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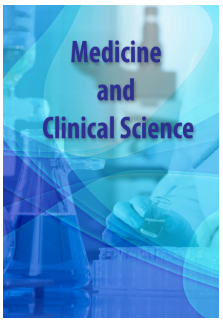

An observational study of invasive mechanically ventilated critically ill SARS-CoV-2 patients

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Abstract

Purpose: The coronavirus disease 2019 causes unique lung injury and multiorgan failure, even in young patients without predisposed comorbidity. Our aim was to use a treatment protocol of early intubation, light sedation, and restrictive fluid strategy, with the intention to reduce the length of stay (LOS) in the intensive care unit (ICU) and the mortality.

Methods: This retrospective single-centre descriptive study was performed from March 10 to May 4, 2020, covering our experiences in the treatment of COVID-19 patients with respiratory failure admitted to the ICU for mechanical ventilation. Early intubation was performed when the patient presented hypoxemia, which no longer responded to treatment with high oxygen concentration, showing excessive work-of-breathing and a paO_2/FiO_2 ratio <200mmHg. During mechanical ventilation, non/light sedation and restrictive fluid strategies were used.

Results: A total of 26 patients with suspected or confirmed COVID-19 were referred to our ICU. 10 patients had laboratory-confirmed RT-PCR for SARS-CoV-2 and were intubated due to hypoxemic respiratory failure with increased work-of-breathing. The median duration of mechanical ventilation was 5,5 days. All 10 patients were discharged from the ICU, the median length of stay in the ICU was 6,8 days. The median Richmond Agitation Scale Score was -3 on day 1 and declined to -1 on day 5. The median cumulative fluid balance upon discharge was -374 ml.

Conclusion: Early intubation, light or nonsedation and a restrictive fluid strategy was a suitable protocol in our limited population of mechanically ventilated, critically ill COVID-19 patients. All 10 patients survived their COVID-19 disease.

Introduction

The coronavirus 2019 (COVID-19) pandemic is characterized by different clinical presentations. Most patients are asymptomatic or present mild symptoms, but some experience severe illness with fatal outcome. In the early phase, the patients present symptoms of mild upper respiratory infection. Approximately 14% develop moderate respiratory insufficiency and about 5% become critically ill, with respiratory failure and multiorgan dysfunction or failure. In older patients, the presence of comorbidities and the development of complications such as acute renal failure are poor prognostics factors [1].

COVID-19 primarily injures the vascular endothelium and is initially characterized by hypoxemia and normal respiratory lung compliance. In many cases, the disease can stabilize at this stage without substantial deterioration. For some patients, the severity of the disease or the loss of response to oxygen treatment will result in persistent excessive work of breathing and fatigue which will in turn contribute to self-induced lung injury (P-SILI). If the process is not interrupted, the progressive lung damage can result in a clinical picture of Adult Respiratory Distress Syndrome (ARDS) [2].

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can be associated with hemodynamic instability, distributive hypovolemia, vasoplegia and myocardial depression. Given the disrupted vasoregulation and increased capillary permeability, an unplanned fluid administration can promote lung edema and iatrogenic damage. In addition, mechanical ventilation and pulmonary vascular dysfunction can further produce Right Ventricular (RV) failure, either by preload insufficiency or by excessive afterload. The dynamics of vascular pressure and prolonged mechanical ventilation may contribute to ventilator-induced injury (VILI) [3].

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Mechanically ventilated patients are often sedated to improve patient tolerance, ensure oxygenation and reduce discomfort. Previous clinical trials suggest an association between deep sedation strategy and increased time to extubation, prolonged length of stay (LOS) in the intensive care unit (ICU) and increased mortality [4,5]. Sedation protocols have changed dramatically, as guidelines now recommend protocols based on non or light-sedation strategies with the use of validated sedation scales such as the Richmond Agitation-Sedation Scale (RASS) [6]. However, deep sedation is required in patients with severe ARDS who receive neuromuscular blocking agents in order to ensure patients do not consciously experience paralysis [7].

Previous studies suggest that a conservative fluid resuscitation strategy could be beneficial for patients with ARDS [8,9]. Goal-directed strategies using pulse pressure variation (PPV), systolic pressure variation (SPV) and echocardiography as dynamic assessments of the fluid therapy, appear to be associated with reduced mechanical ventilation time, reduced LOS in the ICU and reduced mortality [8-11].

