Nalla AK, u. a. Covid-19 in Critically Ill Patients in the Seattle Region — Case Series. N Engl J Med [Internet]. 30. März 2020 [zitiert 29. Mai 2020]; Verfügbar unter: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7143164/

10. Yang F, Shi S, Zhu J, Shi J, Dai K, Chen X. Analysis of 92 deceased patients with COVID-19. J Med Virol. 15. April 2020;

11. Máca J, Jor O, Holub M, Sklienka P, Burša F, Burda M, u. a. Past and Present ARDS Mortality Rates: A Systematic Review. Respir Care. Januar 2017;62(1):113–22.

12. Raymondos K, Dirks T, Quintel M, Molitoris U, Ahrens J, Dieck T, u. a. Outcome of acute respiratory distress syndrome in university and non-university hospitals in Germany. Crit Care [Internet]. 30. Mai 2017 [zitiert 29. Mai 2020];21. Verfügbar unter: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5448143/

13. Wichmann D, Sperhake J-P, Lütgehetmann M, Steurer S, Edler C, Heinemann A, u. a. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. Ann Intern Med. 6. Mai 2020;

14. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA. 22. Dezember 1993;270(24):2957–63.

15. Cullen DJ, Civetta JM, Briggs BA, Ferrara LC. Therapeutic intervention scoring system: a method for quantitative comparison of patient care. Crit Care Med. April 1974;2(2):57–60.

Tables

Table 1: baseline characteristics[a]

	non-survivors (n=17)	survivors (n=17)	all patients (n=34)
number of patients	17 (50%)	17 (50%)	34
age, years	70±10 (49-86)	64±14 (31-84)	67±13 (31-86)
age range, years			
30-49	1 (5.8%)	2 (11.8%)	3 (8.8%)
50-59	2 (11.8%)	4 (23.5%)	6 (17.6%)
60-69	5 (29.4%)	4 (23.5%)	9 (26.5%)
70-79	6 (35.3%)	5 (29.4%)	11 (32.4%)
≥80	3 (17.6%)	2 (11.8%)	5 (14.7%)
sex			
female	4 (23.5%)	2 (11.8%)	6 (17.6%)
DNR order	4 (23.5%)	1 (5.9%)	5 (14.7%)
location of admisson			
home/ER	4 (23.5%)	1 (5.9%)	5 (14.7%)
internal hospital ward	6 (35.3%)	9 (52.9%)	15 (44.1%)
hospital transfer	7 (41.2%)	7 (41.2%)	14 (41.2%)
severity scores			
SAPS II score	**50±7 (42-70)**	**42±14 (15-69)**	46 ±12 (15-70)
TISS score	16±5 (10-28)	8±23 (0-31)	14.8±7 (0-31)
Inpuls®	5.5±0.5 (5-6)	5.2±0.8 (3-6)	5.3±0.7 (3-6)
ARDS			
mild	0	0	0
moderate	7 (41.2%)	9 (52.9%)	17 (50%)
severe	10 (58.8%)	7 (41.2%)	17 (50%)
comorbidites			
BMI (kg/m²)	29±5.5 (18-39)	28±3.7 (23-35)	28±4.6 (18-39)
≥26 kg/m²	13 (76.5%)	13 (76.5%)	26 (76.5%)
≥30 kg/m²	6 (35.3%)	5 (29.4%)	11 (32.4%)

hypertension	9 (52.9%)	9 (52.9%)	18 (52.9%)
diabetes	4 (23.5%)	8 (47.1%)	12 (35.3%)
HbA1c ≥ 6.5%	2 (11.8%)	8 (47.1%)	10 (29.4%)
coronary artery disease	5 (29.4%)	3 (17.6%)	8 (23.5%)
other cardiac disease[b]	5 (29.4%)	1 (5.9%)	6 (17.6%)
chronic respiratory disease	3 (17.6%)	2 (11.8%)	5 (14.7%)
tobacco smoking	6 (35.3%)	4 (23.5%)	10 (29.4%)
chronic kidney failure	6 (35.3%)	2 (11.8%)	8 (23.5%)
cancer	4 (23.5%)	4 (23.5%)	8 (23.5%)
immunosuppression	1 (5.9%)	3 (17.6%)	4 (11.8%)
frailty[c]	6 (35.3%)	1 (5.9%)	7 (20.6%)

