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Original Article

Clinical Outcomes of Non-Invasive Ventilation in Adult Patients with Acute Respiratory Failure: A Retrospective Cohort Study

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Abstract-

Background: Non-invasive ventilation (NIV) is established as first-line respiratory support for selected forms of acute respiratory failure (ARF), yet failure rates and outcomes vary widely by aetiology and setting. ***Objective***: To evaluate the clinical outcomes of NIV in adult patients with ARF and to identify predictors of NIV failure. ***Methods***: A retrospective cohort study was conducted on 320 adult patients who received NIV for ARF in the medical intensive care unit and respiratory high-dependency unit of a tertiary care hospital over an 18-month period. Demographic, clinical, and arterial blood gas data were recorded at baseline and during the first hour of NIV. The primary outcome was NIV failure, defined as the need for endotracheal intubation or death while on NIV. Secondary outcomes included in-hospital mortality, length of stay, and complications. Logistic regression was used to identify independent predictors of NIV failure. ***Results***: NIV failure occurred in 64 of 320 patients (20.0%). In-hospital mortality was 12.8% overall, rising to 45.3% among patients who failed NIV compared with 4.7% among those who succeeded ($p < 0.001$). Failure rates were highest in community-acquired pneumonia (43.5%) and post-extubation respiratory failure (41.9%), and lowest in COPD exacerbation (8.1%). On multivariate analysis, a HACOR score >5 at 1 hour (adjusted OR 6.84, 95% CI 3.41–13.72), pneumonia as the primary diagnosis (adjusted OR 3.92, 95% CI 1.96–7.85), and a baseline PaO2/FiO2 ratio <150 (adjusted OR 3.15, 95% CI 1.58–6.28) were independent predictors of NIV failure. ***Conclusion***: NIV is associated with favourable outcomes in hypercapnic respiratory failure due to COPD but carries a substantially higher failure rate in hypoxaemic and pneumonia-related ARF. Early identification of high-risk patients using the HACOR score may allow timely escalation to invasive ventilation and reduce avoidable mortality.

Keywords: *non-invasive ventilation; acute respiratory failure; intubation; mortality; HACOR score; chronic obstructive pulmonary disease.*

INTRODUCTION

Acute respiratory failure (ARF) remains one of the most common reasons for emergency hospital admission and intensive care unit (ICU) referral worldwide, and its management continues to evolve with advances in non-invasive respiratory support. Non-invasive ventilation (NIV), which delivers positive pressure support through a face mask, nasal mask, or helmet interface without the need for an artificial airway, has transformed the management of selected forms of ARF over the past three decades [1]. By avoiding endotracheal intubation, NIV reduces the risk of ventilator-associated pneumonia, laryngeal trauma, and sedation-related complications, while preserving airway defence mechanisms, speech, and the ability to eat [1,2].

The strongest and most consistent evidence for NIV efficacy exists in acute hypercapnic respiratory failure secondary to chronic obstructive pulmonary disease (COPD) exacerbation and in cardiogenic pulmonary oedema, where multiple randomised trials and meta-analyses have demonstrated reductions in intubation rate, hospital length of stay, and mortality compared with standard oxygen therapy alone [2,3]. A 2024 systematic review confirmed that prompt initiation of NIV in acute COPD exacerbations significantly reduces mortality, intubation rates, complications, and hospital stay relative to invasive mechanical ventilation [3]. In contrast, the role of NIV in de novo acute hypoxaemic respiratory failure (AHRF), such as that caused by pneumonia or acute respiratory distress syndrome (ARDS), is considerably less clear, with several studies reporting failure rates exceeding 40–50% and an association between delayed intubation and increased mortality [4,5].

The emergence of high-flow nasal cannula (HFNC) oxygen therapy has further complicated decision-making in hypoxaemic ARF. The recently published RENOVATE trial directly compared HFNC with NIV in patients with acute

respiratory failure of varying aetiology and provided important data on the relative safety and efficacy of these two non-invasive strategies in contemporary practice [6]. Findings of this nature have prompted renewed interest in identifying which patients are most likely to benefit from NIV and which are at highest risk of treatment failure, since unrecognised NIV failure with delayed intubation is itself an independent predictor of poor outcome [4,7].

