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Factors influencing the prognosis of COVID-19 patients treated with High-Flow Nasal Oxygen Therapy (HFNOT) — a retrospective analysis

Short title: Martyna Wyszyńska-Gołaszewska, Wojciech Naumnik, Factors influencing the prognosis of COVID-19 patients treated with High-Flow Nasal Oxygen Therapy (HFNOT)

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ABSTRACT

Introduction: HFNOT plays an essential role in the management of respiratory failure in COVID-19 patients. However, identifying precise prognostic factors to predict HFNOT outcomes remains crucial for optimizing patient management.

Materials and methods: A retrospective analysis was made of 103 patients treated with HFNOT in Temporary Hospital nr 1 in Białystok. HFNOT failure group (58 pts; 56.3%) was defined as patients requiring treatment escalation, intubated, and/or patients who died. The

rest was the success group (45 pts; 43.7%). Clinical factors and laboratory tests were analyzed at the beginning of HFNOT, after 2, 24, and 72 hours after the start of treatment, and at the end of treatment. Statistical analysis was run in R software, version R4.1.2.

Results: It was found that age, arterial hypertension, heart failure, HFNOT duration days and levels of C-reactive protein, procalcitonin, number of white blood cells close to termination of the therapy, the oxygen content of the respiratory mixture (%) in 24h, heart rate in 72h, partial pressure of oxygen (mmHg) at the beginning of therapy and saturation during treatment are prognostic factors allowing to predict the effect of HFNOT therapy ($p < 0,05$). The use of convalescent plasma, remdesivir, tocylizumab, and olumiant has not been shown to improve the impact of the HFNOT used.

Conclusions: This study highlights critical prognostic factors that influence the outcomes of COVID-19 patients treated with HFNOT. Further research is needed to refine these prognostic models and to explore the potential of early invasive ventilation in patients with unfavorable prognostic indicators.

Keywords: COVID-19, HFNOT (high-flow nasal oxygen therapy), prognosis of COVID-19 patients

Introduction

High-Flow Nasal Oxygen Therapy (HFNOT) is recommended by the National Institutes of Health (NIH) and the Surviving Sepsis Campaign guidelines for the treatment of acute hypoxemic respiratory failure during COVID-19, requiring support beyond conventional oxygen devices [1, 2]. HFNOT is a safe method of respiratory support in COVID-19 patients, reducing the need for invasive ventilation and therapy escalation compared to Conventional Oxygen Therapy (COT) in patients with COVID-19 and acute hypoxemic respiratory failure [3]. Additionally, it significantly reduces the number of intubations and subsequent invasive mechanical ventilation [4]. However, no specific defined factors affect the prognosis of patients treated with this method.

The main objective of this analysis was to determine the factors influencing the prognosis of patients with COVID-19 treated with high-flow nasal oxygen therapy.

Materials and methods

A retrospective analysis was made of 103 patients treated with HFNOT in Temporary Hospital nr 1 in Białystok from December 2020 to April 2022. Clinical factors and laboratory tests were analyzed at the beginning of HFNOT, after 2, 24, and 72 hours after the start of

treatment, and at the end of treatment. The criterion for initiating high-flow oxygen therapy was $SpO_2 \leq 92\%$ and/or RR ≥ 25 times/min while using conventional oxygen therapy. In most patients, the HFNOT flow was 30–60 L/min, FiO_2 100% to maintain oxygen saturation at 92–96%. HFNOT failure group (58 pts; 56.3%) was defined as patients requiring treatment escalation, intubated, and/or patients who died. The rest was the success group (45 pts; 43.7%). Patients undergoing high-flow oxygen therapy received treatment by applicable standards for the treatment of COVID-19 infection with respiratory failure.

Statistical analysis was run in R software, version R4.1.2. Groups were compared with the t-student independent test, Mann–Whitney U-test, Pearson chi-square test, or Fisher exact test, as appropriate. Two-step logistic regression was used to quantify the impact of selected predictors on the odds of therapy failure. All tests assumed statistical significance when $p < 0.05$.