Abbreviations: ICU, intensive care unit; BMI, body mass index (calculated in kilograms divided by height in meters squared); ER, emergency room; SAPS II score, Simplified Acute Physiology Score(14); TISS Score, Therapeutic Intervention Scoring System(15); Inpuls®, Intensivpflege- und Leistungserfassungssystem, intensive care nursing and activity recording system (Inpuls®, Heidelberg, Germany); ARDS = acute respiratory distress syndrome in accordance with the Berlin classification.(6)

If values of non-survivors and survivors were significantly different (p<0.05), we displayed them bold: SAPS II score p=0.037.

[a] Baseline characteristics are displayed for all patients, non-survivors and survivors. Data are n (%) or mean with standard deviation and range.

[b] Other cardiac condition = valve operation or chronic heart failure.

[c] Frailty was clinically judged.

Table 2: ICU resources and therapy[a]

	non-survivors (n=17)	survivors (n=17)	all patients (n=34)
length of ICU stay	17±17 (2-72)	25±22 (1-81)	21±19 (1-81)
ventilation			
NIV +/- IMV	5 (29.4%)	8 (47.1%)	13 (38.2%)
NHF +/- IMV	5 (29.4%)	8 (47.1%)	13 (38.2%)
intubation	17 (100%)	14 (82.4%)	31 (91.2%)
IMV days	16±18 (1-77)	22±23 (0-79)	19±21 (0-79)
weaned respirator	**2 (11.8%)**	**12 (70.6%)**	14 (41.2%)
day 1 (at controlled ventilation with highest PEEP level)			
lowest PaO2/FiO2[d]	109±42 (60-227)	129±19 (82-148)	114±33 (60-227)
FiO2 (%)	66±19 (40-100)	67±19 (40-100)	66±19 (40-100)
PEEP (mbar)	13±3 (7-18)	12±3 (7-17)	13±3 (7-18)
P peak (mbar)	29±5 (17-37)	27±5 (19-36)	28±5 (17-37)
compliance (ml/mbar)	51±30 (18-101)	50±28 (20-120)	51±28 (18-120)
resistance (mbar/sec)	12±3 (7-17)	12±4 (3-17)	12±4 (3-17)
tidal volume (ml)	490±140 (270-780)	430±120 (260-600)	460±130 (270-780)
first spontaneous breathing (> 10min.) in the first 24h hours	10 (58.8%)	15 (88.2%)	25 (73.5%)
-			
ECMO	5 (29.4%)	3 (17.6%)	8 (23.5%)
ECMO days	22±30 (2-75)	16±7 (8-20)	20±23 (2-75)
weaned ECMO	0/8	3/8	3 (8.8%)
therapeutic positioning			
overall therapeutic positioning maneuvers[b]	16 (94.1%)	14 (82.4%)	30 (88.2%)
proning	12 (70.6%)	11 (64.7%)	23 (67.6%)
rotational bed	1 (5.9%)	1 (5.9%)	2 (5.9%)
135°/pilot	3 (17.6%)	2 (11.8%)	5 (14.7%)
supine bedding	1 (5.9%)	3 (17.6%)	4 (11.8%)

acute kidney injury[c]	15 (88.2%)	14 (82.4%)	29 (85.3%)
renal replacement therapy	6 (35.3%)	6 (35.3%)	12 (35.3%)
overall vasopressor therapy[e]	**17 (100%)**	**11 (64.7%)**	28 (82.4%)
no vasopressors	0 (0%)	6 (35.3%)	6 (17.6%)
low vasopressors	4 (23.5%)	8 (47.1%)	12 (35.3%)
mod. vasopressors	4 (23.5%)	1 (5.9%)	5 (14.7%)
high vasopressors	9 (52.9%)	2 (11.8%)	11 (32.4%)
packed red blood cells	**12 (70.6%)**	**5 (29.4%)**	17 (50%)

