Corticosteroids are associated with a decrease in mortality in a multicenter cohort of mechanically ventilated COVID-19 patients.

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INTRODUCTION

In late 2019, the virus responsible for Covid-19 was identified and called SARS-CoV-2. In China, 5% of COVID-19 patients were admitted in ICU, 2,3% were ventilated and 1,4% died. In early 2020, COVID-19 quickly spread in Europe and was responsible for high mortality. Since the start of the SARS-CoV-2 pandemic, the need for trials to assess the benefit of antiviral treatment, anti-cytokine drugs, convalescent plasma and hydroxychloroquine has been advocated by the world health organization. However, evidence of the efficacy of such strategies is still lacking.

OBJECTIVES

This observational multicentric study aimed to identify prognostic factors and therapies which could be valuable in mechanically ventilated COVID-19 patients for respiratory insufficiency.

METHODS

The method consisted in a multicentric retrospective analysis in all consecutive COVID-19 patients admitted to intensive care unit (ICU) and mechanically ventilated for more than 24 hours from March 1 to April 25, 2020, in 12 hospitals. The study protocol was approved by our Ethics Committee and, due to the retrospective nature of the data collected, no consent from the patient was required.
Admission date, age, sex, body mass index, underlying conditions, treatments, physiological values, use of vasopressors, renal replacement therapy (RRT) and extracorporeal membrane oxygenation (ECMO), duration of mechanical ventilation, length of ICU stay, ICU and ventilator-free days at day 42 were collected. The primary outcome was survival during the hospital stay. Secondary outcomes included use of vasopressors, RRT or ECMO, ICU and ventilator-free days at day 42, and evolution of the main physiological values between days 0 and 7. Simple and multiple time-dependent Cox regression models were used to assess the effects of factors on survival.

Table 1: Baseline characteristics and treatment, and association with survival in mechanically ventilated COVID-19 patients

Variable	All N=247 N (%) or median (Q1-Q3)	N Missing	Survivors N=136 N (%) or median (Q1-Q3)	Non-survivors N=111 N (%) or median (Q1-Q3)	Simple Cox p-value	Multiple Cox-adjusted p-value
Male sex	172 (69.6)	-	95 (69.9)	77 (69.4)	0.92	-
Age (years)	65 (57-72)	-	63 (55-69)	69 (60-77)	<0.0001	<0.0001
BMI (kg/m²)	29 (26-33)	14	29 (26-33)	30 (26-33)	0.88	-
Tobacco	21 (8.5)	1	8 (5.9)	13 (11.7)	0.05	0.07
Chronic kidney disease	26 (10.5)	-	8 (5.9)	18 (16.2)	0.0007	0.71
Diabetes	88 (35.8)	1	48 (35.6)	40 (36.0)	0.98	-
Hypertension	141 (57.1)	-	77 (56.6)	64 (57.7)	0.71	-
COPD	32 (13.0)	-	13 (9.6)	19 (17.1)	0.09	0.63
Cancer	11 (6.1)	66	5 (5.3)	6 (7.0)	0.74	-
Immunodeficiency	16 (6.5)	-	6 (4.4)	10 (9.0)	0.22	-
SOFA	6 (4-8)	-	5 (3-7)	7 (5-9)	<0.0001	0.27
PaO₂ (mmHg)	74 (62-90)	25	72 (62-90)	75 (64-91)	0.95	-
FiO₂ (%)	80 (60-90)	17	78 (60-90)	80 (65-100)	0.09	0.19
PaO₂ / FiO₂	103 (82-132)	25	108 (83-140)	96 (79-128)	0.83	-
Platelet count (10³/mm³)	207 (156-290)	-	209 (160-285)	207 (155-293)	0.79	-
Bilirubin (mg/dl)	0.64 (0.49-0.94)	1	0.67 (0.50-0.97)	0.60 (0.42-0.93)	0.42	-
Glasgow coma scale = 15	185 (77.4)	8	109 (82.6)	76 (71.0)	0.05	0.49
Creatinin (mg/dl)	1.00 (0.78-1.37)	1	0.91 (0.71-1.21)	1.20 (0.88-1.73)	<0.0001	<.0001
MAP < 70 mmHg	89 (36.0)	-	37 (27.2)	52 (46.8)	0.0004	0.01
Norepinephrin use	128 (51.8)	-	58 (42.6)	70 (63.1)	0.0021	0.41
Diuresis		1			<0.0001	0.25
≥ 500 ml/day	226 (91.9)		132 (97.1)	94 (85.5)		
200-500 ml/day	11 (4.5)		4 (2.9)	7 (6.4)		
≤ 200 ml/day	9 (3.7)		0 (0.0)	9 (8.2)		
CRP (mg/l)	175 (108-258)	-	172 (107-243)	179 (109-261)	0.33	-
D-dimer (ng/ml)*	1500 (868-3832)	84	1305 (843-3190)	1938 (990-4000)	0.13	-
Lymphocyte count (10³/mm³)*	0.80 (0.55-1.05)	2	0.84 (0.60-1.10)	0.75 (0.51-1.02)	0.06	0.02
Ferritin (mcg/l)*	1185 (582-3053)	163	1281 (578-2790)	1041 (587-3196)	0.43	-
Hydroxychloroquin use	225 (91.1)	-	128 (94.1)	97 (87.4)	0.02	0.46
Azythromycin use	107 (43.3)	-	59 (43.4)	48 (43.2)	0.82	-
Corticosteroids use	58 (23.5)	-	38 (27.9)	20 (18.0)	0.05	0.01

