

Comparison of initial oxygen therapy provided through high-flow nasal cannula versus noninvasive ventilation in patients with acute heart failure

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Abstract

Background: Oxygen therapy with high-flow nasal cannula (HFNC) is being increasingly used in patients with acute heart failure (AHF), but its impact on short-term outcomes has been poorly reported. This study aims to compare short-term outcomes in patients with AHF and respiratory distress who received initial oxygen therapy with HFNC versus noninvasive ventilation (NIV) in the emergency department (ED).

Methods: In this retrospective analysis of prospectively collected data from a multicenter registry, we included all patients diagnosed with AHF in 35 Spanish EDs during January–February 2022 who received either HFNC or NIV as initial oxygen therapy. Patient allocation to initial HFNC or NIV was left to the discretion of the treating emergency physician. The primary outcome was 30-day all-cause mortality. Secondary outcomes included treatment failure (defined as the need for switch of oxygen therapy techniques or escalation to NIV to mechanical ventilation), intensive care unit admission, endotracheal intubation, in-hospital mortality, a composite endpoint of intubation or 7-day mortality, and prolonged hospitalization (>7 days). Associations were expressed as adjusted odds ratios (aOR) with 95% confidence intervals (CIs), using age, sex, and significant patient- and episode-related characteristics as covariates.

Results: Of 4301 patients with AHF, 330 (7.7%) were included (median age: 83 years; 57% women): 71 received HFNC and 259 received NIV. No statistically significant between-group differences were detected in the measured baseline characteristics; however, residual imbalance and unmeasured confounding cannot be excluded. A total of 66 (20.1%) patients died during 30-day follow-up with no significant difference between HFNC (21.4%) and NIV (19.8%) groups (aOR: 1.09; 95% CI: 0.55–2.17). HFNC was more frequently followed by a change or escalation in respiratory support (23.9% vs. 2.3%, aOR: 17.9; 95% CI: 5.90–54.2). This composite outcome was mainly driven by switches from HFNC to NIV (13/17 cases in the HFNC group) rather than by escalation to invasive mechanical ventilation, and should not be interpreted as direct evidence that HFNC was clinically inferior to NIV. But no significant differences were found for the other secondary endpoints.

Conclusion: In this analysis of patients with AHF treated in the ED, no statistically significant between-group difference in 30-day mortality was detected between initial HFNC and NIV. However, given the wide confidence intervals, these findings do not establish equivalence. Larger randomized trials are warranted to confirm the comparative effectiveness of these two oxygenation strategies.

Keywords: Acute heart failure, Emergency department, High-flow nasal cannula, Noninvasive ventilation

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

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Introduction

Noninvasive ventilation (NIV) is commonly used for the management of acute heart failure (AHF) and is especially recommended in case of respiratory distress, respiratory acidosis, or persistent hypoxemia despite supplemental oxygen.^[1, 2] Studies have shown that NIV has beneficial hemodynamic effects in cardiogenic pulmonary edema by reducing venous return, afterload, and myocardial oxygen consumption and can help relieve symptoms, decrease intubation rates, and improve short-term outcomes.^[3, 4] It is also used in the prehospital field with encouraging results.^[5, 6] However, its use can be limited by patient discomfort, difficulties in tolerance, and the need for close monitoring and expertise from physicians to ensure optimal settings and avoid potential complications such as gastric insufflation or hemodynamic instability.^[7]

