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The Impact of Comorbidities on the Effectiveness of Noninvasive Ventilation in Patients with Chronic Obstructive Pulmonary Disease

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Abstract. ***Background:*** Noninvasive ventilation (NIV) is a cornerstone treatment for hypercapnic respiratory failure in patients with chronic obstructive pulmonary disease (COPD). The aim of this study was to evaluate the impact of selected comorbidities on the effectiveness of NIV in these patients, and to compare clinical characteristics and outcomes between continuous positive airway pressure (CPAP) and bilevel positive airway pressure (BiPAP) modalities.

Materials and methods: This prospective, randomized, single-center study included 80 patients with hypercapnic respiratory failure due to COPD, randomized 1:1 to CPAP or BiPAP. Demographic and clinical data, comorbidities, vital signs, and arterial blood gas parameters were recorded at admission and during NIV. The primary outcome was pCO_2 reduction at the end of treatment compared with baseline.

Results: Arterial hypertension significantly enhanced pCO_2 reduction with CPAP, but not with BiPAP. Systolic and mean arterial pressure independently predicted the magnitude of pCO_2 reduction, regardless of NIV modality. Patients treated with BiPAP more frequently had decompensated cor pulmonale and severe pulmonary hypertension, while pneumonia was more common in the CPAP group. NIV modality itself was not an independent predictor of pCO_2 reduction.

Conclusion: Systemic hemodynamic status and arterial hypertension influence NIV effectiveness in hypercapnic COPD. The cardiovascular status should be considered alongside respiratory parameters when selecting the NIV strategy.

Keywords: arterial pressure, chronic obstructive pulmonary disease, hypertension, hypercapnia, noninvasive ventilation.

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Gretutinių ligų įtaka pacientų, sergančių lėtine obstrukcine plaučių liga, neinvazinės ventiliacijos veiksmingumui

Santrauka. ***Įvadas:*** Neinvazinė ventiliacija (NIV) yra pagrindinis sergančių lėtine obstrukcine plaučių liga (LOPL) pacientų hiperkapninio kvėpavimo nepakankamumo gydymo būdas. Tyrimo tikslas buvo įvertinti šių pacientų pasirinktų gretutinių ligų įtaką NIV veiksmingumui bei palyginti klinikines charakteristikas ir rezultatus taikant nuolatinio teigiamo kvėpavimo takų slėgio (CPAP) ir dviejų lygių teigiamo kvėpavimo takų slėgio (BiPAP) metodus.

Medžiagos ir metodai: Šiame perspektyviajame, atsitiktinių imčių, vieno centro tyrime dalyvavo 80 pacientų su hiperkapniniu kvėpavimo nepakankamumu dėl LOPL, atsitiktinai paskirstytų santykiu 1:1 į CPAP arba BiPAP grupes. Pacientų demografiniai ir klinikiniai duomenys, gretutinės ligos, gyvybiniai požymiai ir arterinio kraujo dujų parametrai buvo registruojami priėmimo metu ir taikant NIV. Pirminis rezultatas – pCO_2 sumažėjimas gydymo pabaigoje, palyginti su pradiniu lygiu.

Rezultatai: Arterinė hipertenzija žymiai sustiprino pCO_2 sumažėjimą naudojant CPAP, bet ne BiPAP. Sistolinis ir vidutinis arterinis spaudimas nepriklausomai prognozavo pCO_2 sumažėjimo dydį, neatsižvelgiant į NIV metodą. Pacientai, gydyti BiPAP, dažniau turėjo dekompensuotą plautinę širdies ligą ir sunkią plaučių hipertenziją, o pneumonija buvo dažnesnė CPAP grupėje. Pats NIV metodas nebuvo nepriklausomas pCO_2 sumažėjimo prognozės veiksnys.

Išvada: Sisteminė hemodinamika ir arterinė hipertenzija daro įtaką NIV veiksmingumui hiperkapnijos LOPL atveju. Renkantis NIV strategiją, kartu su kvėpavimo parametrais reikėtų atsižvelgti ir į širdies bei kraujagyslių būklę.

