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# Comparison of clinical outcomes between non-invasive ventilation and high-flow nasal cannula use in patients with acute pancreatitis

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## Abstract

**Background** Noninvasive ventilation (NIV) and high-flow nasal cannula (HFNC) are widely used respiratory support strategies, but their comparative effectiveness in acute pancreatitis remains unclear. Therefore, we analyzed clinical outcomes associated with these interventions using the National Inpatient Sample database (2016–2022).

**Methods** This retrospective study compared clinical outcomes between patients treated with NIV and those treated with HFNC, focusing on mortality, intubation rates, complications, length of stay (LOS), and healthcare costs. We conducted univariate and multivariate logistic regression analyzes, adjusting for patient demographics, hospital characteristics, and comorbidities.

**Results** HFNC treatment was associated with higher mortality (25.7% vs. 15.9%), intubation rates (39.1% vs. 23.6%), and pulmonary complications (pneumonia: 35.2% vs. 23.9%; pulmonary embolism: 6.6% vs. 2.8%) compared to NIV. patients receiving HFNC had longer hospital stays (20.38 vs. 13.62 days) and incurred higher healthcare costs ($302,387.31 vs. $198,870.53) (all $P < 0.001$).

**Conclusion** In this retrospective analysis, initial management with NIV was associated with better clinical outcomes and reduced healthcare resource utilization compared to HFNC in patients with acute pancreatitis. These findings warrant validation in prospective studies.

**Keywords** Acute pancreatitis, Non-invasive ventilation, High-flow nasal cannula, Acute respiratory distress syndrome, National Inpatient Sample

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## Introduction

Acute pancreatitis often triggers a systemic inflammatory response that can progress to multi-organ dysfunction, with the lungs being particularly vulnerable [1]. This frequently leads to acute respiratory failure; the development of ARDS is a common and lethal complication, underscoring the critical need for effective respiratory support [2, 3]. Two primary non-invasive modalities for this are NIV and HFNC. While NIV is effective at reducing intubation rates, its use can be limited by poor patient tolerance [4]. Conversely, HFNC is better tolerated but provides less ventilatory support, which may be inadequate in severe failure [4]. Despite the central role of respiratory support in acute pancreatitis, comparative evidence guiding the choice between NIV and HFNC in this specific population remains scarce.

To address this knowledge gap, we used the National Inpatient Sample (NIS) database to comprehensively compare clinical outcomes between NIV and HFNC in patients with acute pancreatitis, including mortality, intubation rates, complications, LOS, and healthcare costs.

## Materials and methods

### Data source

This retrospective study utilized the NIS, the largest all-payer hospitalization database in the United States. As a key component of the Healthcare Cost and Utilization Project supported by the Agency for Healthcare Research and Quality, the NIS includes data from over 1,000 hospitals, capturing approximately one-fifth of all annual hospital admissions nationwide. In our study, we collected detailed demographic information on patients as well as relevant hospital characteristics. In addition to demographic and hospital data, we included economic factors and LOS in our analysis. Using this information, we developed a robust statistical model to compare outcomes across different patient groups and hospital settings. As our study used anonymized public data, ethics committee approval was not required. The NIS database is accessible at https://www.hcup-us.ahrq.gov.

### Data collection

This study analyzed adult patients (≥18 years) with acute pancreatitis from the NIS database (2016–2022) who received exclusively either NIV or HFNC, having excluded those with sequential or alternating use of both therapies. To ensure a direct comparison, we excluded patients who had undergone surgical procedures or had a history of intubation prior to admission or before receiving NIV or HFNC. Patients treated with NIV were identified using relevant ICD-10 procedure codes (5A09357, 5A09358, 5A09457, 5A09458, 5A09557, 5A09558), while those who received HFNC were identified through the corresponding ICD-10 procedure codes (5A0935A, 5A0945A, 5A0955A). Additional ICD-10 diagnosis and procedure codes were used to define pancreatitis, as well as associated comorbidities and complications, including intubation and tracheotomy. We examined patients' demographic profiles, hospital characteristics, and various outcome measures such as length of hospital stay, economic indicators, and in-hospital mortality. Relevant information on comorbidities and complications was extracted from the ICD-10 diagnosis codes within the database.

