Predictors Of Successful Outcome Of Self-Proning And High Flow Nasal Oxygen Therapy In Patients With COVID-19 Pneumonia: A Retrospective Analysis

Hani Lababidi (hanilab@hotmail.com)
King Fahad Medical City
Bassem Daoud
King Fahad Medical City
Mohamad Alghamdi
King Fahad Medical City
Taher Alhawdar
King Fahad Medical City
Ahmed Alhomoud
King Fahad Medical City
Ahmed Basardah
King Fahad Medical City
Yasser Qasem
King Fahad Medical City
Mahmoud Yamani
King Fahad Medical City
Moustafa Yasawy
King Fahad Medical City
Mohammad AlMaani
King Fahad Medical City

Research Article

Keywords: Awake self-prone positioning, SPP, High flow nasal oxygen, HFNO, APACHE-II score, coronavirus disease 2019 (COVID-19)

Posted Date: March 18th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1412839/v1

Abstract

Background: Proning improves oxygenation and outcome in intubated patients with acute respiratory distress syndrome (ARDS). Awake self proning position (SPP) may lead to clinical improvement in COVID-19 cases with severe hypoxemia. We describe our experience of the impact of awake SPP with high flow nasal oxygen (HFNO) in COVID-19 patients on oxygenation and survival.

Methods: A retrospective study of patients with moderate to severe ARDS due to COVID-19 pneumonia treated with SPP-HFNO admitted from May to July 2020 to ICU. The primary outcomes were avoidance of invasive or non-invasive ventilation or death. The secondary outcomes were improvement of oxygenation (SpO_2), reduction in respiratory rate (RR), and/or reduction in heart rate (HR) after at least 30 minutes of SPP-HFNO.

Results: A total of 110 ICU patients received SPP-HFNO and full data was available on 71 patients. The median age was 55 years with male predominance at 86%. The success group had lower APACHE II score (12.47 vs. 16.97, p<0.001), lower ICU-LOS (6.21 vs 13.19, p<0.001), higher pre and post SpO_2 (90.64 vs 88.42, p=0.015 and 96.09 vs 93.22, p<0.001), and lower pre HR (91.03 vs. 99.08, p=0.04). The survival rate was much higher in HFNO & SPP successful group (97% vs. 51%, p<0.001). The significant covariates in the success group were lower APACHE II score (HR=0.91), lower WBC (HR=0.88), lower post-SPP RR (HR=1.40), and treatment with convalescent plasma (HR=2.33).

Conclusion: Awake SPP-HFNO in patients with moderate to severe COVID-19 pneumonia is associated with improved oxygenation, reduced intubation rate, and improved survival.

Background

COVID-19 is a new disease arising from the novel SARS-CoV-2. It caught the world by surprise to reach pandemic threshold levels in no time. During the pandemic, the healthcare systems worldwide were faced with unprecedented challenges of rapid consumption of resources and high disease infectivity. Patients rapidly became critically ill and died from an illness that did not fit with any existing model, and for which there has been no existing treatment [1]. Sick patients flooded the hospitals, and a substantial proportion was rapidly progressing into acute respiratory failure that required mechanical ventilation and ICU admission. In a significant proportion of these patients, severe hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS) occurred, yet with a stable clinical condition. This combination of signs and symptoms has been called “happy hypoxia” [2].

Health care systems have been exploring therapeutic and oxygenation support strategies in an attempt to conserve medical resources and minimize pressure on diminishing intensive care services. One such modality is prone positioning. It is a ventilatory support strategy that improved oxygenation levels and mortality in mechanically ventilated patients with acute ARDS [3]. Based on prior literature with other causes of ARDS, prone ventilation in unconscious patients is labor-intensive and is associated with various complications [4]. It was thus speculated that prone ventilation is done on awake patients to improve oxygenation, prevent or delay intubation and minimize complications as well. The prone positioning in patients with ARDS favors lung recruitment by improving ventilation-perfusion (V/Q) mismatch [5]. The homogeneous distribution of ventilation minimizes the risk of ventilator-induced lung injury, barotrauma, atelectasis, and mortality [6]

Recent case reports and series showed that early use of awake self-proning position (SPP) with oxygen therapy can be used successfully in non-COVID-19 ARDS to prevent intubation [7]. Mechanism of action behind improved oxygenation involves reducing ventilation/perfusion (V/Q) mismatch and making lung perfusion more uniform [6]. Experts extrapolated the use of awake SPP to patients with COVID-19 pneumonia and severe hypoxemic respiratory failure and showed improved oxygenation, prevention of intubation, and improved outcome [7–9].

More information is needed about the utility, timing, effectiveness, and outcome predictors of awake SPP-HFNO in the treatment of critical COVID-19 pneumonia. Our study aims at exploring the outcome of moderate to severe COVID-19 pneumonia patients who underwent early awake SPP-HFNO. The primary outcome is to determine the success rate of SPP-HFNO defined as the avoidance of non-invasive or invasive ventilation and/or death. The secondary outcome is the efficacy of SPP-HFNO on oxygenation, heart rate, and respiratory rate after at least 30 min of initiation of treatment.

Methods

Study design:

This is a retrospective study of all patients with COVID-19 pneumonia who underwent treatment with SPP-HFNO in the ICU at King Fahad Medical City (KFMC) in Riyadh, Saudi Arabia from May to July 2020. The study was approved by the ethics committee at KFMC.

