Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a retrospective cohort study of 1069 patients

Abstract:

Introduction: The COVID-19 pandemic has brought the management of hypoxemic respiratory distress into question given the limited capacity of the intensive care units who are strained by the high mortality of the disease and the large numbers of patients requiring prolonged periods of hospitalization, as well as mechanical ventilatory support equipment such as ventilators and intensive care units.

The objective of the study: The early and prolonged prone position (PP) reduces the mortality in patients with acute respiratory distress syndrome (ARDS) going under invasive ventilatory support, but its role in conscious patients remains a subject of debate and research. The main aim of this study is to evaluate the efficiency of the prone position for preventing intubation and mortality in spontaneously ventilated patients with COVID-19 and presenting an acute respiratory distress syndrome.

Methods: This is a retrospective, monocentric, descriptive and analytical cohort conducted over a period of 22 months from March 2020 to December 2021 and involving 1069 patients hospitalized in the intensive care unit of our hospital for the management of acute respiratory failure caused by COVID-19.

Results: The median survival in the total sample was 12 ± 3 days with extremes ranging from 2 days to 39 days, the survival of the awake prone position group was superior to that of the non-prone position group, these results were significant with a $p < 0.0001$. We observed a statistically significant increase in the mean ratio during the awake prone position compared to that at admission (143.85 ± 41.56 vs 124.30 ± 36.41; $p<0.0001$), the same when we compared the ratio after prone position to the ratio calculated at admission (131. 91 ± 41.02 vs 124.30 ± 36.41; $p<0.0001$), The rate of intubation at day 28 is about 33.20% for the general population, 25.58% in the awake prone position group and 46.16% in the non-prone position group.

Conclusion: Awake prone positioning was significantly associated with a reduction in 28-day mortality; its use in ARDS deserves to be further studied in randomized controlled trials.

Keywords: Acute respiratory distress syndrome, awake prone position, mortality, intubation, COVID-19.

Introduction:

The early and prolonged prone position (PP) reduces the mortality in patients with acute respiratory distress syndrome (ARDS) going under invasive ventilatory support, but its role in conscious patients is uncertain **(1).** Very few studies have examined the physiological effects of awake prone position in patientswith ARDS and this strategy has not been largely adopted. **(1)**

We have used the awake prone position in patients suffering from ARDS associated with the COVID-19 requiring oxygen therapy and performed a retrospective study objectifying our experience, reporting the physiological changes, as well as the duration and tolerance of the awake prone position.

The upsurge in the COVID-19 pandemic is placing enormous pressure on medical facilities worldwide. The massive number of cases admitted to emergency departments and the rapid progression to respiratory failure rapidly depleted critical care resources, including respiratory support equipment, such as ventilators, and intensive care unit beds **(2).**

In this circumstance, any oxygenation or therapeutic support that conserves medical resources should be welcomed. Prone positioning is a well-known ventilatory support strategy to improve oxygenation levels, usually applied in mechanically ventilated patients with acute respiratory distress syndrome (ARDS). The suggested mechanism of this strategy is to reduce the ventilation/perfusion (V/Q) mismatch and make lung perfusion more uniform **(2).**

Methods and materials:

1. The study type:

This is a single-center retrospective cohort conducted in the intensive care unit of our university hospital.

2. Inclusion criteria:

We enrolled all patients (1069 patients) with ARDS due to SARS-CoV2, confirmed by nasopharyngeal swab, who were hospitalized in COVID-19 intensive care unit from 1 March 2020 to 31 December 2021. These 1069 patients were divided into 2 groups:

- group A, which includes the 681 patients who were placed in the awake prone position.

- group B, which includes the remaining 388 patients who did not practice the prone position**. (figure 1)**

3. Exclusion criteria:

Patients with negative PCR (polymerase chain reaction) (n=82), who were younger than 18 years of age (n=14), patients who died or intubated on the day of admission (n=78) and those intubated on the day of admission (n=125) were excluded from the study. **(figure 1).**

4. Prone position procedure and the judgment criteria:

Each prone position session had a minimum duration of 1 hour and a maximum of 12 hours for a minimum of 3 session per day. FiO2 and PaO2 parameters were measured in patients who were put on prone position in three phases: SP1 (supine position), PP1 (10 min after prone positioning), SP2 (1 hour after resuming supine position). The positive response to prone position was estimated by calculating the PaO2/FiO2 ratio. A response to prone position was defined as an improvement in the PaO2/FiO2 ratio by 10%, whereas non-response was defined as no improvement or a deterioration of the ratio.
The primary outcome was the death within 28 days of hospitalization. Secondary outcome (all censored at 28 days after enrollment) were: intubation rate, length of stay in intensive care units, length of time from hospitalization to death, length of time from hospitalization to intubation.

5. Data collection and statistical analysis:

Epidemiological, clinical, paraclinical and therapeutic data were collected. These data were then computerized and analyzed using IBM SPSS version 21 software. Qualitative variables were described as numbers and/or percentages, and quantitative variables as mean ± standard deviation, or as median with interquartile range for variables not having a normal distribution.
A comparison between PaO2/FiO2 ratios at admission, during PP and 1hour after PP were performed in pairs using Student's t-test for paired series after graphical verification of the normality of the distributions.
To determine the factors associated with a positive response to PP, an univariate analysis between responders and non-responders and other variables was performed in the PP patients,using the chi-square test or Fisher's exact test for comparison of percentages, and Student's T-test or Wilcoxon & Mann-Whitney test for comparison of means according to the distribution of variables (normal or not), after a multivariate analysis by binary logistic regression was performed, a $p \leq 0.10$ was chosen as a threshold to introduce the variables into the initial model by proceeding with the stepwise descending method;
A survival analysis was performed to determine the factors associated with poor prognosis in the entire sample, our outcome was the death at day28; first a univariate analysis by Kaplan Meier method was performed, then a multivariate analysis by Cox regression (stepwise descending)was performed, PP setting was considered as our main explanatory factor, a $p \leq 0.10$ was chosen as a threshold to determine the variables to be included in the initial model still following the stepwise descending procedure.

