REUE | Original Article

Evaluation of the clinical impact of noninvasive respiratory support vs conventional oxygen therapy in acute respiratory failure with SpO_2/FiO_2 280–400

Isabel Gil Rosa[1], Juan Javier García Fernández[2], Sonia Galicia Puyol[3], Juan José Guerras Conesa[4], José Andrés Sánchez Nicolás[5], César Cinesi Gómez[5]

INTRODUCTION. The objective of this study was to evaluate filed initial respiratory support (conventional oxygen therapy vs noninvasive respiratory support) in patients with SpO_2/FiO_2 between 280 and 400.

MATERIALS AND METHODS. We conducted a retrospective observational cohort study of patients with acute respiratory failure and SpO_2/FiO_2 between 280 and 400 who entered the emergency respiratory circuit created during the COVID-19 pandemic. The study was conducted at *Hospital General Universitario Reina Sofía* (Murcia, Spain) from March 2020 through June 2021.

RESULTS. A total of 348 (4.31%) out f 8,074 patients assessed were ultimately included. The failure rate of initial therapy was 24.1% (12.5% in the noninvasive respiratory support group and 12.5% in the conventional oxygen therapy group; OR, 0.383; 95%CI, 0.181–0.808; *P* = .01).

CONCLUSIONS. Early use of noninvasive respiratory support in patients with acute respiratory failure and SpO_2/FiO_2 between 280 and 400 may reduce the risk of initial respiratory support failure, particularly in patients with acute heart failure.

Keywords: Acute respiratory failure. SpO_2/FiO_2. PaO_2/FiO_2. Noninvasive respiratory support. Conventional oxygen therapy.

Evaluación del impacto clínico del soporte respiratorio no invasivo frente a la oxigenoterapia convencional en la insuficiencia respiratoria aguda con SpO_2/FiO_2 280-400

INTRODUCCIÓN. El objetivo de este estudio fue evaluar el fracaso del soporte respiratorio inicial (oxigenoterapia convencional comparada con soporte respiratorio no invasivo) en los pacientes con SpO_2/FiO_2 entre 280-400.

MATERIAL Y MÉTODOS. Estudio observacional de cohortes retrospectivo, de pacientes con insuficiencia respiratoria aguda con SpO_2/FiO_2 entre 280-400 que entraban en el circuito respiratorio de urgencias creado en la pandemia COVID-19, en el Hospital General Universitario Reina Sofía de Murcia entre marzo de 2020 y junio 2021.

RESULTADOS. De los 8.074 pacientes elegibles, se incluyeron 348 (4,31). El fracaso de la terapia inicial fue del 24,1%, siendo del 12,5% en soporte respiratorio no invasivo y 12,5 en oxigenoterapia convencional (OR 0,383 IC 95%: 0,181-0,808, p = 0,01).

CONCLUSIONES. El uso precoz de soporte respiratorio no invasivo en pacientes con insuficiencia respiratoria aguda con SpO_2/FiO_2 entre 280-400 puede reducir el riesgo de fracaso del soporte respiratorio inicial, sobre todo en pacientes con insuficiencia cardiaca aguda.

Palabras clave: Insuficiencia respiratoria aguda. SpO_2/FiO_2. PaO_2/FiO_2. Soporte respiratorio no invasivo. Oxigenoterapia convencional.

Author Affiliations: [1]Servicio de Urgencias y Emergencias Médicas 061, Gerencia 061, Murcia, Spain. [2]Centro de Salud de San Diego, Murcia, Spain. [3]Servicio de Urgencias, Hospital General Los Arcos del Mar Menor, Murcia, Spain. [4]Servicio de Urgencias, Hospital Rafael Méndez, Murcia, Spain. [5]Servicio de Urgencias, Hospital General Universitario Reina Sofía, Murcia, Spain.
Corresponding Author: Isabel Gil Rosa. Escultor José Sánchez Lozano, 7. 30005 Murcia, Spain.
E-mail: igilrosa@yahoo.es
Article Information: Received: 3-2-2025. Accepted: 23-6-2025. *Online:* 26-6-2025.
Editor in Charge: Guillermo Burillo-Putze.

Introduction

Acute respiratory failure (ARF) is one of the most common conditions encountered in emergency departments (EDs). It is a potentially life-threatening syndrome characterized by the inability to maintain adequate arterial oxygen levels and/or an appropriate carbon dioxide exchange to meet the demands of cellular metabolism.[1,2] ARF is defined as a partial pressure of arterial oxygen < 60 mm Hg while breathing room air at sea level, thus with a fraction of inspired oxygen (FiO_2) of 0.21.[3] Currently, for assessing the severity of oxygenation deficit, the PaO_2/FiO_2 ratio is used, based on expert consensus, and is included in the Berlin criteria for acute respiratory distress syndrome (ARDS). A PaO_2/FiO_2 between 200–300 mm Hg, 100–200 mm Hg, and < 100 mm Hg classifies oxygenation deficits as mild, moderate, or severe, respectively.[4]

In EDs and emergency medical systems, respiratory support for ARF includes conventional oxygen therapy (COT), high-flow nasal cannula therapy (HFNC), noninvasive mechanical ventilation (NIMV), and invasive mechanical ventilation (IMV). HFNC and NIMV are referred to collectively as noninvasive respiratory support (NIRS).[5] In general terms, COT is recommended for mild hypoxemia (PaO_2/FiO_2 200–300 mm Hg), NIRS for moderate hypoxemia (PaO_2/FiO_2 100–200 mm Hg), and IMV for severe hypoxemia (PaO_2/FiO_2 < 100 mm Hg).[3,5]