Raktažodžiai: arterinis spaudimas, lėtinė obstrukcinė plaučių liga, hipertenzija, hiperkapnija, neinvazinė ventiliacija.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality worldwide and is frequently complicated by acute hypercapnic respiratory failure requiring ventilatory support [1]. *Noninvasive Ventilation* (NIV) represents the cornerstone of management in this setting, as it significantly reduces the need for endotracheal intubation and improves survival [2–4]. Both *Continuous Positive Airway Pressure* (CPAP) and *Bilevel Positive Airway Pressure* (BiPAP) are widely used in clinical practice; however, available evidence does not demonstrate a clear superiority of one modality over the other for most major outcomes, thereby underscoring the importance of individualized patient selection [5–7].

Patients with COPD commonly suffer from multiple comorbidities that substantially influence disease progression, ventilatory mechanics, and clinical outcomes. Cardiovascular disorders, including arterial hypertension, *Chronic Heart Failure* (HF), and *Pulmonary Hypertension* (PH), are among the most prevalent and clinically relevant comorbidities in this population. These conditions not only increase overall morbidity and mortality but may also directly affect gas exchange, hemodynamic stability, and the physiological response to positive pressure ventilation [8–10].

Although the overall efficacy of NIV in acute hypercapnic respiratory failure is well established, the role of comorbidities as modifiers of NIV response remains insufficiently characterized [11,12]. Data on the influence of arterial hypertension and systemic hemodynamic parameters on carbon dioxide elimination during NIV are scarce. Moreover, the issue whether such cardiovascular factors differentially affect the performance of CPAP and BiPAP has not been adequately explored [8,11,12].

Therefore, the primary aim of this study was to evaluate the impact of selected comorbidities, and particularly arterial hypertension, on the effectiveness of NIV in patients with hypercapnic respiratory failure due to COPD. In addition, we sought to investigate the association between systemic blood pressure parameters and partial pressure of carbon dioxide (pCO_2) reduction.

Materials and Methods

Study design and population

This prospective, single-center, randomized, controlled trial included 80 patients with hypercapnic acute-on-chronic respiratory failure due to COPD treated with NIV in the Non-Surgical Intensive Care Unit at General Hospital "Prim. Dr. Abdulah Nakaš", Sarajevo. Patients were randomized in a 1:1 ratio by using a computer-generated random sequence to receive NIV in either the CPAP or BiPAP mode (40 patients per group).

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of the General Hospital "Prim. Dr. Abdulah Nakaš" (approval number: 100-80/18). All participants provided written informed consent prior to enrollment.

Inclusion and exclusion criteria

Eligible patients were adults (≥18 years) with COPD and hypercapnic respiratory failure confirmed by *Arterial Blood Gas* (ABG) analysis on admission, accompanied by moderate to severe dyspnea and/or persistent tachypnoea resistant to initial oxygen therapy. All patients were enrolled during acute exacerbation or acute-on-chronic deterioration of COPD requiring hospital treatment and NIV.

Patients were excluded if they were unable to cooperate or protect the airway, had severely impaired consciousness (Glasgow Coma Scale, GCS <8), marked hemodynamic or respiratory instability, metabolic acidosis, advanced congestive HF (New York Heart Association, NYHA III–IV), or respiratory failure due to other primary causes (e.g. neuromuscular disease, obesity hypoventilation, obstructive sleep apnea, cardiogenic pulmonary oedema, acute respiratory distress syndrome – ARDS, interstitial lung disease). Patients with acute life-threatening conditions (e.g. septic shock, acute myocardial infarction, pulmonary embolism) or contraindications to mask application were also excluded.

Clinical assessment and outcomes

On admission, demographic data, comorbidities (with focus on arterial hypertension, chronic HF and PH), vital signs, and ABG parameters were recorded.

