

Original Research Article

COMPARISON OF NUTRITIONAL AND RADIOLOGICAL PROFILE OF ACUTE EXACERBATION IN COPD PATIENTS WITH HYPERCAPNIC RESPIRATORY FAILURE WITH NON – HYPERCAPNIC RESPIRATORY FAILURE – A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) complicated by respiratory failure have substantial morbidity, but the relationship of nutritional depletion and structural lung disease with hypercapnia remains incompletely defined. The objective is to compare nutritional and radiological profiles of patients with AECOPD and hypercapnic versus non-hypercapnic respiratory failure.

Materials and Methods: In this prospective cross-sectional study, 400 admitted patients with COPD-related respiratory failure were analyzed; 220 had PaCO₂ >45 mmHg and 180 had PaCO₂ ≤45 mmHg. Arterial blood gases, nutritional and biochemical indices, chest imaging, radiological severity, and short-term outcomes were compared. Multivariable logistic regression identified factors associated with hypercapnia.

Results: Hypercapnic patients had lower pH, PaO₂, BMI, total lymphocyte count, total protein, serum albumin, transferrin, and serum iron, and higher PaCO₂ and urea (all p<0.001 except where stated). Severe radiological disease occurred in 46.8% versus 16.7% (p<0.001). Treatment success was lower with hypercapnia (73.2% vs 93.3%; p<0.001). Greater radiological severity was independently associated with hypercapnia (adjusted OR 3.73 per grade, 95% CI 2.30-6.04). The multivariable model showed strong apparent discrimination (AUC 0.945) and no important multicollinearity (maximum VIF 1.75).

Conclusion: Hypercapnic respiratory failure in AECOPD was associated with poorer nutritional indices, greater radiological severity, and less favorable short-term outcomes. Integrated nutritional, biochemical, and imaging assessment may improve bedside risk characterization.

Keywords: COPD; acute exacerbation; hypercapnia; respiratory failure; nutritional status; computed tomography; emphysema.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a heterogeneous respiratory disorder characterized by persistent airflow obstruction, chronic respiratory

symptoms, and structural abnormalities of the airways and alveoli. It remains a major global health problem. A systematic review and modelling analysis estimated a substantial worldwide prevalence of COPD in 2019, with marked variation according to age, sex, geography, smoking exposure, and

socioeconomic conditions.^[1] Global Burden of Disease analyses similarly demonstrate that COPD continues to cause millions of deaths and substantial disability despite reductions in age-standardized mortality in several regions.^[2] These observations emphasize the need to identify clinically relevant phenotypes that influence deterioration during acute illness.

Acute exacerbations are pivotal events in the natural history of COPD because they worsen health status, increase subsequent exacerbation risk, accelerate functional decline, and contribute to hospitalization and mortality. Contemporary reviews describe COPD as a multidimensional disease in which prognosis reflects more than spirometric impairment alone.^[3] Symptoms, systemic manifestations, comorbidities, gas-exchange abnormalities, respiratory muscle reserve, and structural lung damage all contribute to clinical severity.^[4] During a severe exacerbation, failure of alveolar ventilation may cause carbon-dioxide retention and respiratory acidosis, frequently requiring close monitoring and ventilatory support. Hypercapnia may arise through severe airflow obstruction, dynamic hyperinflation, ventilation-perfusion mismatch, increased physiological dead space, respiratory muscle fatigue, or reduced ventilatory drive.

Exacerbations themselves represent complex clinical events rather than isolated increases in cough, sputum, or dyspnea.^[5] Nutritional status may be particularly relevant because COPD can produce reduced oral intake, systemic inflammation, elevated energy expenditure, and progressive loss of skeletal and respiratory muscle mass. Malnutrition has been associated with impaired muscle function, reduced exercise tolerance, greater healthcare utilization, and adverse prognosis in COPD.^[6] A recent systematic review and meta-analysis also documented a substantial burden of malnutrition or nutritional risk and linked poor nutritional status with worse lung function, dyspnea, exercise limitation, and mortality.^[7]