However, this approach to ARF support in emergency and prehospital care presents several practical barriers. The first concerns obtaining arterial blood gas (ABG), which is a technically demanding, painful procedure and not without complications.[6,7] Moreover, ABG is not usually available in prehospital emergency systems, making pulse oximetry-derived oxygen saturation (SpO_2), and by extrapolation SpO_2/FiO_2, an acceptable surrogate measure of oxygenation.[8,9] Numerous studies have shown a reliable correlation between PaO_2/FiO_2 and SpO_2/FiO_2.[9-17] The limitations of SpO_2 are its poor correlation at values > 97% or < 80%, its inability to assess ventilation status, and inaccurate readings in specific conditions such as shock.[7,18,20-24] Even with these limitations, and without renouncing the initial acquisition of ABG, SpO_2/FiO_2 is a rapid and reliable measure of oxygenation status in both EDs and prehospital emergency care.[7,18,25]

The second difficulty in applying these criteria in urgent care is that they are based on expert opinion rather than strong evidence. The most controversial criterion is the cut-off for starting NIRS, currently defined as PaO_2/FiO_2 < 2 00 mm Hg[3,5] (approximate SpO_2/FiO_2 of 280).[25] The debate, particularly after the COVID-19 pandemic, has focused on moving this cut-off to an earlier threshold of 250 mm Hg (approximate SpO_2/FiO_2 of 400),[25] as already suggested in the Berlin definition for mild ARDS.[4]

Our hypothesis is that in patients with ARF who present SpO_2/FiO_2 between 280–400, regardless of etiology, initiating treatment with NIRS may achieve better clinical outcomes compared with COT.

Therefore, our objective was to evaluate the failure of initial respiratory support (COT vs NIRS) in patients with SpO_2/FiO_2 between 280–400.

Materials and methods

We conducted a retrospective observational cohort study in the ED of *Hospital General Universitario Reina Sofía* (HGURS) of Murcia (Spain), a 350-bed facility serving a reference population of 250,000 people and managing an average of 93,000 emergencies annually. The study began on March 8th, 2020, and ended on June 28th, 2021.

All patients > 18 years admitted consecutively to the dedicated respiratory circuit created during the COVID-19 pandemic were included. Patients entered this circuit if they presented with fever, clinical signs of respiratory infection, diarrhea, dyspnea, or chest radiography/computed tomography showing a pattern consistent with respiratory infection. Exclusion criteria were absence of ARF within the SpO_2/FiO_2 interval of 280–400 or requirement for emergent orotracheal intubation (OTI).

The primary (dependent) variable was failure of initial respiratory therapy. In the COT group, this was defined as the need to initiate invasive/noninvasive respiratory support or death during hospitalization. In the NIRS group, failure was defined as the need for OTI or death. Transient use of oxygen therapy while preparing another modality was not considered failure.

Collected variables included demographics (age, sex), comorbidities [chronic obstructive pulmonary disease (COPD), sleep apnea or sleep apnea-hypopnea syndrome, chronic heart failure, hypertension (HTN), diabetes mellitus (DM), dyslipidemia, smoking, asthma, hyperuricemia, chronic kidney disease, ischemic heart disease], chronic home oxygen therapy, home CPAP (continuous positive airway pressure) or BiPAP (bilevel positive airway pressure), vital signs on ED arrival, laboratory data (glucose, urea, creatinine, sodium, potassium, NT-proBNP, C-reactive protein, procalcitonin, IL-6, SpO_2, pH, pCO_2, HCO_3, lactate, bilirubin, hemoglobin, leukocytes, neutrophils), COVID-19 test (antigen and/or PCR), radiological data (chest radiography or CT), use of COT or NIRS, need for OTI, and final diagnosis [acute heart failure (AHF), COPD exacerbation (AE-COPD), pneumonia, COVID-19, or others].

Statistical analysis was performed with SPSS Statistics v21 (IBM, New Castle, NY, USA). Qualitative variables were expressed as absolute and relative frequencies, and quantitative variables as mean ± standard deviation. Distribution was assessed with the Kolmogorov-Smirnov test. Qualitative variables were compared using chi-square or Fisher's exact tests, as appropriate. Quantitative variables were compared with Student t test for normally distributed data or Mann-Whitney U test for nonparametric distributions. Logistic regression was used to assess the association of factors with the