To avoid patient self-induced lung injury and to optimize the course of critical illness for COVID-19 patients, we designed a treatment protocol based on the principles of early intubation, light/nonsedation and conservative fluid management.

The aim of this study is to describe the demographic characteristics, coexisting conditions and outcomes among our unselected population of consecutive SARS-CoV2 patients admitted to the ICU.

Methods

The present study is a retrospective single-centre descriptive study, including patients with a positive SARS-CoV2 test, admitted to the intensive care unit at the Hospital of South-West Jutland, Denmark, from March 10 to May 4, 2020. Approval from the local ethical committee was obtained prior to data collection (S-20202000-73).

All patients with suspected SARS-CoV2 respiratory insufficiency were seen in the emergency department by a trained intensivist before referral to the ICU.

Patients initially treated with non-invasive oxygen therapy with subsequent life-threatening hypoxemia, no longer responding to high fractional inspired oxygen (FiO_2), with an arterial oxygen partial pressure (PaO_2) to FiO_2 ratio (P/F ratio) less than 200 mmHg, and showing increased respiratory distress (tachypnea greater than 30 per minute), were admitted for intubation and ventilator therapy in the critical care unit.

The rooms in the intensive care COVID-19 unit were equipped with negative air pressure [12]. The intubation protocol was based on propofol, fentanyl and rocuronium. The intubation was performed with video laryngoscopy. After intubation patients were sedated with continuous infusion of propofol and fentanyl or if possible kept awake with morphine bolus injections in order to accept the endotracheal tube. A light sedation strategy in order to achieve a RASS score of -2 was applied. To facilitate patient comfort with minimal sedation, continuous dexmedetomidine infusion was started early, and propofol/fentanyl infusion withdrawn if possible. Daily wake up assessments were made. If patients experienced dyssynchronous respiration despite deep sedation, continuous infusions of cisatracurium or bolus injections of rocuronium were administered [13].

Lung protective ventilation recommended in ARDS protocols was applied (4 to 8 mL/kg of predicted body weight (PBW)) with pressure-regulated volume control modus (PRVC) or adaptive support ventilation control [14]. The plateau pressure (Pplat) was kept at less than 30 cm H_2O. The initially positive end-expiratory pressure (PEEP) was 10 cm H_2O. Lung ultrasound examination was performed daily, focusing on B-lines, lung-sliding, consolidation and pleural fluid.

Most patients were monitored by pulse or systolic pressure variation (PPV/SPV). Transthoracic echocardiography (TTE) was performed in all patients on a daily basis to evaluate fluid management, define the right and left ventricular function and to present abnormalities such as diastolic dysfunction and acute pleural or pericardial effusion. A conservative approach to fluid resuscitation was taken guided by static and dynamic parameters of fluid responsiveness using point-of-care echocardiography.

The first choice of antibiotics was piperacillin-tazobactam and the second choice was meropenem. Oseltamivir was administered until a negative influenza PCR was obtained.

Within the first 24 hours upon admission APACHE II, SAPS II/III and SOFA scores were calculated on all ICU patients. SOFA score was calculated daily.

Statistical Analysis

Data analysis was performed with STATA 16 and distribution test was performed on all data. In case of non-parametric distribution, data has been presented in medians and interquartile range (IQR) otherwise in means and 95% confidence interval (CI).

Results

From March 10 to May 4 2020, a total of 26 patients with suspected or confirmed COVID-19 were referred to the ICU. 16 of the patients had negative test results for SARS-CoV-2. 10 critically ill patients had laboratory-confirmed RT-PCR for SARS-CoV-2, severe hypoxemia no longer responding to high FiO_2 administration, P/F ratio <200 and respiratory rate >30. All 10 patients were admitted to the ICU for intubation and ventilatory support.

Demographic and Clinical Characteristics

Demographic and clinical characteristics of the patients are summarized in Table 1. 90% (9 of 10 patients) were male, the median age was 67 years (IQR 48;71) and the median BMI was 27.1 (IQR 26;31.6). Chronic medical conditions were found in 8 (80%) of the patients. The most common comorbidities were hypertension in 6(60%), hypercholesterolemia in 4(40%) and cardiovascular disease in 3(30%) in the form of carotid artery stenosis and/or a history of stroke. None had diabetes mellitus. Six patients (60%) had more than one coexisting condition. Two patients had no coexisting conditions.