Acute hypercapnic respiratory failure is especially important because it reflects inadequate alveolar ventilation rather than hypoxaemia alone. The arterial carbon-dioxide level integrates ventilatory load, respiratory muscle capacity, and effective minute ventilation. Patients with similar oxygenation may differ substantially in carbon-dioxide retention and clinical reserve. Recognizing hypercapnia-associated characteristics may help identify patients needing repeated blood-gas assessment, noninvasive ventilatory support, or escalation of care during hospital admission. Nutritional depletion may impair respiratory muscle performance, while advanced emphysematous or airway disease may increase mechanical load and dead-space ventilation. Evaluating these domains together offers a practical framework for understanding why some exacerbations progress to ventilatory failure. Thoracic imaging provides complementary information regarding emphysema, hyperinflation,

airway abnormalities, bronchiectatic change, infiltrates, and overall structural disease burden. Yet nutritional depletion and radiological severity are rarely evaluated together in hospitalized AECOPD patients with respiratory failure. Identifying routinely available nutritional and imaging features associated with hypercapnia could improve early clinical characterization when formal pulmonary-function testing is impractical. Therefore, this study compared nutritional and radiological profiles in AECOPD patients with hypercapnic versus non-hypercapnic respiratory failure, examined relationships between PaCO₂ and nutritional or radiological severity, and evaluated independent factors associated with hypercapnia.

MATERIALS AND METHODS

Study design and setting: This prospective cross-sectional study was conducted over six months in the Departments of Respiratory Medicine and Emergency Medicine at Himalayan Hospital, Jolly Grant, Dehradun, India. Adults admitted with an acute exacerbation of established COPD complicated by respiratory failure were eligible. COPD diagnosis and exacerbation status were documented by the treating respiratory team using contemporary clinical principles consistent with the Global Initiative for Chronic Obstructive Lung Disease strategy.^[8] The study protocol planned enrollment of 400 participants and specified informed consent from participants or legally authorized representatives. Patients in whom another condition was considered the dominant cause of respiratory failure were excluded.

Exposure definition and participants: The analysis included 400 complete records. Hypercapnic respiratory failure was operationally defined as PaCO₂ >45 mmHg and non-hypercapnic respiratory failure as PaCO₂ ≤45 mmHg; these thresholds reproduced the recorded group labels without discordance. Arterial pH, PaCO₂, and PaO₂ were analyzed as continuous variables. The clinical relevance of identifying acute hypercapnic respiratory failure in COPD is supported by ERS/ATS guidance on noninvasive ventilation.^[9] Demographic variables included age and sex; treatment history and comorbidities were recorded descriptively.

Nutritional assessment: Weight and height were measured or recorded during admission, and BMI was calculated as weight in kilograms divided by height in meters squared. The dataset's ordinal nutritional category corresponded exactly to BMI cut points: none, BMI ≥18.5 kg/m²; mild underweight, 17.0-18.49; moderate underweight, 16.0-16.99; and severe underweight, <16.0 kg/m². Because GLIM diagnosis requires both phenotypic and etiologic assessment, these BMI-only categories were treated as underweight severity rather than as definitive GLIM malnutrition.^[10] Additional variables were total lymphocyte count, total protein, serum albumin,

urea, creatinine, transferrin, and serum iron. BMI and albumin were retained because nutritional measures have shown prognostic value in COPD with respiratory failure.^[11]

Radiological and outcome assessment: Chest radiograph findings, CT lung patterns, and a recorded ordinal radiological severity grade (mild, moderate, severe) were abstracted directly from study records. CT provides structural information complementary to functional assessment by characterizing emphysema, air trapping, lung volumes, and airway abnormalities.^[12] Short-term outcomes were treatment success, clinical improvement, and radiological improvement, each recorded as yes or no. The study protocol did not provide a reproducible scoring rubric for radiological grade or formal operational definitions for the three clinical outcomes; analyses therefore used the recorded classifications without retrospective redefinition.

Data quality and sample size: The prespecified target sample was 400 participants, and all 400 available records met the completeness requirements for the variables used in analyses; therefore, no imputation was performed. Range and consistency checks were undertaken for demographic, gas-exchange, nutritional, biochemical, imaging, and outcome variables before analysis. Group coding was cross-checked against PaCO₂ values. Because the original protocol did not specify the assumptions used for its sample-size calculation, no post hoc reconstruction of effect size or power was introduced into the manuscript. This avoids presenting unverified design assumptions as if they had been prespecified.