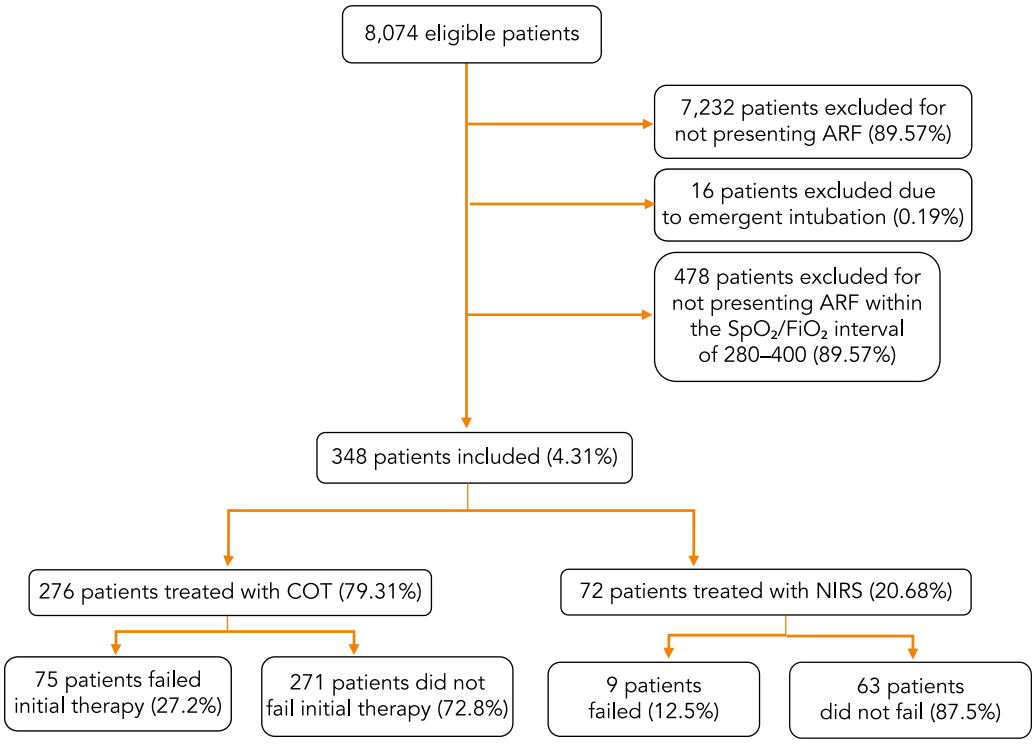

Figure 1. Flowchart of patient inclusion.
ARF: acute respiratory failure; COT: conventional oxygen therapy; NIRS: noninvasive respiratory support.

dependent variable of therapy failure. All analyses were two-tailed, and statistical significance was defined as $P < .05$ or a 95% confidence interval (CI) of the odds ratio (OR) excluding the value 1.

This study was conducted in full compliance with applicable laws and regulations and was approved by the HGURS Clinical Research Ethics Committee (CE04220).

Results

Of the 8074 cases evaluated, 7726 (95.7%) were excluded: 7232 (89.5%) for not presenting ARF, 16 (0.2%) for early IMV, and 478 (5.9%) for not meeting ARF criteria with SpO_2/FiO_2 between 280 and 400. Finally, 348 patients (4.3%) were included (Figure 1).

The mean age was 72.24 ± 15.58 years, and 42.5% were women. The most prevalent comorbidities were hypertension (73.9%), dyslipidemia (53.4%), and diabetes mellitus (39.9%). Regarding home respiratory treatment, 23.9% received long-term oxygen therapy (LTOT), 13.3% CPAP, and 8.3% BiPAP. Respiratory rate was recorded in 147 patients (42.2%). The most frequent diagnoses were acute heart failure (AHF, 26.7%), COVID-19 (19.3%), and COPD exacerbation (AE-COPD, 15.5%).

As initial respiratory therapy, 276 patients (79.3%) received COT and 72 (20.7%) received NIRS, including 66 with NIMV and 6 with HFNC. Clinical-analytical characteristics according to initial therapy are shown in Table 1.

A total of 18 patients (5.2%) required intensive care admission: 5 initially treated with COT (1.8%) and 13 with NIRS (18%), showing a significant association (OR, 11.942; 95% CI, 4.100–34.747; $P < .001$). Mean length of stay was 9.94 ± 13.5 days in the COT group and 8.73 ± 5.7 days in the NIRS group, without statistically significant differences between them ($P = .494$). Overall, mean length of stay was 9.68 ± 12.2 days.

Failure of initial therapy occurred in 84 cases (24.1%): 75 (27.2%) with COT and 9 (12.5%) with NIRS (OR, 0.383; 95% CI, 0.181–0.808; $P = .01$). In the COT group, 45 (16.3%) required NIRS, 6 (2.1%) IMV, and 47 (17%) died. Of these, 18 had received NIRS after initial failure and 29 had not (OR, 4.64; 95% CI, 2.278–9.466; $P < .01$). Initiation of NIRS in these cases occurred at a mean of 62.69 hours (median, 24 hours). Table 2 presents the relationships between studied variables and failure of initial respiratory support.

According to primary diagnosis, failure rates of initial support differed significantly ($P < .001$), as shown in Table 3. Rates were 17.2% in AHF, 13% in AE-COPD, 20.5% in pneumonia, 50.7% in COVID-19, and 20% in other diagnoses. In AHF patients, NIRS use was associated with a lower failure rate than COT (OR, 0.163; 95% CI, 0.035–0.765; $P = .011$). In the other diagnoses, no statistically significant differences were observed between NIRS and COT, although there was a consistent trend toward lower failure with NIRS.

A binary logistic regression was performed to analyze factors associated with failure of initial respiratory

Table 1. Clinical and analytical characteristics of the sample and study according to whether conventional oxygen therapy or noninvasive respiratory support was administered