The most common symptoms were fever (10 of 10 patients), and coughing (9/10). 4(40%) patients had sputum production and subjective dyspnea was seen on 7(70%). The average duration of symptoms before hospitalisation was 11,5 days.

Median time in the emergency or medical COVID-19 department before referral to the ICU was 2,1 days (IQR: 0,9;3,5 min/max: 0,4/7,3).

Severity of illness is summarized in Table 2. Upon admission to the ICU, the median SOFA score was 9(IQR 7; 10), APACHE II score 20.5(IQR 17;27), SAPS II score 43(34; 50) and SAPS III 54.5(IQR 54;62).

Table 1. *Demographic data and clinical characteristics on day of admission to ICU*

Gender (Female)	9 (1)
Age	67 (48;71)
Body Mass Index (BMI), kg/m^2	27.1 (26;31.6)
Temperature	38.3 (IQR 38;38.5)
Comorbidity, N:	
Arterial hypertension	6
Cardiovascular disease	2
Hypercholesterolaemia	4
Obesity BMI > 30?	1
Asthma	1
Polymyalgia rheumatica	1
Malignancy	1
Chronic kidney disease	1
None	2
Time in the hospital before admission to ICU, days median (IQR)	2,1 (0,9, 3,5)

ICU: Intensive Care Unit; N: number of treated patients

Table 2. *Characteristics and Severity off Illness on day of admission to ICU*

	Median (IQR)
Sequential Organ Failure Assesment score (SOFA)	9 (7;10)
Acute Physiology and Chronic Health Evaluation II (APACHE II)	20,5 (17; 27)
Simplified Acute Physiology Score II (SAPS II)	43 (34; 50)
Simplified Acute Physiology Score III (SAPS III)	54,5 (54;62)
Respiratory rate	32 (30;38)
P/F ratio, mmHg	151 (133;163)
PaO_2, kpa	8,1 (7,6;8,8)
$PaCO_2$, kpa	4,1 (3,8-4,5)
pH	7,44 (7,39;7,49)
Heart Rate, breaths per minute	96 (82;104)
Systolic Blood Pressure, mmHg	122 (106; 135)
Diastolic Blood Pressure, mmHg	73 (65; 79)
Lymfocyte count x109L	1 (0,5;1,3)
Ferritin, ug/L	2394 (1447;2768)
C-Reactive Protein mg/L	245 (146;285)
D-dimer, mg/L	0,9 (0,5;2,6)

Microbiological results

SARS-CoV2 was confirmed in all patients by a real-time polymerase chain reaction (RT-PCR) assay of a pharyngeal swab or sputum. In one patient, the pharyngeal swab was negative for SARS-COV2, but due to sustained clinical suspicion a sputum test was done finding the patient positive for SARS-COV2. Five patients were tested by pharyngeal swabs alone and 5 with sputum as well as pharyngeal swabs.

Laboratory findings

The laboratory finding on admission are summarized in Table 2. 7 of 10 (70%) patients had lymphocytopenia and the median count was 1 (IQR: 0,5; 1,3). Median ferritin upon admission was 2394 ug/l (IQR: 1447; 2768) and the median C-reactive protein (CRP) on admission was 245 mg/l (IQR: 145,50; 284,5). Table 3 summarizes the laboratory findings in the patients during the first 5 days of the ICU course.

Radiologic findings

A chest radiograph was obtained in all patients upon ICU admission and showed bilateral pulmonary opacities in 9 (90%) patients.Computed tomographic scan of the chest was obtained in 8 patients (80 %).

Distribution of pulmonary lesions was predominantly bilateral (8 of 8) peripheral (6 of 8) and posterior (6 of 8). In all scans, extensive patchy bilateral ground glass opacities were found, as well consolidations. Crazy paving appearance was present in 4(40%). 7(70%) patients had vascular dilatation. Bronchiectasia was seen in 2(20%) patients and 3(30%) presented pulmonary nodules. No pleural effusions were seen.

Sedation

Clinical characteristics are summarized in Table 4. Median RASS score on the first day was -3(IQR -4;-3). On day 3, RASS score increased to -2 (IQR-3;-1) and on day 5 to -1 (IQR-3;0). On day 1, continuous infusion of sedative (propofol, fentanyl and/or dexmedetomidine) was administered in 9 (90%) of patients, while only 2(20%) of patients received continuous infusion after day 5. One patient received sevoflurane via AnaConDa (anesthetic conserving device) on days 6 to 7.