### Data analysis

Analysis was conducted using Statistical Package for the Social Sciences (SPSS) 25.0 statistical software. Differences between groups were assessed using appropriate methods based on data type. Continuous variables were analyzed with independent t-tests, while categorical variables were evaluated using chi-square tests. To identify factors influencing respiratory support outcomes, we developed a logistic regression model incorporating all relevant variables from the NIS database. This model systematically evaluated demographic characteristics, hospital profiles, and comorbidities. Regression analysis was used to generate quantitative measures, including odds ratios (OR) with corresponding 95% confidence intervals (CI) for each variable [5]. Throughout the analysis, results with $P<0.05$ were considered statistically significant.

Inverse probability of treatment weighting (IPTW) was performed because of the inherent likelihood of selection bias between HFNC and NIV-only patients [4]. IPTW based on propensity scores was applied to minimize potential selection bias between patients receiving HFNC and those treated with NIV. A logistic regression model was used to estimate each patient's propensity score for receiving HFNC, with baseline demographic and clinical characteristics entered as covariates, including sex, age group, ethnicity (White and Hispanic), primary payer, hospital control and region, teaching status, and a comprehensive set of comorbidities (valvular disease, alcohol abuse, renal failure, pulmonary circulation disorders, peripheral vascular disease, congestive heart failure, chronic pulmonary disease, coagulopathy, obesity, diabetes, weight loss, hypertension, hypothyroidism, liver disease, electrolyte disorders, smoking, cardiac arrhythmia, gallstone disease, cholecystitis, and varying degrees of malnutrition). Weights were derived as the inverse of the estimated probability of receiving the treatment actually received, corresponding to the average treatment effect estimand; thus, each HFNC patient was assigned a weight of 1/PS and each NIV patient a weight of 1/(1 – PS), where PS denotes the individual's propensity score. Stabilized weights were used to improve efficiency and mitigate the influence of extreme values, and

**Table 1** Association analysis of outcomes and complications after inverse Probability of Treatment Weighting (IPTW) adjustment

| Outcomes | HFNC (*N* = 727) | NIV (*N* = 6447) | OR | 95% CI | *P* value |
|---|---|---|---|---|---|
| Intubation | 284(39.1%) | 1524(23.6%) | 1.64 | 1.36–1.97 | < 0.001 |
| Pneumonia | 256(35.2%) | 1539(23.9%) | 1.64 | 1.34–1.99 | < 0.001 |
| Pulmonary embolism | 48(6.6%) | 183(2.8%) | 2.18 | 1.50–3.16 | < 0.001 |
| DIED | 187(25.7%) | 1022(15.9%) | 1.43 | 1.17–1.76 | < 0.001 |
| Tracheostomy | 13(1.8%) | 81(1.3%) | 1.13 | 0.58–2.21 | 0.713 |
| Complications | | | | | |
| Systemic InflammatoryResponseSyndrome | 337(46.4%) | 2100(32.6%) | 1.46 | 1.21–1.76 | < 0.001 |
| Pancreatic necrosis | 140(19.3%) | 768(11.9%) | 1.56 | 1.24–1.97 | < 0.001 |
| Sepsis | 412(56.7%) | 2680(41.6%) | 1.46 | 1.21–1.75 | < 0.001 |
| Acute renal insufficiency | 468(64.4%) | 3479(54.0%) | 1.28 | 1.06–1.55 | 0.009 |
| Deep vein thrombosis (DVT) | 49(6.7%) | 233(3.6%) | 1.57 | 1.10–2.24 | 0.012 |
| Gastrointestinal bleeding | 40(5.5) | 269(4.2) | 1.55 | 0.97–2.45 | 0.061 |
| Bronchiolitis | 136(18.7%) | 972(15.1%) | 1.22 | 0.96–1.54 | 0.088 |
| Encephalopathy | 201(27.6%) | 1395(21.6%) | 1.19 | 0.97–1.45 | 0.092 |
| Pancreatic pseudocyst | 64(8.8%) | 452(7.0%) | 1.05 | 0.75–1.46 | 0.762 |
| Acute cardiogenic pulmonary edema | 1(0.1%) | 12(0.2%) | 0.96 | 0.12–7.45 | 0.973 |