Outcomes:

The primary outcomes for the efficacy of SPP-HFNO were the rate of avoidance of invasive or non-invasive ventilation and/or death. The SPP-HFNO intervention was labeled as a success if patients survived and avoided invasive or non-invasive ventilation; otherwise, it was labeled as a failure. The secondary outcomes were improvement of oxygen saturation determined by pulse oximetry (SpO_2), reduction in respiratory rate (RR), and/or reduction in heart rate (HR) after at least 30 minutes of SPP-HFNO.

Data collection:

The following information was collected from the medical records on all patients included in the study: Patient characteristics (age, sex, BMI, APACHE II score, source of admission whether from the emergency department (ED) or hospital ward, ICU length of stay (ICU LOS), total hospital length of stay (TOTLOS), and survival), 2) Laboratory evaluation (WBC, platelet count, Bun, creatinine, ALT, LDH, ferritin, D-Dimer, and CRP), 3) Physiologic parameters (HFNO & SPP time, maximum FiO_2 on HFNO, maximum flow of HFNO, SpO_2, RR, and, HR before and after HFNO &SPP), 4) Comorbidities (diabetes, hypertension, cancer, cardiac, CNS, pulmonary, and kidney diseases), 5) COVID-19 treatment (antiviral, azithromycin, corticosteroids, statins, anticoagulation, Tocilizumab, and convalescent plasma exchange).

Statistical analysis:

Descriptive statistics for quantitative variables was carried out by calculating the mean, standard deviation, median, quartiles, minimum and maximum. The analysis of qualitative variables was carried out by calculating the number and percentage of occurrences of each value. The comparison of values of qualitative variables in

groups was done by using Fisher's exact test. The quantitative variables comparison of the values in two groups was performed using Welch's two-sample t-test. The significance level of P values < 0.05 was assumed in the analysis. All statistical analysis was carried out in the R program, version 1.4.1103.

Regression analysis models:

The primary dependent variable was the success of SPP-HFNO. Cox proportional hazards model was used to determine the association between the success of SPP-HFNO in COVID-19 pneumonia and the covariates in the 5 different categories i.e., demographics, laboratory evaluation, physiologic parameters, comorbidities, and treatment.

Results

A total of 110 patients received awake SPP-HFNO in the ICU during the study period. Thirty-nine patients were excluded for incomplete records leaving 71 patients who form the basis of this study.

General Characteristics:

The median age was 55 years with male predominance at 86% (Figure-1). The SPP-HFNO success group had statistically significant lower APACHE II score (12.47 ± 3.34 vs. 16.97 ± 8.14, p < 0.003) and ICU LOS (6.21 ± 4.63 vs. 13.19 ± 9.44, p < 0.001). However, the total hospital stay was comparable between the 2 groups (18.12 ± 13.00 vs. 20.62 ± 11.10, p = 0.388) with much better survival in the population whom SPP-HFNO intervention was successful (97% vs. 51%, p < 0.001). The most common comorbidities were diabetes (54%) and hypertension (45%). There were no statistically significant differences between the SPP-HFNO success and failure groups in the frequency of comorbidities (Table-1).

Laboratory Evaluation:

The SPP-HFNO success group had a statistically significantly higher platelets count (288 ± 122 vs. 237 ± 84). Otherwise, the laboratory tests of both groups were comparable including COVID-19 inflammatory markers namely LDH, ferritin, D-Dimer, and CRP (Table-2).

Physiologic Parameters:

The Physiologic parameters of the COVID-19 patients who received SPP-HFNO are presented in table-3. The SPP-HFNO success group had statistically significantly higher time in days spent on HFNO and SPP (5.03 ± 2.84 vs. 3.38 ± 3.11, p = 0.022 and 5.26 ± 2.99 vs. 3.35 ± 2.93, p = 0.008 respectively), higher pre and post SPP-HFNO SpO2 (90.64 ± 4.11 vs. 88.42 ± 3.16, p = 0.015 and 96.09 ± 2.07 vs. 93.22 ± 4.03, p < 0.001 respectively), and lower pre SPP-HFNO HR (91.03 ± 18.24 vs. 99.08 ± 12.97, p = 0.04) (Table-3).

Treatment:

More patients received convalescent plasma transfusion in the success group when compared to the failure group (44% vs. 13%, p = 0.007). All other treatment modalities were similar (Table-4).

Cox Proportional Hazards Model:

The hazard ratios of the success of the SPP-HFNO, as the dependent variable, and the covariates of the general characteristics, laboratory tests, physiologic parameters, comorbidities, and treatment are presented in Figs. 2 to 6 respectively. The significant covariates in the success group were lower APACHE II score (HR = 0.91, C.I: 0.82-1.0, p = 0.045), lower WBC (HR = 0.88, C.I: 0.80–0.95, p = 0.005), higher D-Dimer (HR = 1.01, C.I: 1.00-1.03, p = 0.057), higher post-SPP RR (HR = 1.40, C.I: 1.05–1.87, p = 0.022), and treatment with convalescent plasma transfusion (HR = 2.33, C.I: 1.03–5.3, p = 0.043).