Abbreviations: BMI: body mass index; COPD: chronic obstructive pulmonary disease; SOFA: sequential organ failure assessment; MAP: mean arterial pressure; CRP: C- reactive protein. *Cox model on log-transformed values.

RESULTS

Out of 2003 patients hospitalized for SARS-CoV-2, 361 were admitted to the participating ICUs, 257 were ventilated for more than 24 hours and 247 were included in the study. The length of stay in ICU was 21 (12-32) days, the median survival time was 82 days, and the mortality rate was 45%. Corticosteroid therapy was started in 58 (23%) patients between days 0 and 7 of ICU admission and 225 (91%) received hydroxychloroquine alone or in combination with corticosteroid and/or azythromycin. Mortality of the patients who received corticosteroids was 34% (20/58) while it was 48% (91/189) in patients who did not (p = 0,01) (Figure 1). Sixty-nine (28%) patients needed RRT and 215 patients (87%) were treated with norepinephrine during their ICU stay. Four patients (1,6%) were on ECMO. Using multiple regression, the predictors of mortality were age, creatinine value, mean arterial pressure lower than 70 mmHg, lymphocytes count on day 0 and absence of corticosteroid use (Table 1). Survival probability was significantly higher in patients who received corticosteroids (p = 0,01)(Figure 1). Survival probability was 75% at 23 days in patients who received corticosteroids versus at 10 days for those who did not.

Figure 1: Kaplan-Meier survival probability plot of COVID-19 patients treated with and without corticosteroids during their first week of mechanical ventilation (adjusted p value = 0,01).
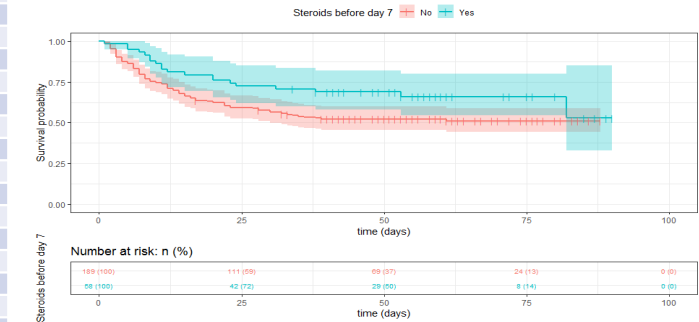
CONCLUSIONS

Retrospectively analyzing the data of a multicenter cohort, we observed that mortality of patients with SARS-CoV-2 pneumonia treated with mechanical ventilation was as high as 45% and median survival time was 82 days. In this series, the risk factors for mortality included age, renal and circulatory dysfunction, lymphopenia and the absence of corticosteroid use during the first week of mechanical ventilation. Corticosteroid therapy during the first week of mechanical ventilation decreased mortality from 48% to 34% (p = 0,01).