Results

Characteristics of all patients and their comparison between failure and success groups

The study group consisted of 103 patients aged 68.83 ± 15.00 years on average treated with HFNOT in Temporary Hospital nr 1 in Białystok, out of which 45.6% were female. Over half of the patients suffered from arterial hypertension (AH), one-third were obese, and roughly one out of five had atrial fibrillation (AF), heart failure (HF), or type 2 diabetes mellitus (T2DM). HFNOT lasted typically 6.00 days. Patients were treated with remdesivir or tocylizumab, less frequently with olumiant or plasma. Over one-third of patients were intubated, and a similar proportion of patients died. Detailed basic characteristics are presented in Table 1.

HFNOT failure group was defined as patients requiring treatment escalation, intubated, and/or patients who died. It consisted of n = 58 patients (56.3%). The rest was defined as a success group (n = 45, 43.7%). The average age was significantly higher in the failure group. The failure group suffered from AH and HF significantly more often compared to the success group. The proportion of patients with AH in the failure group was 75.9% and in the success group, it was 53.3%. The proportion of patients with HF in the failure group was 32.8% while in the success group, n = 3 patients suffered from HF. HFNOT lasted three days in the failure group and 11.00 days in the success group, difference was statistically

significant. Non-invasive ventilation (NIV) was added to the therapy in the case of half of the failure group (53.7%) (Table 2).

At the start of HFNOT patients who died and/or were intubated differed from the success group with procalcitonin (PCT) level, which was significantly higher in the failure group. At the end of the therapy patients with failed outcomes had significantly higher levels of C-reactive protein (CRP), PCT, D-dimer, ferritin, white blood cells (WBC), aspartate transaminase (AST), creatinine and interleukin-6 (IL-6) compared to patients with positive outcome of the therapy (Table 3).

Failure and success groups were significantly differentiated with FiO_2 levels after 24h and 72h, respectively. Also, HR and PO_2/FiO_2 differed between the groups after 72h. HR was higher within the failure group. PO_2/FiO_2 was lower in patients who failed the therapy. Ph after 24h was significantly lower within the failure group. PO_2 at the therapy start had a significantly lower level in the failure group. Saturation was significantly lower in the failure group at every record (Table 4).

Logistic regression analysis — parameters determining the odds of therapy failure

Two-step logistic regression was performed to identify factors impacting the odds of HFNOT failure. In the univariate step, it was found that age impacts the odds significantly. In the case of patients one year older, the chance of therapy failure was 4% higher. AH and HF would increase the odds of failure almost 3× and 7×, respectively.

One more day of therapy duration was associated with 22% lower odds of failure. Using NIV was associated with 8× higher odds of failure. CRP, PCT, and WBC close to termination of the therapy determined its outcome in a significant way. CRP and WBC higher by one resulted in 7% and 17% higher failure odds, respectively. PCT effect size was substantial when the factor was higher by one unit. Additionally, substantially increased odds of therapy failure were observed with FiO_2 24h increase by one unit.

Higher HR 72h was associated with increased odds of failure. The partial pressure of oxygen (mmHg) at the beginning of therapy higher by one decreased the odds by 27%. Saturation higher by one percentage point meant decreased odds of failure by 10–20%, depending on the timing of measurement (Table 5).

In the multivariate analysis, the odds of therapy failure were dependent on saturation at 24h and 72h, HR at 72h, and HF disease. Saturation after 24h higher by one percentage point was associated with 51% higher odds of failure. Saturation after 72h higher by one

percentage point was associated with 20% lower odds of failure. HR after 72h higher by one resulted in 9% higher odds of failure. HF disease resulted in 14× increased odds of failure. Other predictors included in the multivariate model (saturation after 2h, AH disease, and FiO_2 after 24h) did not prove to impact failure odds significantly.

Discussion

The application of High-Flow Nasal Oxygen Therapy in managing acute hypoxemic respiratory failure, particularly among COVID-19 patients, has revolutionized treatment protocols by minimizing the necessity for invasive mechanical ventilation (IMV) [5, 6]. However, identifying precise prognostic factors to predict HFNOT outcomes remains crucial for optimizing patient management.

Our findings indicate that age is a significant prognostic factor for HFNOT outcomes. Advanced age is well-documented as a predictor of poor prognosis in COVID-19 patients due to a higher incidence of comorbidities and diminished physiological reserve. In the present study, each additional year of age increased the odds of HFNOT failure by 4%. This is consistent with studies showing that older adults are particularly vulnerable to severe outcomes in COVID-19, especially when requiring respiratory support [7]. A study by Grasselli et al. corroborates this, demonstrating that advanced age is a critical determinant of mortality among COVID-19 patients in intensive care units [8].