In recent years, oxygen therapy provided through high-flow nasal cannula (HFNC) has emerged as another option for managing acute respiratory failure. By delivering heated and humidified oxygen at high flow rates, it enhances oxygenation, reduces respiratory effort, and provides a mild positive airway pressure effect.^[8–10] Unlike NIV, HFNC does not require a tight-fitting

mask, making it more comfortable and potentially easier to use in some patients.^[11, 12] Initially, HFNC was compared with conventional oxygen therapy in different types of respiratory failure, showing benefits in terms of symptom relief and respiratory support.^[12–16] More recently, studies have compared the effects of HFNC and NIV and evaluated their role specifically in AHF. A recent meta-analysis^[17] only found 2 studies (102 patients) that had evaluated discomfort and clinical tolerance,^[18, 19] but only one used an objective discomfort scale.^[18] In The High-Flow Nasal Oxygen Cannula Compared to Non-Invasive Ventilation in Adult Patients With Acute Respiratory Failure (RENOVATE) trial, there was no significant difference in the primary outcome of intubation or 7-day mortality in HFNC and NIV subgroups, and HFNC was better tolerated and associated with fewer interface-related complications.^[20] However, this study was conducted in the intensive care unit (ICU), whereas the initial management of most of these patients takes place in the emergency department (ED). In this context, we aimed to compare the effect of HFNC and NIV on short-term outcomes in patients presenting to the ED with AHF.

Methods

We conducted a retrospective exploratory analysis of prospectively collected data from a cohort of consecutive patients diagnosed with acute heart failure in 35 Spanish EDs between January and February 2022 during the eighth phase of patient inclusion in the Epidemiology of AHF in Emergency departments (EAHFE) Registry. The EAHFE registry constitutes a prospective, multipurpose, multicenter registry cohort study initiated in 2007. Every 2–3 years, it carries out a 1- to 2-month recruitment period of all consecutive patients diagnosed with AHF in Spanish EDs. The EAHFE Registry does not include any planned intervention, and the management of patients is entirely based on the attending ED physician's decisions. The only exclusion criterion is the development of AHF during ST-elevation myocardial infarction. Around 300 primary variables are prospectively recorded during a patient's stay in the ED in order to be further used for retrospective analyses like the present one. To date, 8 recruitment phases (in 2007, 2009, 2011, 2014, 2016, 2018, 2019, and 2022) have been performed with the participation of 45 EDs from community and university hospitals across Spain (representing about 15% of hospitals in the Spanish public healthcare system), enrolling a total of 24,947 AHF patients. The AHF diagnosis had to be the principal one, and it was determined by the treating physician and confirmed by the principal investigator of each participating center according to the European Society of Cardiology criteria. All patients had the typical clinical picture plus a natriuretic peptide above the recommended cutoff values or, for those with no natriuretic peptide measurement, diagnostic data of heart failure in an echocardiography made during ED stay.^[21] Complete details of patient recruitment and data recording have been previously published.^[22–24]

For this retrospective analysis, we included only those patients recruited during the eighth phase (2022) who received initial oxygen therapy via HFNC or NIV in the ED. As this was an observational study, the decision to administer oxygen therapy via HFNC or NIV was left at the discretion of the treating emergency physician. Patients were classified into 2 groups based on their first-line oxygen therapy in the ED: “HFNC first” or “NIV first.” No formal sample size calculation was performed, as the eighth phase of patient recruitment for the EAHFE registry was scheduled to last 2 months, due to investigator workload and

budgetary constraints. Consequently, this study was performed using an opportunistic sample size.

The protocol was approved by the Ethics Committees of the Hospital Universitario Central de Asturias (Oviedo, Spain, reference number 15/2022). All participating patients gave informed consent to be included in the registry and to be contacted for follow-up. The present study was carried out in strict compliance with the principles of the Declaration of Helsinki.

Outcomes

The primary outcome of this study was the 30-day all-cause death. The following secondary outcomes were considered: (1) change or escalation in respiratory support, defined as a composite of: (a) switch from HFNC to NIV, (b) switch from HFNC to invasive mechanical ventilation (IMV), or (c) switch from NIV to IMV; (2) need of admission to ICU; (3) need of endotracheal intubation; (4) in-hospital all-cause mortality; (5) a composite endpoint of endotracheal intubation or all-cause mortality within seven days of enrollment; and (6) prolonged hospitalization, considered in every patient with a length of hospitalization, counted from the arrival to the ED until hospital discharge, longer than 7 days. Adjudication of the outcomes was carried out at local level by the principal investigator of the center, without external review. For this purpose, all medical records were electronically reviewed for every patient included in the study between 30 and 90 days after the index episode, and, when no data were available, patients or relatives were interviewed through a phone call.

