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Predictors of high-flow nasal cannula failure in COVID-19 patients in a northern Peruvian hospital

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Abstract

Objectives To determine predictors of high-flow nasal cannula (HFNC) failure in COVID-19 patients in a hospital in northern Peru.

Methodology A retrospective cohort study was conducted during the months of March and May 2021. Data collection was based on a follow-up of 156 hospitalized patients with a diagnosis of COVID-19 who were users of HFNC. Epidemiological factors and clinical outcomes of treatment were analyzed from medical records. Epidemiological, analytical, and HFNC use-related characteristics were described using measures of absolute and relative frequencies, measures of central tendency, and dispersion. A multivariate Poisson regression analysis with robust variance and a 95% confidence interval was performed.

Results We found that age, SpO2/FiO2, work of breathing (WOB scale) at admission, degree of involvement, type of infiltrate on CT scan, lymphocytes, c-reactive protein, and D-dimer were significantly associated with failure of HFNC ($p < 0.05$). In addition, the WOB scale, PaO2/FiO2, SaO2/FiO2, and ROX index were variables that presented statistical significance ($p < 0.0001$). In the multivariate analysis model, a risk of failure of HFNC was determined with age >=60 years [RRa 1.39 (1.05–1.85)] and PaO2/FiO2 score less than 100 [Rra 1.65 (0.99–2.76)].

Conclusions Predictors to failure of HFNC are age older than 60 years and minimally significantly lower PaO2/FiO2 than 100.

Keywords High-flow nasal cannula failure, COVID-19, Mechanical ventilation

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Introduction

In 2019, a new type of coronavirus called "severe acute respiratory syndrome-causing coronavirus 2 (SARS-CoV-2)" was identified [1]. To date, the Americas have exceeded 193 million cumulative cases and almost 3 million deaths [2], and in Peru, the Ministry of Health (MINSA) has reported more than 221 thousand deaths [3]. SARS-CoV-2 infection ranges from asymptomatic to very severe pneumonia, requiring oxygen therapy or assisted ventilation, and is associated with high mortality [4, 5].

Severe COVID-19 frequently progresses to acute hypoxemic respiratory failure, which necessitates high fractional inspired oxygen concentration (FiO2) and the possibility of creating new noninvasive mechanical ventilation (NIV) strategies. This is where the high-flow nasal cannula (HFNC) arises, which uses active humidification that allows the delivery of flow up to 60 L/min in oxygen concentrations ranging from 21 to 100% [6], being a non-invasive strategy that improves oxygenation and carbon dioxide elimination, and in relation to other non-invasive ventilation strategies, provides a greater inspiratory demand for patients [7]. High-flow oxygen therapy provides a mixture of gases with flows that exceed the ventilatory demand of the patient in order to prevent intubation in patients with adult respiratory distress syndrome (ARDS) [8]. Since invasive mechanical ventilation (IMV) is a life support method that must be applied in the intensive care unit (ICU) [9], it has been reported to increase mortality rates compared to non-intubated patients [8, 9]. Although the use of noninvasive ventilatory support in acute respiratory failure due to viral infections continues to have conflicting data on benefits for major outcomes, noninvasive ventilatory support strategies were widely and variably used during the pandemic [10].

A systematic review study found that, compared to standard oxygen therapy, HFNC could reduce intubation rates, decrease ICU stays, and increase the number of days free of mechanical ventilation, in addition to improving oxygenation rates [11]. HFNC seems to be useful for ARDS associated with COVID-19 and safer for healthcare professionals, as it is associated with lower in-hospital mortality compared to mechanical ventilation; however, there is still contradictory data on the benefits of its use depending on the severity of acute respiratory failure [12]. In addition, the severity of ARDS with PaO2/FiO2 < 150 and a respiratory rate > 35/min can be considered a predictor of intubation [13].

Other studies have pointed out that the HFNC represents the most common and successful ventilatory support method for patients with COVID-19 associated with acute respiratory failure [14]. In addition, it was noted that patients with a lower PaO2/FiO2 ratio were more likely to experience failure in the use of this cannula, and that the overall intubation rate was as high as 15% among those with severe acute respiratory failure [14]. HFNC continues to play a pivotal role in the management of COVID-19 in patients with hypoxemic respiratory failure. However, those with at least one comorbidity or immunosuppression, as well as elevated inflammatory markers, higher SOFA scores, and elevated lactate levels, have been observed to have a higher likelihood of not responding satisfactorily to HFNC therapy [15]. Given its effectiveness in preventing intubation and associated complications, the use of HFNC may be considered the first treatment option for ARDS [8].