Cardiovascular comorbidities, such as arterial hypertension and heart failure, were also found to be significant predictors of HFNOT failure in the present analysis. Patients with AH had nearly a threefold increased risk of therapy failure, while those with HF faced a sevenfold increase in risk. In the present study, in the case of patients treated with HFNOT, heart failure increased the odds of therapy failure almost 7 times. These findings are supported by existing literature, which indicates that patients with pre-existing cardiovascular conditions have a higher susceptibility to severe COVID-19 complications and poorer outcomes when subjected to non-invasive respiratory support [9–11]. For instance, Chatrath et al. highlighted the poor prognosis for COVID-19 patients with concomitant heart failure, underlining the challenges in managing these high-risk patients [12].

Our study also identified the duration of HFNOT as a critical factor in patient outcomes. Patients in the failure group required therapy escalation within three days, compared to eleven days in the success group. This finding aligns with recent evidence suggesting that prolonged non-invasive support, without timely escalation to IMV, may lead

to worse outcomes, particularly in patients with lower initial PaO_2 values [13, 14]. The systematic review by Ridjab et al. supports early intubation in severe cases of COVID-19-associated ARDS to mitigate the risks associated with delayed invasive ventilation [15]. In the present analysis, NIV was added to the therapy in case of increasing respiratory effort and decreasing saturation in patients treated with HFNOT. Half of the failure group was treated with non-invasive ventilation (53,7%). Necessity of NIV application was associated with 8 times higher odds of failure. It is possible that the older age of the patients and comorbidities worsened the prognosis and also contributed to the failure of NIV.

In the present study, inflammatory markers, including C-reactive protein (CRP), procalcitonin (PCT), and white blood cell (WBC) count, were significantly elevated at the termination of HFNOT in the failure group, suggesting a link between these markers and poor outcomes. The present studies corroborate the findings reported by other authors [16, 17]. Elevated levels of these markers may indicate secondary bacterial infections, a common complication in critically ill COVID-19 patients, which are known to worsen prognosis [16, 17]. Liu et al. have demonstrated that high levels of CRP and PCT are associated with severe disease and poor outcomes in COVID-19 patients, reinforcing the importance of monitoring these biomarkers during HFNOT [18].

Interestingly, the use of adjunctive therapies such as remdesivir, tocilizumab, and convalescent plasma did not significantly improve HFNOT outcomes in the present cohort. This finding is consistent with recent meta-analyses that have questioned the effectiveness of these treatments in altering the course of severe COVID-19, particularly when used alongside advanced respiratory support [19]. A study by Pilgram et al. also concluded that remdesivir did not significantly impact the outcomes of severe COVID-19 cases, suggesting that its role may be limited in the context of advanced respiratory interventions [20].

One limitation of the present study was the inability to calculate the ROX index due to the absence of respiratory rate data. The ROX index has been validated as a predictor of HFNOT success, and its inclusion could enhance the early identification of patients at risk for treatment failure [21]. The work by de Carvalho et al. underscores the utility of the ROX index in predicting the need for mechanical ventilation in COVID-19 patients undergoing HFNOT [22].

Conclusions

In conclusion, this study highlights critical prognostic factors that influence the outcomes of COVID-19 patients treated with HFNOT. Age, cardiovascular comorbidities,

duration of HFNOT, and inflammatory markers are pivotal in predicting therapy success or failure. These findings suggest that an integrated approach, combining close monitoring of clinical parameters with timely therapeutic interventions, is essential for optimizing outcomes in this patient population. Further research is needed to refine these prognostic models and to explore the potential of early invasive ventilation in patients with unfavorable prognostic indicators.

Article information

Data availability statement: *Data reported in this study are available upon request from authors.*

Ethics statement: *The study was approved by the Ethics Committee of the Medical University of Bialystok, Poland (protocol code: APK.002.236.2021, date of approval: 29.04.2021).*

Author contributions: *conceptualization, methodology, investigation, data curation, writing (original draft preparation) — M. Wyszyńska-Gołaszewska; writing (review and editing), supervision — W. Naumnik; all authors have read and agreed to the published version of the manuscript.*

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Supplementary material: *None.*

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Table 1. Basic characteristics in the total group