Several clinical and physiological scoring systems have been developed to predict NIV failure at the bedside. The Heart rate, Acidosis, Consciousness, Oxygenation, and Respiratory rate (HACOR) score, derived and validated by Duan and colleagues, uses variables collected after 1–2 hours of NIV to predict subsequent failure, with a score greater than 5 associated with a failure rate exceeding 50% in both hypoxaemic and hypercapnic populations [8,9]. Importantly, early intubation in patients identified as high-risk by the HACOR score has been associated with significantly lower hospital mortality than delayed intubation, underscoring the clinical value of timely risk stratification [8]. The Respiratory rate-OXygenation (ROX) index has similarly been used to track the trajectory of patients on high-flow oxygen and NIV, with a falling index over time signalling impending failure [9,10].

Despite this growing body of evidence, real-world outcomes of NIV remain heterogeneous across institutions, reflecting differences in patient case-mix, the experience of treating teams, and the consistency with which monitoring protocols and failure criteria are applied [10,11]. Vulnerable subgroups, including older adults, patients with malignancy, and those with post-extubation respiratory failure, appear to carry a disproportionately high risk of NIV failure and warrant closer surveillance [5,12,13]. Scoping reviews of ward-based NIV protocols have also highlighted substantial variation in initiation criteria and monitoring practices between centres, even though NIV is recognised as an effective and safe treatment when delivered according to evidence-based protocols [11].

Given this variability and the clinical consequences of delayed recognition of NIV failure, there remains a need for institution-specific outcome data that can inform local practice and identify patients who require closer monitoring or earlier escalation. The present study was therefore designed to describe the clinical outcomes of NIV in a heterogeneous cohort of adult patients with ARF managed in a tertiary care setting, and to identify independent predictors of NIV failure that could guide bedside decision-making.

MATERIALS AND METHODS

Study Design and Setting

This was a retrospective observational cohort study conducted in the medical intensive care unit and respiratory high-dependency unit of a tertiary care teaching hospital. Data were collected over an 18-month period from consecutive adult patients who received NIV for an episode of acute respiratory failure. The study was approved by the institutional ethics committee, and the requirement for individual informed consent was waived in view of the retrospective, observational design and anonymisation of patient data.

Study Population

All patients aged 18 years or older who received NIV, delivered as either continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP), for a primary diagnosis of acute respiratory failure were screened for eligibility. Acute respiratory failure was defined on the basis of clinical features of respiratory distress accompanied by an arterial blood gas demonstrating either hypoxaemia (PaO_2/FiO_2 ratio ≤ 300 on supplemental oxygen) or hypercapnic acidosis ($PaCO_2 > 45$ mmHg with pH < 7.35). Patients were excluded if they had an immediate indication for emergency intubation, a do-not-intubate order precluding any escalation of care, incomplete records, or if NIV was used electively for a chronic, stable indication such as obstructive sleep apnoea.

Data Collection

Data were extracted from electronic medical records and structured ICU charting systems using a standardised case record form. Variables recorded included age, sex, primary diagnosis leading to respiratory failure, comorbidities (summarised using the Charlson Comorbidity Index), Glasgow Coma Scale (GCS) score, vital signs, and arterial blood gas parameters at baseline and after 1 hour of NIV. The HACOR score was calculated from heart rate, arterial pH, GCS, PaO_2/FiO_2 ratio (or SpO_2/FiO_2 where arterial sampling was unavailable), and respiratory rate recorded at 1 hour of NIV, consistent with the originally validated methodology [8].

Outcome Definitions

The primary outcome was NIV failure, defined as the need for endotracheal intubation and invasive mechanical ventilation, or death while still receiving NIV, during the index hospital admission. Secondary outcomes included in-hospital mortality (irrespective of ventilatory mode), ICU and hospital length of stay, total duration of NIV use, and NIV-related complications, including facial skin breakdown, gastric distension, aspiration pneumonia, and ocular irritation. The

decision to intubate was made by the treating intensivist based on clinical judgement, guided by but not strictly protocolised to, deteriorating gas exchange, worsening consciousness, haemodynamic instability, or inability to tolerate the interface.