Abbreviations: ICU, intensive care unit; IMV, invasive mechanical ventilation; NIV, non-invasive ventilation; NIV +/- IMV or NHF, nasal high flow +/- IMV: Non-invasive strategy (NIV or NHF) followed by intubation or as exclusive strategy during ICU treatment; PEEP, positive end-expiratory pressure; P insp, inspiratory pressure; P peak, measured peak pressure; ECMO, extracorporeal membrane oxygenation.

[a] ICU resources are displayed for all patients, non-survivors and survivors. Data are n (%) or mean with standard deviation and range.

[b] Therapeutic positioning maneuvers included complete proning, incomplete proning (135°), pilot´s seat positioning or the use of a rotational bed.

[c] Acute kidney injury is defined by the RIFLE definition.

If values of non-survivors and survivors were significantly different (p<0.05), we displayed them bold: weaned respirator p<0.0001; vasopressor therapy p=0.007; transfusion p=0.016;

Table 3: complications and outcomes

	non-survivor (n=17)	ICU-survivors (n=17)	all patients (n=34)
complications[a]			
respiratory superinfection (initially)	6 (35.3%)	5 (29.4%)	11 (32.4%)
respiratory superinfection (during treatment)	9 (52.9%)	9 (52.9%)	18 (52.9%)
Serratia marcescens	3 (17.6%)	3 (17.6%)	6 (17.6%)
Aspergillus fumigatus	2 (11.8%)	0 (0%)	2 (5.9%)
other superinfection[b]	4 (23.5%)	6 (35.3%)	10 (29.4%)
pneumothoraxes/pneumomediastinum	4 (23.5%)	2 (11.8%)	6 (17.6%)
pulmonary embolism	2 (11.8%)	3 (17.6%)	5 (14.7%)
Intracerebral hemorrhage	**5 (29.4%)**	**0 (0%)**	5 (14.7%)
delirium	1 (5.9%)	3 (17.6%)	4 (11.8%)
cause of death[c]			
refractory respiratory failure	3 (17.6%)		
refractory multiorgan failure	9 (52.9%)		
fatal intracerebral hemorrhage	3 (17.6%)		
withdrawal due to DNR order	2 (11.8%)		
discharge place			
weaning unit[d]		5 (29.4%)	
rehabilitation (without weaning)		2 (17.6%)	
home		10 (58.8%)	
survival since admission, days			60±8 (51-81)

[a] Complications are displayed for all patients, non-survivors and survivors. Data are n (%).

[b] Other superinfections included *Haemophilus influenza, Streptokokkus pneumonia, Staphylococcus aureus, Pseudomonas aeruginosa.*

If values of non-survivors and survivors were significantly different (p<0.05), we displayed them bold: intracerebral hemorrhage p=0.015

[c] Cause of death was analyzed for the 17 deceased patients according to clinical judgement. No medical autopsies were carried out. Data are n (%).

DNR order = do not resuscitate order.