6. Ethical consideration:

This study complies with the code of ethics of the World Medical Association (Declaration of Helsinki) and was approved by the Oujda Biomedical Research Ethics Committee (N° 017/20). Written informed consent was obtained from each participant. This study is registered in the Research Registry under the number: ****

Results:

1. Descriptive study:

During the study period, of the 1366 patients hospitalized in our department for the management of COVID-19 infection, 1069 patients met our inclusion criteria.

1.1. Demographics and baseline characteristics:

1069 cases were identified over 22 months, with an annual frequency of 651 cases/year.
The mean age of our patients was 63.72 ± 15.86 years, with age extremes ranging from 21 to 101 years, a male predominance was noted, with a sex ratio of 1.54.
The average BMI was 28.45 ± 9.10 kg/m². The most frequent comorbidities in the sample were hypertension (33.70%) and diabetes (33.10%). Baseline demographic and clinical characteristics were well balanced between the two groups **(table 1).**

1.2. Laboratory and radiological findings:

On admission, all 1069 cases underwent laboratory tests, the results of which are presented in **table 1**. Regarding radiological findings, pulmonary involvement was presented according to the CORADS classification system **(table 1).** Chest CT with contrast, when performed, revealed pulmonary embolism in 5.63% of cases.

1.3. Treatment and evolution:

Oxygen supplementation varied from patient to patient according to individual needs, sometimes requiring a more efficient method of oxygenation or ventilation depending on the patient's response and progress. As for medications, the protocol was mainly based on anticoagulation, antiplatelet therapy, corticosteroids, adjuvant therapies (vitamins C and D, zinc), and antibiotics **(table 1).**
The mean time from hospitalization to intubation in our sample was 9 ± 6 days, with extremes ranging from 1 day to 24 days; in the prone position group, the mean time was 12 ± 4 days,while the non-prone position group had a mean time of 6 ± 2 days.
The rate of intubation at day 28 was 33.20% for the total sample, those who practiced PP had a rate of 25.58%, and 46.16% for the non-PP group.

2. Analytic study:

2.1. PP results:

To assess the clinical tolerance of prone position in patients, we monitored respiratory parameters and pulsed oxygen saturations before, during, and after PP, while retaining the average of their respiratory rates and peripheral saturation of oxygen (SpO2) during each of

the three periods. We observed an improvement in both parameters during and after each PP session.

The proportion of responders (SP2/SP1) to PP was 33.00% with a 95% confidence interval [29.50-36.70].

We observed a statistically significant increase in the mean PaO2/FiO2 ratio during PP compared to that at admission (143.85 ± 41.56 vs. 124.30 ± 36.41; p<0.0001), the same when we compared the ratio after PP to the ratio calculated at admission (131.91 ± 41.02 vs. 124.30 ± 36.41; p<0.0001). **(figure 2)**

The results showed that the mean age of the patients who responded positively to the prone position was significantly lower than the mean age of the patients who did not respond to the PP (61.89 ± 14.15 vs. 64.64 ± 14.10 years; p=0.017). The mean length of stay in the intensive care unit was also lower in the patients who responded to the PP (19.83 ± 3.62 vs. 28.72 ± 8.43 days; p<0.0001).

Regarding pathological history, we did not find any significant difference between the two groups **(table 2).** As for toxic history, the results showed that smoking was significantly related to a lower response to PP (17.90 vs 33.90 %; p= 0.040).

The proportion of responders in patients with abnormally high lactate levels was significantly lower than in patients with normal lactate levels (23.40 vs. 35.00%; p=0.047), and similarly, patients with respiratory complications, and more specifically those with Pneumothorax, had a lower response to PP (6.70 vs. 33.60%; p=0.027). The univariate analysis is summarized in **table 2**.

Multivariate analysis showed that length of hospitalization, presence of tumor terrain, elevated lactate levels and presence of Pneumothorax were significantly associated with response to prone position, the degree of lung involvement was also associated with patients' response to PP **(table 2),** patients with critical parenchymal involvement were less likely to respond to PP, compared to those with involvement that did not exceed 25%, (RR=0. 34 with 95% CI [0.15-0.76]; p=0.009).

2.1. survival analysis:

Concerning mortality, it was 26.28% (n=281) in the total sample. On average, patients with SARS CoV-2 in the study series were hospitalized for 20 ± 11 days, with extremes ranging from 3 days to 42 days. The average length of hospitalization in the PP group was 26 ± 8 days, while in the non-PP group it was 9 ± 5 days.

The median survival in the total sample was 12 ± 3 days with extremes ranging from 2 days to 39 days, survival in the PP group was higher than in the non-PP group, (p< 0.0001) **(figure 3).**

The cumulative incidence of mortality at day 28 was lower in the PP group than in the non-PP group **(Figure 3a, Table 3),** (HR=0.044 with 95% CI [0.03-0.06]; p<0.0001).