*OR* Odds ratio, *CI* Confidence interval

**Table 2** Relationship between complications and HFNC or NIV use

| Complications | Univariate Analysis | | | Multivariate Logistic Regression | | |
|---|---|---|---|---|---|---|
| | HFNC (*N* = 727) | NIV (*N* = 6447) | *P* value | OR | 95% CI | *P* value |
| Sepsis | 412(56.7%) | 2680(41.6%) | < 0.001 | 1.487 | 1.25–1.76 | < 0.001 |
| Deep vein thrombosis | 49(6.7%) | 233(3.6%) | < 0.001 | 1.380 | 0.98–1.93 | 0.060 |
| Acute cardiogenic pulmonary edema | 1(0.1%) | 12(0.2%) | 0.770 | 0.707 | 0.07–7.16 | 0.769 |
| Pancreatic necrosis | 140(19.3%) | 768(11.9%) | < 0.001 | 1.347 | 1.08–1.66 | 0.006 |
| Pancreatic pseudocyst | 64(8.8%) | 452(7.0%) | 0.076 | 1.021 | 0.76–1.36 | 0.890 |
| Encephalopathy | 201(27.6%) | 1395(21.6%) | < 0.001 | 1.135 | 0.94–1.36 | 0.178 |
| Acute renal insufficiency | 468(64.4%) | 3479(54.0%) | < 0.001 | 1.327 | 1.11–1.58 | 0.002 |
| Bronchiolitis | 136(18.7%) | 972(15.1%) | 0.010 | 1.170 | 0.95–1.43 | 0.137 |
| Systemic Inflammatory Response Syndrome | 337(46.4%) | 2100(32.6%) | < 0.001 | 1.442 | 1.21–1.70 | < 0.001 |
| Gastrointestinal bleeding | 40(5.5) | 269(4.2) | 0.094 | 1.127 | 0.79–1.60 | 0.507 |

*OR* Odds ratio, *CI* Confidence interval

covariate balance between treatment groups before and after weighting was assessed using standardized mean differences, with values below 0.1 indicating adequate balance. The weighted cohort was subsequently analyzed using survey-weighted generalized linear models (family = quasibinomial) to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for each outcome comparing HFNC and NIV, with all analyzes performed in R (version 4.3.2) using the WeightIt, cobalt, and survey packages. Table 1 presents the analysis results based on IPTW adjustment. Due to its methodological difference (weighting approach) from Table 2 (standard regression adjustment approach), the effect estimates (ORs) between the two tables should not be compared directly. In multivariate logistic regression, an odds ratio (OR) greater than 1 indicates a positive association between the variable and receiving HFNC (compared to NIV), while an OR less than 1 indicates a negative association. When the 95% confidence interval (CI) includes 1, the association is not statistically significant ($p > 0.05$).

## Results

### Demographic and clinical characteristics of patients

Application of the study criteria identified a cohort of 7,174 patients with acute pancreatitis, of whom 727 were managed with HFNC and 6,447 with NIV (Fig. 1). Baseline characteristics are summarized in Table 3. The groups were notable for significant differences in age, primary payer, hospital characteristics, and comorbidity profiles (all $P < 0.001$), with the HFNC group being marginally younger.

### Two groups of hospital characteristics

Comparative analysis of hospital characteristics revealed significant differences in hospital ownership, hospital type, and hospital location ($P < 0.001$). Regarding hospital