Independent variables

We also recorded 32 independent variables. They included 2 demographics (age and sex), 9 comorbidities (hypertension, diabetes mellitus, coronary artery disease, previous AHF episodes, atrial fibrillation, chronic kidney disease, heart valve disease, chronic obstructive pulmonary disease [COPD], and dementia), 6 chronic heart failure treatments (diuretics, beta-blockers, renin-angiotensin system inhibitors, mineral corticosteroid-receptor antagonists, neprilysin inhibitors, and sodium-glucose cotransporter inhibitors), 3 variables that classify the baseline functional situation of the patient (general functional capacity assessed by Barthel Index, respiratory capacity according to New York Heart Association [NYHA] class, and type of heart failure based on the left ventricular ejection fraction), 5 precipitants of the decompensation that were assigned by local physicians and investigators after reviewing all clinical data (infection, rapid atrial fibrillation, hypertensive crisis, anemia, and acute coronary syndrome), 3 vitals at ED arrival (systolic blood pressure, heart rate, pulse oximetry), and 4 analytical parameters obtained at the ED (hemoglobin, estimated glomerular filtration rate, NT-proBNP, troponin).

Statistical analysis

Categorical variables were reported as numbers and percentages, while continuous variables were reported as medians with interquartile ranges. Comparisons between the “HFNC first” and “NIV first” groups were performed using bivariable analyses, with a chi-square or Fisher exact test for categorical variables and a Student *t* test or Mann–Whitney *U* test for continuous variables, as appropriate. The association between treatment groups and each outcome was assessed using logistic regression, unadjusted and adjusted for age, sex, and any independent variables that, in the comparison between groups in the bivariable

analysis, obtained a P value <0.20 , and such associations were expressed as odds ratio (OR) and adjusted OR (aOR), respectively, with 95% confidence interval (CI). For the multivariate model, missing values were replaced by multiple imputation using chained equations. The Mersenne Twister was used as a pseudorandom number generator, with seed number 2,000,000, to generate 10 imputed datasets, including all cases without missing values in adjustment variables. In the adjusted models, a first-degree interaction between the presence or absence of infection as a precipitating factor for the AHF episode and treatment group was examined in relation to outcomes.

Statistical significance was defined as $P < 0.05$ or 95% CI not including 1. All analyses were performed using SPSS version 29.0 for Mac (IBM Corp., Armonk, NY, USA).

Results

Among the 4301 patients diagnosed with AHF during the enrollment period, 330 (7.7%) met the inclusion criteria, with 71 (22%) in the “HFNC first” group and 259 (78%) in the “NIV first” group (Fig. 1). For the included patients, the median patient age was 83 years and 57% were female. A majority (72%) had had previous episodes of AHF. The most common precipitating factor of cardiac decompensation was infection (41%), and there was no identifiable precipitating factor in 19.4% of cases (15.4% in the HFNC group and 20.2% in the NIV group, $P = 0.421$). The rest of the baseline characteristics of the patients are shown in Table 1. None of the baseline characteristics significantly differ between groups.

The primary endpoint (30-day all-cause death) was met in 66 out of 328 patients (2 cases with 30-day follow-up lacking), resulting in a 30-day mortality rate of 20.1%. There was no significant association between the first-intention treatment for oxygen supplementation and the primary endpoint (21.4% in HFNC vs. 19.8% in NIV; OR for patients treated with HFNC of 1.11, 95% CI: 0.58–2.12, Table 2).