The primary outcome for this analysis was a reduction in pCO_2 at the end of NIV treatment compared with the baseline (admission), analyzed as a binary variable (yes/no). Additional analyses evaluated the relationships between the NIV modality (CPAP vs. BiPAP), arterial hypertension, and pCO_2 reduction. pCO_2 was measured by arterial blood gas analysis. Arterial blood gas and acid-base status analyses were performed by using a COBAS blood gas analyzer (*Roche*, Germany). The reference range for $PaCO_2$ was 4.67–6.13 kPa.

Noninvasive ventilation

After randomization, patients were treated with NIV in either the CPAP or BiPAP mode according to standard intensive care unit protocols. NIV settings were individually adjusted to achieve adequate oxygenation and ventilation. Arterial blood gases were evaluated during treatment and at the end of NIV.

The end of NIV treatment was determined according to clinical stabilization and successful weaning from NIV. Clinical stabilization was defined by respiratory rate <24 breaths/min, heart

rate <110 beats/min, pH ≥7.35, and SaO_2 ≥90%. After these criteria had been achieved, a trial of NIV discontinuation was performed. In patients treated with CPAP, oxygen support was continued while using a partial rebreathing mask, whereas, in patients treated with BiPAP, IPAP was gradually reduced by 2 cmH_2O. NIV treatment was considered completed if the patient remained clinically stable without the need for NIV reapplication for 24 consecutive hours.

NIV was discontinued earlier in cases of treatment failure requiring endotracheal intubation and invasive mechanical ventilation. Need for endotracheal intubation was considered a NIV treatment failure and was recorded as an in-hospital outcome.

Statistical analysis

Descriptive statistics were used to summarize baseline characteristics. Continuous variables were expressed as the mean ± standard deviation or the median (interquartile range), and categorical variables were expressed as frequencies and percentages. Associations between categorical variables were tested by using the chi-square test or Fisher's exact test, as appropriate. To evaluate the joint effects of NIV modality, arterial hypertension, and pCO_2 reduction, a hierarchical log-linear analysis was performed to assess main effects and interaction effects among the three categorical variables.

Independent predictors of pCO_2 reduction at the end of the treatment were identified by using multivariable binary logistic regression. The dependent variable was pCO_2 reduction (yes/no). Systolic and mean arterial pressure were entered as primary predictors and adjusted for the NIV modality, heart rate, respiratory rate, diuresis, and diastolic blood pressure. The results were expressed as *Odds Ratios* (OR) with 95% *Confidence Intervals* (CI). The model fit was evaluated by using the Hosmer–Lemeshow test and pseudo-R^2 measures (Cox & Snell R^2 and Nagelkerke R^2). All tests were two-tailed, and $p < 0.05$ was considered statistically significant. Statistical analyses were performed by using *SPSS*, version 18.0.

Results

Demographic and clinical characteristics of the study population are presented in Table 1. Patients treated with CPAP had a significantly higher body mass index ($p = 0.023$), body weight ($p = 0.001$), and body height ($p = 0.027$) compared with those treated with BiPAP. No significant differences were observed between the groups with regard to age, sex distribution, smoking status, and length of hospitalization.

During hospitalization, endotracheal intubation was required in 18 (22.5%) patients, including 11 (27.5%) patients in the BiPAP group and 7 (17.5%) patients in the CPAP group, without a statistically significant difference between the groups. In-hospital mortality occurred in 21 (26.3%) patients, including 12 (30.0%) patients treated with BiPAP and 9 (22.5%) patients treated with CPAP, also without a statistically significant difference between the groups.

On admission, pneumonia was significantly more frequent among patients treated with CPAP (40%) than among those treated with BiPAP (20%) ($p = 0.042$). Chronic HF including the cor pulmonale status was recorded in all patients. Overall, decompensated HF or decompensated cor pulmonale on admission was present in 46 (57.5%) patients, including 25 (62.5%) patients in the BiPAP group and 21 (52.5%) patients in the CPAP group. The distribution of HF/cor pulmonale subtypes differed significantly between the groups ($p = 0.012$): decompensated cor pulmonale was more frequent in the BiPAP group (45.0% vs. 17.5%), whereas decompensated HF due to other causes was more frequent in the CPAP group (35.0% vs. 17.5%). PH was also more prevalent in the BiPAP group, predominantly severe PH (40.0% vs. 7.5%), with a statistically significant difference between the groups ($p = 0.006$) (Table 2).