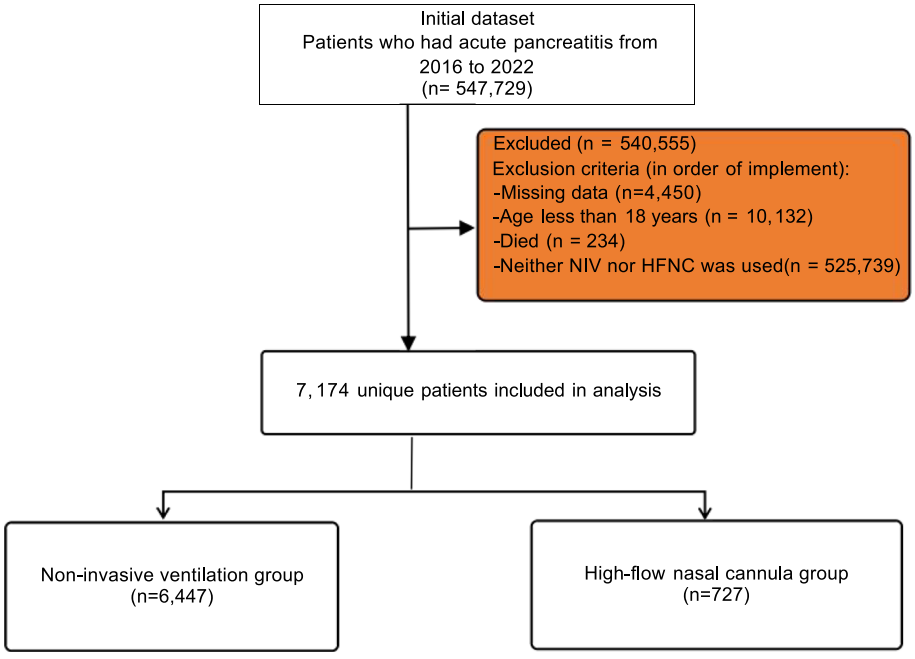


**Fig. 1** Study flowchart. The numbers for the exclusion criteria are not mutualy exclusive, as patients may meet more than one criterion

ownership, both groups were predominantly treated in private nonprofit institutions, with the HFNC group showing a higher proportion than the NIV group. The HFNC group also had higher percentages of patients in government non-federated institutions, while the NIV group had a greater proportion treated in private for-profit institutions. Regarding hospital type, both groups were predominantly treated in urban teaching hospitals. However, the NIV group had higher proportions in rural and urban nonteaching hospitals compared to the HFNC group. In terms of hospital location, most patients in both groups were treated in the South. Compared to the NIV group, the HFNC group had higher proportions in the Northeast and Midwest, while the NIV group had higher proportions in the South and West.

Regarding comorbidities, the HFNC group had higher rates of alcohol abuse, coagulation disorders, fluid and electrolyte imbalances, weight loss, and severe malnutrition. In contrast, the NIV group showed higher proportions of chronic pulmonary disease, chronic renal failure, obesity, hypertension, smoking, and congestive heart failure (Table 4).

### Clinical outcomes and resource utilization

Comparative outcomes are summarized in Table 5. The HFNC group exhibited significantly increased odds of in-hospital mortality, intubation, pneumonia, and pulmonary embolism (all $P<0.001$). The rate of tracheostomy did not differ significantly between the two cohorts.

Regarding resource utilization, patients in the NIV group experienced shorter hospital stays and incurred lower total hospitalization costs compared to those in the HFNC group (Table 6). Logistic regression analysis was performed to identify factors associated with the use of HFNC and NIV, revealing several risk indicators for acute pancreatitis in HFNC patients. These included sepsis (OR = 1.487; 95% CI = 1.25–1.76), deep vein thrombosis (DVT) (OR = 1.380; 95% CI = 0.98–1.93), pancreatic necrosis (OR = 1.347; 95% CI = 1.08–1.66), encephalopathy (OR = 1.135; 95% CI = 0.94–1.36), acute renal insufficiency (OR = 1.327; 95% CI = 1.11–1.58), and systemic inflammatory response syndrome (OR = 1.442; 95% CI = 1.21–1.70) (Table 2).

## Discussion

The present study provides a comprehensive health-economic evaluation associating NIV and HFNC therapy with clinical outcomes. It showed that patients in the HFNC group had higher mortality rates (25.7% vs. 15.9%) and a significantly greater incidence of pulmonary complications (35.2% vs. 23.9%). The HFNC group also exhibited slightly higher tracheotomy rates compared to the NIV group (1.8% vs. 1.3%). Conversely, the NIV group showed a higher rate of progression to respiratory failure, including ARDS (4.6% vs. 2.2%). Economic analysis revealed that HFNC therapy was associated with longer hospital stays, extending the average length of stay by 6 to 7 days, and resulted in a substantial 52.05% increase in healthcare-related costs. The observational nature of this study, mandates a cautious interpretation of our results. The potential for selection bias and unmeasured confounding is paramount, as the choice of respiratory