Regarding secondary outcomes (Table 2), there was a higher rate of change or escalation in respiratory support in the HFNC group (17 cases [23.9%], with 13 switching to NIV and 4 requiring IMV) than in the NIV group (6 cases [2.3%], all requiring IMV, with no switches to HFNC), with an OR of 13.2 (95% CI: 5.00–35.2). It is noteworthy that the difference in this composite outcome was

predominantly driven by the 13 switches from HFNC to NIV, which represent a change between non-invasive modalities rather than an escalation to invasive ventilation. There were no significant differences in the other secondary endpoints: need of ICU admission was observed in 5.5% of cases (2.9% vs. 6.2%), intubation in 3.0% of cases (5.6 vs. 2.3%), in-hospital death in 16.1% (15.5% vs. 16.2%), intubation or 7-day death in 12.4% (15.5% vs. 11.6%), and prolonged hospitalization in 55.9% (52.1% vs. 57.0%).

The multivariate models used age, sex, previous episodes of AHF, chronic treatment with beta-blockers, pulse oximetry at ED arrival, and hemoglobin and NT-proBNP measured in the ED as covariates to adjust the effect estimation of the treatment group on primary and secondary outcomes. Using this adjustment strategy, we did not observe changes on what we found in the unadjusted analysis; the primary outcome remained unassociated with the kind of initial approach used for oxygen treatment, with an aOR for the HFNC group of 1.09 (95% CI: 0.55–2.17); the treatment failure also remained significantly higher for the group of HFNC (aOR: 17.9; 95% CI: 5.90–54.2), and the remaining secondary outcomes remained not statistically significant (Fig. 2). No interaction of the presence or absence of infection as precipitant of the AHF episode and treatment group was present for any of the outcomes ($P > 0.05$ for all outcomes).

Discussion

In this comparison of 330 patients treated for AHF in the ED and receiving either HFNC or NIV as first-line therapy, there was no significant difference in the primary outcome of 30-day mortality. Among the secondary outcomes evaluated in the present study, the need for escalation of oxygen therapy technique was more frequent in the HFNC group, but the need for ICU admission, intubation, in-hospital death, or length of hospitalization did not differ between the 2 groups.

Optimal management of AHF in the ED remains debated, with studies providing only a low level of evidence for effective treatments, most of which referred to the use of drugs, and less studies dedicated to other nonpharmacological interventions.^[25–30] Although NIV or HFNC are not frequently needed in patients with AHF (they were initiated in less than 10% of cases coming to the ED), emergency physicians might consider either technique, as no statistically significant between-group difference was detected in the secondary endpoints; however, the confidence intervals were wide, and clinically important differences in either direction cannot be excluded. In some cases, in the present study, HFNC/NIV was initiated in patients with pulse oximetry values above 90% at ED arrival. Although the specific indication for HFNC/NIV use was not recorded, we hypothesize that its initiation may have been driven by severe respiratory distress or by subsequent deterioration in oxygen saturation during the patient’s stay in the ED. In patients with COPD, HFNC may be considered as an alternative to NIV if the latter fails due to intolerance, and should also be considered and preferred to conventional oxygen therapy at NIV breaks and weaning.^[31] Finally, HFNC should also be preferred as first-line oxygen treatment in acute exacerbations of COPD patients without respiratory acidosis.^[31] A meta-analysis of studies comparing HFNC versus NIV in patients with AHF updated to March 2024 found that, overall, treatment failure rate was 24% and 13% in patients with HFNC and NIV, respectively,^[17] and in randomized controlled studies, such rates were 20% and 13%, respectively, with an OR for HFNC respect to NIV of 1.7 (95% CI: 0.9–3.1; $P = 0.09$).