	Total N = 348 n (%)	Conventional oxygen therapy N = 276 n (%)	NIRS N = 72 n (%)	*P*-value
Female sex	148 (42.5)	111 (40.2)	37 (51.4)	.088
Hypertension	257 (73.8)	200 (72.5)	57 (79.2)	.249
Type 2 diabetes mellitus	139 (39.9)	109 (39.5)	30 (41.4)	.737
Dyslipidemia	186 (53.4)	143 (51.8)	43 (59.7)	.231
Smoker	38 (10.9)	26 (9.4)	12 (16.7)	.079
OSA	21 (6)	12 (4.3)	9 (12.5)	.01
OSAHS	41 (11.8)	35 (12.7)	6 (8.3)	.308
Long-term home oxygen therapy	83 (23.91)	62 (22.5)	21 (29.2)	.235
Home CPAP	46 (13.2)	35 (12.7)	11 (15.3)	.562
Home BiPAP	29 (8.3)	15 (5.4)	14 (19.4)	< .01
Asthma	34 (9.8)	30 (10.9)	4 (5.6)	.176
COPD	81 (23.3)	66 (23.9)	15 (20.8)	.582
Heart failure	73 (21)	53 (19.2)	20 (27.8)	.111
Ischemic heart disease	53 (15.2)	42 (15.2)	11 (15.3)	.99
Chronic kidney disease	74 (21.3)	62 (22.5)	12 (16.7)	.284
Chest CT performed	20 (5.7)	20 (100)	0 (0)	.019
Age (years)*	77.24 ± 13.58	77.14 ± 13.84	77.65 ± 12.64	.775
SBP (mm Hg)*	129.18 ± 27.3	128.51 ± 26.86	131.69 ± 29.86	.38
DBP (mm Hg)*	73.09 ± 14.97	72.94 ± 14.92	73.67 ± 15.25	.71
Heart rate (bpm)*	87.9 ± 19.33	87.17 ±19.08	91.07 ± 20.09	.128
Respiratory rate (rpm)*	24.07 ± 7.39	23.59 ± 7.33	25.6 ± 7.45	.16
RALE chest X-ray score*	1.92 ± 2.48	1.89 ± 2.42	2.04 ± 2.69	.63
Glucose (mg/mL)*	167.17 ± 97.95	164 ± 100.74	179.3 ± 86.06	.24
Urea (mg/mL)*	60.12 ± 44.71	60.47 ± 43.08	58.81 ± 50.66	.77
Creatinine (mg/mL)*	1.53 ± 1.46	1.54 ± 1.35	1.47 ± 1.8	.69
Sodium (mg/mL)*	137.43 ± 6.08	137.6 ± 6.1	136.78 ± 6	.3
Potassium (mg/mL)*	4.42 ± 0.76	4.37 ± 0.73	4.59 ± 0.85	.02
NT-proBNP (pg/dL)*	4.281.58 ± 6.608.0	4.660.28 ± 7.501.07	3387.19 ± 3649.72	.154
LDH (U/L)*	306.39 ± 206.55	305.79 ± 218.08	308.85 ± 151.5	.92
C-reactive protein (mg/dL)*	8.57 ± 8.87	8.86 ± 8.81	7.43 ± 9.11	.25
Procalcitonin (mg/mL)*	1.22 ± 5.06	1.13 ± 3.58	1.57 ± 8.87	.54
IL-6 (pg/mL)*	272.68 ± 681.98	240.29 ± 568.92	411.46 ± 1032.41	.27
SpO_2/FiO_2*	345.7 ± 33.3	345.2 ± 31.7	347.4 ± 38.9	.663
pH*	7.36 ± 0.07	7.37 ± 0.65	7.32 ± 0.09	.6
pCO_2 (mm Hg)*	51.76 ± 17.02	49.3 ± 14.54	60.78 ± 21.89	< .01
HCO_3^- (mmol/L)*	27.86 ± 5.78	27.42 ± 5.08	29.5 ± 7.65	.03
Lactate (mg/mL)*	2.09 ± 1.70	2.04 ± 1.29	2.28 ± 2.74	.48
Bilirubin (mg/dL)*	0.68 ± 0.53	0.66 ± 0.54	0.75 ± 0.50	.23
Hemoglobin (g/dL)*	12.5 ± 2.17	12.53 ± 2.04	12.39 ± 2.63	.65
Leukocytes*	11.624.43 ± 9.042.97	11.843.84± 9.917.94	10798.61 ± 4354.55	.38
Neutrophils*	8.530.09 ± 4.594.57	8.571.66 ± 4.732	8373.61 ± 4059.9	.74
Time on NIRS (hours)*	76.93 ± 106.1	110.74 ± 129.6	51.89 ±78.2	< .001
Diagnoses				
Acute heart failure	93 (26.7)	55 (59.1)	38 (40.9)	< .01
AE-COPD exacerbation	54 (15.5)	44 (15.9)	10 (13.9)	
Pneumonia	39 (11.2)	33 (12)	6 (8.3)	
COVID-19	67 (19.3)	57 (20.7)	10 (13.9)	
Other	95 (27.3)	87 (31.5)	8 (8.4)	
Invasive mechanical ventilation	10 (2.9)	6 (2.2)	4 (5.6)	.126
Death	54 (15.5)	47 (17)	7 (9.7)	.127
Failure	84 (24.1)	75 (27.2)	9 (12.5)	.01

* Results shown as mean (standard deviation).
NIRS: noninvasive respiratory support; OSA: obstructive sleep apnea; OSAHS: obstructive sleep apnea–hypopnea syndrome; CPAP: continuous positive airway pressure; BiPAP: bilevel positive airway pressure; COPD: chronic obstructive pulmonary disease; AE-COPD: acute exacerbation of chronic obstructive pulmonary disease; SBP/DBP: systolic/diastolic blood pressure; RALE: Radiographic Assessment of Lung Edema; NT-proBNP: N-terminal pro–B-type natriuretic peptide; LDH: lactate dehydrogenase; IL-6, interleukin 6; pCO_2: partial pressure of carbon dioxide; HCO_3^-: bicarbonate.

support. The model included type of support, sex, systolic blood pressure, RALE (Radiographic Assessment of Lung Edema) score, CRP, lactate, LDH, and diagnosis. In the final model, COVID-19 diagnosis, type of support, RALE index, and CRP were identified as independent variables (Table 4).

