

Original Research Article

HIGH-FLOW NASAL CANNULA OXYGEN THERAPY AND NON-INVASIVE VENTILATION IN ACUTE HYPERCAPNIC COPD EXACERBATIONS: A COMPARATIVE ANALYSIS

Sachin Baliyan¹, Davinder Kumar Kundra², Vikas Jaiswal³

¹Senior Consultant, Department of Pulmonary Medicine, Oncoplus Hospital, Delhi, India.

²Senior Consultant, Unit Head, Department of Pulmonology (Respiratory and Sleep Medicine), Manipal Hospital, Dwarka, Delhi, India.

³Senior Resident, Consultant Pulmonologist, Department of Respiratory Medicine, Rajinder Integrated Multispeciality Hospital & Research Centre, Varanasi, Uttar Pradesh, India.

Received : 24/08/2026
Received in revised form : 22/09/2026
Accepted : 03/10/2026

Corresponding Author:

Dr. Sachin Baliyan,
Senior Consultant, Department of
Pulmonary Medicine, ONCOPLUS
Hospital, Delhi, India.
Email: drbaliyan.ucms@gmail.com

DOI: 10.70034/ijmedph.2026.4.76

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2026; 16 (4); 513-518

ABSTRACT

Background: High-flow nasal cannula (HFNC) therapy may be better tolerated than non-invasive ventilation (NIV) during acute exacerbations of chronic obstructive pulmonary disease (COPD), but their comparative performance in hypercapnic respiratory failure remains uncertain.

Materials and Methods: This study included 102 adults with COPD and acute hypercapnic respiratory failure: 51 initially treated with HFNC and 51 with NIV. The planned comparisons include arterial blood gases, respiratory rate, treatment failure, clinical outcomes and treatment-related complications. Treatment failure comprises intubation or a switch from the initial support modality.

Results: Baseline characteristics were similar between groups. At 24 hours, among patients still assessed on initial support, NIV was associated with lower PaCO₂ (54.8 versus 59.4 mmHg; p=0.033), higher pH (7.36 versus 7.33; p=0.012) and lower respiratory rate (23.6 versus 25.4 breaths/min; p=0.038). Treatment failure occurred in 10/51 NIV patients (19.6%) and 17/51 HFNC patients (33.3%; p=0.178). HFNC had a higher comfort score (7.5 versus 6.3; p<0.001) and fewer pressure-related skin injuries (2.0% versus 17.6%; p=0.016). In-hospital mortality did not differ significantly.

Conclusion: The study findings suggest better 24-hour ventilatory measures with NIV and greater comfort with HFNC. The non-significant treatment-failure comparison does not establish equivalence.

Keywords: Chronic obstructive pulmonary disease; acute hypercapnic respiratory failure; high-flow nasal cannula; non-invasive ventilation; treatment failure.

INTRODUCTION

Acute exacerbations of chronic obstructive pulmonary disease (COPD) can cause worsening airflow obstruction, dynamic hyperinflation and respiratory muscle fatigue. When alveolar ventilation becomes inadequate, carbon dioxide accumulates and arterial pH falls, producing acute hypercapnic respiratory failure. These patients need prompt treatment of the exacerbation, controlled oxygen delivery and close assessment for ventilatory support.^[1]

Non-invasive ventilation (NIV) delivers positive pressure through a mask, increasing alveolar ventilation and reducing the work of breathing. Trials have shown that NIV reduces endotracheal intubation and in-hospital mortality in selected patients with acute COPD exacerbations.^[2,3] Accordingly, ERS/ATS guidelines recommend bilevel NIV when an exacerbation causes respiratory acidosis (pH ≤7.35) [4]. Its effectiveness, however, may be limited by mask discomfort, air leaks, skin injury and difficulty clearing secretions.