**Table 3** Demographics and patient characteristics

| | HFNC (*n* = 727) | NIV (*n* = 6447) | *P* value |
|---|---|---|---|
| Male sex, n(%) | 423(58.2%) | 3775(58.6%) | 0.848 |
| Age, (mean, SD) | 59.3(16.4) | 61.0(15.5) | < 0.001 |
| Age, y | | | 0.070 |
| 18–34 | 58(8.0%) | 393(6.1%) | |
| 35–49 | 141(19.4%) | 1071(16.6%) | |
| 50–64 | 225(30.9%) | 2141(33.2%) | |
| 65–79 | 220(30.3%) | 2092(32.4%) | |
| ≥ 80 | 83(11.4%) | 750(11.6%) | |
| Hispanic, n(%) | 84(11.6%) | 658(10.2%) | 0.258 |
| White, n(%) | 465(64.0%) | 4264(66.1%) | 0.240 |
| Primary expected payer | | | < 0.001 |
| Medicare, n(%) | 312(42.9%) | 3278(50.8%) | |
| Medicaid, n(%) | 157(21.6%) | 968(15.0%) | |
| Private insurance, n(%) | 201(27.6%) | 1745(27.1%) | |
| Self-pay, n(%) | 34(4.7%) | 244(3.8%) | |
| No charge, n(%) | 3(0.4%) | 22(0.3%) | |
| Other, n(%) | 20(2.8%) | 190(2.9%) | |
| Control/ownership of the hospital | | | < 0.001 |
| Government/nonfederal | 101(13.9%) | 710(11.0%) | |
| Private/nonprofit | 589(81.0%) | 4848(75.2%) | |
| Private | 37(5.1%) | 889(13.8%) | |
| Hospital type | | | < 0.001 |
| Rural | 30(4.1%) | 437(6.8%) | |
| Urban/non teaching | 86(11.8%) | 1300(20.2%) | |
| Urban/teaching | 611(84.0%) | 4710(73.1%) | |
| Hospital location | | | < 0.001 |
| Northeast | 124(17.1%) | 1014(15.7%) | |
| Midwest | 213(29.3%) | 1477(22.9%) | |
| South | 256(35.2%) | 2578(40.0%) | |
| West | 134(18.4%) | 1378(21.4%) | |
| LOS (mean, SD) | 20.38(20.4) | 13.62(15.0) | < 0.001 |
| TOTCHE (mean, SD) | 302,387.31(443,759.9) | 198,870.53(320,494.3) | < 0.001 |

*LOS* Length of stay, *TOTCHE* Total charge

support in clinical practice is not random. HFNC may have been preferentially used in patients with either milder disease or specific contraindications to NIV (e.g., agitation) [6], while NIV might have been initiated in those with more evident severity [7]. The absence of critical physiological data, such as baseline $PaO_2/FiO_2$ ratios, prevents adequate adjustment for illness severity. Therefore, the poorer outcomes associated with HFNC may reflect these underlying patient differences rather than a direct effect of the therapy. Moreover, we revealed that HFNC therapy was significantly associated with increased risks of systemic complications, including sepsis, acute renal insufficiency, SIRS, and pancreatic necrosis. After a systematic evaluation, we identified a strong correlation between complications and these variables within the HFNC group (Table 2).

In our study, HFNC therapy was associated with a higher incidence of sepsis compared to NIV. However, it is crucial to interpret this finding with caution. This observed association may not imply a direct causal effect of HFNC. An alternative and perhaps more plausible explanation is the presence of confounding by indication and unmeasured severity. Clinicians may preferentially opt for HFNC in patients who are more critically ill or have a higher baseline inflammatory burden, such as those with established pancreatic necrosis (which was more common in the HFNC group, as shown in Table 2), but who cannot tolerate NIV interfaces. These patients are inherently at a higher risk for developing sepsis, which could explain the association we observed. Furthermore, while HFNC can aid secretion clearance and potentially reduce pulmonary infection risk, treatment failure or delayed escalation of therapy in severely ill patients managed with HFNC could potentially contribute to this outcome [8, 9]. This contrasts with findings from Zhu et al., who reported no increased sepsis