Table 2. Clinical and analytical characteristics of the sample and study according to initial therapy failure

	Total N = 348 n (%)	Failure N = 84 n (%)	Success N = 264 n (%)	*P*-value
Female sex	148 (42.5)	26 (31)	122 (46.2)	.014
Hypertension	257 (73.8)	61 (72.6)	196 (774.2)	.768
Diabetes mellitus	139 (39.9)	34 (40.5)	105 (39.8)	.909
Dyslipidemia	186 (53.4)	42 (50)	144 (54.5)	.467
Smoker	38 (10.9)	6 (7.1)	32 (12.1)	.203
OSA	21 (6)	5 (6)	16 (6.1)	.971
OSAHS	41 (11.8)	9 (10.7)	32 (12.1)	.397
Long-term home oxygen	83 (23.91)	17 (20.2)	66 (25)	.372
Home CPAP	46 (13.2)	10 (11.9)	36 (13.6)	.683
Home BiPAP	29 (8.3)	3 (3.6)	26 (9.8)	.07
Asthma	34 (9.8)	6 (7.1)	28 (10.6)	.352
COPD	81 (23.3)	18 (21.4)	63 (23.9)	.646
Heart failure	73 (21)	12 (14.3)	61 (23.1)	.084
Ischemic heart disease	53 (15.2)	9 (10.7)	44 (16.7)	.186
Chronic kidney disease	74 (21.3)	18 (21.4)	56 (21.2)	.966
Chest CT performed	20 (5.7)	7 (8.3)	13 (4.9)	.242
Age (years)*	77.24 ± 13.58	77.24 ± 15.17	77.25 ± 13.1	.996
SBP (mm Hg)*	129.18 ± 27.3	122.2 ± 24.6	131.3 ± 27.7	.008
DBP (mm Hg)*	73.09 ± 14.97	71.9 ± 14.4	73.4 ± 15.1	.425
Heart rate (bpm)*	87.9 ± 19.33	88.4 ± 18.2	87.8 ± 19.7	.809
Respiratory rate (rpm)*	24.07 ± 7.39	26.2 ± 9.4	23.4 ± 6.5	.111
RALE CXR score*	1.92 ± 2.48	3.16 ± 3	1.53 ± 2.1	< .001
Glucose (mg/mL)*	167.17 ± 97.95	193.3 ± 155	158.7 ± 68.9	.098
Urea (mg/mL)*	60.12 ± 44.71	72.5 ± 54.4	56.1 ± 40.4	.073
Creatinine (mg/mL)*	1.53 ± 1.46	1.57 ± 0.9	1.51 ± 1.5	.774
Sodium (mg/mL)*	137.43 ± 6.08	136.4 ± 7.8	137.7 ± 5.3	.104
Potassium (mg/mL)*	4.42 ± 0.76	4.4 ± 0.8	4.42 ± 0.7	.788
NT-proBNP (pg/dL)*	4.281.58 ± 6.608.0	7.079 ± 10.838.2	3.571.1 ± 4.816.6	.069
LDH (U/L)*	306.39 ± 206.55	397.3 ± 284.4	274.1 ± 159.6	< .001
C-reactive protein (mg/dL)*	8.57 ± 8.87	12.5 ± 9.9	7.2 ± 8.1	< .001
Procalcitonin (mg/mL)*	1.22 ± 5.06	1.31 ± 3.5	1.19 ± 5.4	.849
IL-6 (pg/mL)*	272.68 ± 681.98	397.6 ± 860.4	226.4 ± 598.9	< .001
SpO_2/FiO_2*	345.7 ±33.3	351.7 ± 37.6	343.7 ± 31.6	.103
pH*	7.36 ± 0.07	7.36 ± 0.08	7.35 ± 0.07	.739
pCO_2 (mm Hg)*	51.76 ± 17.02	51.5 ± 21.2	51.8 ± 15.4	.885
HCO_3^- (mmol/L)*	27.86 ± 5.78	27.4 ± 6.7	28 ± 5.4	.437
Lactate (mg/mL)*	2.09 ± 1.70	2.38 ± 1.6	2 ± 1.7	.018
Bilirubin (mg/dL)*	0.68 ± 0.53	0.76 ± 0.53	0.65 ± 0.54	.131
Hemoglobin (g/dL)*	12.5 ± 2.17	12.39 ± 2.3	12.54 ± 2.1	.62
Leukocytes*	11.624.43 ± 9.042.97	11.372.2 ± 10.797	11.704.9 ± 8.428.8	.771
Neutrophils*	8.530.09 ± 4.594.57	8.368.6 ± 4.738.2	8.581.6 ± 4.555.8	.714
Time on NIRS (hours)*	76.93 ± 106.1	103.5 ± 123.1	49.1 ± 78.5	.014
Type of support				
Conventional oxygen therapy	276 (79.3)	75 (89.3)	201 (76.1)	.001
HFNC	6 (1.7)	1 (1.2)	5 (1.9)	
Noninvasive mechanical ventilation	66 (18.9)	8 (9.5)	58 (21.9)	

* Results expressed as mean (standard deviation).
OSA: obstructive sleep apnea; OSAHS: obstructive sleep apnea–hypopnea syndrome; CPAP: continuous positive airway pressure; BiPAP: bilevel positive airway pressure; COPD: chronic obstructive pulmonary disease; SBP/DBP: systolic/diastolic blood pressure; RALE: Radiographic Assessment of Lung Edema; NT-proBNP: N-terminal pro–B-type natriuretic peptide; LDH: lactate dehydrogenase; IL-6: interleukin 6; pCO_2: partial pressure of carbon dioxide; HCO_3^-: bicarbonate; NIRS: noninvasive respiratory support; HFNC: high-flow nasal cannula.

Discussion

This study provides evidence of the relationship between type of initial respiratory support (COT vs NIRS) in patients with ARF and SpO_2/FiO_2 between 280 and 400, and the success or failure of such support. In this range—traditionally considered mild hypoxemia—we observed an overall failure rate of 24.1%, questioning the safety of maintaining conservative strategies such as COT in this group.