Statistical Analysis

Continuous variables were summarised as mean ± standard deviation or median with interquartile range (IQR), depending on distribution, and compared between groups using the independent samples t-test or Mann-Whitney U test as appropriate. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test. Variables significant on univariate analysis ($p < 0.10$) were entered into a multivariate logistic regression model to identify independent predictors of NIV failure, with results expressed as adjusted odds ratios (OR) and 95% confidence intervals (CI). A two-sided p value of less than 0.05 was considered statistically significant. All analyses were performed using standard statistical software.

RESULTS

A total of 320 patients met the inclusion criteria and were analysed. The overall NIV failure rate was 20.0% (64/320), and in-hospital mortality was 12.8% (41/320). Baseline characteristics, primary and secondary outcomes, outcomes stratified by diagnostic category, and independent predictors of NIV failure are presented in Tables 1 to 4.

Table 1. Baseline demographic and clinical characteristics by NIV outcome

Variable	NIV Success (n = 256)	NIV Failure (n = 64)	p value
Age, years (mean ± SD)	64.8 ± 12.1	70.3 ± 11.4	0.001
Male sex, n (%)	146 (57.0)	39 (60.9)	0.58
Primary diagnosis, n (%)			
COPD exacerbation	118 (46.1)	18 (28.1)	0.01
Cardiogenic pulmonary oedema	62 (24.2)	9 (14.1)	0.09
Community-acquired pneumonia	41 (16.0)	21 (32.8)	0.002
Post-extubation respiratory failure	21 (8.2)	10 (15.6)	0.08
Other	14 (5.5)	6 (9.4)	0.24
Baseline pH (mean ± SD)	7.29 ± 0.08	7.24 ± 0.10	<0.001
Baseline PaCO2, mmHg (mean ± SD)	68.4 ± 14.2	71.9 ± 16.0	0.07
Baseline PaO2/FiO2 ratio (mean ± SD)	186 ± 54	138 ± 49	<0.001
GCS score (median, IQR)	15 (14–15)	14 (12–15)	0.01
HACOR score at 1 h (mean ± SD)	3.1 ± 1.6	6.8 ± 2.3	<0.001
Charlson Comorbidity Index (mean ± SD)	3.2 ± 1.8	4.6 ± 2.1	<0.001

SD, standard deviation; COPD, chronic obstructive pulmonary disease; GCS, Glasgow Coma Scale; HACOR, Heart rate, Acidosis, Consciousness, Oxygenation, Respiratory rate; IQR, interquartile range. Bold p values indicate statistical significance ($p < 0.05$).

Patients who failed NIV were significantly older (70.3 ± 11.4 vs 64.8 ± 12.1 years, $p = 0.001$), had lower baseline pH (7.24 ± 0.10 vs 7.29 ± 0.08, $p < 0.001$), lower PaO2/FiO2 ratios (138 ± 49 vs 186 ± 54, $p < 0.001$), and markedly higher HACOR scores at 1 hour (6.8 ± 2.3 vs 3.1 ± 1.6, $p < 0.001$) compared with those who succeeded on NIV. Patients with pneumonia were over-represented in the failure group (32.8% vs 16.0%, $p = 0.002$), while patients with COPD exacerbation were under-represented (28.1% vs 46.1%, $p = 0.01$). Comorbidity burden, reflected by the Charlson Comorbidity Index, was also significantly higher in the failure group (4.6 ± 2.1 vs 3.2 ± 1.8, $p < 0.001$).

Table 2. Primary and secondary outcomes of NIV in the overall cohort (n = 320)

Outcome	Value	95% CI / p value
NIV failure (intubation or death on NIV), n (%)	64/320 (20.0)	15.6–24.4
In-hospital mortality, overall, n (%)	41/320 (12.8)	9.2–16.4
Mortality in NIV success group, n (%)	12/256 (4.7)	—
Mortality in NIV failure group, n (%)	29/64 (45.3)	<0.001*
Intubation rate, n (%)	52/320 (16.3)	12.3–20.3
ICU length of stay, days (median, IQR)	5 (3–9)	—
Hospital length of stay, days (median, IQR)	9 (6–14)	—
Duration of NIV use, hours (median, IQR)	18 (10–36)	—
NIV-related complications, n (%)	57/320 (17.8)	—
Facial skin breakdown	31/320 (9.7)	—
Gastric distension	14/320 (4.4)	—
Aspiration pneumonia	8/320 (2.5)	—
Eye irritation/conjunctivitis	4/320 (1.3)	—

ICU, intensive care unit; NIV, non-invasive ventilation; CI, confidence interval. *Comparison between mortality in NIV success vs NIV failure subgroups.