Table 1. Demographic, baseline clinical characteristics, and in-hospital outcomes

Parameter		BiPAP* (n = 40)	CPAP† (n = 40)	*p*-value
Age		66.6 ± 8.6, 67.0 [12.0]	66.6 ± 8.6, 67.0 [12.0]	0.097
Sex	Male	14 (35%)	17 (42.5%)	0.491
	Female	26 (65%)	23 (57.5%)	
BMI‡		23.7 ± 3.9, 22.5 [6.5]	26.4 ± 3.5, 25.0 [4.6]	0.023
Body weight (kg)		67.5 ± 10.9, 65.0 [22.0]	79.2 ± 11.7, 80.0 [18.0]	0.001
Body height (cm)		168.7 ± 5.1, 168.0 [5.0]	173.0 ± 6.9, 170.0 [10.0]	0.027
Smoking status:				0.150
	Non-smoker	0 (0%)	4 (10%)	
	Current smoker	27 (67.5%)	26 (65%)	
	Former smoker	13 (32.5%)	10 (25%)	
Length of hospitalization (days)		14.0 ± 6.8, 13.0 [10.0]	12.1 ± 8.9, 11.0 [13.0]	0.461
Intubation				0.284
	No	29 (72.5%)	33 (82.5%)	
	Yes	11 (27.5 %)	7 (17.5%)	
In-hospital mortality				0.446
	No	28 (70%)	31 (77.5%)	
	Yes	12 (30%)	9 (22.5%)	

Note. Abbreviations in use: *Bilevel Positive Airway Pressure; †Continuous Positive Airway Pressure; ‡Body Mass Index. $p < 0.05$ is considered statistically significant.

Table 2. Comorbidities on admission

	Comorbidity	BiPAP* (n = 40)	CPAP† (n = 40)	p-value
Pneumonia	No	32 (80.0%)	24 (60.0%)	0.042
	Yes	8 (20.0%)	16 (40.0%)	
Influenza	No	37 (92.5%)	36 (90.0%)	1.000
	Yes	3 (7.5%)	4 (10.0%)	
Bronchiectasis	No	40 (100.0%)	38 (95.0%)	0.494
	Yes	0 (0.0%)	2 (5.0%)	
Lung cancer	No	40 (100.0%)	39 (97.5%)	1.000
	Yes	0 (0.0%)	1 (2.5%)	
Previous pulmonary tuberculosis	No	38 (95.0%)	37 (92.5%)	1.000
	Yes	2 (5.0%)	3 (7.5%)	
Chronic HF‡	Decompensated cor pulmonale	18 (45%)	7 (17.5%)	0.012
	Compensated cor pulmonare	11 (27.5%)	8 (20%)	
	Compensated HF‡ (other causes)	4 (10%)	11 (27.5%)	
	Decompensated HF‡ (other causes)	7 (17.5%)	14 (35%)	
PH§	Severe PH§	16 (40%)	3 (7.5%)	0.006
	Moderate PH§	5 (12.5%)	6 (15%)	
	Mild PH§	4 (10%)	6 (15.0%)	
	No PH§	15 (37.5%)	25 (62.5%)	

Note. Abbreviations in use: *Bilevel Positive Airway Pressure; †Continuous Positive Airway Pressure; ‡Heart Failure; §Pulmonary Hypertension. $p < 0.05$ is considered statistically significant.

At the end of the NIV treatment, pCO_2 normalization compared with the baseline was achieved in 19 (23.8%) patients, including 7 (17.5%) patients in the BiPAP group and 12 (30.0%) patients in the CPAP group, without a statistically significant difference between the groups ($p = 0.189$). A reduction in pCO_2 compared with the baseline was observed in 41 (51.3%) patients, including 23 (57.5%) patients treated with BiPAP and 18 (45.0%) treated with CPAP; this difference was not statistically significant, either ($p = 0.263$).