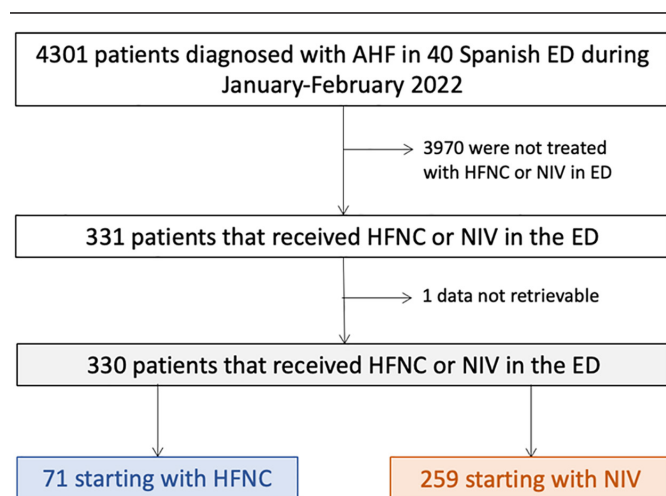


Figure 1. Flow chart for patient inclusion. AHF, acute heart failure; ED, emergency department; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation.

Table 1**Clinical Characteristics**

Characteristics	All Patients, N = 330 n (%)	Missing Values n (%)	Starting With HFNC, n = 71 n (%)	Starting With NIV, n = 259 n (%)	P Value
Demographic data					
Age (yr), median (IQR)	83 (75–88)	0 (0)	82 (75–87)	83 (74–89)	0.889
Sex female	189 (57.4)	1 (0.3)	35 (49.3)	154 (59.7)	0.117*
Comorbidity					
Hypertension	280 (85.9)	4 (1.2)	63 (88.7)	217 (85.1)	0.437
Previous episodes of AHF	236 (71.7)	4 (1.2)	45 (63.4)	191 (74.0)	0.078*
Atrial fibrillation	144 (49.3)	4 (1.2)	35 (49.3)	109 (42.7)	0.326
Diabetes mellitus	140 (42.9)	4 (1.2)	30 (42.3)	110 (43.1)	0.894
Chronic kidney disease	110 (33.7)	4 (1.2)	28 (39.4)	82 (32.2)	0.251
COPD	91 (27.9)	4 (1.2)	19 (26.8)	72 (28.2)	0.806
Heart valve disease	77 (23.6)	4 (1.2)	13 (18.3)	64 (25.1)	0.234
Coronary artery disease	71 (21.8)	4 (1.2)	15 (22.1)	56 (22.0)	0.880
Dementia	41 (12.6)	4 (1.2)	9 (12.7)	32 (12.5)	0.977
Chronic treatments at home					
Diuretics	235 (72.1)	4 (1.2)	47 (67.1)	188 (73.4)	0.298
RAAS inhibitors	183 (56.1)	4 (1.2)	36 (51.4)	147 (57.4)	0.371
Beta-blockers	158 (48.5)	4 (1.2)	28 (40.0)	130 (50.8)	0.110*
Aldosterone antagonists	57 (17.5)	4 (1.2)	9 (12.9)	48 (18.8)	0.250
Neprilysin inhibitors	11 (3.4)	4 (1.2)	1 (1.4)	10 (3.9)	0.309
SGLT2 inhibitors	42 (12.9)	4 (1.2)	11 (15.7)	31 (12.1)	0.425
Baseline status					
Barthel index (points), median (IQR)	80 (50–100)	45 (13.6)	50 (50–95)	80 (50–100)	0.851
NYHA III–IV	64 (23.8)	61 (18.5)	10 (22.2)	54 (24.1)	0.786
LVEF (%), median (IQR)	57 (47–65)	140 (42.4)	59 (49–65)	56 (45–65)	0.448
Trigger of decompensation					
Infection	119 (40.9)	39 (11.8)	18 (36.0)	101 (41.9)	0.439
Rapid atrial fibrillation	58 (19.9)	39 (11.8)	11 (22.0)	47 (19.3)	0.687
Hypertensive crisis	34 (11.7)	39 (11.8)	5 (10.0)	29 (12.0)	0.684
Anemia	27 (9.3)	39 (11.8)	7 (14.0)	20 (8.3)	0.206
Acute coronary syndrome	18 (6.1)	36 (10.9)	3 (5.8)	15 (6.2)	0.907
Vitals at arrival to the ED					
Heart rate (bpm), median (IQR)	88 (75–110)	20 (6.1)	87 (76–117)	89 (75–110)	0.931
SBP (mm Hg), median (IQR)	141 (119–163)	7 (2.1)	144 (124–163)	140 (119–163)	0.717
Pulse oximetry (%), median (IQR)	93 (89–97)	9 (2.7)	95 (90–97)	93 (88–97)	0.173*
Blood test at ED arrival					
Hemoglobin (g/L), median (IQR)	123 (108–139)	1 (0.3)	127 (112–148)	123 (107–138)	0.077*
eGFR (mL/min), median (IQR)	46 (32–73)	6 (1.8)	49 (35–69)	46 (31–75)	0.655
NT-proBNP (pg/mL), median (IQR)	4810 (2397–11168)	28 (8.5)	3795 (1860–9988)	4874 (2525–11793)	0.178*
Raised troponin (>99th centile)	112 (52.1)	115 (34.8)	27 (52.9)	85 (51.8)	0.890