Since 2019, when the first cases were reported, there have been no studies on this topic in our country. Therefore, we hope that this research will provide data that will allow us to make more effective proposals for the management of severe acute respiratory syndromes. In addition, we seek to contribute to the availability of information that may be useful for future research in this field.

The main objective of the present study was to determine the predictors of failure of HFNC in patients with COVID-19 in a hospital in northern Peru during the second wave of the pandemic. In addition, we seek to describe the sociodemographic and clinical characteristics of patients with COVID-19 who use HFNC, as well as measure the time delay in the use of high-flow devices and identify the predictor indices of failure of HFNC in patients with COVID-19.

Materials and methods

Study design, population and sample

A longitudinal observational study with a retrospective cohort analytical design was conducted at the Hospital Almanzor Aguinaga Asenjo (HAAA) in Lambayeque, Peru. The study population included 162 patients hospitalized for COVID-19 who used HFNC during the months of March to May 2021, in the context of the second pandemic wave.

The study sample consisted of 112 patients hospitalized for COVID-19. A sample size was estimated based on the comparison of respiratory rate means in patients using noninvasive ventilation and with oxygen system failure results (30 ± 8) and those without noninvasive ventilation failure (26 ± 7) at 24 h, taking into account a confidence level of 95%, a power of 80%, and a between-group ratio of 1:1 [16]. However, a total of 156 patients could be captured. Non-probability convenience sampling was used.

Eligibility criteria

Adult patients over 18 years of age hospitalized on the general ward with a diagnosis of COVID-19 confirmed by antigenic, molecular, or serologic testing and who received treatment with HFNC were selected. Patients

whose medical records did not contain the outcome variables of interest were excluded; those with severe chronic lung disease or chronic respiratory failure were also excluded. We excluded six patient histories whose medical records did not contain the outcome variable.

Variables

The dependent variable was treatment failure with HFNC, operationally defined as the presence of at least 1 criterion: hemodynamic instability, shock, vasopressor requirements, PaO2/FiO2 less than 100, PaC02 greater than 40, increased work of breathing with paradoxical breathing, and persistent respiratory rate greater than or equal to 30 per minute.

The independent variables were: sex, age, type of comorbidity, oximetry on admission without oxygen therapy, work of breathing (WOB) scale on admission using variables such as respiratory rate, nasal flaring, use of sternocleidomastoid and abdominal muscles during inspiration and expiration, and ranging from 1 to 7 [17], SpO2/FiO2 on admission, relative lymphocytes, polymerase chain reaction (PCR), lactate dehydrogenase (LDH), D-dimer, glucose, type of infiltrate, and pulmonary involvement. Likewise, those related to the use of HFNC were respiratory frequency, ROX index, WOB scale, arterial oxygen pressure/inspired oxygen fraction (PaO2/FiO2), and ratio of peripheral oxyhemoglobin saturation/inspired oxygen fraction (SaO2/FiO2) taken between 12 and 24 h after the start of HFNC use.

Procedures and techniques

The medical records of the patients included in the study were obtained through the institutional research and ethics committee of the HAAA. After approval of the protocol, permission was obtained from the heads of the respective services to access the follow-up database and thus identify our population of interest. Subsequently, data collection was completed by reviewing the medical records stored in the Occupational Health and Safety Management System.

Data collection was carried out through continuous follow-up with the patients by the research team. Medical records were examined for risk factors, focusing on the outcome of interest. A data collection form was prepared, which included epidemiological characteristics (age, sex, comorbidities, respiratory rate oximetry, SpO2/FiO2, and WOB scale on admission), analytical (lymphocytes, C-reactive protein, lactate dehydrogenase, D-dimer, glucose, type of infiltrate, and pulmonary involvement), and related to the use of HFNC (respiratory frequency, ROX index, WOB scale, PaO2/fiO2, SatO2/FiO2) of the patient.

The primary outcome evaluated was HFNC device failure, and the secondary outcome was mortality, which is not detailed in this study.