The patients were categorized according to the NIV modality (CPAP or BiPAP), the presence or absence of arterial hypertension, and pCO_2 reduction from the baseline, which served as the basis for the subsequent hierarchical log-linear analysis. Table 3 shows statistically significant interaction between NIV modality and arterial hypertension on pCO_2 reduction.

Among the pairwise associations, the strongest statistically significant association was observed between the NIV modality and the presence or absence of arterial hypertension, followed by the association between pCO_2 reduction and the arterial hypertension status (Table 3).

Table 3. Results of the hierarchical log-linear analysis and partial associations between NIV* modality, arterial hypertension, and pCO_2 reduction

Full model (K-way effects)					
	K	Likelihood ratio		Pearson	
		Chi-square	*p*-value	Chi-square	*p*-value
K-way and higher-order effects[a]	1	35.124	<0.001	27.000	<0.001
	2	14.144	0.007	9.062	0.060
	3	4.415	0.036	3.044	0.081
K-way effects	1	20.980	<0.001	17.938	<0.001
	2	9.729	0.021	6.019	0.111
	3	4.415	0.036	3.044	0.081

Partial associations		
Effect	Partial Chi-Square	*p*-value
BiPAP†-CPAP‡: pCO_2 reduction	2.520	0.112
BiPAP†-CPAP‡: Arterial hypertension on admission	5.627	0.018
pCO_2 reduction: Arterial hypertension on admission	4.114	0.043
BiPAP†: CPAP‡	0.000	1.000
pCO_2 reduction	0.050	0.823
Arterial hypertension on admission	20.930	<0.001

Note. Abbreviations in use: *Noninvasive Ventilation; †Bilevel Positive Airway Pressure; ‡Continuous Positive Airway Pressure.

[a]Tests in which K-way and higher-order effects were set to zero. [b] Tests in which K-way effects were set to zero. *$p < 0.05$ is considered statistically significant.

Parameter estimates confirmed a significant association between the NIV modality (BiPAP vs. CPAP) and arterial hypertension, as well as a strong main effect of arterial hypertension (Table 4).

No statistically significant association was found between the arterial hypertension status and pCO_2 reduction from admission in the patients treated with BiPAP ($p = 0.481$). In contrast, among the patients treated with CPAP, pCO_2 reduction from admission was observed exclusively in those with arterial hypertension (18/34), whereas none of the patients without hypertension showed pCO_2 reduction (0/6), with a statistically significant association confirmed by the chi-square test (Pearson's $\chi^2 = 5.775$, Fisher's exact $p = 0.024$).

Table 4. Parameter estimates of the log-linear model for NIV* modality, pCO_2 reduction, and arterial hypertension

Effect	Estimate	SE†	Z	*p*-value	95% CI‡	
					Lower	Upper
BiPAP§-CPAP II: pCO_2 reduction: Arterial hypertension on admission	-0.278	0.205	-1.358	0.175	-0.680	0.123
BiPAP§-CPAP II: pCO_2 reduction	-0.363	0.205	-1.769	0.077	-0.765	0.039
BiPAP§-CPAP II: Arterial hypertension on admission	0.427	0.205	2.083	0.037	0.025	0.829
pCO_2 reduction: Arterial hypertension on admission	0.391	0.205	1.909	0.056	-0.010	0.793
BiPAP§-CPAP II	0.286	0.205	1.393	0.164	-0.116	0.688
pCO_2 reduction	0.250	0.205	1.218	0.223	-0.152	0.652
Arterial hypertension on admission	-0.708	0.205	-3.455	0.001	-1.110	-0.307

Note. Abbreviations in use: *Noninvasive Ventilation; †Standard Error; ‡Confidence Interval; §Bilevel Positive Airway Pressure; IIContinuous Positive Airway Pressure. $p < 0.05$ is considered statistically significant.