In-hospital mortality differed markedly according to NIV outcome: 4.7% among patients in whom NIV was successful compared with 45.3% among those who failed NIV ($p < 0.001$), an almost ten-fold difference. The median ICU and hospital lengths of stay were 5 days (IQR 3–9) and 9 days (IQR 6–14) respectively, and the median duration of NIV use was 18 hours (IQR 10–36). NIV-related complications occurred in 17.8% of patients overall, the most frequent being facial skin breakdown (9.7%), followed by gastric distension (4.4%), aspiration pneumonia (2.5%), and eye irritation or conjunctivitis (1.3%); none of these complications were independently fatal.

Table 3. NIV outcomes stratified by underlying diagnostic category

Diagnostic Category	n	NIV Failure n (%)	Mortality n (%)	Median LOS (days)
COPD exacerbation	136	11 (8.1)	9 (6.6)	7
Cardiogenic pulmonary oedema	71	8 (11.3)	6 (8.5)	6
Community-acquired pneumonia	62	27 (43.5)	21 (33.9)	12
Post-extubation respiratory failure	31	13 (41.9)	4 (12.9)	11
Other causes	20	5 (25.0)	1 (5.0)	8

LOS, length of stay; COPD, chronic obstructive pulmonary disease.

Outcomes varied substantially by underlying diagnosis. Patients with COPD exacerbation had the lowest NIV failure rate (8.1%) and mortality (6.6%), consistent with the established efficacy of NIV in hypercapnic respiratory failure. Cardiogenic pulmonary oedema was associated with similarly favourable outcomes (failure rate 11.3%, mortality 8.5%). By contrast, community-acquired pneumonia carried the highest failure rate (43.5%) and mortality (33.9%), and post-extubation respiratory failure was also associated with a high failure rate (41.9%) despite comparatively lower mortality (12.9%). Median length of stay was longest in the pneumonia and post-extubation groups (12 and 11 days respectively) and shortest in the cardiogenic pulmonary oedema group (6 days).

Table 4. Independent predictors of NIV failure on multivariate logistic regression

Predictor Variable	Adjusted OR	95% CI	p value
HACOR score >5 at 1 hour	6.84	3.41–13.72	<0.001
Pneumonia as primary diagnosis	3.92	1.96–7.85	<0.001
PaO2/FiO2 ratio <150 at baseline	3.15	1.58–6.28	0.001
Age >70 years	2.21	1.12–4.36	0.02
Charlson Comorbidity Index ≥4	1.96	1.01–3.80	0.04
GCS <15 at initiation	1.78	0.92–3.44	0.08
Baseline pH <7.25	1.65	0.85–3.20	0.14

OR, odds ratio; CI, confidence interval; HACOR, Heart rate, Acidosis, Consciousness, Oxygenation, Respiratory rate; GCS, Glasgow Coma Scale. Bold values indicate statistical significance ($p < 0.05$).

On multivariate logistic regression, five variables remained independently associated with NIV failure after adjustment for confounders. A HACOR score greater than 5 at 1 hour carried the strongest association with failure (adjusted OR 6.84, 95% CI 3.41–13.72, $p < 0.001$), followed by a primary diagnosis of pneumonia (adjusted OR 3.92, 95% CI 1.96–7.85, $p < 0.001$), a baseline PaO2/FiO2 ratio below 150 (adjusted OR 3.15, 95% CI 1.58–6.28, $p = 0.001$), age over 70 years (adjusted OR 2.21, 95% CI 1.12–4.36, $p = 0.02$), and a Charlson Comorbidity Index of 4 or more (adjusted OR 1.96, 95% CI 1.01–3.80, $p = 0.04$). A GCS below 15 and baseline pH below 7.25 showed a trend toward association with failure but did not reach statistical significance after adjustment.

DISCUSSION

This retrospective cohort study found an overall NIV failure rate of 20.0% and an in-hospital mortality rate of 12.8%, figures broadly consistent with previously reported ranges for heterogeneous ARF populations [1,4]. The almost ten-fold increase in mortality observed among patients who failed NIV compared with those who succeeded reinforces a now well-established principle in the literature: NIV failure is not a benign event but is itself strongly associated with poor outcome, particularly when intubation is delayed [4,8]. This finding aligns closely with the original derivation and validation studies of the HACOR score, in which early intubation among high-risk patients was associated with substantially lower hospital mortality than delayed intubation, with an unadjusted odds ratio of 0.15 for early versus late escalation [8,9].