The presence of critical lung injury and high lactate levels were significantly associated with a high mortality rate (HR=8.43 with 95% CI [2.08-34.20]; p<0.003 / HR=1.55 with 95% CI [1.13-2.14]; p<0.007) **(Figure 3b,3c; Table 3).**

Discussion:

The PP improves the homogeneity of pulmonary ventilation through the back-lung segments, reducing ventilation-perfusion mismatch, and ameliorates the high pressure variations that exacerbate regional hyperinflation that exacerbate lung injury **(15).**

This treatment modality could prevent disease progression by reducing the work of breathing, given that the high transpulmonary pressure that occurs with high work of breathing, exacerbates the underlying lung damage **(14).**

Our results agree with previous studies of awake prone position in non-intubatedpatients showing an improvement in oxygenation and a tendency to improvement in symptoms **(3-5).** For example, Sartini found an improvement in oxygenation in the 15 non invasive ventilation (NIV) patients with mild to moderate ARDS who practiced vigilant PPfor 3 hours per day **(6).** Or Coppo who found a significant improvement in the PaO2/FiO2 ratio before and during conscious PP (primary outcome) performed for a minimum of 3 hours in patients under oxygen therapy or NIV. The effect was maintained in about 50% of patients however this result was not significant **(7).**

Tolerance of vigilant PP may be a means of selecting patients in whom those who will have a favorable evolution with an improvement of the clinical signs. For example, in their prospective single-center feasibility study, Elharrar et al. sought to assess the responder rate to awake prone position, characterized by an increase in PaO2 of more than 20% between a blood gas analysis performed before and during the session. The rate was 25%. Of the responders, half were persistent responders (defined as an increase in PaO2 of more than 20% on blood gas before and 12 hours after DV) **(8).**

The use of prone positioning in spontaneously breathing patients has been reported previously. In 2003, Valter and colleagues **(9)** reported on four patients in whom prone positioning in an awake state rapidly increased oxygenation and avoided oxygenation and intubation. Feltracco and colleagues **(10,11)** reported on five lung transplant recipients who successfully underwent awake prone positioning with NIV, with resolution of refractory hypoxemia. Scaravilli and colleagues **(12)** performed a retrospective study in 2015 of 15 non-intubated patients who underwent a total of 43 prone positioning procedures. They found that the procedure was feasible in 95% of all procedures and reported a significant increase in PaO2 compared with before prone positioning.
However, the study by Scaravilli and colleagues is limited by its retrospective nature, the variation in interface and ventilatory settings between procedures, and the small number of patients.

An important study on this topic is a 2020 trial by Ding and colleagues **(4),** in which the authors evaluated the effect of adding prone positioning to the use of high-flow nasal cannulas and noninvasive ventilation in 20 patients with moderate to severe ARDS. They

found that the addition of prone positioning could have helped avoid intubation in 11 of 20 patients, and that the PaO2/FiO2 ratio was significantly higher in patients who avoided intubation.
A systematic review examined the effect of awake prone position on oxygenation variables in a heterogeneous group of adult patients with COVID-related hypoxemic respiratory failure19. The patients with Pao2/Fio2 greater than 150 showed a relatively greater improvement in oxygenation, the clinical significance of this result is difficult to determine **(13).**

To note that this study has its limitations:

- First, although we used robust statistical techniques for adjustment, PP was not randomized.
- Second, note that several studies have been found to be inconsistent regarding intubation. Some studies suggest a prevention of intubation with awake PP, but this has not confirmed in other studies **(16-21),** It should be noted that the different studies currently published concerning awake PP in acute respiratory failure patients with COVID-19 use a wide variety of judgment criteria. We will take as an example, an observational pilot study, in which awake PP was set up from arrival in the emergency room until the patient was taken to the ward and analyzed the median SpO2 with oxygen therapy.
- Third, this is a retrospective cohort and the collection of patients were not monitored, therefore we did not evaluate the tolerance during each of the PP sessions, in addition to the significant heterogeneity of the included patient populations and the lack of data on co-interventions used (steroids, antiviral therapies).
- Fourth, the fact that the intervention was performed in some cases under conditions of pandemic stress that affected the availability of resources.

On the whole, these considerations should not distract from the pragmatic observation that this positioning reduces intubation and mortality, regardless of the underlying mechanism of this effect. These limitations are counterbalanced by the advantage of rapidly setting up an international randomized study generating high-level evidence in a short period of time frame.

PP in mechanically ventilated patients with ARDS requires the concomitant use of sedatives and, often, neuromuscular blocking agents. Pressure sores and compressive neuropathy are recognized complications. In our retrospective review, few complications were noted, even for longer periods of time than previously reported in conscious patients **(4,6,7)** and when performed over several consecutive days. Conscious patients were able to adjust their position, which probably contributes to the reduction in complications. Alternative methods with the use of pillows and blankets were performed in our study to reduce the adverse effects.
These results highlight the need to standardize PP practices for better comparison.
It is possible that some patients may be able to self-position, but their ability to remain in that position for extended periods of time is unclear. Similarly, patients who can get into the PP

are likely to be younger, less frail and require less assistance. All these factors introduce a selection bias when interpreting the potential benefits of PP.
The selection of an appropriate patient would be the key to the success of adoption of awake PP. Recent studies suggest that patients with mild-moderate ARDS (Pao2/Fio2 between 100 and300) and a respiratory rate of less than 40 breaths/min may be considered for PP **(22,23).**
A study by Mathews et al (11) strongly supports the strategy of awake prone positioning forCOVID-19 related respiratory failure **(24).**
Future studies must adjust for these confounding factors in relation to patient selection.

Conclusion :

Prone positioning appears to be a safe and inexpensive strategy to improve outcomes and save limited resources.
Until further studies confirm or refute our findings, we recommend early and frequent use of the awake prone positioning in the hope that it will improve the decrease in the rate of death and delay or prevent intubation.
Prospective efforts are needed to better define the effect of awake recumbent positioning on oxygenation and to improve the ability of patients to tolerate this procedure.