Continuous fentanyl infusion was administered in 6(60%) on day 1 and on day five 3(30%) patients received fentanyl infusion (median rate of 0,03 ug/kg/min.). Continuous propofol infusion was administered in 6(60 %) on day 1 (median rate 0,84 mg/kg/hour) and on day five 2(20%) patients received continuous propofol infusion (rate of 0,48 to 3,6 mg/kg/hour). Dexmedetomidine was administered in 7(70%) patients on day 1 and no patients received infusion after day 4. 1(10%) patient did not receive any kind of sedation.

Respiratory findings

Prior to intubation the median P/F ratio was 151 (IQR: 133; 163). Median saturation was 93% (IQR: 90%; 94%) and there was a median respiratory rate of 32 (IQR: 30; 38) (Table 2).

All patients were invasively mechanically ventilated and the median P/F ratio on day 1 was 178 (IQR, 157;193) Institution of mechanical ventilation was associated with improved P/F ratio, and reached 207 (IQR: 134;226) on day 5 (Table 4)

The median duration of mechanical ventilation was 5,5 days (IQR 5; 9. min./max.: 4/24) (Table 5).

One patient developed severe lung consolidation, low compliance and was placed in prone position on day 5. On day 7, because of a P/F ratio of 89 mmHg, the same patient was transferred in order to receive Extracorporeal Membrane Oxygenation (ECMO). The patient was later successfully extubated, discharged from our ICU and subsequently from the hospital after 28 days.

Table 3. *Laboratory parameters for the first 5 days after intubation, median (IQR)*

	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**
Neutrophil count, × 109 L	5,9 (4,3;8,5)	8,6 (4,6;9,6)	6,2 (4,6;7,0)	5,5 (4,5;5,9)	5,7 (4,4;7,3)
Lymphocyte count, × 109 L	0,6 (0,5;1,4)	0,7 (0,5;0,9)	0,9 (0,6;1,5)	0,9 (0,5;1,9)	0,9 (0,9;1,7)
Neutrophil/Lymphocytes NLR	8,7 (3.3;15.5)	7,7 (6;14,4)	9,2 (3.1;12.1)	6,4 (3.1;8.1)	4.7 (3.9;5.3)
Platelet count, × 109 L	165 (144;268)	171 (135;197)	221 (168;250)	237 (197;267)	256 (203;295)
D-dimer, mg/L	0.95 (0,5;2,6)	1,6 (1,0;1,7)	1.2 (0.8;1.6)	1.4 (1.2;3.2)	1.5 (0.9;3.2)
Prothrombin time, s/ INR	1.0 (0,9;1,1)	1,1 (1,1;1,2)	1,1 (1,0;1,2)	1,1 (1,1;1,1)	1,1 (1,1;1,2)
Albumin, g/L	35 (34;37)	31,5 (30;34,5)	31,5 (29;33,5)	29,5 (27,5;30,5)	27 (25;31)
Alanine aminotransferase, U/L	103 (46;124)	83 (28;174)	78 (34;147)	52 (42;114)	70 (46;128)
Billirubin mmol/l	11 (8;16)	9 (8;18)	9.5 (7;13)	10 (6;11)	8 (7;13)
Creatinine, µmol/L	100 (80;182)	100 (80;126)	103 (88;121)	96 (84;122)	107 (95;133)
Hypersensitive troponin I, pg/L	7.5 (5;20.5)	25 (3;30)	23 (6;33)	11 (6;60)	11 (2;36)
C-Reactive Protein, mg/L	194 (128;285)	212 (146;279)	197 (146;317)	178 (151;302)	150 (132;199)
Serum ferritin, ng/mL	1691 (1311;2789)	1614 (148;2684)	1530 (1171;4960)	1095 (991;3233)	1480 (767;3099)
Lactate dehydrogenase (LDH), U/l	331 (280;451)	355 (286;459)	388 (349;490)	366 (255;520)	345 (295;500)