High-flow nasal cannula (HFNC) therapy supplies warmed, humidified oxygen at high flow rates. It may improve comfort, wash carbon dioxide from upper-airway dead space and provide modest positive airway pressure.^[5,6] In a physiological trial involving 24 patients with COPD exacerbations, high-flow therapy produced a small reduction in transcutaneous carbon dioxide compared with standard nasal oxygen.^[5] Whether these effects provide sufficient ventilatory support during respiratory acidosis remains uncertain. Current ERS guidance suggests a trial of NIV before HFNC in COPD-related acute hypercapnic respiratory failure.^[6]

Comparative trials have yielded differing results. Cortegiani and colleagues found HFNC non-inferior to NIV for reducing arterial carbon dioxide after two hours, although 32% of HFNC recipients required NIV within six hours.^[7] In contrast, Tan and colleagues reported higher treatment failure (25.7% versus 14.3%) and intubation (14.2% versus 5.4%) with HFNC.^[8] The RENOvATE trial met its prespecified non-inferiority criterion for a COPD subgroup, but 23% of patients assigned to high-flow oxygen required rescue NIV.^[9] Further direct comparison of gas exchange, treatment failure, tolerance and clinical outcomes is therefore warranted. So, this study aimed to compare HFNC oxygen therapy and NIV as initial respiratory support in patients with acute COPD exacerbation and hypercapnic respiratory failure, with respect to early gas exchange, treatment failure, clinical outcomes and treatment tolerance.

MATERIALS AND METHODS

Study design and setting

This prospective comparative observational study was conducted in the department of Pulmonology in collaboration with emergency department of tertiary care center of North India over a period of 12 months between January 2024 and December 2024. Adults admitted with an acute exacerbation of chronic obstructive pulmonary disease (COPD) complicated by acute hypercapnic respiratory failure were assessed for eligibility. Patients received either high-flow nasal cannula (HFNC) oxygen therapy or non-invasive ventilation (NIV) as their initial respiratory support, according to the treating clinician's assessment. The study included 102 patients: 51 initially treated with HFNC and 51 with NIV. Treatment allocation was not randomised.

Eligibility criteria

Patients aged 18 years or older were eligible if they had an established diagnosis of COPD, an acute worsening of respiratory symptoms requiring hospital admission, and an arterial blood gas sample obtained before respiratory support showing a partial pressure of carbon dioxide (PaCO_2) >45 mmHg with $\text{pH} \leq 7.35$. COPD diagnosis was based on documented prior spirometry where available, supported by clinical history and previous treatment

records. Patients requiring immediate endotracheal intubation, those unable to protect their airway, and those with respiratory or cardiac arrest were excluded. Other exclusions were haemodynamic instability, an untreated pneumothorax, recent facial trauma or surgery preventing NIV use, and a primary cause of respiratory failure other than COPD exacerbation.

Respiratory support and concurrent treatment

HFNC was administered through a heated, humidified nasal cannula. Flow and inspired oxygen concentration were adjusted according to respiratory effort, tolerance and oxygenation. NIV was delivered through an appropriately fitted face mask using bilevel positive airway pressure; inspiratory and expiratory pressures were adjusted in response to respiratory rate, patient comfort, mask leak and arterial blood gas findings. In both groups, supplemental oxygen was titrated to a target peripheral oxygen saturation of 88–92%.

All patients received usual care for COPD exacerbation as clinically indicated, including inhaled bronchodilators, systemic corticosteroids, antibiotics when bacterial infection was suspected, and treatment of associated conditions. Clinicians could change the mode of respiratory support or proceed to invasive ventilation if the patient deteriorated. The timing and reason for each change were recorded.

Data collection and outcomes

Baseline data included age, sex, smoking history, comorbidities, documented Global Initiative for Chronic Obstructive Lung Disease (GOLD) airflow limitation grade, vital signs, respiratory rate, oxygen saturation and arterial blood gas values. Arterial pH, PaCO_2 and partial pressure of oxygen were reassessed at 24 hours; additional measurements were obtained when clinically required. Treatment failure was defined as escalation to invasive mechanical ventilation or a switch from the initial support modality because of worsening respiratory status. Secondary outcomes included changes in arterial blood gases and respiratory rate, duration of respiratory support, hospital stay, complications and in-hospital mortality. Prespecified subgroup comparisons examined baseline PaCO_2 and GOLD grade.