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Tables and figures :

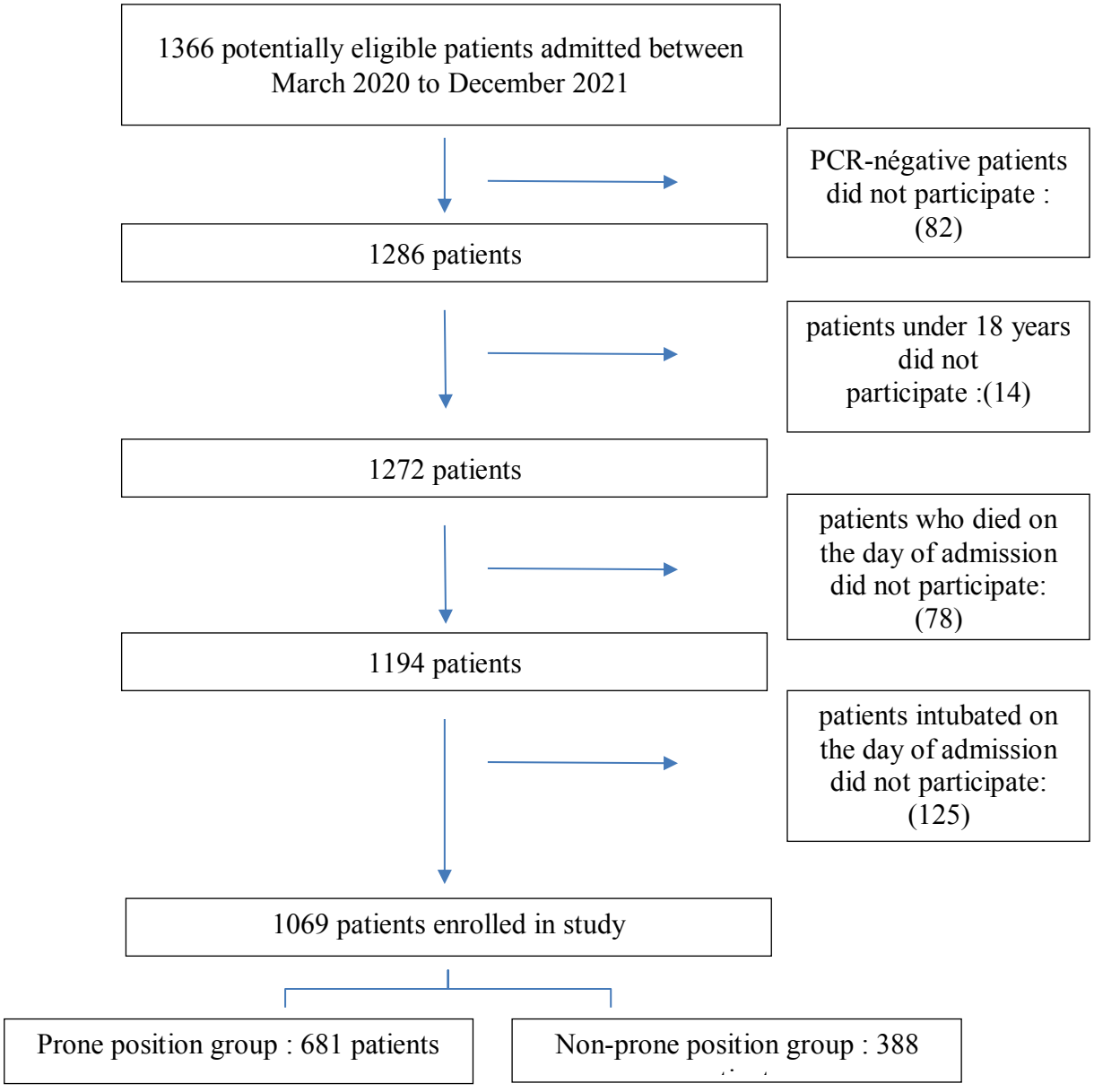

Figure 1: Study profile

Tableau 1 : Summary of the demographic and baseline characteristics, laboratory/radiological findings, and Treatments/outcome of the patients:

Demographic and baseline characteristics	Prone position group(n=681)	Non-prone position group(n=388)
Age, years (mean ± SD)	63.73±14.17	63.70±18.49
Sex n (%):		
Female	246 (36.10)	174 (45.10)
Male	436 (63.90)	212 (54.90)
IMC kg/m2 (mean ± SD)	28.4 (4.70)	28.4 (4.70)
Time between symptom and admission at hospital, days (mean ± std deviation)	3 (1.30±2)	3 (1.20±2)
Symptoms, n (%)		
Fever	582 (85.00)	325 (84.80)
Chills	287 (42.30)	166 (43.10)
Dyspnea	589 (86.20)	329 (85.40)
Cough	513 (75.80)	294 (76.10)
Anosmia	83 (12.40)	51 (13.30)
Asthenia	493 (72.30)	279 (72.50)
Digestives signs	238 (35.30)	135 (35.60)
Clinical parameter: mean (±SD)		
Respiratory rate	32(5.40)	31(6.10)
PaO2	87(10.40)	88(11.20)
PaO2/FiO2	139(39.20)	143(41.50)
Co morbidities: n (%)		
Obesity (BMI >30)	107 (15.70)	64 (16.50)
HTA	230 (33.70)	124 (32.00)
Diabetes	226 (33.10)	131 (33.90)
Smoker	39 (5.70)	36 (9.30)
Preexisting respiratory diseases	13 (1.90)	12 (3.10)
Cardiopathy	85 (12.50)	73 (18.90)
Cancer	23 (3.40)	21 (5.40)
Chronic renal failure (DFG<59)	3 (0.44)	2 (0.51)
Immunodepression	0 (0)	0 (0)
Complications		
Pulmonary embolism, n (%)	25 (3.67)	23 (5.92