The study focused on failure of initial support—defined as the need for escalation of therapy or death—and compared respiratory techniques accordingly. From this perspective, the relevant issue is not only whether COT or NIRS was administered but how that initial choice influenced subsequent clinical evolution. Our results showed a significant difference in failure rates: 27.2% in the COT group vs 12.5% in the NIRS group (*P* = .01), with an adjusted OR of 3.145.

Table 3. Failure of initial respiratory support according to main diagnosis and type of treatment (COT vs NIRS)

Diagnosis	Therapy	n (%)	Failure n (%)	Success n (%)	*P*-value	OR	95% CI
AHF	NIRS	38 (40.9)	2 (5.3)	36 (94.1)	.011	0.163	(0.035-0.765)
	COT	55 (59.1)	14 (25.5)	41 (74.5)			
AE-COPD	NIRS	10 (18.51)	0 (0)	10 (100)	.176	N/A	(N/A)
	COT	44 (81.48)	7 (15.9)	37 (84.1)			
Pneumonia	NIRS	6 (15.38)	1 (16.7)	5 (13.3)	.743	0.800	(0.074-7.436)
	COT	33 (84.61)	7 (21.2)	26 (78.81)			
COVID-19	NIRS	10 (14.92)	5 (50)	5 (50)	.959	0.966	(0.252-3.702)
	COT	57 (85.07)	20 (50.9)	28 (49.1)			
Other	NIRS	8 (8.42)	1 (12.5)	7 (87.5)	.575	0.548	(0.063-4.742)
	COT	87 (91.57)	18 (20.7)	69 (79.3)			

AHF: acute heart failure; AE-COPD: acute exacerbation of chronic obstructive pulmonary disease; NIRS: noninvasive respiratory support; COT: conventional oxygen therapy; OR: odds ratio; CI: confidence interval; N/A: not applicable.

Table 4. Multivariate logistic regression model: predictors of failure of initial respiratory support

Variable	aOR	95% CI	*P*-value
COT	3.145	1.314-7526	.01
COVID-19	2.249	1.062-4.763	.034
CRP	1.035	1.002-1.069	.038
RALE score	1.169	1.017-1.343	.028

Adjustment variables: Type of support (COT vs NIRS), sex, SBP, RALE score, CRP, lactate, LDH, and diagnosis (AHF, AE-COPD, pneumonia, COVID-19, and others).
aOR: adjusted odds ratio; CI: confidence interval; COT: conventional oxygen therapy; NIRS: noninvasive respiratory support; CRP: C-reactive protein; RALE: Radiographic Assessment of Lung Edema; AHF: acute heart failure; AE-COPD: acute exacerbation of chronic obstructive pulmonary disease; LDH: lactate dehydrogenase; SBP: systolic blood pressure.

This difference should not be interpreted as intrinsic superiority of one type of support over the other, but rather as an indication that early initiation of NIRS may anticipate clinical deterioration, preventing progression to severe forms requiring IMV or increasing mortality risk.

The importance of early NIRS initiation was reflected in the subgroup of patients who began with COT and later required NIRS after a median of 24 hours (mean, 62.7 hours). In this group, mortality was 40%, suggesting that delay in support escalation may have significant clinical consequences. This finding aligns with the principle of a "therapeutic window," widely accepted in acute pulmonary edema management, where NIMV benefit is greatest when applied early.[28]

Multivariate analysis showed that, in addition to type of support, other variables were independently associated with failure: COVID-19 diagnosis, RALE score, and CRP levels. These variables reflect more severe pulmonary involvement and systemic inflammation. Thus, failure of initial support appears as dependent on the patient's clinical and pathophysiological profile as on the applied technique.

By diagnosis, results were heterogeneous. In AHF patients, NIRS was associated with a lower failure rate (5.3%) compared with COT (25.5%), the only category with a statistically significant difference. This finding is consistent with clinical guidelines recommending NIMV as the treatment of choice in acute pulmonary edema.[28] The positive pressure generated by NIRS reduces preload and afterload, improves oxygenation, and relieves dyspnea rapidly and effectively.

In AE-COPD patients, no significant differences were observed, although the trend favored NIRS. Most AE-COPD patients did not present respiratory acidosis at admission, likely explaining the lower use of NIMV. In this context, recent studies have explored HFNC as a safe and effective alternative, particularly in mild AE-COPD or without acidosis, thereby expanding NIRS applicability.[29,30]

In pneumonia and COVID-19 patients, both groups showed high failure rates without significant differences between COT and NIRS. In COVID-19, this may be explained by high clinical variability and unmeasured factors such as ventilation modality, parameters used, or inflammatory burden. Previous studies also reported high failure rates in COVID-19 patients treated with NIRS, reinforcing the need to tailor support to individual patient characteristics.[31]

A variable not included in the final model that could have influenced failure prediction was respiratory rate, a key parameter in ARF severity assessment. Its limited documentation may have led to exclusion from the model, representing a study limitation.

Recent studies have shown that combining respiratory rate and oxygenation, expressed as the ROX index, reliably predicts outcomes in NIRS-treated patients.[32] Systematic inclusion of this index in clinical practice may improve decision-making and prevent delays in support escalation.

Another limitation was the retrospective design, with risk of selection and information bias. However, consecutive inclusion of all eligible patients during the study period and thorough review of electronic health records partially mitigated this risk.

Of note, clinical diagnosis was made by the attending physician without standardized verification, possibly introducing diagnostic variability, mainly in differentiating AHF from COVID-19.