Data analysis plan

The data were entered and analyzed using Stata version 17.0. To describe the sociodemographic and clinical characteristics of the patients, tables of absolute and relative percentage frequencies were prepared. To measure the delay time in the use of high-flow devices, statistical measures of central tendency and dispersion were used. A bivariate analysis was performed using chi-square and Fisher's exact tests according to criteria, the Student's t-test, and Mann-Whitney U tests according to normality, in addition to relative risk and 95% confidence intervals with a $p<0.05$. Finally, to evaluate the association between clinical-epidemiological factors and failure of HFNC, which translates as mechanical ventilation criteria, a multivariate Poisson regression analysis with robust variance was performed. The risk ratio (RR) and 95% confidence intervals (95%CI) were estimated. Collinearity was evaluated in the variables of interest.

Ethical considerations

The present research was approved by the ethics committee of the Faculty of Human Medicine of the Universidad de San Martín de Porres (N°. 0103–2024 – CIEI-FMH-USMP). Additionally, it was approved by the HAAA research committee (CIEI-RPLAMB. N°056). The information obtained was used only for research purposes, so strict confidentiality measures were taken to protect the identity of our study group. Since the information was obtained from the patients' medical records and there was no direct contact with them, the ethics committee determined that it was not necessary to obtain their informed consent.

Results

Characteristics of the HFNC user population

The sample consisted of 156 patient histories of COVID-19 users of HFNC. Table 1 shows that among the epidemiological characteristics, the minimum age was 23 years and the maximum was 93 years. The patients older than 60 years were 77 (49.3%); an association was found between age older than 60 years and HFNC failure ($p<0.0001$). Among the comorbidities, we found 2/156 patients with cardiovascular disease, 1/156 with COPD/DPID (chronic obstructive pulmonary disease/diffuse interstitial lung disease), 4/156 with cancer, 4/156 with cirrhosis, and 5/156 with ESRD (chronic end-stage renal disease).

With respect to clinical characteristics, dyspnea was present in 85.8% of the patients and in 69.2% of those with HFNC failure. At hospital admission, the values for

Table 1 Epidemiological characteristics of patients with COVID-19 users of HFNC according to device failure

Variable	*n* (156)	Failure of the HFNC		*p*-value
		Yes	No	
Age	58.4 ± 12.9 **	61.5 ± 12.0**	51.8 ± 12.6**	< 0.001[a]
Sex				
Male	99(63.5) *	67(67.7) *	32(32.3) *	0.746[a]
Female	57(36.5) *	40(70.2) *	17(29.8) *	
Comorbidity				
HTA	46(29.7) *	36(78.3) *	10(21.7) *	0.086[a]
Obesity	27(17.3) *	18(66.7) *	9(33.3) *	0.813[a]
Diabetes Mellitus type 2	33(21.2) *	24(72.7) *	9(27.3) *	0.564[a]
Oximetry admission without oxygen therapy (%)[¥]	88.5 (82–90) **	88 (81–90)**	89 (86–91) **	0.399[a]
Respiratory frequency at admission (respirations/minute) [¥]	26 (24–30)**	26 (24–30)**	25 (22–32) **	0.509[a]
WOB scale at admission				
4–6 points	68 (54.4) *	53 (60.1) *	15 (39.5) *	0.027
SpO2/FiO2 at admission	101.5 (96–105)	100 (93–104) **	105 (101–112)**	0.001[a]
< 160	141(92.8) *	103(73.1) *	38 (26.9)	0.013[a]
≥ 160	11(7.2) *	2(18.2) *	9(81.8)	

*Absolute and relative frequency, **mean and standard deviation, and/or median and interquartile range, ap-values were calculated using the χ^2 test, Fisher's exact test, Student's t-test, and Mann-Whitney U test, as appropriate. ¥ It details missing values in variables such as time of illness, admission saturation, respiratory frequency (RF), work of breathing (WOB) scale, ratio of peripheral oxyhemoglobin saturation/inspired oxygen fraction (SaO2/FiO2), and arterial hypertension (HTA)