Pleurisy	0 (0)	0 (0)
Pneumothorax	2 (0.29)	1 (0.25)
Degree of pulmonary involvement in CT, n (%)		
Atteinte Modérée <25%	39 (5.72)	45 (11.60)
Atteinte importante (25-50%)	121 (17.74)	80 (20.70)
Atteinte sévère (50-75%)	290 (42.52)	166 (42.90)
Atteinte critique >75%	231 (34.02)	97(24.80)
Oxygène delivery interface at admission, n (%)		
Nasal oxygen therapy	47 (7.00)	34 (9.00)
High concentration oxygen therapy	129 (19.10)	87 (22.00)
High flow nasal oxygen therapy	202 (29.50)	120 (31.00)
Continuous positive airway pressure (CPAP) therapy	108 (16.00)	54 (14.00)
Noninvasive ventilation (NIV)	195 (28.40)	93 (24.00)
Laboratory and radiological findings		
High WBC, n (%)	299 (44.05)	166 (43.01)
Leucopenia, n (%)	34 (4.92)	19 (4.83)
Lymphocytopenia n (%)	585 (86.70)	329 (85.80)
Thrombocytosis, n (%)	204 (29.17)	112 (28.24)
CRP, mean (range) (mg/L)	398 (10 – 837)	379 (10-826)
Ferritin, mean (range) (µg/L)	1742,2 (10 – 4000)	1724,5 (10 – 4000)
Procalcitonin, mean (range) (ng/L)	207,17 (0,12 – 692)	202,17 (0,12 – 692)
Interleukin 6, mean (range) (pg/mL)	194,82 (0,35 – 6000)	192,82 (0,35 – 6000)
D-dimers mean (range) (mg/L)	7,23 (0,31 – 45,20)	7,16 (0,31 – 45,20)
Fibrinogen, mean (+/-SD) (g/L)	5.25 ±2,79 (0,41 – 9,10)	5.24 ±2,79 (0,41 – 9,10)
Corticosteroids therapy, n (%)		
Methylprednisolone	374 (55,64)	217 (56,34)
Dexamethasone	82 (12,65)	47 (12,53)
Hydrocortisone	231 (3,47)	12 (3,51)
Anticoagulation, n (%)		
Enoxaparine	652 (95,60)	376 (96,30)
Tinzaparine	29 (4,40)	12 (3,70)
Platelet anti-aggregation inhibitors, n (%)		
Acetylsalicylic acid	531 (78,84)	306 (79,67)
Anti-interleukin-6 therapy		
Tocilizumab	129 (18,45)	69 (18,65)

Antibiotics, n (%)		
Amoxicillin + clavulanic acid	217 (32,20)	128 (33,70)
Ceftriaxone	306 (44,70)	170 (43,90)
Ceftriaxone + ciprofloxacin	102 (14,40)	58 (14,70)
Piperacillin-Tazobactam + voriconazole + amikacin	61 (8,70)	32 (8,90)