Discussion

Our study showed a success rate of awake SPP-HFNO in COVID-19 patients of 48%. We believe this intervention is worth trying since it is a simple technique to correct hypoxemia thus avoiding the need for intubation with few side effects. In a cohort of 56 patients with COVID-19, proning was feasible in 84% with substantial improvement of oxygenation [11]. The addition of non-invasive ventilation (NIV), in the form of applying continuous positive airway pressure of 10 cm H2O and 60% FiO2, to prone position to COVID-19 patients outside of ICU resulted in improvement in oxygenation and respiratory rate [12]. The early application of SPP-HFNO avoided intubation in 7 out of 20 patients with moderate ARDS and baseline SpO2 > 95% [7].

The main challenge in SPP-HFNO is patient fatigue and delaying invasive mechanical ventilation. In a prospective, multicenter study of COVID-19 patients receiving HFNO therapy, there were no effects of SPP on intubation rate or mortality [13]. In our study, patients were monitored in the ICU and the average time spent on SPP-HFNO was 5.26 days in the success group versus 3.38 days in the failure group. Furthermore, the mortality rate in the SPP-HFNO success group was 3% versus 49% in those who required intubation and mechanical ventilation.

There have been several attempts to investigate predictors of failure of NIV and/or HFNO in patients with COVID-19 pneumonia such as HACOR score [14] and ROX index [15]. More recently a machine learning algorithm based on vital signs, laboratory values, and demographic data outperformed the ROX index in predicting the need for intubation in COVID-19 patients [16]. The baseline physiologic parameters (i.e. RR, HR, SpO2) in our cohort were comparable except for statistically significant lower HR in the success group (91 vs. 98 bpm, p = 0.04). Those who responded to SPP-HFNO therapy had statistically significant improvement in their SpO2 (96% vs. 93%, p < 0.001), and lower RR (HR = 1.40, CI: 1.05–1.87, p = 0.022). Similar findings showing improvements in SpO2 and RR have been reported previously [11, 12].

Multiple blood tests were shown to be associated with independent risk for poor ICU outcomes in COVID-19 patients. Elevated white blood cell count and neutrophils and low lymphocyte count are directly proportional to the severity of COVID-19 [17]. Moreover, elevated biomarkers of inflammation in COVID-19 namely: D-dimer, CRP, LDH, and ferritin, are independently associated with higher ICU admission, invasive ventilatory support, and death [18]. In our study, the SPP-HFNO successful group had lower WBC and is a predictor of outcome (HR = 0.88, CI: 0.80–0.95, p = 0.005). The biomarkers of inflammation, except for D-Dimer, were more elevated in the SPP-HFNO failure group but did not reach statistical significance. We found the D-dimer was more elevated in the SPP-HFNO successful group, but with a wide range, and was not statistically significant. The hazard ratio for D-Dimer was mildly elevated with a marginal p-value (HR = 1.01, CI: 1.00-1.03, p = 0.057).

The APACHE-II score was designed to measure the severity of disease in patients admitted to the ICU and to predict mortality [19]. In our cohort of patients, APACHE-II was a significant covariate in the success group (HR = 0.91, CI: 0.82-1.0, p = 0.045), indicating an improved survival of 9% with every 1.0-point decrease in the APACHE II score. Studies have shown that the APACHE-II score accurately predicts the severity of illness in patients with COVID-19 disease admitted to ICU [20, 21].

Advanced age and obesity were previously reported as predictors of poor outcomes in COVID-19 patients, but this association was lacking in our study. A meta-analysis showed that age is an important indicator for predicting the severity and outcome of COVID-19, with a relative risk of 3.59 (95% CI: 1.87–6.90, p < 0.001) [22]. Although an association between severity of COVID-19 disease and comorbidities has been reported [23], this relationship was not revealed in our cohort of patients. Diabetes and hypertension are very common comorbidities in the Saudi population [24]. In addition, our cohort of patients was too small to detect association with other comorbidities like cancer. Regarding the treatment modalities and the predictability of successful SPP-HFNO in COVID-19 patients, treatment with convalescent plasma was associated with better outcomes in our study (HR = 2.33, CI: 1.03–5.3, p = 0.043). Initial reports on treatment with convalescent plasma for severe COVID-19 pneumonia showed promising results [25]; however, a recent randomized trial failed to demonstrate significant improvement in mortality [26].

A major limitation of this study is being retrospective with no control arm to compare. Second, the unavailability of complete data on 39 out of 110 patients. Third, measures of symptoms of dyspnea or comfort after prone positioning were not collected.

Conclusion

Our study showed that awake SPP-HFNO in patients with moderate to severe COVID-19 pneumonia is associated with improved oxygenation, reduced intubation rate, and improved survival. We identified several predictors of success of SPP-HFNO including lower WBC, lower APACHE II score, lower RR post SPP-HFNO, and treatment with convalescent plasma.

Declarations

Ethical Approval:

The research was approved by the Internal Review Board at King Fahad Medical City in Riyadh, Saudi Arabia (IRB log number 20-341; IRB registration number with KACST, KSA: H-01-R-012; IRB registration number with OHRP/NIH, USA: IRB00010471; Approval number Federal Wide Assurance NIH, USA: FWA0018774).

Consent for Publication:

The manuscript is the authors' original work and the manuscript has not received prior publication and is not under consideration for publication elsewhere. If the paper is finally accepted by the journal for publication, we confirm that we will either publish the paper in this journal.