Table 2 Radiologic and laboratory variables according to HFNC failure

Variable	*N* (156)	Failure of the HFNC		*p*-value [a]
		Yes	No	
Type of infiltrate [¥]				
Tarnished glass	22(14.10) *	11(50) *	11(50) *	0.193
Cobblestone	2(1.28) *	1(50) *	1(50) *	
Consolidation	9(5.77) *	6(66.7) *	3(33.3) *	
Mixed	22(14.10) *	6(27.3) *	16(72.7) *	
Commitment [¥]				
Mild	4(5.33) *	1(25) *	3(75) *	0.04
Moderate	22(29.33) *	9(40.9) *	13(59.1) *	
Severe	49(65.33) *	33(67.3) *	16(32.7) *	
Analytics [¥]				
Lymphocytes (%)	8 (5-13.9)	6.8 (4.8–10)	14.2 (8.2–19.2)	< 0.0001
PCR (mg/dl)	10.2 (2.6–18.5)	12.5 (5.8–23.8)	7.2 (4.1–12.7)	0.003
LDH (mg/dl)	639.1 ± 224.0	666.9 ± 240.2	583.6 ± 189.9	0.442
D-dimer (ug/ml)	1.22 (0.6–2.56) **	1.35 (0.78–3.09 **	0.6 (0.45–2.07) **	0.024
Glucose (mg/dl)	98 (83–125) **	99 (85–130) **	94 (80–113) **	0.100

* Absolute and relative frequency; ** mean and standard deviation, and/or median and interquartile range; p-values were calculated using the χ^2 test, Fisher's exact test, Student's t test, and Mann-Whitney U test, as appropriate; polymerase chain reaction (PCR); lactate dehydrogenase (LDH); ¥ Missing values for all laboratory and imaging variables are detailed

respiratory rate were a minimum of 18 and a maximum of 89/min; for the WOB scale, a minimum of one point and a maximum of six points; and for SpO2/FiO2, a minimum of 42 and a maximum of 260, respectively. A statistical association was found between the WOB scale and SpO2/FiO2 on admission with HFNC failure.

The mean hospital stay prior to the use of HFNC was 2.6 ± 2.3 days, with a minimum of one day and a maximum of 20 days. Table 2 shows the laboratory tests performed at hospital admission. The minimum lymphocyte value was found to be 1, and the maximum was 45%. Patients with PCR ≥ 10 mg/dl were 50.88% (range: 0.3–154), LDH ≥ 450 was found in 70.37% (range: 266–1128), D-dimer ≥ 0.5ng/dl in 85.12% (range: 0.25-29), and glucose with values from 71 to 179 mg/dl in 85.31% of patients (range: 11–735). Of all the variables described, significant differences were only found with relative lymphocytes ($p < 0.031$), PCR ($p < 0.021$), and D-dimer ($p < 0.0001$).

Table 3 Clinical outcomes in patients with high-flow cannula use according to HFNC failure criteria

Variable	*n*	Failure of the HFNC		*p*-value
		Yes	No	
Respiratory rate with HFNC (respirations / minute)	24 (20–30) **	28 (22–30) **	22 (20–24) **	0.085[a]
WOB scale with HFNC 4–6 points[¥]	57.5 ± 15.1 **	59.6 ± 14.6 **	51.6 ± 15.0 **	0.018[a]
PaO2/FiO2 with HFNC [¥]	88 (65.5–121) **	72.6 (62–100) **	121 (103–159) **	< 0.0001[a]
SaO2/FiO2 with HFNC	103 (93.5-125.5) **	98 (90–107)**	118 (106–158)**	< 0.0001[a]
ROX index[¥]	4.4 (3.23–5.83) **	3.99 (3-4.6) **	6 (4.92–7.79) **	< 0.0001[a]

** Standard deviation; *mean and percentage; p-values were calculated using the χ^2 test, Fisher's exact test, Student's t test, and Mann-Whitney U test, as appropriate; work of breathing (WOB) scale; ratio of peripheral oxyhemoglobin saturation/inspired oxygen fraction (SaO2/FiO2); arterial oxygen pressure / inspired oxygen fraction (PaO2/FiO2); and high flow nasal cannula (HFNC). ¥ Missing values in variables such as ROX index, WOB scale, and PaO2/fiO2 are detailed

Table 4 Multivariate analysis

Failure of the HFNC	Adjusted risk ratio (rRa)	*p*-value	[95% confidence interval]	
Age >= 60 years	**1.39**	**0.023**	**1.05**	**1.85**
WOB scale at admission	1.28	0.170	1.05	1.81
Lymphocytes <= 10%	1.35	0.09	0.95	1.91
PaO2/FiO2 with HFNC < 100	1.65	0.056	0.99	2.76
ROX index with HFNC < 3.85	1.11	0.96	0.89	1.41

Poisson regression model with adjusted risk ratio at $p < 0.05$, HFNC: high-flow nasal cannula, WOB scale: work of breathing

Clinical results of treatment with HFNC

Table 3 shows the oxygen parameters 12–24 h after starting HFNC. We found that patients with a respiratory frequency higher than 20 breaths/min were 74.83% (values between 16 and 50); in addition, in HFNC users, we found PaO2/FiO2 values < 100 in 59.38% (values between 42 and 377), SaO2/FiO2 lower than 160 in 89.74% (values between 32 and 317), and a ROX index lower than 3.88 in 99.3% (values between 1.06 and 23). A statistical association was found between HFNC failure and WOB scale >= 4 points ($p < 0.027$), PaO2/FiO2 < 100 ($p < 0.0001$), SaO2/FiO2 < 160 ($p < 0.0001$), and ROX index < 3.85 ($p < 0.0001$).