Multivariable logistic regression analysis was performed with the objective to assess which vital parameters and NIV modality influenced pCO_2 reduction at the end of the treatment compared with the baseline. The final model identified the systolic and mean arterial pressure as the only significant predictors of pCO_2 reduction, whereas the NIV modality (BiPAP vs. CPAP) was not a significant factor. The model showed an acceptable overall fit (Cox & Snell $R^2 = 0.176$, Nagelkerke $R^2 = 0.234$, Hosmer–Lemeshow $\chi^2 = 9.814$, df = 8, $p = 0.278$). The effects of systolic and mean arterial pressure were adjusted for the NIV modality (BiPAP vs. CPAP), heart rate, respiratory rate, diuresis, and diastolic blood pressure.

A 1-mmHg increase in the systolic arterial pressure was associated with a 6.2% increase in the odds of pCO_2 reduction, whereas a 1-mmHg increase in the mean arterial pressure was associated with an approximately 11.2% decrease in the odds of pCO_2 reduction (Table 5).

Table 5. Logistic regression analysis of pCO_2 change according to arterial pressure in hypercapnic respiratory failure

Factor	OR*	95% CI†	*p*-value
Systolic arterial pressure	1.062	1.002 – 1.125	0.042
Mean arterial pressure	0.888	0.815 – 0.967	0.006

Note. Abbreviations in use: *Odds ratio; †Confidence interval. $p < 0.05$ is considered statistically significant.

Limitations

This study has several limitations. It was conducted as a single-center study with a relatively small sample size, which limits the generalizability of the findings. The observational design precludes causal inference, and residual confounding cannot be excluded despite multivariable adjustment. In addition, long-term outcomes after the hospital discharge were not assessed. Future multicenter prospective studies with larger patient populations are warranted to validate these results and to further explore the mechanistic links between systemic hemodynamics, arterial hypertension, and pCO_2 clearance during NIV.

Discussion

The present study has demonstrated that arterial hypertension significantly modified the effect of CPAP on pCO_2 reduction, with a more pronounced decrease observed in hypertensive patients treated with CPAP, whereas no such effect was observed in the BiPAP group. In addition, systolic and mean arterial pressure independently predicted the magnitude of pCO_2 reduction, regardless of the NIV modality used. These findings suggest that the systemic hemodynamic status plays a key role in determining the effectiveness of NIV, beyond the choice of the ventilatory mode itself.

In the present study, NIV was initiated because of acute exacerbation of COPD complicated by hypercapnic respiratory failure. Hypercapnia should therefore be interpreted as a physiological manifestation of ventilatory failure and a criterion for NIV initiation, rather than as the underlying cause of respiratory deterioration. The underlying clinical condition requiring ventilatory support was COPD-related ventilatory failure, frequently accompanied with relevant cardiopulmonary comorbidities.

The association between higher systolic and mean arterial pressure and greater pCO_2 reduction is physiologically plausible, as an improved cardiac output and pulmonary perfusion facilitate more efficient carbon dioxide elimination during NIV. Conversely, impaired hemodynamic parameters may limit the ventilatory efficiency despite adequate airway pressure support [13–15]. Although both CPAP and BiPAP improve gas exchange and reduce the work of breathing in COPD, current evidence does not demonstrate consistent superiority of one modality over the other, and modality selection is often driven by the underlying comorbidity profile rather than inherent efficacy [5,6,11]. Importantly, direct evidence specifically linking arterial hypertension to enhanced pCO_2 reduction, particularly with CPAP, remains scarce in the literature, thereby highlighting the novelty of our findings [16,17].

In our cohort, pneumonia as a comorbidity was diagnosed twice as often in patients treated with CPAP than in those treated with BiPAP. Guideline recommendations advise caution when applying NIV in the presence of pneumonia because of an increased risk of treatment failure [18,19]. Shah et al., in a large ten-year observational study including more than eight million patients, reported an increasing use of NIV in patients with COPD and pneumonia with a reduced need for invasive mechanical ventilation, but also a higher overall risk of mortality and morbidity among patients requiring ventilatory support, particularly in those with multiple comorbidities such as sepsis and congestive HF [20]. Previous studies have also demonstrated a favorable response to NIV in selected patients with pre-existing cardiac or pulmonary disease who develop acute pneumonia, while emphasizing the risk of delayed intubation after NIV failure [20,21]. In a systematic review, Vanoni et al. showed that CPAP was superior to conventional oxygen therapy in reducing intubation rates and improving oxygenation parameters in community-acquired pneumonia, which is partly consistent with the frequent use of CPAP in pneumonia observed in our routine clinical practice [21].