Data Availability Statement:

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests:

We confirm that all authors of the manuscript have no conflict of interests to declare.

Funding:

No funding received for this research.

Authors' Contributions

All authors listed on the title page and in this form have contributed significantly to the work, have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to this journal.

Acknowledgements

Not Applicable

References

1. Fauci AS, Lane HC, Redfield RR. Covid-19 - Navigating the Uncharted. N Engl J Med. 2020;382(13):1268–1269. doi:10.1056/NEJMe2002387
2. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes?. Intensive Care Med. 2020;46(6):1099–1102. doi:10.1007/s00134-020-06033-2
3. Guérin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013;368(23):2159–2168. doi:10.1056/NEJMoa1214103
4. Kallet RH. A Comprehensive Review of Prone Position in ARDS. Respir Care. 2015;60(11):1660–1687. doi:10.4187/respcare.04271
5. Zarantonello F, Andreatta G, Sella N, Navalesi P. Prone Position and Lung Ventilation and Perfusion Matching in Acute Respiratory Failure due to COVID-19. Am J Respir Crit Care Med. 2020;202(2):278–279. doi:10.1164/rccm.202003-0775IM
6. Qadri SK, Ng P, Toh TSW, et al. Critically Ill Patients with COVID-19: A Narrative Review on Prone Position. Pulm Ther. 2020;6(2):233–246. doi:10.1007/s41030-020-00135-4
7. Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. Crit Care. 2020;24(1):28. Published 2020 Jan 30. doi:10.1186/s13054-020-2738-5
8. Gattinoni L, Busana M, Giosa L, Macrì MM, Quintel M. Prone Positioning in Acute Respiratory Distress Syndrome. Semin Respir Crit Care Med. 2019;40(1):94–100. doi:10.1055/s-0039-1685180
9. Caputo ND, Strayer RJ, Levitan R. Early Self-Proning in Awake, Non-intubated Patients in the Emergency Department: A Single ED's Experience During the COVID-19 Pandemic. Acad Emerg Med. 2020;27(5):375–378. doi:10.1111/acem.13994

10. Elharrar X, Trigui Y, Dols AM, et al. Use of Prone Positioning in Nonintubated Patients With COVID-19 and Hypoxemic Acute Respiratory Failure. JAMA. 2020;323(22):2336–2338. doi:10.1001/jama.2020.8255
11. Coppo A, Bellani G, Winterton D, et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. Lancet Respir Med. 2020;8(8):765–774. doi:10.1016/S2213-2600(20)30268-X
12. Sartini C, Tresoldi M, Scarpellini P, et al. Respiratory Parameters in Patients With COVID-19 After Using Noninvasive Ventilation in the Prone Position Outside the Intensive Care Unit. JAMA. 2020;323(22):2338–2340. doi:10.1001/jama.2020.7861
13. Ferrando C, Mellado-Artigas R, Gea A, et al. Awake prone positioning does not reduce the risk of intubation in COVID-19 treated with high-flow nasal oxygen therapy: a multicenter, adjusted cohort study. Crit Care. 2020;24(1):597. Published 2020 Oct 6. doi:10.1186/s13054-020-03314-6
14. Guia MF, Boléo-Tomé JP, Imitazione P, et al. Usefulness of the HACOR score in predicting success of CPAP in COVID-19-related hypoxemia. Respir Med. 2021;187:106550. doi:10.1016/j.rmed.2021.106550
15. Vega ML, Dongilli R, Olaizola G, et al. COVID-19 Pneumonia and ROX index: Time to set a new threshold for patients admitted outside the ICU. Pulmonology. 2022;28(1):13–17. doi:10.1016/j.pulmoe.2021.04.003
16. Arvind V, Kim JS, Cho BH, Geng E, Cho SK. Development of a machine learning algorithm to predict intubation among hospitalized patients with COVID-19. J Crit Care. 2021;62:25–30. doi:10.1016/j.jcrc.2020.10.033
17. Luo J, Zhou L, Feng Y, Li B, Guo S. The selection of indicators from initial blood routine test results to improve the accuracy of early prediction of COVID-19 severity. PLoS One. 2021;16(6):e0253329. Published 2021 Jun 15. doi:10.1371/journal.pone.0253329
18. Ayanian S, Reyes J, Lynn L, Teufel K. The association between biomarkers and clinical outcomes in novel coronavirus pneumonia in a US cohort. Biomark Med. 2020;14(12):1091–1097. doi:10.2217/bmm-2020-0309
19. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med. 1985;13(10):818–829.
20. Pannu AK, Kumar M, Singh P, et al. Severe Acute Respiratory Infection Surveillance during the Initial Phase of the COVID-19 Outbreak in North India: A Comparison of COVID-19 to Other SARI Causes. Indian J Crit Care Med. 2021;25(7):761–767. doi:10.5005/jp-journals-10071-23882
21. Wilfong EM, Lovly CM, Gillaspie EA, et al. Severity of illness scores at presentation predict ICU admission and mortality in COVID-19. J Emerg Crit Care Med. 2021;5:7. doi:10.21037/jeccm-20-92
22. Noor FM, Islam MM. Prevalence and Associated Risk Factors of Mortality Among COVID-19 Patients: A Meta-Analysis. J Community Health. 2020;45(6):1270–1282. doi:10.1007/s10900-020-00920-x
23. Thakur B, Dubey P, Benitez J, et al. A systematic review and meta-analysis of geographic differences in comorbidities and associated severity and mortality among individuals with COVID-19. Sci Rep. 2021;11(1):8562. Published 2021 Apr 20. doi:10.1038/s41598-021-88130-w
24. Sheshah E, Sabico S, Albakr RM, et al. Prevalence of diabetes, management and outcomes among Covid-19 adult patients admitted in a specialized tertiary hospital in Riyadh, Saudi Arabia. Diabetes Res Clin Pract. 2021;172:108538. doi:10.1016/j.diabres.2020.108538