The ventilatory support time with HFNC was 7.0 ± 5.8 days, and the initial device flow was 60 (50–70) liters/minute. We found that 106 patients (68.4%) had HFNC failure at 12 to 24 h.

Multivariate model

Three prognostic models were initially created. The first model included epidemiological variables: age > 60 [RR 1.65 (1.31–2.08)], WOB scale on admission [RR 1.06 (0.99–1.14)] ($p = 0.08$), and SaO2/FiO2 on admission [RR 0.98 (0.98–0.99)]. The second with analytical variables: PCR >= 10 mg/dl [RR 1.24 (0.94–1.65)] ($p = 0.125$), relative lymphocytes [RR 1.49 (1.04–2.14)]; the rest of the variables were not considered due to missing data greater than 20%. The third has variables related to treatment with HFNC at 12–24 h: PaO2/FiO2 [RR 1.73 (1.09–2.75)], ROX index [RR 1.11 (0.89–1.39)] ($p = 0.32$), SaO2/FiO2 [RR 0.78 (0.31–1.96)] ($p = 0.59$), and the WOB scale [RR 1.21 (0.89–1.66)] ($p = 0.22$). Measurement parameters such as the SaO2/FiO2 and the WOB scale have similarities in their measurement sub-variables.

Based on that, a final model was constructed, taking into account that the numerical variables were categorized based on the literature and in a linear sense. In the final prognostic model, we found that age >= 60 years [Rra 1.39 (1.05–1.85)] and a minimally significant PaO2/FiO2 score less than 100 [Rra 1.65 (0.99–2.76)] predicted treatment failure with a high-flow device and therefore the need for invasive mechanical ventilation (Table 4).

Discussion

The role of HFNC in respiratory failure by COVID-19

Oxygen therapy is one of the fundamental pillars in the therapy of critically ill patients with respiratory diseases; however, conventional systems do not have adequate heating, humidification, or a reliable fraction of inspired oxygen. [18, 19]. HFNC is a noninvasive ventilation system that has become one of the main strategies for noninvasive ventilatory support in acute hypoxemic respiratory failure, mainly in the context of the COVID-19 pandemic [20]. It has several advantages, such as high FiO2 delivery, low positive pressure levels, inspiratory pressure reduction, humidified ventilatory support, and optimization of mucociliary function. It can also decrease dead space, leading to decreased respiratory rate and effort [20–22]; however, its effects on dyspnea reduction are still debated among studies pre-pandemic [23].

Evaluation of the predictive model for HFNC failure

In the present study, we found a HFNC failure rate of 68.4%. This is related to other studies where it ranges between 32 and 53% with maximums of 92% [11]. In addition, Pisciotta W et al. in a systematic review found failure rates between 11 and 69.3% with the use of HFNC [24] and Wang et al. in another systematic review found failure rates in those with PaO2/FiO2 < 200 between 34 and 54% and values of 0–43% in those with PaO2/FiO2 > 20 [25]. While Cárcamo P et al. in the Peruvian population who used HFNC found device failure in 29.7%, these results do not coincide with our study, probably because in the population evaluated, 68% were under 60 years of age, while in our study and the rest of the detailed investigations the average age was 55–65 years, so we assume other factors such as comorbidities and frailty could also be present.

In addition, it was shown that of the 156 hospitalized patients using HFNC, age greater than 60 years and minimally significantly lower PaO2/FiO2 than 100 predicted HFNC failure.

This model is contradicted by other studies, such as that of Panadero C. et al. in Spain, where HFNC failure was associated with a ROX index lower than 4.94 measured 2 to 6 h after initiation of therapy [8]. Although the ROX index has been considered a predictor of HFNC failure in patients with COVID-19, with a high sensitivity and specificity even for lower values, without being affected by comorbidity, age, or blood tests [26], it should be measured between 2 and 6 h after the start of the oxygen therapy modality to predict the need for IMV [11]. However, values close to 5 at 24 h may also predict the failure of HFNC [26]. Our measurement value was 3.88 and was measured between 12 and 24 h after the initiation of HFNC, in many cases because no protocol for the management of these patients was followed.