[d] Transferals to weaning units included 4 transferals to an incorporated weaning unit and 1 transferal to an external weaning unit.
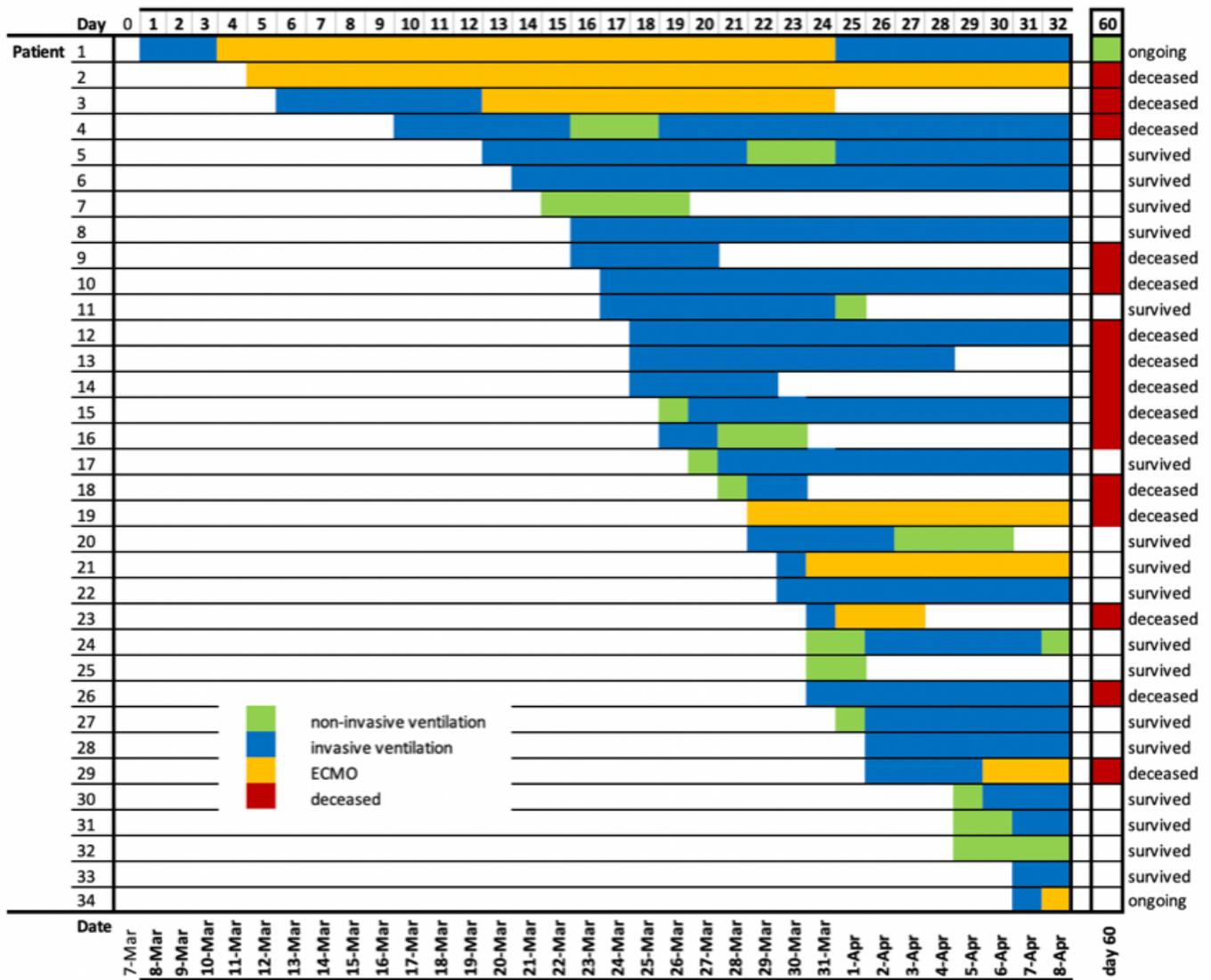
Figures