This, however, reflects real-world ED settings, where decisions are made in real time with limited information. In COVID-19 cases, all patients had confirmed positive tests (antigen or PCR), while negative cases had negative PCR, reinforcing diagnostic validity in that subgroup.

Additionally, limitation of therapeutic effort was not analyzed, which could have influenced group composition. However, in clinical practice, and according to local NIRS protocol, these patients are not candidates for IMV and typically receive only COT or HFNC with comfort care. Their exclusion therefore has limited impact, since the study's primary focus was on patients potentially eligible for support escalation.

Based on our findings, we propose reconsidering current thresholds for mild and moderate hypoxemia classification. Traditionally, PaO_2/FiO_2 < 200 has been considered the threshold to initiate NIRS. However, our data suggest

that an estimated PaO_2/FiO_2 of 200–250 (SpO_2/FiO_2 between 280–400) may benefit from a more aggressive approach.

This hypothesis justifies the need for prospective studies validating a more dynamic classification framework that incorporates underlying pathophysiology and other relevant clinical parameters such as respiratory rate.

Finally, our results support the implementation of clinical algorithms integrating risk of initial support failure into therapeutic strategy selection, prioritizing early NIRS initiation in higher-risk profiles.

This approach would improve clinical outcomes and optimize resource use in high-demand ED and emergency contexts.

In conclusion, initiating noninvasive support in patients with ARF and SpO_2/FiO_2 between 280–400 may reduce failure risk, particularly in AHF cases. Rethinking this threshold could optimize decision-making in EDs and emergency settings.

ARTICLE INFORMATION

Conflict of Interest Disclosures: None reported.

Funding: The authors declare the non-existence of funding in relation to this article.

Ethical responsibilities: The authors have confirmed the maintenance of confidentiality and respect for the patient rights, agreement of publication, and transfer of rights to Revista Española de Urgencias y Emergencias.

Data availability: Data are available upon request from the corresponding author.

Author's contributions (CRediT): All authors contributed to study conception and design; data collection; data analysis and interpretation; and drafting, reviewing, and approving the submitted manuscript.

Use of generative artificial intelligence tools: The authors declare no use of AI tools in preparing this article.

Article not commissioned by the Editorial Board and with external peer review.

Note of the editors: This is a BOWMAN-generated English translation of the officially indexed Spanish-language article, which should be cited as Rev Esp Urg Emerg. 2025;4:162-169. In this translated version, the editors have supervised the process; however, it cannot be ruled out that some errors resulting from the artificial intelligence translation process may have gone unnoticed.