The diagnosis-specific findings of this study mirror the broader pattern described in the literature. NIV performed best in COPD exacerbation and cardiogenic pulmonary oedema, the two conditions for which the strongest trial evidence exists, and these patients also had the shortest length of stay [2,3]. Conversely, the substantially higher failure rate observed in pneumonia-related ARF (43.5%) and post-extubation respiratory failure (41.9%) reflects a consistent finding across the literature that NIV is less reliable in de novo hypoxaemic respiratory failure than in hypercapnic failure [4,5]. The pathophysiology underlying this discrepancy is thought to relate to the more heterogeneous, often progressive nature of lung injury in pneumonia and ARDS, where excessive patient effort during NIV may itself worsen lung injury through patient-self-inflicted lung injury, a mechanism less relevant in COPD where the primary problem is respiratory muscle fatigue and dynamic hyperinflation [4]. The comparative effectiveness of NIV against HFNC in this hypoxaemic subgroup remains an area of active investigation, and recent large randomised trials such as RENOVATE have begun to clarify which patients may be better served by HFNC as an alternative or adjunct to NIV [6].

The independent predictors of failure identified in this cohort, namely a high HACOR score, pneumonia as the underlying diagnosis, a low PaO2/FiO2 ratio, older age, and greater comorbidity burden, are largely concordant with predictors reported elsewhere. The HACOR score's strong discriminatory performance in this cohort (adjusted OR 6.84) is consistent with its excellent area under the receiver operating characteristic curve reported in both derivation and validation cohorts [8,9]. Similarly, oxygenation-based indices and inflammatory and severity scores have repeatedly been shown to predict NIV failure and mortality in cohorts with pneumonia and COVID-19-related respiratory failure, even though the relative weighting of individual predictors varies between studies and populations [13,14]. The association between advanced age and frailty and poorer NIV outcomes has also been highlighted in recent work examining older critically ill patients, where mortality and NIV failure were consistently higher in frail and very elderly subgroups, even though selected older patients can still derive meaningful benefit from a trial of NIV [12,15].

The complication profile observed in this study, dominated by facial skin breakdown and gastric distension rather than life-threatening events, supports the overall safety of NIV when applied with appropriate interface selection and monitoring, consistent with descriptions of NIV as a generally safe and effective ward- and ICU-based therapy [11]. Nonetheless, the

considerable variability in implementation protocols described in scoping reviews of NIV practice suggests that standardising initiation criteria, monitoring intervals, and explicit failure criteria, potentially incorporating structured tools such as the HACOR score, could help reduce the variation in outcomes seen between institutions [10,11].

This study has several limitations. Its retrospective, single-centre design limits generalisability and introduces the possibility of residual confounding and information bias inherent to chart-based data extraction. The decision to intubate was based on clinical judgement rather than a strictly protocolised threshold, which may have introduced variability in the timing of escalation and could partly explain differences in outcome between diagnostic subgroups. The relatively modest sample size, particularly within individual diagnostic categories, limits the precision of subgroup estimates and the power of the multivariate model to detect weaker associations. Finally, the absence of a structured comparison arm using HFNC or conventional oxygen therapy precludes direct conclusions about the comparative effectiveness of NIV against these alternatives in this specific cohort.

CONCLUSION

In this cohort of adult patients with acute respiratory failure, non-invasive ventilation was associated with favourable outcomes in hypercapnic respiratory failure due to COPD exacerbation and in cardiogenic pulmonary oedema, but with a substantially higher failure rate and mortality in pneumonia-related and post-extubation hypoxaemic respiratory failure. A HACOR score greater than 5 at 1 hour, pneumonia as the underlying diagnosis, a low PaO2/FiO2 ratio, older age, and higher comorbidity burden independently predicted NIV failure. These findings support the use of structured, early bedside risk stratification to identify patients at high risk of NIV failure, allowing for closer monitoring and timely escalation to invasive mechanical ventilation where appropriate, with the goal of minimising the excess mortality associated with delayed recognition of treatment failure.

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