Variable	All patients (n = 103)
Sex, female [n (%)]	47 (45.6)
Age [years]	68.83 ± 15.00
Weight [kg]	90.24 ± 17.97
Height [m]	1.69 ± 0.09
BMI [kg/m^{2}]	31.67 ± 5.52
Comorbidities [n (%)]	
AH	68 (66.0)
T2DM	19 (18.4)
COPD/Asthma	8 (7.8)
CKD	6 (5.8)
Obesity	35 (34.0)
AF	23 (22.3)
HF	22 (21.4)
Mental illness	7 (6.8)
Active cancer	3 (2.9)
Other disease	42 (40.8)
HFNOT duration [days]	6.00 (2.00;11.00)
NIV [n (%)]	26 (35.6)
Drugs [n (%)]	
Remdesivir	26 (25.2)
Tocilizumab	24 (23.3)
Plasma	2 (1.9)
Olumiant	13 (12.6)
HRCT [points]	18.00 (13.25;20.00)
HRCT [%]	62.73 ± 19.86
Intubation [n (%)]	35 (34.0)
Death [n (%)]	27 (32.5)

BMI — body mass index; AH — arterial hypertension; T2DM — type 2 diabetes mellitus; COPD — [please expand]; CKD — [please expand]; AF — atrial fibrillation; HF — heart failure; HFNOT — high-flow nasal oxygen therapy; NIV — non-invasive ventilation; HRCT — [please expand]

Data presented as n (%) for categorical parameters and mean ± standard deviation or median (interquartile range), depending on distribution normality, for numerical parameters

Table 2. Basic characteristics — comparison between failure and success groups

Variable	HFNOT failure (n = 58)	HFNOT success (n = 45)	MD (95% CI)	p
Sex, female [n (%)]	29 (50.0)	18 (40.0)	–	0.417
Age [years]	72.71 ± 15.16	63.82 ± 13.37	8.88 (3.21;14.56)	**0.002**[1]
Weight [kg]	88.75 ± 16.85	91.95 ± 19.45	–3.20 (–14.11;7.71)	0.557[1]
Height [m]	1.68 ± 0.09	1.70 ± 0.09	–0.01 (–0.07;0.04)	0.627[1]
BMI [kg/m^2]	31.74 ± 5.23	31.60 ± 5.96	0.14 (–3.04;3.32)	0.930[1]
Comorbidities [n (%)]				
AH	44 (75.9)	24 (53.3)	–	**0.029**
T2DM	13 (22.4)	6 (13.3)	–	0.356
COPD/Asthma	4 (6.9)	4 (8.9)	–	0.727[2]
CKD	5 (8.6)	1 (2.2)	–	0.228[2]
Obesity	20 (34.5)	15 (33.3)	–	> 0.999
AF	15 (25.9)	8 (17.8)	–	0.460
HF	19 (32.8)	3 (6.7)	–	**0.003**
Mental illness	4 (6.9)	3 (6.7)	–	> 0.999[2]
Active cancer	3 (5.2)	0 (0.0)	–	0.255[2]
Other disease	23 (39.7)	19 (42.2)	–	0.951
HFNOT duration days	3.00 (2.00;5.00)	11.00 (7.00;16.00)	–8.00 (–10.00;–6.00)	**< 0.001**
NIV [n (%)]	22 (53.7)	4 (12.5)	–	**0.001**
Drugs [n (%)]				
Remdesivir	15 (25.9)	11 (24.4)	–	> 0.999
Tocylizumab	12 (20.7)	12 (26.7)	–	0.634
Plasma	1 (1.7)	1 (2.2)	–	> 0.999[2]
Olumiant	5 (8.6)	8 (17.8)	–	0.276
HRCT [points]	19.00 (14.75;21.00)	17.00 (12.00;20.00)	2.00 (–1.00;4.00)	0.272
HRCT [%]	66.25 ± 19.20	58.50 ± 20.82	7.75 (–10.07;25.57)	0.375[1]

MD — mean or median difference (failure vs success); CI — confidence interval; BMI — body mass index; AH — arterial hypertension; T2DM — type 2 diabetes mellitus; COPD — [please expand]; CKD — [please expand]; AF — atrial fibrillation; HF — heart failure;

HFNOT — high-flow nasal oxygen therapy; NIV — non-invasive ventilation; HRCT — [please expand]

Data presented as n (%) for categorical parameters and mean ± standard deviation or median (interquartile range), depending on distribution normality, for numerical parameters. Failure is defined as death and/or intubation. Success is defined as not intubated and not dead