REFERENCES

1. Romero-Dapueto C, Budini H, Cerpa F, Caceres D, Hidalgo V, Gutiérrez T, et al. Pathophysiological Basis of Acute Respiratory Failure on Non-Invasive Mechanical Ventilation. Open Respir Med J. 2015;9:97-103.
2. Williams JW Jr, Cox CE, Hargett CW, Gilstrap DL, Castillo CE, Govert JA, et al. Noninvasive Positive-Pressure Ventilation (NPPV) for Acute Respiratory Failure [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012; 68. (Consultado 18 Mayo 2025). Disponible en: https://ncbi.nlm.nih.gov/books/NBK99179/
3. Luján M, Peñuelas Ó, Cinesi Gómez C, García-Salido A, Moreno Hernando J, Romero Berrocal A, et al. Resumen de recomendaciones y puntos clave del consenso de las sociedades científicas españolas (SEPAR, SEMICYUC, SEMES; SECIP, SENEO, SEDAR, SENP) sobre el uso de ventilación no invasiva y oxigenoterapia de alto flujo con cánulas nasales en pacientes adultos, pediátricos y neonatales con insuficiencia respiratoria aguda grave. Med Intensiva. 2021;45:298-312.
4. ARDS Definition Task Force; Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307:2526-33.
5. Cinesi Gómez C, Carratalá Perales JM; grupo multidisciplinar de manejo de la IRA secundaria al COVID-19. Soporte respiratorio en el paciente adulto con insuficiencia respiratoria aguda secundaria a COVID-19. Emergencias. 2020;32:197-200.
6. Bilan N, Dastranji A, Ghalehgolab Behbahani A. Comparison of the SpO2/fio2 ratio and the paO_2/FiO_2 ratio in patients with acute lung injury or acute respiratory distress syndrome. J Cardiovasc Thorac Res. 2015;7:28-31.
7. Wick KD, Matthay MA, Ware LB. Pulse oximetry for the diagnosis and management of acute respiratory distress syndrome. Lancet Respir Med. 2022;10:1086-98.
8. Lobete C, Medina A, Rey C, Mayordomo-Colunga J, Concha A, Menéndez S. Correlation of oxygen saturation as measured by pulse oximetry/fraction of inspired oxygen ratio with PaO_2/fraction of inspired oxygen ratio in a heterogeneous sample of critically ill children. J Crit Care. 2013;28:538.
9. Khemani RG, Patel NR, Bart RD 3rd, Newth CJL. Comparison of the pulse oximetric saturation/fraction of inspired oxygen ratio and the PaO2/fraction of inspired oxygen ratio in children. Chest. 2009;135:662-8.
10. Rice TW, Wheeler AP, Bernard GR, Hayden DL, Schoenfeld DA, Ware LB; National Institutes of Health, National Heart, Lung, and Blood Institute ARDS Network. Comparison of the SpO_2/FIO_2 ratio and the PaO2/FIO_2 ratio in patients with acute lung injury or ARDS. Chest. 2007;132:410-7.
11. Khemani RG, Thomas NJ, Venkatachalam V, Scimeme JP, Berutti T, Schneider JB, et al. Pediatric Acute Lung Injury and Sepsis Network Investigators (PALISI). Comparison of SpO_2 to PaO_2 based markers of lung disease severity for children with acute lung injury. Crit Care Med. 2012;40:1309-16.
12. Pandharipande PP, Shintani AK, Hagerman HE, St Jacques PJ, Rice TW, Sanders NW, et al. Derivation and validation of SpO_2/FiO_2 ratio to impute for PaO_2/FiO_2 ratio in the respiratory component of the Sequential Organ Failure Assessment score. Crit Care Med. 2009;37:1317-21.
13. Xu W, Li C, Chen Y, Duan H, Diao L, Yang X, et al. Comparison of pulse oxygen saturation/fraction of inhaled oxygen and arterial partial pressure of oxygen/fraction of inhaled oxygen in the assessment of oxygenation in acute respiratory distress syndrome patients at different high altitudes in Yunnan Province. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2021;33:826-31.
14. Bonaventura A, Mumoli N, Mazzone A, Colombo A, Evangelista I, Cerutti S, et al. Correlation of SpO_2/FiO_2 and PaO_2/FiO_2 in patients with symptomatic COVID-19: An observational, retrospective study. Intern Emerg Med. 2022;17:1769-75.
15. Chen W, Janz DR, Shaver CM, Bernard GR, Bastarache JA, Ware LB. Clinical characteristics and outcomes are similar in ARDS diagnosed by oxygen saturation/FiO_2 ratio compared with paO_2/FiO_2 ratio. Chest. 2015;148:1477-83.
16. Jubran A. Pulse oximetry. Crit Care. 2015;19:272.
17. Collins JA, Rudenski A, Gibson J, Howard L, O'Driscoll R. Relating oxygen partial pressure, saturation and content: the haemoglobin-oxygen dissociation curve. Breathe (Sheff). 2015;11:194-201.
18. Gadrey SM, Lau CE, Clay R, Rhodes GT, Lake DE, Moore CC, et al. Imputation of partial pressures of arterial oxygen using oximetry and its impact on sepsis diagnosis. Physiol Meas. 2019;40:115008.
19. Grasselli G, Calfee CS, Camporota L, Poole D, Amato MBP, Antonelli M et al; European Society of Intensive Care Medicine Taskforce on ARDS. ESICM guidelines on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies. Intensive Care Med. 2023;49:727-59.
20. Perkins GD, McAuley DF, Giles S, Routledge H, Gao F. Do changes in pulse oximeter oxygen saturation predict equivalent changes in arterial oxygen saturation? Crit Care. 2003;7:R67.
21. O'Driscoll BR, Howard LS, Davison AG; British Thoracic Society. BTS guideline for emergency oxygen use in adult patients. Thorax. 2008;63 Suppl 6:vi1-68. Erratum in: Thorax. 2009;64(1):91.
22. Wilson BJ, Cowan HJ, Lord JA, Zuege DJ, Zygun DA. The accuracy of pulse oximetry in emergency department patients with severe sepsis and septic shock: a retrospective cohort study. BMC Emerg Med. 2010;10:9.
23. Pretto JJ, Roebuck T, Beckert L, Hamilton G. Clinical use of pulse oximetry: official guidelines from the Thoracic Society of Australia and New Zealand. Respirology. 2014;19:38-46.
24. Ekström M, Engblom A, Ilic A, Holthius N, Nordström P, Vaara I. Calculated arterial blood gas values from a venous sample and pulse oximetry: Clinical validation. PLoS One. 2019;14:e0215413.
25. Cinesi-Gómez C, García-García P, López-Pelayo I, Giménez JI, González-Torres LM, Bernal-Morell E. Correlación entre la saturación de oxihemoglobina por pulsioximetría y la presión arterial de oxígeno en pacientes con insuficiencia respiratoria aguda. Rev Clin Esp (Barc). 2017;217:522-5.
26. Sanz F, Dean N, Dickerson J, Jones B, Knox D, Fernández-Fabrellas E, et al. Accuracy of PaO_2/FiO_2 calculated from SpO_2 for severity assessment in ED patients with pneumonia. Respirology. 2015;20:813-8.
27. Bianquis C, De Leo G, Morana G, Duarte-Silva M, Nolasco S, Vilde R, et al. Highlights from the Respiratory Failure and Mechanical Ventilation Conference 2024. Breathe (Sheff). 2024;20:240105.
28. Masip J, Peacock WF, Price S, Cullen L, Mar-

tin-Sanchez FJ, Seferovic P, et al. Indications and practical approach to non-invasive ventilation in acute heart failure. Eur Heart J. 2018;39:17-25.
29. Wang M, Zhao F, Sun L, Liang Y, Yan W, Sun X, et al. High-Flow Nasal Cannula versus Noninvasive Ventilation in AECOPD Patients with Respiratory Acidosis: A Retrospective Propensity Score-Matched Study. Can Respir J. 2023;6377441.
30. Cortegiani A, Longhini F, Madotto F, Groff P, Scala R, Crimi C, et al. H. FAECOPD study investigators. 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.
31. García-Fernández JJ, Sánchez-Nicolás JA, Galicia-Puyol S, Gil-Rosa I, Guerras-Conesa JJ, Bernal-Morell E. Failure of Non-Invasive Respiratory Support in Patients with SARS-CoV-2. J Clin Med. 2023;12:6537.
32. Roca O, Caralt B, Messika J, Samper M, Sztrymf B, Hernández G, et al. An Index Combining Respiratory Rate and Oxygenation to Predict Outcome of Nasal High-Flow Therapy. Am J Respir Crit Care Med. 2019;199:1368-76.