25. Rajendran K, Krishnasamy N, Rangarajan J, Rathinam J, Natarajan M, Ramachandran A. Convalescent plasma transfusion for the treatment of COVID-19: Systematic review. J Med Virol. 2020;92(9):1475–1483. doi:10.1002/jmv.25961
26. Simonovich VA, Burgos Pratx LD, Scibona P, et al. A Randomized Trial of Convalescent Plasma in Covid-19 Severe Pneumonia. N Engl J Med. 2021;384(7):619–629. doi:10.1056/NEJMoa2031304

Tables

Table-1: General characteristics of the COVID-19 patients who received awake SPP-HFNO

Characteristics		All (N=71)	Success (N=34)	Fail (N=37)	p-value
Age (Mean ± SD)		56.11 ± 12.02	56.12 ± 10.02	56.11 ± 13.74	0.9973
Male (N, %)		(61) 86%	(32) 94%	(29) 78%	0.0875
BMI (Mean ± SD)		29.08 ± 5.59	28.31 ± 4.46	29.80 ± 6.44	0.2566
APACHE II (Mean ± SD)		14.82 ± 6.76	12.47 ± 3.34	16.97 ± 8.14	0.0033
ED Source (N, %)		(N=38) 53%	(N=21) 62%	(N=17) 46%	0.2356
Survival (N, %)		(N=52) 73%	(N=33) 97%	(N=19) 51%	< 0.001
ICU length of stay (Mean ± SD)		9.84 ± 8.27	6.21 ± 4.63	13.19 ± 9.44	< 0.001
Total length of stay (Mean ± SD)		19.42 ± 12.03	18.12 ± 13.00	20.62 ± 11.10	0.388
Comorbidities	Diabetes mellitus (N, %)	N=38, 54%	N=17, 50%	N=21, 57%	0.6377
	Hypertension (N, %)	N=32, 45%	N=17, 50%	N=15, 40%	0.479
	Cardiac disease (N, %)	N=13, 18%	N= 4, 12%	N=9, 24%	0.225
	Liver disease (N, %)	N=0, 0%	N=0, 0%	N=0, 0%	NA
	Neurologic disease (N, %)	N=4, 6%	N=0, 0%	N=4, 11%	0.116
	Cancer (N, %)	N=3, 4%	N=1, 3%	N=2, 5%	1
	Pulmonary disease (N, %)	N=7, 9%	N=2, 6%	N=5, 11%	0.432
	Kidney disease (N, %)	N=9, 13%	N=3, 9%	N=6, 16%	0.482

Table-2: Laboratory evaluation of the COVID-19 patients who received awake SPP-HFNO

Characteristics	All (N=71) (Mean ± SD)	Success (N=34) (Mean ± SD)	Fail (N=37) (Mean ± SD)	p-value
WBC	14.47 ± 7.17	12.82 ± 4.72	15.96 ± 8.72	0.062
Hemoglobin	14.18 ± 1.96	14.45 ± 1.52	13.91 ± 2.31	0.249
Platelets	261 ± 106	288 ± 122	237 ± 84	0.049
INR	1.23 ± 0.27	1.24 ± 0.25	1.22 ± 0.29	0.825
BUN	10.03 ± 6.85	9.29 ± 5.78	10.69 ± 7.81	0.389
Creatinine	104.2 ± 71.49	88.82 ± 30.07	118.2 ± 90.97	0.079
ALT	111.62 ± 106.70	125.10 ± 122.28	98.92 ± 91.69	0.314
AST	95.32 ± 60.19	96.65 ± 56.57	94.11 ± 64.87	0.861
LDH	992.90 ± 1999.19	753.70 ± 204.79	1213 ± 2762.12	0.320
Ferritin	2537.30 ± 6613.82	1916.60 ± 2148.14	3108 ± 8951.35	0.437
D-Dimer	7.52 ± 20.80	11.58 ± 28.26	3.78 ± 8.90	0.132
Lactate	2.75 ± 1.55	2.63 ± 1.22	2.85 ± 1.81	0.563
CRP	119.96 ± 80.43	112.41 ± 72.19	126.90 ± 88.76	0.452

Table-3: Physiologic parameters of the COVID-19 patients who received awake SPP-HFNO