**Table 4** Relationship between comorbidities and HFNC or NIV use

| Comorbidities | HFNC (*n* = 727) | NIV (*n* = 6447) | *P* value |
|---|---|---|---|
| Valvular disease | 52(7.2%) | 434(6.7%) | 0.669 |
| Alcohol abuse | 182(25.0%) | 1296(20.1%) | 0.002 |
| Chronic Renal failure | 140(19.3%) | 1730(26.8%) | < 0.001 |
| Pulmonary circulation disorders | 51(7.0%) | 394(6.1%) | 0.338 |
| Peripheral vascular disorders | 59(8.1%) | 466(7.2%) | 0.384 |
| Congestive heart failure | 201(27.6%) | 2100(32.6%) | 0.007 |
| Chronic pulmonary disease | 195(26.8%) | 2118(32.9%) | < 0.001 |
| Coagulopathy | 246(33.8%) | 1503(23.3%) | < 0.001 |
| Obesity | 182(25.0%) | 2658(41.2%) | < 0.001 |
| Diabetes, uncomplicated | 93(12.8%) | 1085(16.8%) | 0.005 |
| Weight loss | 209(28.7%) | 1304(20.2%) | < 0.001 |
| Hypertension | 441(60.7%) | 4758(73.8%) | < 0.001 |
| Hypothyroidism | 84(11.6%) | 822(12.8%) | 0.358 |
| Fluid and electrolyte disorders | 590(81.2%) | 4381(68.0%) | < 0.001 |
| Liver Disease | 208(28.6%) | 1671(25.9%) | 0.118 |
| Smoking | 72(9.9%) | 1127(17.5%) | < 0.001 |
| Arrhythmia | 217(29.8%) | 2015(31.3%) | 0.438 |
| Gallstone disease | 35(4.8%) | 397(6.2%) | 0.149 |
| Cholecystitis | 17(2.3%) | 162(2.5%) | 0.775 |
| Mild malnutrition | 13(1.8%) | 63(1.0%) | 0.043 |
| Moderate malnutrition | 50(6.9%) | 276(4.3%) | 0.001 |
| Severe malnutrition | 106(14.6%) | 604(9.4%) | < 0.001 |
| Unspecified malnutrition | 36(5.0%) | 317(4.9%) | 0.967 |

risk with HFNC [10], underscoring the need for careful patient selection and prospective validation. The higher incidence of SIRS in the HFNC group (13.8% compared to NIV) should be interpreted in the context of disease severity rather than as a direct pro-inflammatory effect of the therapy. The progression to severe acute pancreatitis is itself a potent trigger for SIRS [11, 12]; thus, the association likely reflects the patient population selected for HFNC. Although experimental models suggest ventilation patterns can influence cytokine release [13], extrapolating this to HFNC in clinical pancreatitis remains speculative. The observed association is more parsimoniously explained by residual confounding.

In contrast, NIV provides more robust oxygenation support [14]. The higher sepsis risk observed with HFNC may therefore reflect its limitations in managing severe cases, which is consistent with our finding that HFNC was associated with a 1.2-fold increased risk of acute kidney injury (AKI) compared to NIV. Sepsis is a leading cause of AKI in critically ill patients [15, 16], often through direct or immune-mediated mechanisms [17]. The difference in AKI risk may also align with the complex hemodynamic effects of HFNC, which could influence renal perfusion [18, 19].

Physiologically, while HFNC provides positive airway pressure and reduces anatomical dead space, it may not achieve the same consistent alveolar recruitment and ventilatory support as NIV with PEEP in severely compromised patients [13]. This relative insufficiency could, in some cases, contribute to patient self-inflicted lung injury due to high respiratory effort [20]. Conversely, NIV itself carries risks of volutrauma or barotrauma if not carefully titrated [13]. The higher SIRS incidence in the HFNC group may thus result from an interplay where, in patients with high respiratory drive, insufficient support from HFNC fails to adequately mitigate work of breathing and protect the lungs, potentially exacerbating systemic inflammation.