Table 3. Laboratory tests outcomes in split-to-failure and success groups

Variable	HFNOT failure (n = 58)	HFNOT success (n = 45)	MD (95% CI)	p
At HFNOT start				
CRP	114.50 (83.86;191.25)	131.00 (84.00;205.00)	–16.50 (–45.00;16.00)	0.382
PCT	0.22 (0.09;0.72)	0.09 (0.05;0.27)	0.14 (0.00;0.17)	**0.009**
D–dimer	1283.00 (680.50;1796.50)	1086.00 (737.00;2160.00)	197.00 (–271.00;408.00)	0.668
Ferritin	1356.00 (817.00;2850.00)	1135.50 (778.50;1588.00)	220.50 (–122.00;706.00)	0.193
WBC	7.06 (5.23;9.29)	6.40 (4.67;8.62)	0.66 (–0.45;1.97)	0.230
RBC	4.27 ± 0.66	4.49 ± 0.60	–0.22 (–0.47;0.03)	0.083[1]
HGB	12.94 ± 1.85	13.52 ± 1.75	–0.58 (–1.30;0.14)	0.110[1]
PLT	192.55 ± 81.50	189.22 ± 83.03	3.33 (–29.32;35.97)	0.840[1]
AST	61.50 (44.00;83.00)	55.00 (40.00;83.00)	6.50 (–6.00;18.00)	0.270
ALT	38.50 (26.25;57.50)	36.00 (24.00;54.00)	2.50 (–5.00;12.00)	0.476
Creatinine	1.04 (0.84;1.35)	0.91 (0.77;1.08)	0.13 (–0.03;0.27)	0.122
IL-6	94.50 (59.25;169.25)	86.00 (55.80;167.00)	8.50 (–27.00;36.80)	0.676
HFNOT termination				
CRP	77.73 (38.00;150.00)	2.67 (0.97;5.09)	75.06 (62.01;101.09)	**< 0.001**
PCT	0.35 (0.10;2.67)	0.05 (0.05;0.07)	0.30 (0.20;0.84)	**< 0.001**
D–dimer	3149.00 (1347.50;6054.50)	841.00 (511.50;1919.50)	2308.00 (750.00;3197.00)	**< 0.001**
Ferritin	1512.00 (917.50;3612.50)	665.00 (516.00;916.00)	847.00 (121.00;2386.00)	**0.015**
WBC	11.22 (8.93;15.60)	8.16 (5.94;11.44)	3.06 (1.31;4.88)	**0.001**
RBC	4.23 ± 0.71	4.21 ± 0.55	0.01 (–0.25;0.27)	0.928[1]
HGB	12.87 ± 2.02	12.76 ± 1.61	0.10 (–0.65;0.86)	0.786[1]
PLT	232.62 ± 82.44	226.47 ± 87.62	6.15 (–29.07;41.37)	0.729[1]
AST	40.00 (30.75;60.00)	26.00 (21.00;38.00)	14.00 (6.00;20.00)	**< 0.001**
ALT	38.50 (29.75;53.50)	46.00 (28.00;72.00)	–7.50 (–17.00;4.00)	0.263
Creatinine	0.93 (0.71;1.31)	0.79 (0.60;0.93)	0.14 (0.04;0.33)	**0.013**
IL-6	51.50 (31.05;138.00)	8.40 (2.60;57.50)	43.10 (16.70;58.80)	**< 0.001**

MD — mean or median difference (failure vs success); CI — confidence interval; HFNOT — high-flow nasal oxygen therapy; CRP — C-reactive protein, PCT — procalcitonin, WBC — white blood cells; RBC — red blood cells; HGB — [please expand]; PLT — [please expand]; AST — aspartate transaminase; ALT — [please expand]; IL-6 — interleukin-6

Data presented as mean ± standard deviation or median (interquartile range), depending on distribution normality. Failure is defined as death and/or intubation. Success is defined as not intubated and not dead. Comparisons made with t-Student independent test[1] or Mann–Whitney U test, as appropriate

Table 4. Respiratory and cardiological parameters over time in split into failure and success groups