Statistical analysis

The data was analysed using SPSS 20.0. Continuous variables were presented as mean $\pm$ standard deviation, and categorical variables as frequencies and percentages. Between-group comparisons used Welch's independent-samples *t* test for continuous variables and Fisher's exact test for categorical variables. Arterial pH, PaCO_2 and respiratory rate were compared between groups separately at 6 and 24 hours; these tests did not assess within-patient change from baseline. The 24-hour analysis included only patients with available measurements who remained on their initial respiratory support. Treatment failure was defined as intubation or a switch from the initial support modality.

Comparisons stratified by baseline PaCO₂, arterial pH and GOLD grade were exploratory; no interaction tests or multivariable regression were performed. A two-sided *p* value <0.05 was considered statistically significant.

Ethical considerations

The study was approved by institutional ethics committee. Patient identifiers were removed from the analysis dataset.

RESULTS

In present study the mean age was 64.8 ± 8.9 and 65.3 ± 9.1 years, respectively; approximately 71% of patients were men. Baseline respiratory rate, arterial pH and PaCO₂ were similar between groups. The proportions with GOLD grade III–IV airflow limitation, pH <7.25 and PaCO₂ >70 mmHg also showed no statistically significant between-group differences (all *p*>0.05). [Table 1]

Table 1: Baseline demographic, clinical and arterial blood gas characteristics of patients initially treated with HFNC or NIV

Characteristic	HFNC (n=51)	NIV (n=51)	p value
	Frequency (%) / Mean ± SD		
Age, years	64.8 ± 8.9	65.3 ± 9.1	0.780
Male gender	37 (72.5)	36 (70.6)	1.000
Body mass index, kg/m ²	22.1 ± 3.4	22.6 ± 3.5	0.466
Current or former tobacco smoking	40 (78.4)	39 (76.5)	1.000
History of biomass smoke exposure	8 (15.7)	10 (19.6)	0.796
Duration of COPD, years	8.1 ± 5.2	8.8 ± 5.5	0.510
GOLD grade III–IV airflow limitation	34 (66.7)	35 (68.6)	1.000
Hospitalisation for COPD exacerbation in preceding year	24 (47.1)	22 (43.1)	0.842
Hypertension	20 (39.2)	22 (43.1)	0.841
Diabetes mellitus	13 (25.5)	14 (27.5)	1.000
Respiratory rate, breaths/min	30.8 ± 4.9	31.2 ± 5.1	0.687
Arterial pH	7.27 ± 0.05	7.27 ± 0.05	1.000
PaCO ₂ , mmHg	68.9 ± 11.3	68.5 ± 10.9	0.856
PaCO ₂ >70 mmHg	18 (35.3)	17 (33.3)	1.000
Arterial pH <7.25	14 (27.5)	13 (25.5)	1.000

COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; HFNC, high-flow nasal cannula; NIV, non-invasive ventilation; PaCO₂, arterial partial pressure of carbon dioxide.

At 6 hours, arterial pH, PaCO₂ and respiratory rate did not differ significantly between groups. At 24 hours, patients still assessed on their initial support

had a higher mean pH with NIV than HFNC (7.36 ± 0.05 versus 7.33 ± 0.06; *p*=0.012), lower PaCO₂ (54.8 ± 9.5 versus 59.4 ± 10.7 mmHg; *p*=0.033) and lower respiratory rate (23.6 ± 3.8 versus 25.4 ± 4.3 breaths/min; *p*=0.038). These comparisons exclude patients who had already changed support or required escalation. [Table 2]