Table 4. *Clinical characteristics for the first 5 days after intubation*

	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**
SOFA	8,5 (7;10)	7 (6;9)	6 (3;8)	5 (4;7,5)	5 (3;6)
Respiratory data					
Invasive Mechanical Ventilation, N	10	10	10	8	5
P/F ratio, median (IQR)	178 (157;193)	211 (182;234)	197 (160;231)	206 (156;234)	207 (134;226)
PEEP, cm H_2O, median (IQR)	13 (10;15)	12(12;14)	11 (9;14)	9,5 (8;15)	9 (7;12)
Tidal volume ml/kg PBW, median (IQR)	7.3 (6.6;7.9)	7,8 (7,3;8,11)	7,5 (6,88;8,33)	6,9 (6,4;7,4)	7,3 (6,8;8,1)
Peak pressure, cm H_2O, median (IQR)	23 (21;27)	22 (18;25)	20 (15;25)	17 (14;24)	17 (14;25)
Circulatory data					
Heart Rate, median (IQR)	93 (78;103)	82 (59;85)	81 (76;86)	82 (75;96)	79 (75;92)
MAP, mmHg, median (IQR)	89 (82;100)	80 (77;87)	79 (76;101)	89 (80;100)	82 (79;89)
CVP mmHg, median (IQR)	7.5 (3;22)	13 (7;13)	12 (6;14)	9 (7;17)	11 (3;15)
Fluid balance, ml, median (IQR)	117 (-489;1212)	-456 (-759;805)	-166 (-698;69)	-359 (-519;87)	-36 (-214;267)
Norephinephrine, N	5	3	2	2	2
ug/kg/min, median (IQR)	0,04 (0,01; 0,04)	0,03 (0,02;0,03)	0,02 (0,01;0,03)	0,02 (0,01; 0,02)	0,06 (0,03;0,09)
Sedation					
RASS	-3 (-4;-3)	-3 (-4;-2)	-2 (-3;-1)	-2 (-3;-1)	-1 (-3;0)
Sedated, N	9	9	8	5	2
Fentanyl inf., N	6	4	3	3	3
ug/kg/min., median (min;max)	0,014 (0,008;0,02)	0,03 (0,008;0,03)	0,03 (0,008;0,03)	0,03 (0,008;0,03)	0,03 (0,008;0,03)
Propofol inf. N	6	4	3	2	2
mg/kg/hour, median (min;max)	0,84 (0,24; 2,4)	0,51 (0,24;2,4)	0,54 (0,48;2,4)	1,44 (0,48;2,4)	2,04 (0,48;3,6)
Dexmedetomidine inf. N	7	6	4	3	
ug/kg/hour, median (min;max)	0,6 (0,6; 1,2)	0,6 (0,6; 1,2)	0,9 (0,6;1,2)	0,6 (0,6;1,2)	

Table 5. *Clinical outcomes*

Discharged from hospital and alive, N	10
Days in ICU, median (IQR)	6,8 (5,7; 9,8)
Days of invasive mechanical ventilation, median (IQR)	5,5 (5; 9)
Days of vasopressor support, median (IQR)	2 (1,3;2,5)
LOS in hospital, median (IQR)	17,5 (15; 19)
Alives at 90-days, N	10

N: Number of patients treated; ICU: Intensive Care Unit; LOS: Length of Stay

Circulatory findings

Critical care echocardiography performed upon admission, presented good Left Ventricular Ejection Fraction (LVEF), normal ventricular dimensions and normal RV function in all 10 patients. No abnormal mitral inflow or high left atrial pressure was recorded.

On day 1 the median left ventricular outflow tract velocity time integral (LVOT-VTI) was 20 cm/s (IQR: 19; 21). 8 patients (80%) presented transient hypotension related to intubation and sedation, requiring vasopressors to maintain mean pressure above 70 mmHg. Vasopressor therapy was needed for 48 hours in 5 patients (50%) and 2 patients (20%) required vasopressors for more than 48 hours. Fluid balance was conservative and the cumulative fluid balance upon discharge was a median of -374 ml (IQR: -2562;426).

Outcomes

All 10 patients were discharged from the ICU. The median length of stay in the ICU was 6,8 days (IQR: 5,7; 9,8). The median length of stay in hospital after discharge from the ICU was 6,5 days (IQR: 6,1; 8,0). The median total length of stay in hospital was 17,5 days (IQR: 15; 19). All patients survived. (Table 5).

Discussion

We present an unselected cohort of 10 mechanically ventilated patients, with moderate SARS-CoV2 respiratory insufficiency, admitted to the ICU. Upon referral to the ICU, the median P/F ratio was 151 (IQR: 133; 163) mmHg and the median RF was 32 (IQR: 30;38). SOFA score was 9 (IQR 7; 10). APACHE II score 20.5 (IQR 17; 27), and SAPS III 54.5 (IQR 54;62). To avoid SILI and to optimize the course of critical illness, a treatment protocol was designed using early intubation, light/nonsedation and conservative fluid management.