Figure 1

Clinical courses and outcomes of critically ill COVID-19 patients. Date of admission, clinical course and outcomes are depicted for each patient until 05/28/2020. Days with non-invasive ventilation (non-invasive oxygen support; green), invasive ventilation (blue) and additional extracorporeal membrane oxygenation (ECMO; orange) are displayed.
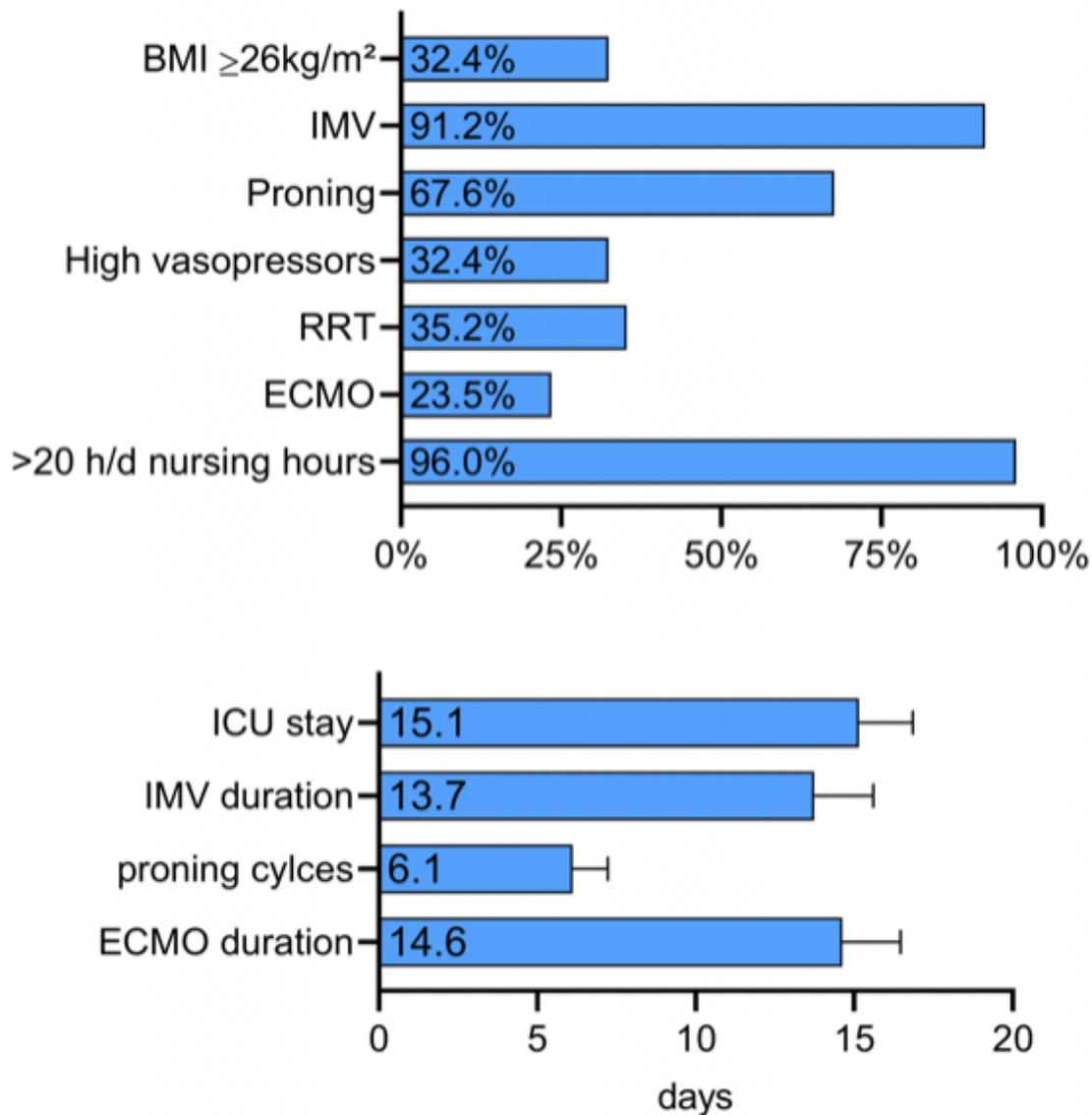
Figure 2

Intensive care resources and therapies in critically ill COVID-19 patients. Cumulative intensive care resources and therapies are displayed in %. The average of length of stay, invasive mechanical ventilation (IMV) days, proning cycles and days of extracorporeal membrane oxygenation (ECMO) therapy are displayed in days or cycles.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 4SupplementalmaterialCOVID19ICU.docx