**Table 5** Outcomes

| Outcomes | HFNC | NIV | *P* value | OR | 95% CI | *P* value |
|---|---|---|---|---|---|---|
| Deaths, n(%) | 187(25.7%) | 1022(15.9%) | < 0.001 | 1.503 | 1.235–1.830 | < 0.001 |
| Pneumonia, n(%) | 256(35.2%) | 1539(23.9%) | < 0.001 | 1.509 | 1.271–1.791 | < 0.001 |
| Pulmonary embolism, n(%) | 48(6.6%) | 183(2.8%) | < 0.001 | 1.945 | 1.380–2.741 | < 0.001 |
| Intubation, n(%) | 284(39.1%) | 1524(23.6%) | < 0.001 | 1.608 | 1.350–1.914 | < 0.001 |
| Tracheostomy, n(%) | 13(1.8%) | 81(1.3%) | 0.232 | 1.039 | 0.559–1.931 | 0.903 |

**Table 6** Resource consumption

| Resource consumption | Study cohorts | | |
|---|---|---|---|
| | HFNC | NIV | *P* value |
| Length of stay (Days) | | | < 0.001 |
| 25-75th percentile | 8.00–24.00 | 5.00–17.00 | < 0.001 |
| Median | 15 | 9 | < 0.001 |
| Total charge (USDs) | | | < 0.001 |
| 25-75th percentile | 99,834–345,216 | 50,639.00–231690.00 | < 0.001 |
| Median | 183,416.00 | 109,234.00 | < 0.001 |
| Age in years at admission | | | < 0.001 |
| 25-75th percentile | 48.00–72.00 | 51.00–72.00 | < 0.001 |
| Median | 62 | 62 | < 0.001 |

Our findings are consistent with the known epidemiology of acute pancreatitis, wherein the development of pancreatic necrosis is a key indicator and defining component of severe acute pancreatitis (SAP), affecting approximately 10–20% of patients [12]. Furthermore, prolonged SIRS duration is associated with a higher incidence of infectious pancreatic necrosis [21], which may be linked to HFNC's correlation with increased SIRS susceptibility.

In addition, our analysis demonstrated a higher incidence of pulmonary complications in patients receiving HFNC therapy. Although HFNC delivers warmed and humidified oxygen that helps prevent viscous secretions and atelectasis [22], the PEEP effect generated by HFNC is inherently "passive," reliant on the patient's respiratory rate, tidal volume, and the nasal obstruction model [14]. This distinction is particularly critical in patients with acute pancreatitis, where abdominal hypertension and restricted diaphragmatic movement significantly impair respiratory efficiency. In such cases, the positive pressure support provided by NIV may help prevent inadequate alveolar ventilation and alveolar collapse [23]. It is important to note that in clinical practice, NIV is typically used for patients with more pronounced respiratory distress, while HFNC is often reserved for those with relatively better respiratory function [6, 24]. This selection bias may contribute to the delayed recognition of clinical deterioration.

Herein, patients receiving HFNC therapy experienced significantly longer hospital stays, extending six to seven days beyond those treated with NIV. This disparity in resource utilization can be understood through the distinct clinical trajectories of the two cohorts. The HFNC group exhibited a higher burden of systemic complications, such as sepsis, acute kidney injury, and pancreatic necrosis (Table 2). Conditions that typically demand prolonged and multidisciplinary inpatient care. Moreover, the markedly elevated intubation rate in the HFNC group (39.1% vs. 23.6%) likely further extended hospitalization, as invasive mechanical ventilation is often associated with longer weaning periods and heightened risks of subsequent complications [25]. In turn, extended hospitalization increases the risk of secondary complications, including pulmonary embolism and deep vein thrombosis [26]. Importantly, the HFNC group exhibited a heightened occurrence of pulmonary complications, including pneumonia, which necessitates a more lengthy diagnostic and therapeutic approach, thus prolonging hospital stays [27]. In summary, these factors might explain the less favorable clinical outcomes observed in the HFNC cohort.

The HFNC group tracheostomy rate is slightly higher, but not statistically significant (1.8% vs. 1.3%, $P = 0.232$). The NIS database relies on administrative diagnostic and procedure codes, which may be incomplete or inconsistent in clinical practice. When interpreting this finding, the known coding limitations of the NIS database must be considered, as they may lead to an underestimation of true incidence and complicate direct comparisons of severity between the groups.