AHF, acute heart failure; COPD, chronic obstructive pulmonary disease; ED, emergency department; eGFR, estimated glomerular filtration rate; HFNC, high-flow nasal cannula; IQR, interquartile range; LVEF, left ventricular ejection fraction; NIV, noninvasive ventilation; NT-proBNP, N-terminal pro-brain natriuretic peptide; NYHA, New York Heart Association; RAAS, renin-angiotensin-aldosterone system; SBP, systolic blood pressure; SGLT2, sodium-glucose cotransporter-2.

*Variables with a *P* value <0.20 that were used, on top of age and sex, as covariables in the multivariate models for analysis of outcomes.

Rates of NIV failure in AHF are comparable to those reported when used in broader patient populations, with NIV failure rates of approximately 11%.^[32]

Our results suggest that the short-term benefits of these treatments likely stem from reducing hypoxemia by delivering high oxygen volumes, which both HFNC and NIV achieve. The effects of NIV on respiratory mechanics, which HFNC does not provide, would therefore be more useful in the short-term for immediate symptom relief but might not have a significant long-term impact, as suggested by some studies evaluating NIV.^[3, 33] With respect to HFNC, the High-Flow Oxygen through Nasal Cannula in Acute Hypoxemic Respiratory Failure (FLORALI) study randomized patients admitted to French ICU with acute hypoxemic respiratory failure to start treatment with HFNC or NIV and found that

there was no difference in intubation rates between groups and those treated with NIV, and mortality was even higher in the NIV group.^[11] However, these patients were mainly affected by infectious and septic illnesses (very few patients, if any, had AHF) and may have been more sensitive to the adverse hemodynamic effects of NIV. In the RENOVATE randomized clinical trial run in Brazil, HFNC was not inferior to NIV in terms of intubation or 7-day mortality in the ICU.^[20] However, less than half of patients were initially treated at the ED, and only 15% the cause of respiratory distress was AHF. For this subgroup of patients, no differences in outcomes were found as well. Therefore, the results of our study agree with previous findings. In this scenario, therefore, HFNC could be initially considered in most patients with AHF, especially in less severe cases, closely monitoring the presence of treatment

Table 2**Outcomes and association between use of high-flow nasal cannula and outcomes**

Outcomes	Starting With HFNC Events/Total (%)	Starting With NIV Events/Total (%)	Unadjusted OR for HFNC Starting (95% CI)
Primary outcome			
Death at 30 d	15/70 (21.4)	51/258 (19.8)	1.11 (0.58–2.12)
Secondary outcomes			
Treatment failure (need for escalation in the type of oxygen therapy supplementation)	17/71 (23.9)	6/259 (2.3)	13.2 (5.00–35.2)
ICU admission	2/ 70 (2.9)	16/ 259 (6.2)	0.45 (0.10–1.99)
Endotracheal intubation	4/ 71 (5.6)	6/ 259 (2.3)	2.52 (0.69–9.18)
In-hospital death	11/ 71 (15.5)	42/ 259 (16.2)	0.95 (0.46–1.95)
Endotracheal intubation or death at 7 d	11/ 71 (15.5)	30/ 259 (11.6)	1.40 (0.66–2.95)
Prolonged hospitalization (>7 d)	37/ 71 (52.1)	147/ 258 (57.0)	0.82 (0.48–1.39)

Bold numbers denote statistical significance ($P < 0.05$). One patient had missing data for Death at 30 days.