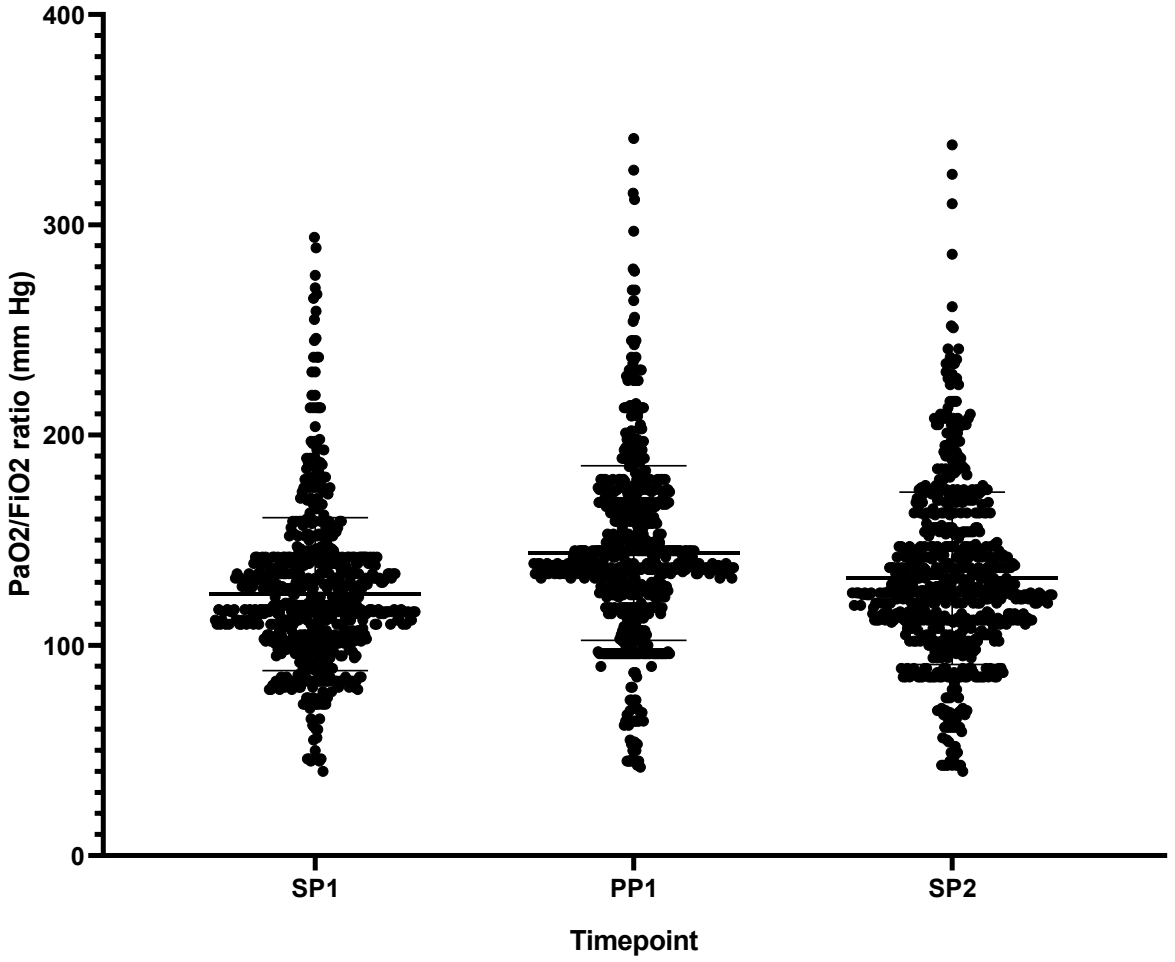

Figure 2 : PaO2/FiO2 ratio per patient, at the three time points of the study, SP1, PP1 and SP2

Each datapoint is showing the PaO2/FiO2 ratio at the three timepoints. Responders were defined as patients with an increased PaO2/FiO2 ratio between SP1 to SP2 for the main analysis. All other patients who were successfully put in the prone position were non-responders. PaO2=partial pressure of oxygen. FiO2=fractional concentration of oxygen in inspired air. SP1=baseline supine position. PP1=10 min after prone positioning. SP2=1 h after resuming supine position

Tableau 2 : Factors associated with a positive response in patients with Covid-19, having benefited from the prone position during their hospitalization in the intensive care unit

Variable	Univariate analysis			Multivariate analysis	
	Responders n (%)	Non- Responders n (%)	P Value	OR [95% CI]	P Value
Age (mean ± SD)	61.89 ± 14.15	64.64 ± 14.10	0.017		
BMI, kg/m^2 (mean ± SD)	26.64 ±3.86	26.72 ± 3.76	0.783		
Respiratory rate at admission, breaths/min (mean ± SD)	34.04 ± 4.61	33.81 ± 4.54	0,540		
Length of hospitalization (median (Q1-Q3)	19.00 (17.00-21.00)	31.00 (26.00-35.00)	<0.0001	**0.828 [0,798-0,858]**	**<0,0001**
Sex					
Male	142 (32,6)	294 (67,4)	0,755		
Female	83 (33,7)	163 (66,3)			
Diabetes	79 (35)	147 (65)	0,442		
hypertension					
Active smoker	7 (17,9)	32 (82,1)	0,040		
Asthma	3 (23,1)	10 (76,9)	0,561		
Obstructive sleep apnea syndrome	2 (66,7)	1 (33,3)	0,254		
Cardiopathy	21 (24,7)	64 (75,3)	0,082		
Gout	4 (20)	16 (80)	0,210		
Hypothyroidism	6 (26,1)	17 (73,9)	0,471		
Chronic obstructive pulmonary disease	4 (50)	4 (50)	0,450		
Cancer	4 (17,4)	19 (82,6)	0,106	**0.156 [0,027-0,910]**	**0,039**
Chronic renal failure	8 (36,4)	14 (63,6)	0,732		
Immunosuppression	3 (23,1)	10 (76,9)	0,561		
Tuberculosis	2 (40)	3 (60)	0,667		
Hemopathy	1 (11,1)	8 (88,9)	0,284		
Stroke					
Pulmonary embolism	12 (33,3)	24 (66,7)	0,964		

Pneumothorax	1 (6,7)	14 (93,3)	0,027	**0.052 [0,005-0,574]**	**0,016**
Pleurisy	14 (26,9)	38 (73,1)	0,329		
Pneumomediastinum	3 (21,4)	11 (78,6)	0,566		
pH			0.252		
High	90 (35.4)	164 (64.6)			
Normal	86 (32.5)	179 (67.5)			
Low	31 (26.7)	85 (73.3)			
Lactate (>2mmol/l)	18 (23,4)	59 (76,6)	0,047	**0.379 [0,188-0,765]**	**0,007**
HCO3			0.013		
High	68 (34.3)	130 (65.7)			
Normal	98 (37.3)	165 (62.7)			
Low	42 (24)	133 (76)			
PaO2			0.093		
Normal	117 (36.2)	206 (63.8)			
Low	108 (30.2)	250 (69.8)			
PaCO2			0.220		
High	18 (24)	57 (76)			
Normal	88 (34.5)	167 (65.5)			
Low	102 (33.4)	203 (66.6)			

Tableau 3 : Survival analysis in patients with Covid-19 during their hospitalization in the intensive care unit

Variables	**Staff**	**Number of deaths**	**Median survival * (IQR)**	**Log Rank test (p)**	**Hazard ratio [IC 95%] (Cox regression)**	**p value**
Sex	1067			0.025		
Men	647	160	**(13 - **)			
Women	420	122	** (24 - **)			
Prone position	1068			<0.0001	**0.044 [0.03- 0.06]**	**<0.0001**
Yes	682	104	** (** -**)			
No	386	178	13 (9 – 18)			
Obesity	1068			0.301		
Yes	171	52	** (17 - **)			
No	897	230	** (23 - **)			
Age	1068			0.001		
<65years	519	112	** (26 - **)			
>65years	549	170	** (18 - **)			