In terms of medical payment frameworks, the HFNC group demonstrated a higher prevalence of Medicaid coverage and self-payment options, while Medicare coverage was observed to be lower in comparison. This trend may be associated with the younger population within the HFNC cohort, potentially reflecting their socio-economic status and access to healthcare services, which can significantly affect adherence to treatment and the length of hospitalization [28]. At the institutional level, notable disparities were identified concerning hospital ownership, type, and geographical location between the two groups. The HFNC cohort was more prominently represented in private non-profit hospitals and urban teaching institutions, thereby underscoring the clinical practice standards and resource distribution practices prevalent in different healthcare settings, which may further influence treatment choices and outcome assessments [29].

This study is subject to several important limitations inherent to its retrospective design and data source. Its retrospective nature introduces a significant potential for selection bias and residual confounding. Moreover, the NIS database lacks granular clinical data, including vital parameters for assessing disease severity (e.g., PaO2/FiO2 ratios), treatment details, and the clinical rationale behind the choice of respiratory support. This fundamentally limits our capacity to adjust for key confounding variables and to draw definitive causal inferences regarding the comparative effectiveness of HFNC versus NIV. Future prospective studies should systematically collect early physiological parameters such as the ROX index [30], its modified versions [31], and the HACOR score [32]. This will allow for more accurate assessment of disease severity, prediction of therapy failure risk, and ultimately, a more balanced comparison of the efficacy of NIV versus HFNC.

The observed discrepancies in outcomes between the two cohorts may be ascribed to treatment selection bias and overlooked confounding variables, such as initial disease severity, variations in comorbidities, and preferences in clinical decision-making. Because it is impossible to clarify the time sequence of complications, there is no time correlation. So, complications may also be comorbidities at the beginning. These limitations impede an evaluation of how patient characteristics and treatment modalities affect outcomes. The HFNC and NIV groups could represent fundamentally distinct clinical populations. The mere difference in treatment selection may introduce a selection bias, rather than simply indicating

a straightforward treatment protocol that leads to variations in outcomes.

## Conclusion

In this large-scale nationwide analysis, NIV was associated with superior clinical outcomes compared to HFNC in acute pancreatitis patients with respiratory insufficiency. Our findings highlight the need for careful patient selection and close monitoring when utilizing HFNC in this population. Future prospective studies are essential to validate these associations and to define the specific roles and optimal application of both NIV and HFNC in the management of acute pancreatitis.

### Abbreviations

| | |
|---|---|
| HFNC | High flow nasal cannula |
| NIV | Non-invasive ventilation |
| AP | Acute pancreatitis |
| SAP | Severe acute pancreatitis |
| ARDS | Acute respiratory distress syndrome |
| DVT | Deep vein thrombosis |
| SIRS | Systemic inflammatory response syndrome |
| MODS | Multiple organ dysfunction syndrome |
| NIS | National Inpatient Sample |
| AECOPD | Acute chronic obstructive pulmonary disease |
| COPD | Chronic obstructive pulmonary disease |
| AKI | Acute kidney injury |
| ALI | Acute lung injury |
| LOS | Length of stay |
| IMV | Invasive mechanical ventilation |
| CI | Confidence intervals |
| OR | Odds ratios |
| PEEP | Positive end expiratory pressure |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-04084-z.

Supplementary Material 1.

### Clinical trial number

Not applicable.

### Authors' contributions

Li Tang: investigation (lead); project administration (lead); formal analysis (equal); visualization (equal); writing — original draft (lead); writing — review and editing (support). Bei Zhang, Jie shan Hu: conceptualization (supporting); formal analysis (equal); visualization (equal); writing — review and editing (supporting). Xiao Yin Li: conceptualization (supporting); formal analysis (equal); visualization (equal); writing — review and editing (supporting). Hao Xie: conceptualization (supporting); project administration (supporting); writing — review and editing (supporting). Nan Feng Huang: conceptualization (lead); project administration (supporting); writing — review and editing (supporting). Min Zhi Di: conceptualization (supporting); project administration (supporting); methodology (lead); formal analysis (equal); visualization(equal); writing — original draft (lead); writing — review and editing (lead).

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None.

### Data availability

The datasets are available at https://www.ahrq.gov/data/hcup/index.html.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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