Other models, such as that of Nevola et al. in their prospective study, found that the predictors of NIV/continuous positive airway pressure failure, defined as rate of orotracheal intubation and death, were advanced age and the need for continuous ventilation over intermittent ventilation [27]. Innocenti et al. found in their retrospective study that predictors of NIV failure (orotracheal intubation or mortality) assessed previously and up to day 5 of treatment were a HACOR scale score > 5 points, ROX index, and PaO2/FiO2 [16]. Although we see variables in common within the predictive models of these studies with a similar population size, it should be considered that the outcomes were not only the failure of the high-flow device, and additionally, the types of devices used as NIV were different.

Evaluation of the variables in the predictive model

Our model found that an important factor leading to the failure of HFNC is age, which could be explained by the fact that in aging, a state of chronic mild inflammation occurs involving various tissues and organs and is characterized by a complex balance between proinflammatory and anti-inflammatory responses [28]. Akbar AN. et al. demonstrated that the presence of excessive inflammation can inhibit immunity in both animals and humans [29]. Liu L. et al. also found in their retrospective study that increasing age is a risk factor for failure of noninvasive devices such as HFNC [30]. In addition, other studies show that older age increases mortality [31–33]. However, Ruiz A. et al. reported that they found no statistically significant differences with age [34], as did Zúñiga J. et al. [35]. This is probably because the aforementioned studies were performed with a smaller population, and our study had an average population age of 58.4 years.

Among other important data found in this research, the PaO2/FiO2 variable stands out, since with a value less than 100, it showed a minimally significant prediction with the criterion of HFNC failure, which agrees with the research. Nevola et al., in their prospective study, demonstrated that the initiation of NIV in patients with mild-moderate ARDS (PaO2/FiO2 < 200) improved survival in comparison with patients with severe ARDS [27]. Wang et al. found that of the 17 patients who used HFNC, 7 patients presented failure, significantly correlating those with PaO2/FiO2 ≤ 200 mm Hg [14], as did the retrospective cohort study published by Delbove et al. in France, where they found a significant association between severity of ARDS by COVID-19 and PaO2/FiO2 < 150 [13]. Similarly, Zúñiga J. demonstrated that at 72 h of HFNC use, failure was found with a PaO2/FiO2 in the range of severe ARDS [35]. It has been shown that the efficacy of HFNC is lower with PaO2/FiO2 < 200 [36], and although our study demonstrates this in a minimally significant way, it is likely that a larger population is required for the study of all the variables involved. In addition, the timing of PaO2/FiO2 value collection between 12 and 24 h after the initial use of the device could also play a role in its assessment.

Other variables possibly associated

In our study, we found no relationship between ROX index and HFNC failure in multivariate analysis, which could be explained because ROX index was not measured at 2, 6, and 12 h as appropriate. I agree with Ait Hamou Z. et al., who reported that the ROX index could not reliably predict HFNC failure with an area under the ROC curve of 0.65 [37]. In contrast, many studies found that this variable does relate to the success or failure of the high-flow device, such as Patel et al. in 2021, who demonstrated that an ROX index value of less than 5 at the onset

of HFNC suggested progression to IMV; furthermore, any further decrease in the ROX index value after the onset of HFNC was predictive of intubation [38]. Similarly, Chandel et al., concurring with Patel's study, found that a ROX index > 3.0 at 2, 6, and 12 h after the onset of HFNC has a sensitivity of 85.3% for identifying the subsequent success of HFNC [39]. Romero I. identified the 12-hour ROX index as the best predictor of failure, with an area under the curve of 0.75 (0.64–0.85) and a cutoff point of 6.23 as the best predictor of intubation [40].

Although the assessment of SpO2/FiO2 and the WOB scale as a measure of respiratory effort prior to HFNC use has not been detailed in previous studies, we were able to find a statistical association that could not be clinically assessed in multivariate analysis. This is also demonstrated by Innocenti et al., in whose retrospective study it could not be determined that oxygenatory measures prior to HFNC use, such as PaO2/FiO2, HACOR, were associated with failure to use the device [16]. And although SaO2/FiO2 < 160, WOB scale >= 4 points measured at 12 to 24 h after HFNC use found significant association, they were not considered for multivariate analysis because they were variables that presented subvariables in common. However, Iglesias A., in his retrospective cohort, found that SpO2/FiO2 proved to be a better method of diagnostic accuracy than the ROX index for predicting the use of IMV [41].