Table 2: Arterial blood gas and respiratory rate measurements at 6 and 24 hours after initiation of HFNC or NIV

Measurement	HFNC	NIV	p value
	Mean ± SD		
At 6 hours	n=48	n=49	
Arterial pH	7.30 ± 0.06	7.32 ± 0.05	0.078
PaCO ₂ , mmHg	63.7 ± 11.1	60.1 ± 10.3	0.101
Respiratory rate, breaths/min	27.2 ± 4.5	25.9 ± 4.2	0.145
At 24 hours	n=44	n=47	
Arterial pH	7.33 ± 0.06	7.36 ± 0.05	0.012
PaCO ₂ , mmHg	59.4 ± 10.7	54.8 ± 9.5	0.033
Respiratory rate, breaths/min	25.4 ± 4.3	23.6 ± 3.8	0.038

Assessments were available for 48 HFNC and 49 NIV patients at 6 hours, and 44 and 47 patients, respectively, at 24 hours. PaCO₂, arterial partial pressure of carbon dioxide.

Treatment failure occurred in 17/51 HFNC patients (33.3%) and 10/51 NIV patients (19.6%), a difference that was not statistically significant

(*p*=0.178). Intubation as the first failure event occurred in eight and four patients, respectively (*p*=0.357). ICU admission, duration of respiratory support, hospital stay and in-hospital mortality did not differ significantly between groups. Five HFNC patients (9.8%) and three NIV patients (5.9%) died during admission (*p*=0.715). [Table 3]

Table 3: Treatment failure and clinical outcomes according to initial respiratory support

Outcome	HFNC (n=51)	NIV (n=51)	p value
	Frequency (%) / Mean ± SD		
Treatment failure	17 (33.3)	10 (19.6)	0.178
Endotracheal intubation as first failure event	8 (15.7)	4 (7.8)	0.357
Switch to the alternative non-invasive modality as first failure event	9 (17.6)	6 (11.8)	0.577

Admission or transfer to intensive care	16 (31.4)	12 (23.5)	0.506
Duration of respiratory support, days	3.6 ± 1.8	4.1 ± 2.0	0.188
Hospital stay, days	7.7 ± 2.8	8.1 ± 3.0	0.488
In-hospital death	5 (9.8)	3 (5.9)	0.715

Treatment failure was defined as intubation or a switch from the initial HFNC/NIV modality; the reported first-failure categories are mutually exclusive. ICU, intensive care unit.

The mean comfort score was higher with HFNC than NIV (7.5 ± 1.4 versus 6.3 ± 1.6; $p < 0.001$). Pressure-

related facial or nasal skin injury was less frequent with HFNC (1/51, 2.0%) than NIV (9/51, 17.6%; $p = 0.016$). Differences in dryness, gastric distension, documented interface intolerance and treatment interruption did not reach statistical significance. [Table 4]

Table 4: Patient comfort and treatment-related complications with HFNC and NIV

Measure	HFNC (n=51)	NIV (n=51)	p value
	Frequency (%)	Mean ± SD	
Patient-reported comfort score (0–10; higher is better)	7.5 ± 1.4	6.3 ± 1.6	<0.001
Facial or nasal pressure-related skin injury	1 (2.0)	9 (17.6)	0.016
Nasal or oral dryness	7 (13.7)	3 (5.9)	0.318
Gastric distension	1 (2.0)	6 (11.8)	0.112
Documented interface intolerance	4 (7.8)	11 (21.6)	0.091
Treatment interruption lasting >15 minutes	7 (13.7)	13 (25.5)	0.212

Treatment failure was more frequent among patients with $\text{PaCO}_2 > 70$ mmHg, $\text{pH} < 7.25$ or GOLD grade III–IV airflow limitation in both treatment groups. For example, failure occurred in 9/18 HFNC patients (50.0%) and 7/17 NIV patients (41.2%) with $\text{PaCO}_2 > 70$ mmHg. None of the within-subgroup

comparisons between HFNC and NIV was statistically significant (all $p > 0.05$). The small subgroup sizes limit conclusions about whether baseline severity changes the relative effect of either treatment. [Table 5]