In our study, endotracheal intubation was considered a marker of NIV treatment failure and escalation to invasive mechanical ventilation. Although intubation was numerically more frequent in the BiPAP group than in the CPAP group, the difference was not statistically significant. This finding should be interpreted in the context of the higher burden of severe PH and decompensated cor pulmonale in the BiPAP group, which may have contributed to a more severe clinical profile.

Current guidelines recognize that patients with acute HF and concomitant COPD are deemed to be at an increased risk of respiratory deterioration [22,23]. Although no randomized trials specifically address NIV use in isolated right-sided HF, experimental and clinical data suggest that positive pressure ventilation may increase right ventricular afterload, and, therefore, it requires careful hemodynamic monitoring [24–26]. In contrast, in patients with COPD and concomitant pulmonary oedema, NIV is considered the treatment of choice because it favorably affects both the respiratory and cardiac function [5,6]. COPD is associated with systemic inflammation and vascular dysfunction, leading to a substantially increased cardiovascular risk. PH develops in a large proportion of

patients with advanced COPD and represents a major contributor to right-sided cardiac involvement [27,28]. Given that most patients in our cohort had severe COPD at admission, the high prevalence of PH and right-sided heart disease is consistent with these pathophysiological mechanisms and explains the heavy cardiovascular burden observed in the BiPAP group.

Previous studies have consistently demonstrated beneficial hemodynamic and gas-exchange effects of NIV in selected patients with acute respiratory failure and cardiopulmonary comorbidity. Celutkiene et al. reported improved gas exchange, reduced need for intubation, and lower mortality in patients with acute exacerbation of COPD and/or acute HF with pulmonary oedema treated with BiPAP [29]. Similarly, Berbenetz et al. observed rapid improvements in arterial oxygenation and pH, along with a reduction in diastolic blood pressure in patients with hypercapnic respiratory failure and acute pulmonary oedema [6]. Held et al. further demonstrated, by using right heart catheterization, that prolonged NIV significantly reduced pulmonary artery pressures, peripheral vascular resistance, and right atrial volume [30]. These data are in line with the hemodynamic and gas-exchange trends observed in our cohort.

Although patients treated with BiPAP more frequently had decompensated cor pulmonale and severe pulmonary hypertension, whereas pneumonia was more common in the CPAP group, this imbalance most likely reflects a random variation related to the relatively small sample size, as treatment allocation was randomized at a 1:1 ratio. The finding that arterial hypertension predicted pCO_2 reduction only in the CPAP group may therefore be explained by differences in the baseline hemodynamic burden between the groups. In the CPAP group, preserved or elevated systemic arterial pressure likely reflected a more stable cardiovascular function, allowing the effects of positive airway pressure on ventilation–perfusion matching and CO_2 elimination to fully manifest.

Conclusions

In conclusion, this study highlights the critical role of cardiovascular comorbidity and the systemic hemodynamic status in shaping the response to NIV in patients with hypercapnic COPD. Importantly, the systolic and mean arterial pressure independently predicted pCO_2 reduction, and arterial hypertension significantly modified the effect of CPAP on carbon dioxide clearance. These findings emphasize that the cardiovascular status, rather than the NIV modality alone, is an important determinant of the ventilatory response and support a more individualized, physiology-guided approach to NIV selection in routine clinical practice.

Author contributions

A. M.: conceptualization, methodology, formal analysis, data curation, investigation, validation, writing – original draft preparation.
N. M.-V.: methodology, formal analysis, data curation, investigation, writing – original draft preparation, writing – review and editing.
N. P.: investigation, writing – review and editing.
A. M.: methodology, validation, supervision, writing – review and editing.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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