Arterial hypertension is recognized as the leading cause of preventable mortality worldwide [42]. Arterial hypertension affects more than 1 billion people worldwide, mostly those in middle- and low-income countries [31]. The results of our study show that a large percentage of patients are hypertensive (46%); however, in the bivariate and multivariate analyses, no association with HFNC failure was found. Zhou F. et al. presented similar results, where arterial hypertension was the most frequent comorbidity (30%), followed by diabetes (19%) [31]. However, the frequency is less than that reported in other studies, such as that of Delgado K. et al., who reported that hypertensive patients accounted for more than half (60%) [43], although no association was found in the predictive models with device failure in these patients, highlighting more other oxygenation parameters and age.

Clinical implications

Although a systematic review based on clinical trials and observational studies shows the benefits of the use of HFNC in patients with COVID-19 versus conventional therapy in the outcome evaluated as intubation rate or device failure [44], our study provides information based on the management of these patients during the second wave of the pandemic in Peru and helps us to understand the need to establish protocols and assess strict follow-up of the use of these devices, taking into account the factors that predict their failure. This may also help us promote their use in the management of other respiratory pathologies outside the context of the pandemic. Studies with a larger sample size, including populations with or without multimorbidity, with or without other strategies such as prone, which were not evaluated in this study, are needed to analyze the effectiveness of HFNC and to measure different outcomes such as length of stay in the ICU, days free of mechanical ventilation, or mortality, which are detailed in other studies and are important at the level of care [25, 45].

Strengths of the study

The study shows the characteristics of the Peruvian population with COVID-19 infection that received oxygen therapy through HFNC during the second wave of the pandemic and is one of the few studies that analyzes the factors associated with the failure of the use of this device in this population, where the lethality was between 40 and 46% during the first two waves [46, 47]. In addition, our study includes an analysis of several clinical and laboratory variables and oxygenation parameters during follow-up, thus allowing us to evaluate the implications of these variables through multivariate analysis.

Limitations of the study

Regarding the limitations of this study, we should highlight that it is a retrospective single-center investigation that included a limited number of patients and clinical histories with incomplete data on some variables of interest, which may generate selection biases, and also that it is not possible to generalize the results of the study. In addition, the variables were not measured at a specific time, so the assessments were made between 12 and 24 h after the use of HFNC. Additionally, the sampling was non-probabilistic, which may affect the internal validity of this study. Additionally, other therapeutic strategies such as prone that are protocolized in the management of patients with severe disease and HFNC users were not considered, which could generate confounding bias [48].

Conclusions

Our study found that in a Peruvian population, predictors of HFNC failure in patients with COVID-19 hospitalized during the second wave of the pandemic were age greater than 60 years and a minimally significant PaO2/FiO2 less than 100.

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None.

Author contributions

Conceptualization, S.T.C.P. and E.D.D.T.; methodology, E.A.M., D.A.L.F. and M.J.V.G.; software, E.A.M. and D.A.L.F.; validation, E.A.M. and S.T.C.P.; formal analysis, E.A.M. and E.D.D.T.; investigation, S.T.C.P. and E.D.D.T.; resources, E.A.M., D.A.L.F. and M.J.V.G.; data curation, S.T.C.P. and E.D.D.T.; writing—original draft

preparation, S.T.C.P., E.D.D.T., E.A.M., D.A.L.F. and M.J.V.G.; writing—review and editing, S.T.C.P., E.D.D.T., E.A.M., D.A.L.F. and M.J.V.G.; visualization, S.T.C.P. and E.D.D.T.; supervision, M.J.V.G.; project administration, E.A.M. All authors have read and agreed to the published version of the manuscript.

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Data availability
Data sets generated and/or analyzed during the present study are not publicly available because they contain information that could compromise the privacy of research participants, but they are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
The present research was approved by the ethics committee of the Faculty of Human Medicine of the Universidad de San Martín de Porres (No. 0103–2024 - CIEI - FMH - USMP). Since the information was obtained from the patient's medical records and there was no direct contact with them, the ethics committee determined that it was not necessary to obtain their informed consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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