Hypertension	1068			0.195		
Yes	354	104	** (20 - **)			
No	714	178	** (22 - **)			
Diabetes	1068			0 .252		
Yes	357	102	** (20 - **)			
No	711	180	** (22 - **)			
Active smoker	1068			0.467		
Yes	75	21	** (16 - **)			
No	993	261	** (22 - **)			
Asthma	1068			0.323		
Yes	25	7	** (12 - **)			
No	1043	275	** (22 - **)			
Obstructive sleep apnea syndrome	1068			0.320		
Yes	3	0	** (** - **)			
No	1065	282	** (21 - **)			
Chronic obstructive pulmonary disease	1068			0.820		
Yes	14	4	** (13 - **)			
No	1054	278	** (22 - **)			
Cardiopathy	1068			0.241		
Yes	158	46	** (17 - **)			
No	910	236	** (23 - **)			
Cancer	1068			0.359		
Yes	44	13	** (13 - **)			
No	1024	269	** (22 - **)			
Chronic renal failure	1068			0.359		
Yes	50	15	34 (18 - **)			
No	1018	267	** (22 - **)			
Immunosuppression	1068			0.053		
Yes	26	10	27 (12 - **)			
No	1042	272	** (22 - **)			
Pulmonary embolism	1068			0.436		
Yes	54	17	** (20 - **)			
No	1014	265	** (22 - **)			
Stroke	1065			<0.0001		
Yes	28	16	14 (06 - **)			
No	1037	266	** (23 - **)			
Pneumothorax	1068			0.339		
Yes	20	8	** (13 - **)			
No	1048	274	** (22 - **)			
Pleurisy	1067			0.072		
Yes	96	33	** (13 - **)			
No	971	249	** (23 - **)			
Pneumomediastinum	1068			0.351		
Yes	14	3	** (** - **)			
No	1054	279	** (21 - **)			
Pulmonary damage (CT scan)	1068					**<0.0001**
<25%	84	2	** (**-**)		**1**	
25 - 50%	201	7	** (**-**)		**0.78 [0.15-4.03]**	**0.768**
50 – 75%	455	118	** (20-**)		**3.75 [0.92-15.26]**	**0.065**
>75%	328	155	27 (09-**)		**8.43 [2.08-34.20]**	**0.003**
Time between symptom and hospitalization	1024			0.009		
<5days	919	242	** (21 - **)			
>5days	105	18	** (** - **)			

Lactate					<0.0001	**1.557 [1.130-2.143]**	**0.007**
	Normal (<2mmol/l)	615	142	** (25 - **)			
	High (>2mmol/l)	126	52	** (12 - **)			
pH					0.229		
	High (>7.35)	387	106	** (21 - **)			
	Normal	420	107	** (21 - **)			
	Low (<7.35)	171	59	** (18 - **)			
HCO3		979			0.041		
	High (>22)	297	68	** (25 - **)			
	Normal	406	112	** (20 - **)			
	Low (<22)	276	92	** (14 - **)			
PaO2		1024			0.015		
	Normal	524	113	** (24 - **)			
	Low	500	161	** (19 - **)			
PaCO2					0.155		
	High	120	41	** (17 - **)			
	Normal	372	95	** (22 - **)			
	Low	486	136	** (20 - **)			

Median survival*: the value of ti for which S(ti) = 0.5: Probability of living being = 50%; IQR: the value of ti for which S(ti) = 0.75 and S(ti) = 0.25 respectively.
(**): Median survival or IQR is not available: ti could not be calculated because we did not observe a percentage of 50% or 75% of deaths.

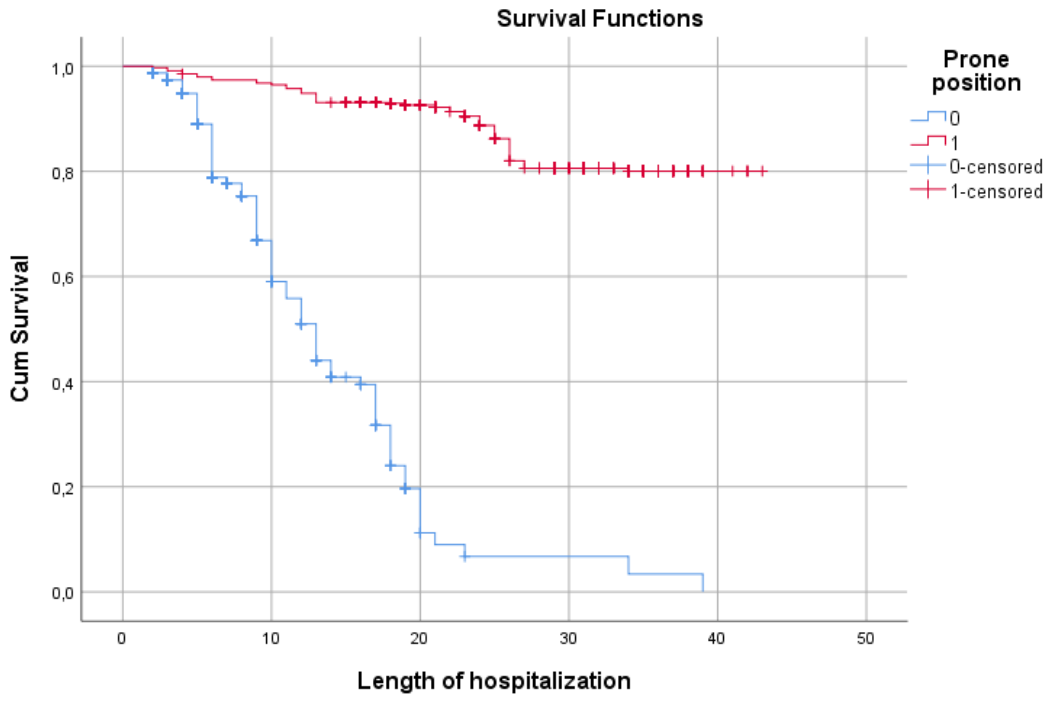

Figure 3a : ***Estimation of the probabilities of survival by the Kaplan Meier method in the study population at day28 according to the practice or not of awake prone positioning***