Statistical analysis: Continuous variables were summarized as mean $\pm$ standard deviation and categorical variables as frequency and percentage. Groups were compared using Welch independent-

samples t tests and chi-square tests. Mean differences were reported with 95% confidence intervals; Hedges g and Cramer's V quantified effect size where appropriate. Spearman correlation assessed PaCO₂ against ordinal underweight and radiological severity. Multivariable logistic regression used hypercapnic respiratory failure as the dependent variable and prespecified demographic, nutritional, biochemical, and radiological covariates. Adjusted odds ratios with 95% confidence intervals were reported. Multicollinearity was assessed using variance inflation factors. Apparent model performance was summarized by area under the receiver-operating-characteristic curve, Brier score, and Hosmer-Lemeshow goodness-of-fit test. Two-sided $p < 0.05$ indicated statistical significance; complete-case analysis was used.

RESULTS

Participant characteristics and gas exchange: All 400 records were complete for variables included in the primary analyses. Hypercapnic respiratory failure was present in 220 patients (55.0%), while 180 (45.0%) were non-hypercapnic. The cohort mean age was 66.63 years and 301 participants (75.3%) were male. Hypercapnic patients were older than non-hypercapnic patients (68.55 $\pm$ 8.86 vs 64.28 $\pm$ 8.22 years), with a mean difference of 4.26 years (95% CI 2.58-5.94; $p < 0.001$). Male sex was more frequent with hypercapnia (79.1% vs 70.6%), although the unadjusted group difference was not statistically significant ($p = 0.064$). Gas-exchange differences were large: pH was lower (7.31 vs 7.39), PaCO₂ higher (64.66 vs 37.98 mmHg), and PaO₂ lower (54.63 vs 60.35 mmHg) in hypercapnic patients (all $p < 0.001$) [Table 1].

Table 1: Demographic and arterial blood gas characteristics

Variable	Hypercapnic (n=220)	Non-hypercapnic (n=180)	Mean difference (95% CI)	Effect size	p value
Age (years)	68.55 $\pm$ 8.86	64.28 $\pm$ 8.22	4.26 (2.58 to 5.94)	$g = 0.50$	< 0.001
Male sex, n (%)	174 (79.1)	127 (70.6)	-	$V = 0.10$	0.064
pH	7.31 $\pm$ 0.04	7.39 $\pm$ 0.03	-0.08 (-0.09 to -0.07)	$g = -2.18$	< 0.001
PaCO ₂ (mmHg)	64.66 $\pm$ 9.43	37.98 $\pm$ 3.84	26.67 (25.30 to 28.04)	$g = 3.57$	< 0.001
PaO ₂ (mmHg)	54.63 $\pm$ 8.13	60.35 $\pm$ 8.34	-5.72 (-7.35 to -4.09)	$g = -0.69$	< 0.001

Values are mean $\pm$ SD unless otherwise indicated. Continuous-variable comparisons used Welch t tests; male sex used chi-square with Yates continuity correction. g, Hedges g; V, Cramer's V.