Table 5: Exploratory treatment-failure comparisons by baseline PaCO_2 , arterial pH and GOLD grade

Baseline subgroup	HFNC failures / subgroup total (%)	NIV failures / subgroup total (%)	p value
$\text{PaCO}_2 \leq 70$ mmHg	8/33 (24.2)	3/34 (8.8)	0.109
$\text{PaCO}_2 > 70$ mmHg	9/18 (50.0)	7/17 (41.2)	0.738
Arterial pH ≥ 7.25	8/37 (21.6)	4/38 (10.5)	0.222
Arterial pH < 7.25	9/14 (64.3)	6/13 (46.2)	0.449
GOLD grade I–II	3/17 (17.6)	1/16 (6.3)	0.601
GOLD grade III–IV	14/34 (41.2)	9/35 (25.7)	0.208

Each pair of rows stratifies the same patients by one characteristic; subgroups across different characteristics overlap. Treatment failure was defined as in Table 3. GOLD, Global Initiative for Chronic Obstructive Lung Disease; PaCO_2 , arterial partial pressure of carbon dioxide.

DISCUSSION

In this study cohort of 102 patients with COPD and acute hypercapnic respiratory failure, baseline pH, PaCO_2 and respiratory rate were comparable between the HFNC and NIV groups. Severe airflow limitation was common in both groups. This baseline similarity helps frame the observed comparisons, although clinically selected treatment may still reflect differences in exacerbation severity that the tables do not capture. Lee et al., likewise evaluated both approaches in COPD exacerbations with moderate hypercapnia, while the observational cohort of Sun et al., found comparable treatment failure with HFNC and NIV in selected patients.^[10,11] Neither study establishes that the two modalities are interchangeable across all degrees of respiratory acidosis.

At six hours, the study groups had similar blood gas values. By 24 hours, NIV was associated with lower PaCO_2 (54.8 versus 59.4 mmHg; $p = 0.033$), higher pH (7.36 versus 7.33; $p = 0.012$) and lower respiratory rate (23.6 versus 25.4 breaths/min; $p = 0.038$). Bilevel NIV directly augments tidal ventilation and unloads inspiratory muscles; HFNC primarily reduces upper-airway dead space while providing humidification and modest expiratory pressure. This mechanism could explain a larger sustained reduction in PaCO_2 with NIV. Yet published physiological results vary: Papachatzakis et al., reported lower PaCO_2 at discharge with HFNC in a small trial involving mixed causes of hypercapnic failure, and Rezaei et al., found short-term improvement with both modalities in 30 patients with COPD exacerbation.^[12,13] Rittayamai et al., showed that HFNC flow affected inspiratory effort, while Haciosman et al., studied different HFNC flow rates in a three-arm trial.^[14,15] Device settings may therefore influence comparisons. The study 24-hour analysis includes only patients still assessed on their initial support, so it's apparent NIV advantage could also reflect earlier escalation of patients with poorer HFNC responses. Treatment failure was numerically higher with HFNC than NIV (33.3% versus 19.6%), but the

difference was not statistically significant ($p=0.178$). Intubation and in-hospital mortality also showed no significant differences. These results cannot demonstrate equivalence, particularly with only 51 patients per group. Pantazopoulos et al., reported failure in 19.6% of patients receiving nasal high flow and 14.8% receiving NIV in a multicentre trial.^[16] A retrospective study by Colaianne-Alfonso et al., found no significant failure difference but reported better early PaCO₂ and respiratory-rate responses with NIV.^[17] In a meta-analysis of four randomised trials involving 486 patients, Qin et al., found higher treatment failure (risk ratio 1.64) and switching rates (risk ratio 2.60) with HFNC, without a demonstrated increase in intubation or mortality.^[18] Rescue NIV may prevent some HFNC failures from progressing to intubation, making the definitions and timing of failure important when comparing studies.