CI, confidence interval; HFNC, high-flow nasal cannula; ICU, intensive care unit; NIV, noninvasive ventilation; OR, odds ratio.

failure. However, it should be emphasized that there is currently a lack of randomized controlled trials in patients with AHF, which precludes making firm recommendations.

Currently, the use of HFNC is not recommended for the management of AHF in the European Society of Cardiology guidelines.^[21] In the present study, due to its observational nature, we were able to notice that, in practice, HFNC is already being used for this indication, likely because some physicians have found it effective, particularly in patients who do not tolerate NIV. Previous experience of use during the COVID-19 pandemic has probably provided a strong experience in intensivists and emergency physicians about the strengths of this technique for oxygen supplementation.^[34] It is remarkable that the rate of change or escalation in respiratory support was higher in the HFNC group, as one in four patients initiated with HFNC required a subsequent switch to NIV or intubation. However, this was largely attributable to switches from HFNC to NIV (18.3% of HFNC patients) rather than to rescue invasive ventilation (5.6%). Consequently, the 17.9-fold higher odds of this composite endpoint should not be interpreted as evidence that HFNC is clinically inferior to NIV. Instead, HFNC may serve as a tolerable initial step, allowing clinicians to avoid immediate NIV while still achieving comparable safety outcomes, as reflected by the lack of significant differences in mortality, intubation, and ICU admission between groups. Although the intubation rate

was lower and the length of hospitalization longer in the NIV group, the differences were not statistically significant. Indeed, ICU admission tended to be higher in the NIV group, which is in accordance with the general practice in which patients treated with NIV require a high level of care.^[35] The absence of statistically significant differences in mortality or intubation does not establish the comparative safety of HFNC and NIV, because the number of events was small and the confidence intervals were wide. However, the selection of oxygenation technique remains nowadays a subjective physician-dependent decision. There is therefore an urgent need to validate HFNC in patients with AHF and provide specific recommendations in the next guidelines about the scenarios where HFNC can be safely used.^[36, 37]

Limitations

First, as a retrospective analysis of a cohort of patients with prospective data collection, there may have been a selection bias regarding which patients received HFNC or NIV. Certainly, although the groups were comparable in their baseline characteristics, particularly in terms of dyspnea (NYHA III and IV), the decision to use HFNC versus NIV was up to the treating physician, who was likely making this decision based on a number of clinical factors that we were not able to adequately adjust for. Second, our study included unselected patients from real clinical