Table 2: Nutritional and biochemical profile by respiratory-failure group

Variable	Hypercapnic (n=220)	Non-hypercapnic (n=180)	Mean difference (95% CI)	Effect size	p value
Weight (kg)	56.31 $\pm$ 12.61	59.90 $\pm$ 11.75	-3.60 (-5.99 to -1.20)	$g = -0.29$	0.003
BMI (kg/m ²)	20.99 $\pm$ 4.18	22.63 $\pm$ 4.03	-1.64 (-2.45 to -0.83)	$g = -0.40$	< 0.001
Total lymphocyte count (cells/mm ³)	1268.84 $\pm$ 373.60	1639.71 $\pm$ 438.91	-370.87 (-452.07 to -289.67)	$g = -0.92$	< 0.001
Total protein (g/dL)	6.29 $\pm$ 0.53	6.65 $\pm$ 0.49	-0.35 (-0.45 to -0.25)	$g = -0.69$	< 0.001
Serum albumin (g/dL)	3.25 $\pm$ 0.45	3.67 $\pm$ 0.44	-0.42 (-0.50 to -0.33)	$g = -0.93$	< 0.001
Urea (mg/dL)	40.58 $\pm$ 13.44	36.27 $\pm$ 9.99	4.31 (2.00 to 6.62)	$g = 0.36$	< 0.001
Creatinine (mg/dL)	1.07 $\pm$ 0.29	0.98 $\pm$ 0.22	0.09 (0.04 to 0.14)	$g = 0.35$	< 0.001
Transferrin	195.27 $\pm$ 32.88	226.32 $\pm$ 37.36	-31.05 (-38.05 to -24.05)	$g = -0.89$	< 0.001
Serum iron	58.24 $\pm$ 17.67	71.80 $\pm$ 20.92	-13.56 (-17.42 to -9.70)	$g = -0.70$	< 0.001

Negative mean differences indicate lower values in the hypercapnic group. BMI, body mass index; g, Hedges g.

Nutritional and biochemical profile: Hypercapnic patients had lower mean weight (56.31 vs 59.90 kg; $p=0.003$) and BMI (20.99 vs 22.63 kg/m²; mean difference -1.64, 95% CI -2.45 to -0.83; $p<0.001$) [Table 2; Figure 1]. Total lymphocyte count was lower by 371 cells/mm³ (95% CI -452 to -290; $p<0.001$). Total protein (6.29 vs 6.65 g/dL), serum albumin (3.25 vs 3.67 g/dL), transferrin (195.27 vs 226.32), and serum iron (58.24 vs 71.80) were also lower (all $p<0.001$). Urea (40.58 vs 36.27 mg/dL) and creatinine (1.07 vs 0.98 mg/dL) were higher (both $p<0.001$). Moderate or severe underweight occurred in 16.4% of hypercapnic patients versus 6.7% of non-hypercapnic patients. The overall underweight-category distribution differed between groups ($p=0.022$; Cramer's $V=0.155$). PaCO₂ correlated weakly with increasing underweight severity (Spearman $\rho=0.123$; $p=0.014$).

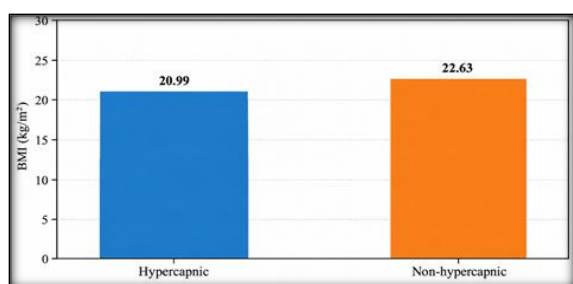


Figure 1: Mean BMI by respiratory-failure group

Radiological profile and short-term outcomes: Radiological severity differed substantially between

groups ($p<0.001$; Cramer's $V=0.435$) [Table 3]. Severe radiological disease was recorded in 46.8% of hypercapnic patients versus 16.7% of non-hypercapnic patients, whereas mild disease occurred in 8.6% versus 42.8% (Figure 2). PaCO₂ correlated positively with radiological grade ($\rho=0.333$; $p<0.001$). CT-pattern distributions also differed ($p<0.001$; Cramer's $V=0.462$), with extensive, panlobular, bullous, and emphysema-plus-bronchiectasis patterns more concentrated in the hypercapnic group. Treatment success was lower with hypercapnia (73.2% vs 93.3%; risk ratio 0.78, 95% CI 0.72-0.86; $p<0.001$). Clinical improvement was also lower (80.9% vs 91.1%; risk ratio 0.89, 95% CI 0.82-0.96; $p=0.004$), while radiological improvement did not differ significantly (71.8% vs 77.8%; $p=0.174$).