Non-Invasive Positive Pressure Ventilation (NIPPV) was not part of the respiratory protocol as the benefits presented in several ARDS studies remain unclear. Previous studies have not been able to report decreased mortality in patients treated with NIPPV for acute hypoxemic respiratory failure. NIPPV may exacerbate lung injury as a consequence of the remaining inspiratory stress. In moderate to severe ARDS or in the presence of other organ failure, NIPPV support presents a high risk of failure [14-17].

ARDS patients that underwent late intubation present markedly higher mortality rates compared to patients intubated early, even when severity of illness is the same [14,15]. Additionally, studies with ARDS patients indicate that it is feasible and important to identify patients with ARDS early, in part to facilitate earlier treatment [14-18]. The present respiratory protocol was designed considering the similarities between ARDS and SARS-CoV2.

Median duration of mechanical ventilation in the present study was 5,5 days (IQR: 5, 9) and the median LOS in the ICU was 6,8 days (IQR: 5,7; 9,8). Comparable results from the Intensive Care National Audit & Research Centre (ICNARC) in the UK reported a median LOS in ICU of 8 days (IQR:5,13) for non-survivors and 13 days (IQR 7;19) for survivors [19], while in the Lombardy Region of Italy the overall mean LOS was 9 days [20] and 14 days in Seattle, USA [21].

In severe ARDS, the need for patient ventilator synchrony can lead to a need for deeper sedation and neuromuscular blockade. In a cohort of critically ill patients identified shortly after the diagnosis of moderate to severe ARDS, the addition of early neuromuscular blockade with concomitant deep sedation did not lower the mortality when compared to a standard or routine approach to mechanical ventilation including lighter sedation strategies [22]. Sedation in order to achieve Low Tidal Volume Ventilation (LTVV) and avoid increased tidal volumes has been associated with adverse outcomes. Application of LTVV to all patients may be harmful [23].

Mechanical ventilation needs to be individualized to reduce the risk of ventilation-induced lung injury (VILI). Benefits of LTVV must be weighed against risks of pharmacologic measures needed to support LTVV.

Some studies have pointed that the use of benzodiazepines is associated with increased delirium, increased time of mechanical ventilation, and increased LOS in the ICU [3]. Recent randomized, placebo-controlled trials report that, in critically ill patients, continuous dexmedetomidine infusion decreases time to successful extubation and is associated with decreased risk of delirium [24-26]. The present treatment protocol was based on a light sedation strategy using low doses of continuous fentanyl and propofol infusion upon admission with early shift to continuous infusion of dexmedetomidine or bolus dosing of intravenous clonidine or morphin to optimize the patient comfort

Conservative fluid management is a key principle of ARDS management and in the FACTT trial, a restrictive fluid strategy increased ventilator-free days [9]. Similarly, the Sepsis Occurrence in Acutely Ill Patients (SOAP) reported positive fluid balance as an independent risk factor for increased mortality [27]. During SARS-Cov2, pulmonary capillary dysfunction is present with capillary leakage with the potential risk of pulmonary oedema and compromised oxygen delivery, making these patients more vulnerable to fluid resuscitation induced lung congestion. In this context, fluid infusion must be carefully monitored and administered in order to avoid fluid overload and to improve respiratory function, while carefully balanced against the risk of inducing acute organ hypoperfusion and renal impairment.

Limitations

Sample size is low, and the number of patients admitted to the ICU never exceeded the reorganized ICU capacity, therefore never stressing the system capability. In addition, this observational case series has no control group, and the findings may not be reproducible. As a result, the outcome should be interpreted with caution and the results are mostly intended to inspire rather than direct.

Conclusion

A treatment protocol of early intubation, light or

nonsedation and a restrictive fluid strategy was suitable in our limited population of 10 mechanically ventilated, critically ill adult patients diagnosed with SARS-CoV2. All 10 patients survived their COVID-19 disease. Further studies that might support this treatment protocol are needed.

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Declarations

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Availability of data and material: Anonymized raw data may be available upon request from the corresponding author if certain legal requirements are fulfilled by the receiving party

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Authors' contributions: All authors contributed to the study conception and design. All authors contributed substantially to data acquisition. All authors read and approved the final manuscript. Data analyses were performed by Jakob Oxlund. The first draft of the manuscript was written by Ricardo Sanchez Garcia and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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