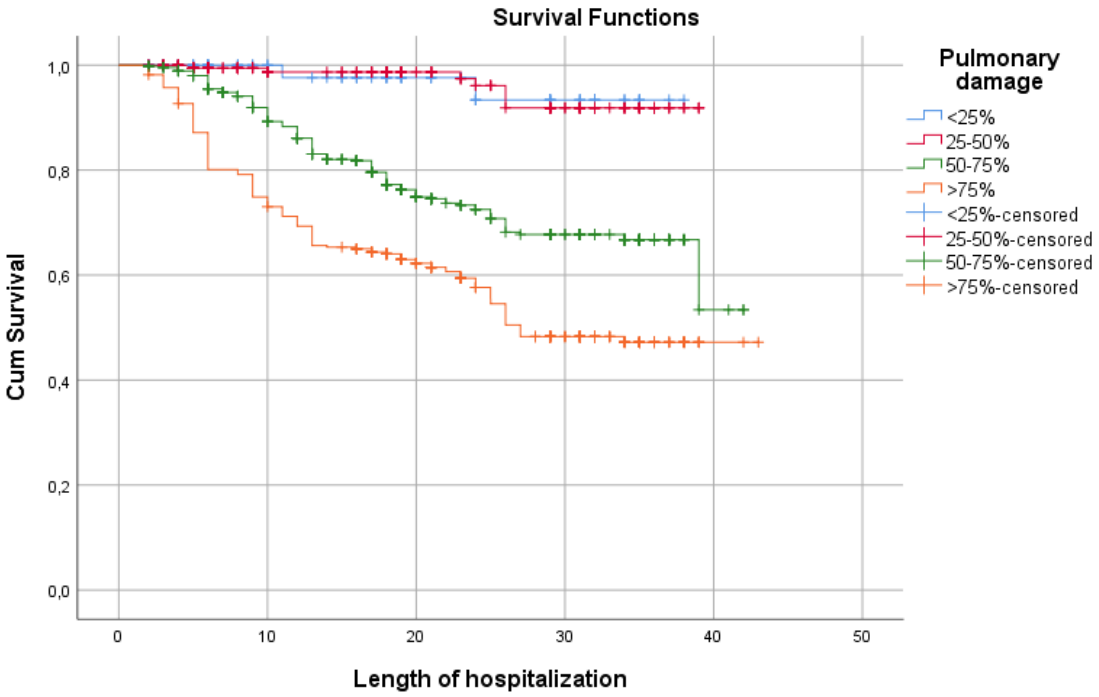

Figure 3b : ***Estimation of survival probabilities by the Kaplan Meier method in the study population at day28 according to the degree of pulmonary damage***

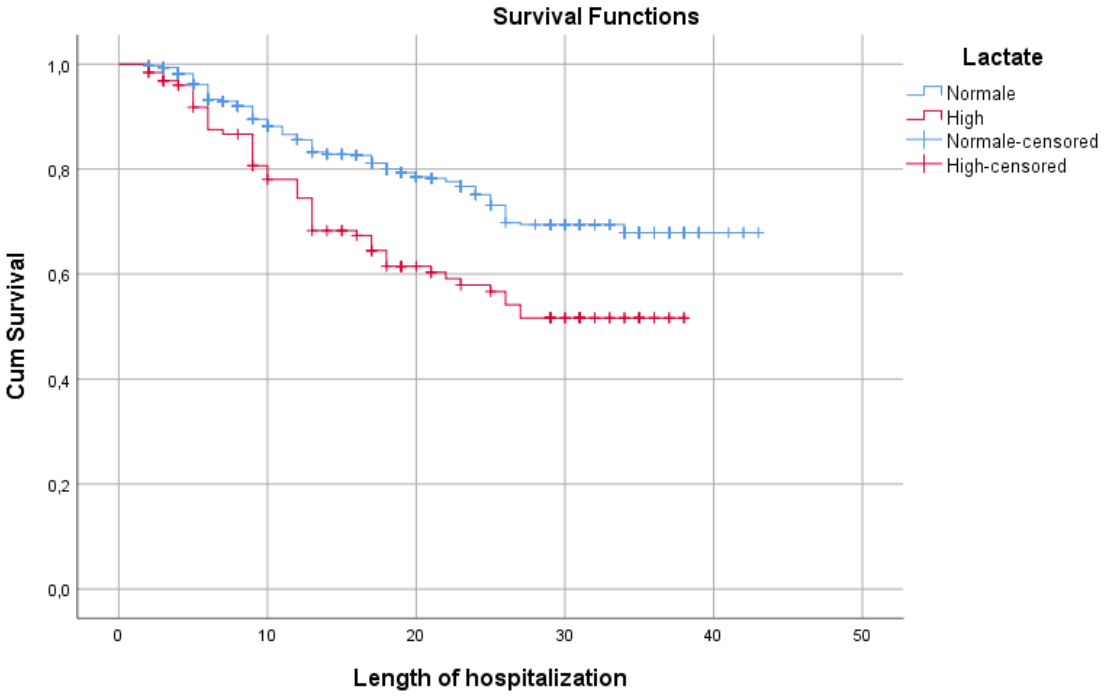

Figure 3c : ***Estimation of survival probabilities by the Kaplan Meier method in the study population at day28 according to the lactate level at admission***