HFNC had a higher comfort score (7.5 versus 6.3; $p<0.001$) and fewer pressure-related skin injuries (2.0% versus 17.6%; $p=0.016$). Its open nasal interface permits communication and secretion clearance without sustained mask pressure. In a trial involving patients with COPD after extubation, Tan et al., also found greater comfort and less nasofacial skin breakdown with HFNC.^[19] Longhini et al., reported improved comfort when HFNC was used during NIV interruptions,^[20] while Yuste et al., studied its use in patients unable to tolerate NIV.^[21] These settings differ from choosing initial support during respiratory acidosis, but they help explain why HFNC may be useful when mask tolerance limits NIV delivery.

Finally, in study, the failure proportions rose in both groups with PaCO₂ >70 mmHg, pH <7.25 and GOLD grade III–IV disease. Confalonieri et al., identified low pH and elevated respiratory rate among predictors of NIV failure in COPD exacerbations,^[22] supporting close reassessment when acidosis is pronounced. The present subgroup comparisons were small and none tested a treatment-by-severity interaction; they cannot identify which patients benefit more from either modality. Taken together, the study findings suggest a trade-off between more effective carbon dioxide clearance with NIV and better interface tolerance with HFNC.

Limitations

The study comparison is limited by its small sample and non-random treatment selection, leaving potential confounding despite similar measured baseline characteristics. Twenty-four-hour blood gases were available only for patients remaining on their initial support, creating possible selection bias. Subgroup comparisons were underpowered, device settings and crossover decisions may have varied, and in-hospital follow-up cannot establish longer-term outcomes. These limitations prevent conclusions about clinical equivalence.

CONCLUSION

In this study cohort, both HFNC and NIV were associated with improvement in respiratory status, while NIV showed lower PaCO₂, higher arterial pH and a lower respiratory rate at 24 hours among patients still receiving their initial support. Treatment failure occurred more often with HFNC, although the difference was not statistically significant; this finding does not establish equivalence. HFNC was associated with greater comfort and fewer pressure-related skin injuries. The pattern supports careful monitoring of gas exchange and readiness to escalate support, particularly in patients with marked acidosis or hypercapnia.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of COPD: 2026 report.
2. Brochard L, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. *N Engl J Med*. 1995;333:817–822. doi:10.1056/NEJM199509283331301.
3. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. *Lancet*. 2000;355:1931–1935. doi:10.1016/S0140-6736(00)02323-0.
4. Rochweg B, et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J*. 2017;50:1602426. doi:10.1183/13993003.02426-2016.
5. Pilcher J, et al. Physiological effects of titrated oxygen via nasal high-flow cannulae in COPD exacerbations: a randomized controlled cross-over trial. *Respirology*. 2017;22:1149–1155. doi:10.1111/resp.13050.
6. Oczkowski S, et al. ERS clinical practice guidelines: high-flow nasal cannula in acute respiratory failure. *Eur Respir J*. 2022;59:2101574. doi:10.1183/13993003.01574-2021.
7. Cortegiani A, et al. High flow nasal therapy versus noninvasive ventilation as initial ventilatory strategy in COPD exacerbation: a multicenter non-inferiority randomized trial. *Crit Care*. 2020;24:692. doi:10.1186/s13054-020-03409-0.
8. Tan D, et al. High flow nasal cannula oxygen therapy versus non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: a randomized controlled non-inferiority trial. *Crit Care*. 2024;28:250. doi:10.1186/s13054-024-05040-9.
9. RENOVATE Investigators and the BRICNet Authors. High-flow nasal oxygen vs noninvasive ventilation in patients with acute respiratory failure: the RENOVATE randomized clinical trial. *JAMA*. 2025;333:875–890. doi:10.1001/jama.2024.26244.
10. Lee MK, Choi J, Park B, et al. High flow nasal cannulae oxygen therapy in acute-moderate hypercapnic respiratory failure. *Clin Respir J*. 2018;12:2046–2056. doi:10.1111/crj.12772.
11. Sun J, Li Y, Ling B, et al. High flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: an observational cohort study. *Int J Chron Obstruct Pulmon Dis*. 2019;14:1229–1237. doi:10.2147/COPD.S206567.
12. Papachatzakis Y, Nikolaidis PT, Kontogiannis S, Trakada G. High-flow oxygen through nasal cannula vs. non-invasive ventilation in hypercapnic respiratory failure: a randomized