Characteristics	All (N=71) (Mean ± SD)	Success (N=34) (Mean ± SD)	Fail (N=37) (Mean ± SD)	p-value
HFNO Time	4.17 ± 3.08	5.03 ± 2.84	3.38 ± 3.11	0.022
SPP Time	4.27 ± 3.09	5.26 ± 2.99	3.35 ± 2.93	0.008
FiO_2 Max	92.61 ± 14.38	86.67 ± 18.27	98.06 ± 6.24	0.001
Flow Max	43.33 ± 6.84	42.73 ± 8.49	43.89 ± 4.94	0.495
Pre SpO_2	89.48 ± 3.76	90.64 ± 4.11	88.42 ± 3.16	0.015
Post SpO_2	94.59 ± 3.50	96.09 ± 2.07	93.22 ± 4.03	< 0.001
Diff SpO_2	5.03 ± 3.72	5.45 ± 3.62	4.64 ± 3.86	0.369
Pre RR	32.03 ± 7.43	31.82 ± 7.10	32.22 ± 7.91	0.824
Post RR	28.29 ± 7.25	27.18 ± 7.26	29.31 ± 7.30	0.230
Diff RR	- 3.85 ± 6.48	- 4.88 ± 6.63	- 2.92 ± 19.17	0.215
Pre HR	95.23 ± 16.00	91.03 ± 18.24	99.08 ± 12.97	0.040
Post HR	88.88 ± 18.53	85.27 ± 16.85	92.19 ± 19.85	0.122
Diff HR	-6.54 ± 15.30	-5.97 ± 10.13	-7.06 ± 19.17	0.767

Table-4: Treatment of the COVID-19 patients who received awake SPP-HFNO

Treatment	All (N=71) (N, %)	Success (N=34) (N, %)	Fail (N=37) (N, %)	p-value
HCQ	N=4, 6%	N=2, 6%	N=2, 5%	1
Azithromycin	N=52, 73%	N=28, 82%	N=24, 65%	0.114
Dexamethasone	N=30, 42%	N=11, 32%	N=19, 51%	0.149
Methylprednisolone	N=47 66%	N=26, 76%	N=21, 57%	0.131
Favipiravir	N=27, 30%	N=13, 38%	N=14, 38%	1
Tocilizumab	N=37, 52%	N=19, 56%	N=18, 49%	0.637
Convalescent Plasma	N=20, 28%	N=15, 44%	N=5, 13%	0.007
Statins	N=28, 39%	N=14, 41%	N=14, 38%	0.812
Anticoagulation	Full=16,Mod=53,Low=2	Full=7,Mod=25,Low=2	Full=9,Mod=28,Low=0	0.510