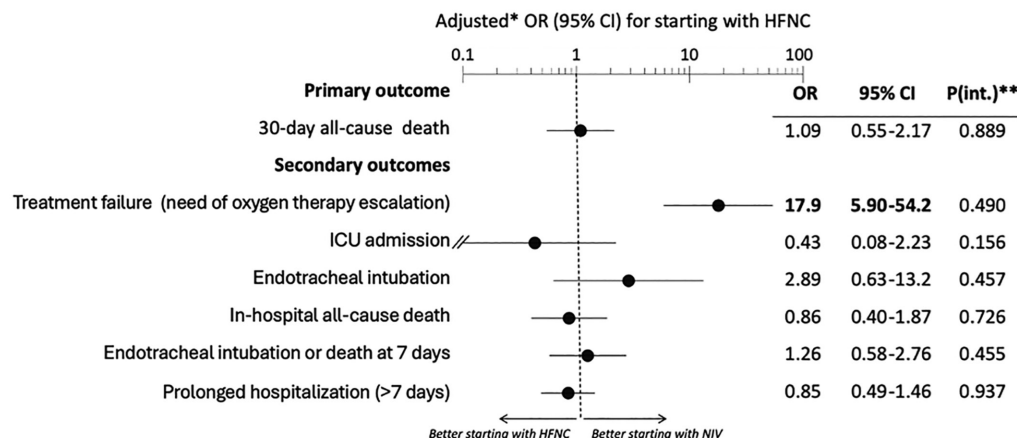


Figure 2. Adjusted analysis of outcomes. *Adjusted by age, sex, previous episodes of acute heart failure, chronic treatment with beta-blockers, pulse oximetry at emergency department arrival, hemoglobin, and NT-proBNP. **Interaction was checked for patients with and without infection as the precipitant of the acute heart failure episode. Bold numbers denote statistical significance ($P < 0.05$). CI, confidence interval; HFNC, high-flow nasal cannula; ICU, intensive care unit; int., interaction; NIV, noninvasive ventilation; NT-proBNP, N-terminal pro-brain natriuretic peptide; OR, odds ratio.

practice of the ED and a high percentage of them were very old (median age 83 years; and a quarter were 88 years or older). In elderly AHF patients, accommodation to NIV could show specific difficulties, and this could have additionally conditioned the selection of a particular technique for oxygen supplementation. Third, the present study did not distinguish between the 2 main NIV techniques: continuous positive airway pressure or bilevel pressure support. Fourth, there was no previous sample size calculation, and the relatively small sample size may have limited the ability to detect a significant difference. Remarkably, the estimation of the association of HFNC with intubation was high, with an aOR of 2.89, as well as with ICU admission was low, with an aOR of 0.43, although the CIs were wide, not allowing to reach statistical significance. We cannot rule out that a beta error was present in these estimations. Fifth, the large number of EDs participating in the study (35) makes it possible that variation in indication or use of HFNC/NIV in patients with AHF could have varied highly. This is illustrated by the fact that while some centers contributed with more than 20 cases, others just included 3 cases during the same recruiting period. Finally, limiting patient recruitment to a 2-month period (January and February) may reduce the generalizability of our findings, as a higher incidence of infections is expected during these months, potentially leading to a greater number of heart failure decompensations related to this factor.

Conclusion

In this observational registry analysis, HFNC was more frequently followed by a change or escalation in respiratory support. We did not detect statistically significant differences in mortality, intensive care unit admission, or intubation, but estimates were imprecise and residual confounding was likely. These findings are exploratory and do not establish the equivalence or comparative safety of HFNC and NIV. The use of HFNC was associated with a higher rate of treatment failure, but not with the risk of ICU admission, intubation, increased length of stay, or mortality. However, as the purpose of this study was to obtain real-world data from unselected consecutive patients on how HFNC is currently used in EDs to treat patients with AHF and whether its use impacts short-term outcomes, our results cannot be used to define a standard of care. Such standards should ideally be established through randomized controlled trials or, alternatively, through pooled analyses of several nonrandomized studies, allowing the inclusion of a larger number of patients than individual studies alone.

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Conflict of interest statement

Yonathan Freund is an Associate Editor of *Emergency and Critical Care Medicine*. The article was subject to the journal's standard procedures, with peer review handled independently of this Associate Editor and their research groups. The authors declare no conflict of interest.

Author contributions

Miró Ò and Gorlicki J designed the study. Miró Ò, Masip J, Llorens P, and Alquézar-Arbé A contributed to patient recruitment and data collection. Miró Ò performed the statistical analysis, and Freund Y interpreted the results. Miró Ò drafted the manuscript, and Freund Y made substantial contributions to its

revision. All authors critically revised the manuscript and approved the final version. All authors take responsibility for the integrity of the work.

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Ethical approval of studies and informed consent

The study followed the principles of the Declaration of Helsinki as revised in 2013. The coordinating-center protocol was approved by the Ethics Committee of Hospital Universitario Central de Asturias (reference 15/2022). Following Spanish legislation, each participating center obtained local approval afterwards before study initiation. All participating patients gave written informed consent to be included in the registry and to be contacted for follow-up.

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