- clinical trial. *Int J Environ Res Public Health*. 2020;17:5994. doi:10.3390/ijerph17165994.
13. Rezaei A, Fakharian A, Ghorbani F, et al. Comparison of high-flow oxygenation with noninvasive ventilation in COPD exacerbation: a crossover clinical trial. *Clin Respir J*. 2021;15:420–429. doi:10.1111/crj.13315.
 14. Rittayamai N, Phuangchoei P, Tscheikuna J, Praphruekit N, Brochard L. Effects of high-flow nasal cannula and non-invasive ventilation on inspiratory effort in hypercapnic patients with chronic obstructive pulmonary disease: a preliminary study. *Ann Intensive Care*. 2019;9:122. doi:10.1186/s13613-019-0597-5.
 15. Haciosman O, Ergenc H, Az A, Dogan Y, Sogut O. A high-flow nasal cannula versus noninvasive ventilation in acute exacerbations of chronic obstructive pulmonary disease. *Am J Emerg Med*. 2025;87:38–43. doi:10.1016/j.ajem.2024.10.043.
 16. Pantazopoulos I, Boutlas S, Mavrovounis G, et al. Nasal high flow or noninvasive ventilation? Navigating hypercapnic COPD exacerbation treatment: a randomized noninferiority clinical trial. *Respir Med*. 2024;232:107762. doi:10.1016/j.rmed.2024.107762.
 17. Colaianne-Alfonso N, Toledo A, Montiel G, Deana C, Vetrugno L, Castro-Sayat M. High-flow nasal cannula versus non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease with acute-moderate hypercapnic respiratory failure: a retrospective study. *Front Med*. 2025;12:1582749. doi:10.3389/fmed.2025.1582749.
 18. Qin J, Wang G, Liao Y, Shang W, Han D. High flow nasal therapy versus noninvasive ventilation for AECOPD with acute hypercapnic respiratory failure: a meta-analysis of randomized controlled trials. *Ann Intensive Care*. 2025;15:64. doi:10.1186/s13613-025-01480-w.
 19. Tan D, et al. High-flow nasal cannula oxygen therapy versus non-invasive ventilation for chronic obstructive pulmonary disease patients after extubation: a multicenter, randomized controlled trial. *Crit Care*. 2020;24:489. doi:10.1186/s13054-020-03214-9.
 20. Longhini F, Pisani L, Lungu R, et al. High-flow oxygen therapy after noninvasive ventilation interruption in patients recovering from hypercapnic acute respiratory failure: a physiological crossover trial. *Crit Care Med*. 2019;47:e506–e511. doi:10.1097/CCM.00000000000003740.
 21. Yuste ME, Moreno O, Narbona S, Acosta F, Peñas L, Colmenero M. Efficacy and safety of high-flow nasal cannula oxygen therapy in moderate acute hypercapnic respiratory failure. *Rev Bras Ter Intensiva*. 2019;31:156–163. doi:10.5935/0103-507X.20190026.
 22. Confalonieri M, Garuti G, Cattaruzza MS, et al. A chart of failure risk for noninvasive ventilation in patients with COPD exacerbation. *Eur Respir J*. 2005;25:348–355. doi:10.1183/09031936.05.00085304.