Variable	Time [h]	HFNOT failure (n = 58)	HFNOT success (n = 45)	MD (95% CI)	p
sBP	0	131.04 ± 19.84	132.00 ± 22.17	–0.96 (–9.47;7.55)	0.823[1]
	2	136.23 ± 21.71	130.48 ± 15.46	5.74 (–3.43;14.92)	0.216[1]
	24	130.16 ± 20.36	125.73 ± 21.97	4.43 (–4.20;13.05)	0.311[1]
	72	130.66 ± 20.18	124.49 ± 19.61	6.17 (–3.34;15.68)	0.200[1]
	Int.	–	–	–	–
dBP	0	75.75 ± 13.60	78.89 ± 13.48	–3.14 (–8.64;2.36)	0.259[1]
	2	76.71 ± 9.81	75.39 ± 10.61	1.32 (–3.63;6.27)	0.596[1]
	24	75.80 ± 11.85	75.53 ± 13.43	0.27 (–4.88;5.42)	0.918[1]
	72	77.00 (70.00;86.00)	76.00 (67.50;81.50)	1.00 (–4.00;9.00)	0.425
	Int.	–	–	–	–
FiO_2	0	0.80 (0.21;0.80)	0.80 (0.80;0.80)	0.00 (0.00;0.00)	0.390
	2	1.00 (1.00;1.00)	1.00 (1.00;1.00)	0.00 (0.00;0.00)	0.467
	24	1.00 (1.00;1.00)	1.00 (0.90;1.00)	0.00 (0.00;0.00)	**0.026**
	72	1.00 (1.00;1.00)	1.00 (0.90;1.00)	0.00 (0.00;0.00)	**0.045**
	Int.	–	–	–	–
HCO_3	0	22.35 ± 4.47	22.39 ± 2.62	–0.05 (–3.01;2.92)	0.975[1]
	2	22.97 ± 4.44	23.82 ± 3.34	–0.85 (–3.80;2.11)	0.565[1]
	24	23.42 ± 3.71	24.31 ± 3.75	–0.90 (–3.24;1.45)	0.445[1]
	72	24.71 ± 3.92	25.15 ± 3.42	–0.43 (–3.31;2.45)	0.760[1]
	Int.	–	–	–	–
HR	0	90.00 (79.50;100.00)	88.00 (75.00;100.00)	2.00 (–5.00;10.00)	0.633
	2	83.14 ± 14.54	78.30 ± 13.70	4.84 (–2.01;11.69)	0.163[1]
	24	84.52 ± 17.45	79.31 ± 15.52	5.21 (–1.55;11.97)	0.129[1]
	72	87.45 ± 13.69	76.52 ± 12.90	10.92 (4.56;17.29)	**0.001**[1]
	Int.	–	–	–	–
Lac	0	2.79 ± 1.37	2.17 ± 0.76	0.62 (–0.77;2.01)	0.348[1]
	2	2.05 (1.67;2.72)	1.70 (1.45;2.05)	0.35 (–0.30;1.10)	0.315
	24	2.38 ± 1.28	1.98 ± 0.49	0.40 (–0.56;1.37)	0.398[1]
	72	2.43 ± 0.95	2.60 ± 0.93	–0.17 (–1.31;0.98)	0.757[1]
	Int.	1.90 (1.85;2.55)	–	–	–
PO_2/FiO_2	0	64.75 (56.28;135.78)	68.75 (65.12;71.25)	–4.00 (–15.96;6.50)	0.254
	2	64.60 (59.75;74.90)	89.60 (70.60;105.80)	–25.00 (–37.49;0.10)	0.060
	24	62.56 (49.90;73.90)	68.22 (59.55;84.30)	–5.67 (–18.44;5.70)	0.310
	72	58.50 (50.90;72.00)	73.30 (62.20;116.90)	–14.80 (–36.70;–0.60)	**0.040**