Figures

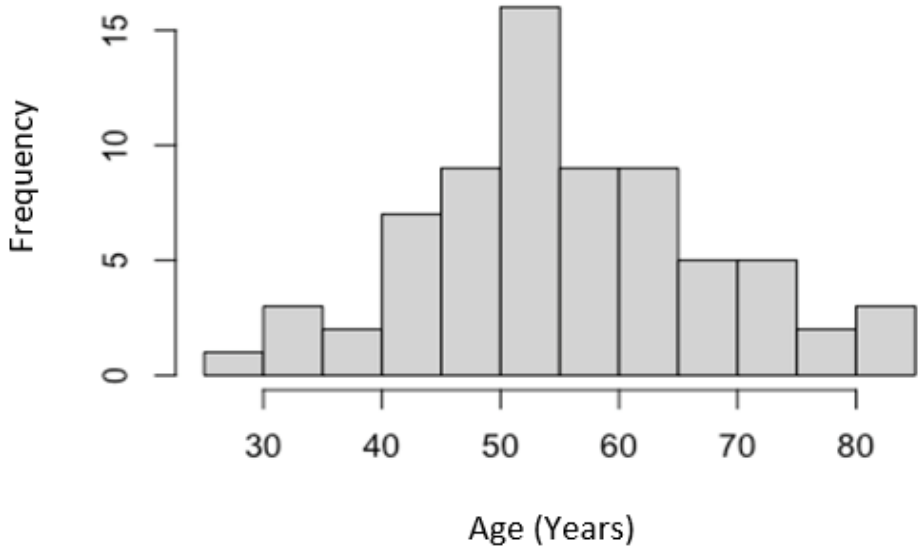

Figure 1

Age distribution of the COVID-19 patients who received awake SPP-HFNO

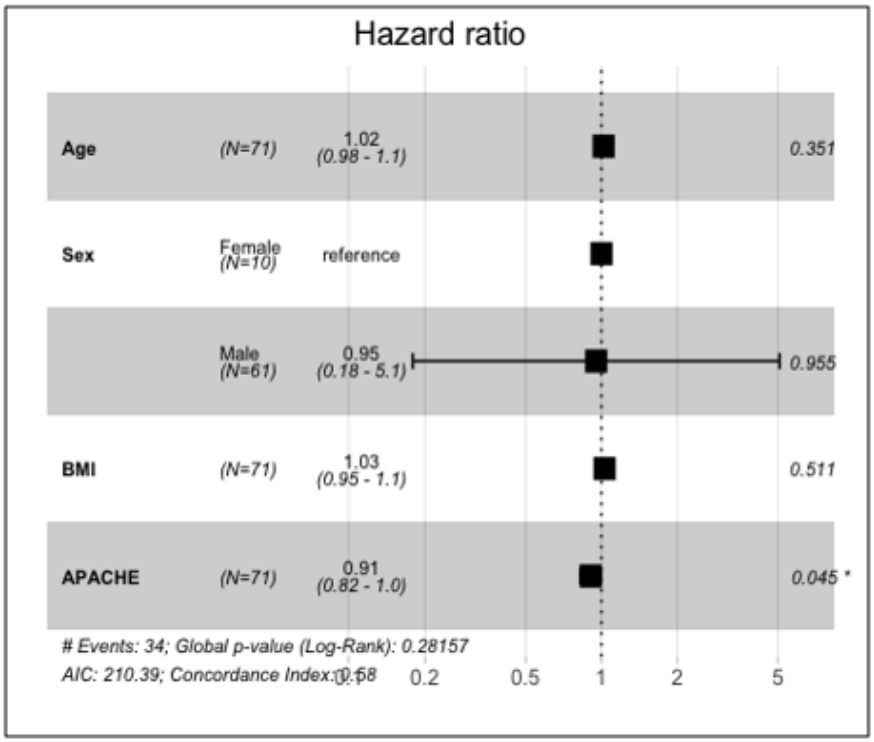

Figure 2

The Hazard ratio for the general characteristics of the COVID-19 patients who received awake SPP-HFNO

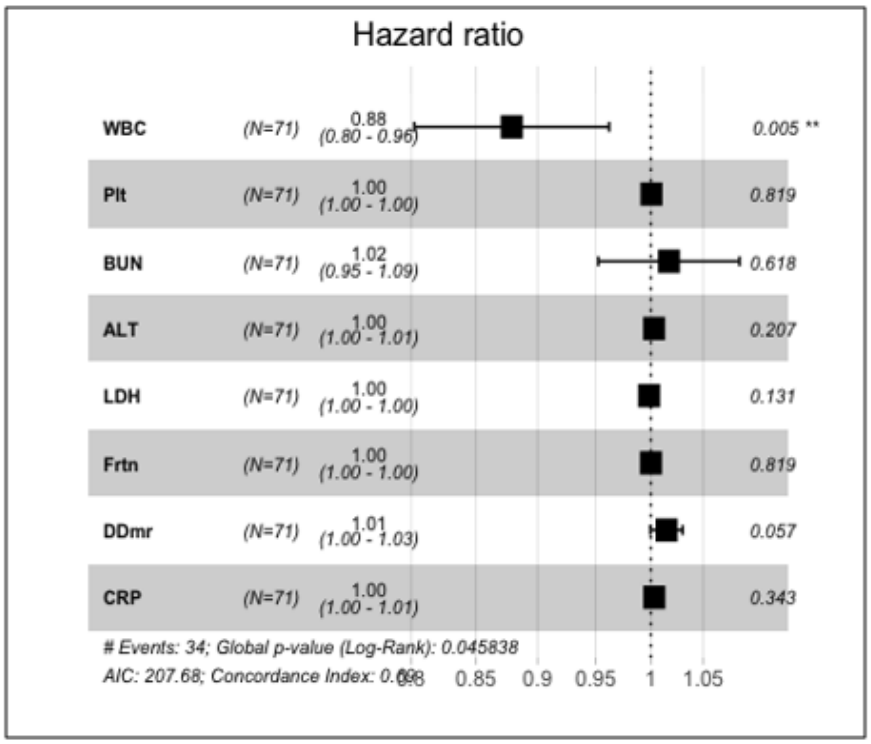

Figure 3

The Hazard ratio for the laboratory tests of the COVID-19 patients who received awake SPP-HFNO

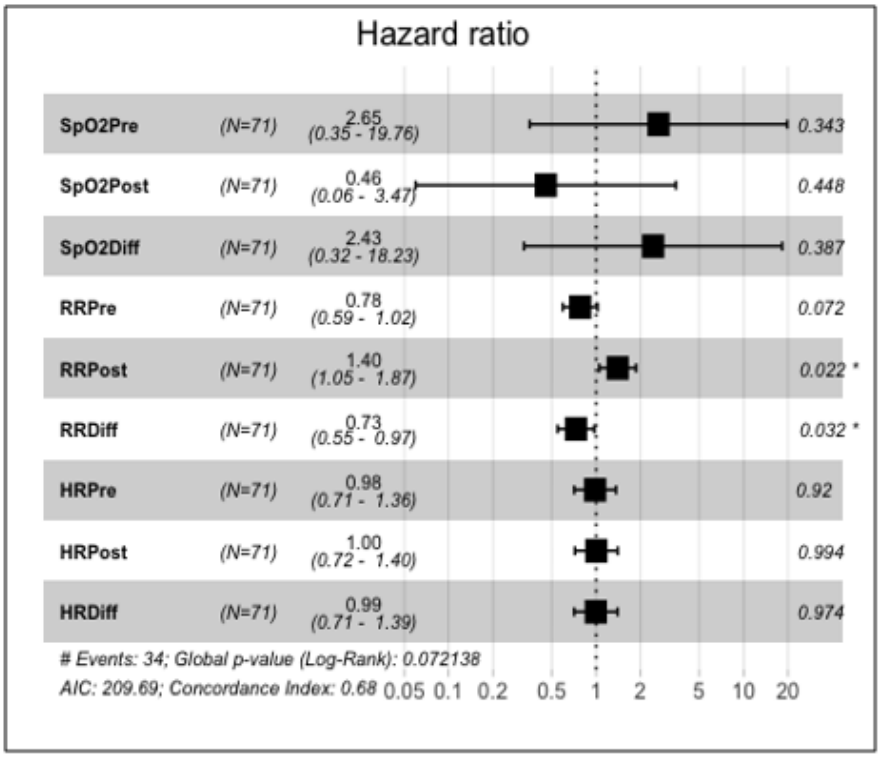

Figure 4

The Hazard ratio for the physiologic parameters of the COVID-19 patients who received awake SPP-HFNO