Variable	Time [h]	HFNOT failure (n = 58)	HFNOT success (n = 45)	MD (95% CI)	p
	Int.	–	–	–	–
pCO_2	0	32.05 (30.35;35.03)	35.35 (29.35;39.22)	–3.30 (–7.30;3.30)	0.435
	2	31.98 ± 5.08	33.95 ± 6.08	–1.96 (–5.63;1.70)	0.285[1]
	24	35.33 ± 5.31	34.61 ± 7.82	0.72 (–3.09;4.53)	0.705[1]
	72	34.00 (30.80;36.20)	36.95 (31.15;40.78)	–2.95 (–6.40;3.10)	0.634
	Int.	–	–	–	–
ph	0	7.43 ± 0.03	7.43 ± 0.07	0.00 (–0.04;0.04)	0.983[1]
	2	7.45 ± 0.04	7.45 ± 0.04	0.00 (–0.02;0.03)	0.793[1]
	24	7.42 ± 0.04	7.46 ± 0.05	–0.03 (–0.06;–0.01)	**0.013**[1]
	72	7.43 (7.41;7.48)	7.45 (7.41;7.49)	–0.02 (–0.06;0.03)	0.474
	Int.	7.43 (7.40;7.47)	–	–	–
PO_2	0	45.30 (41.12;49.55)	54.50 (52.10;56.35)	–9.20 (–15.00;–4.00)	**0.001**[1]
	2	64.60 (58.15;74.90)	72.60 (67.30;105.80)	–8.00 (–32.80;2.00)	0.091
	24	60.50 (49.90;73.90)	65.30 (55.55;76.40)	–4.80 (–14.40;8.10)	0.582
	72	58.50 (50.80;72.00)	71.50 (62.20;116.90)	–13.00 (–34.50;1.80)	0.094
	Int.	–	–	–	–
Sat.	0	83.00 (74.25;86.00)	88.00 (83.00;89.00)	–5.00 (–7.80;–2.00)	< **0.001**
	2	93.00 (91.15;95.15)	95.00 (93.80;96.20)	–2.00 (–3.00;–0.40)	**0.009**
	24	92.25 (86.70;95.00)	95.00 (92.00;96.00)	–2.75 (–4.00;–1.00)	**0.005**
	72	88.90 (82.00;92.80)	96.00 (94.00;98.00)	–7.10 (–10.10;–4.00)	< **0.001**
	Int.	88.20 (83.60;90.00)	–	–	–

HFNOT — high-flow nasal oxygen therapy; MD — mean or median difference (failure *vs.* success); CI — confidence interval; sBP — [please expand]; dBP — [please expand]; FiO_2 — [please expand]; HCO_3 — [please expand]; HR — heart rate; Lac — [please expand]; PO_2/FiO_2 — [please expand]; pCO_2 — [please expand]; ph — [please expand]; PO_2 — [please expand]; Sat. — saturation; Int. — intubation

Data presented as mean ± standard deviation or median (interquartile range), depending on distribution normality. Failure is defined as death and/or intubation. Success is defined as not intubated and not dead. Comparisons made with t-Student independent test[1] or Mann–Whitney U test, as appropriate

Table 5. Logistic regression outcomes for failure of HFNOT. The table presents statistically significant results from the univariate model. For the remaining variables, the regression results were not significant

Variable	Univariate model		
	OR	**95% CI**	**p**
Age [years]	1.04	1.01–1.08	**0.004**
Comorbidities [n (%)]			
AH	2.75	1.20–6.48	**0.018**
HF	6.82	2.12–30.65	**0.004**
HFNOT duration days	0.78	0.70–0.86	**< 0.001**
NIV [n (%)]	8.11	2.61–31.16	**< 0.001**
CRP at HFNOT termination	1.07	1.04–1.11	**< 0.001**
PCT at HFNOT termination	114126.80	379.97–Inf	**< 0.001**
WBC at HFNOT termination	1.17	1.06–1.32	**0.004**
FiO_2			
0	0.46	0.08–2.29	0.348
2	93.20	0.11–289053.23	0.209
24	38693.17	12.62–Inf	**0.025**
72	544726.88	3.75–Inf	0.087
HR			
0	1.00	0.98–1.02	0.876
2	1.03	0.99–1.06	0.163
24	1.02	0.99–1.05	0.132
72	1.06	1.02–1.11	**0.002**
PO_2			
0	0.73	0.54–0.88	**0.009**
2	0.98	0.95–1.01	0.124
24	1.00	0.98–1.03	0.852
72	0.98	0.96–1	0.140
Sat.			
0	0.90	0.84–0.95	**0.001**
2	0.82	0.69–0.95	**0.014**
24	0.88	0.79–0.96	**0.009**
72	0.80	0.70–0.88	**< 0.001**

OR — odds ratio; CI — confidence interval; Sat. — saturation; HFNOT — high-flow nasal oxygen therapy; NIV — non-invasive ventilation; CRP — C-reactive protein; PCT — procalcitonin; WBC — white blood cells; HR — heart rate

Failure is defined as death and/or intubation