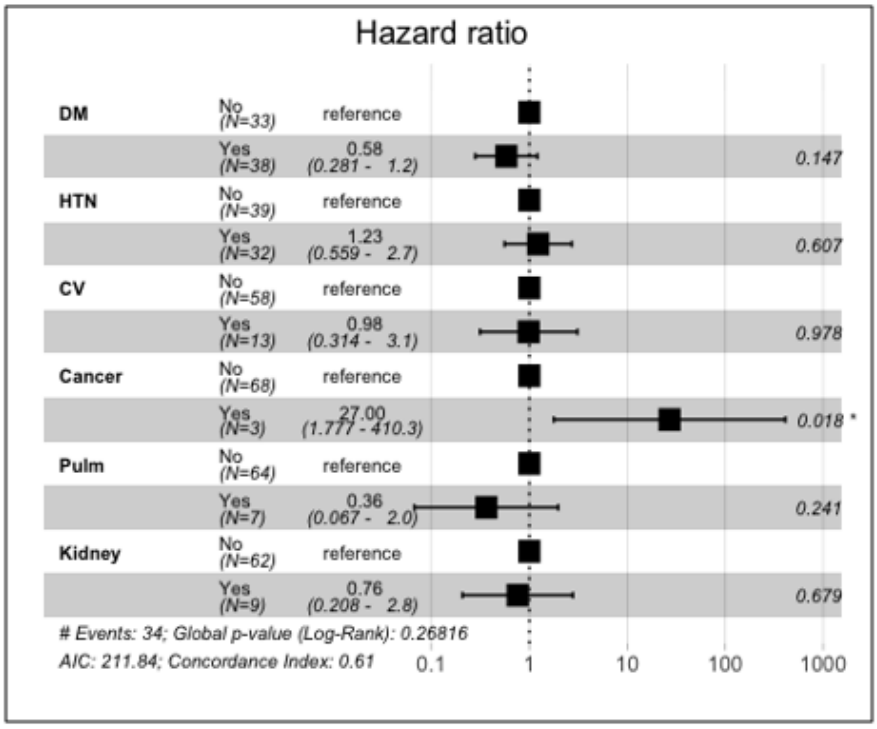

Figure 5

The Hazard ratio for the comorbidities of the COVID-19 patients who received awake SPP-HFNO

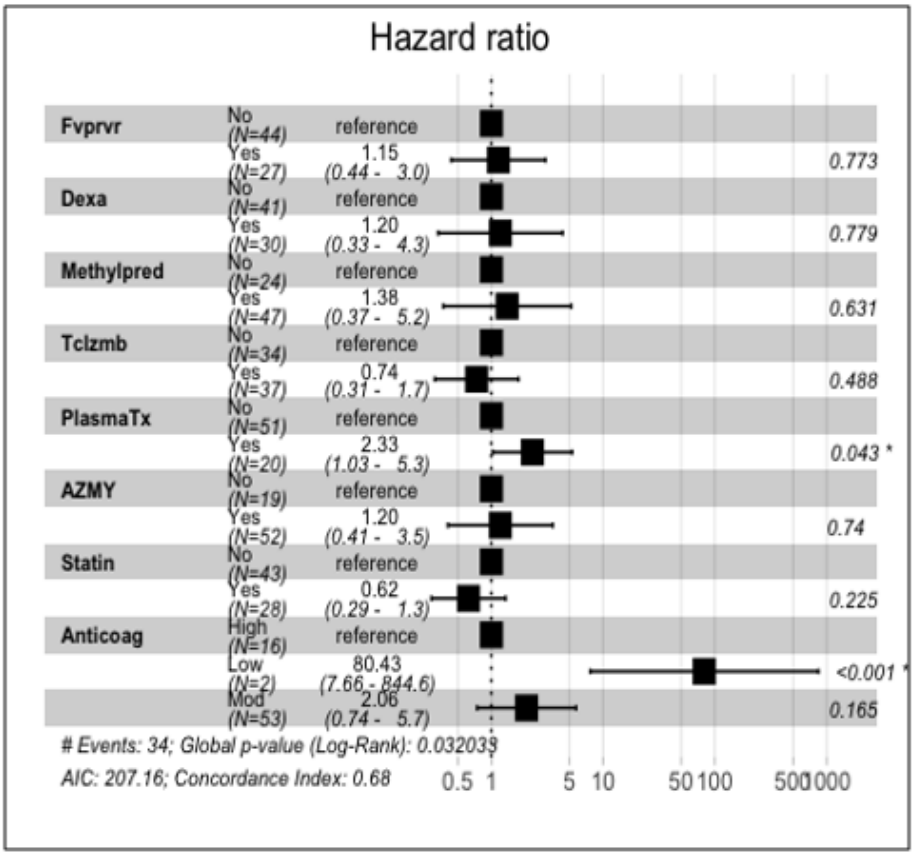

Figure 6

The Hazard ratio for the treatment of the COVID-19 patients who received awake SPP-HFNO