Effect sizes supported the statistical comparisons. The standardized difference was moderate for age (Hedges $g=0.50$), very large for pH ($g=-2.18$) and PaCO₂ ($g=3.57$), and moderate-to-large for PaO₂ ($g=-0.69$). Nutritional differences were largest for serum albumin ($g=-0.93$), total lymphocyte count ($g=-0.92$), transferrin ($g=-0.89$), and serum iron ($g=-0.70$), while BMI showed a smaller-to-moderate difference ($g=-0.40$). These estimates indicate that the observed group differences were not explained solely by the large sample size. For categorical variables, the strongest associations were seen for CT pattern (Cramer's $V=0.462$) and radiological severity ($V=0.435$), while BMI-based underweight severity showed a smaller association ($V=0.155$).

Table 3: Underweight category, CT pattern, radiological severity, and short-term outcomes

Characteristic	Hypercapnic (%)	n	Non-hypercapnic n (%)	Effect estimate	p value
BMI-based underweight: None	161 (73.2)		152 (84.4)	V=0.155	0.022
Mild	23 (10.5)		16 (8.9)		
Moderate	16 (7.3)		5 (2.8)		
Severe	20 (9.1)		7 (3.9)		
CT pattern: Mild centrilobular emphysema	10 (4.5)		39 (21.7)	V=0.462	<0.001
Moderate centrilobular emphysema	43 (19.5)		43 (23.9)		
Mixed emphysema	26 (11.8)		18 (10.0)		
Bullous emphysema	23 (10.5)		11 (6.1)		
Panlobular emphysema	19 (8.6)		2 (1.1)		
Extensive emphysema	38 (17.3)		11 (6.1)		
Emphysema + bronchiectasis	52 (23.6)		18 (10.0)		
Airway wall thickening	3 (1.4)		27 (15.0)		
Focal emphysematous changes	6 (2.7)		11 (6.1)		
Radiological severity: Mild	19 (8.6)		77 (42.8)	V=0.435	<0.001
Moderate	98 (44.5)		73 (40.6)		
Severe	103 (46.8)		30 (16.7)		
Treatment success: Yes	161 (73.2)		168 (93.3)	RR 0.78 (0.72-0.86)	<0.001
Clinical improvement: Yes	178 (80.9)		164 (91.1)	RR 0.89 (0.82-0.96)	0.006
Radiological improvement: Yes	158 (71.8)		140 (77.8)	RR 0.92 (0.82-1.03)	0.213

Overall p values for multi-category variables are Pearson chi-square tests; binary outcomes use chi-square with Yates continuity correction. V, Cramer's V; RR, risk ratio; CI, confidence interval.

Multivariable analysis: After adjustment, older age, male sex, lower BMI, lower lymphocyte count, lower albumin, lower total protein, higher urea, lower transferrin, lower serum iron, and greater radiological severity were independently associated with hypercapnia [Table 4; Figure 3]. Radiological severity showed a strong graded association (adjusted

OR 3.73 per category, 95% CI 2.30-6.04; $p<0.001$). Creatinine and BMI-based underweight grade were not independently significant. The adjusted associations were directionally consistent with the univariable findings. Each 1-year increase in age increased the odds of hypercapnia by 6%, and male sex more than doubled the odds. Conversely, higher

BMI, lymphocyte count, albumin, total protein, transferrin, and iron reduced the adjusted odds. A 10 mg/dL increase in urea increased the odds by approximately 49% after adjustment. Maximum VIF

was 1.75, indicating no important multicollinearity. The model had an apparent AUC of 0.945, Brier score 0.092, McFadden pseudo-R² of 0.569, and Hosmer-Lemeshow p=0.061.

Table 4: Multivariable logistic regression for hypercapnic respiratory failure

Variable	Adjusted OR	95% CI	p value
Age (per year)	1.06	1.02-1.11	0.002
Male sex	2.56	1.15-5.70	0.021
BMI (per kg/m ²)	0.89	0.81-0.98	0.021
Total lymphocyte count (per 100 cells/mm ³)	0.80	0.73-0.88	<0.001
Albumin (per g/dL)	0.11	0.05-0.25	<0.001
Total protein (per g/dL)	0.20	0.10-0.40	<0.001
Urea (per 10 mg/dL)	1.49	1.11-2.00	0.008
Creatinine (per mg/dL)	2.39	0.62-9.16	0.205
Transferrin (per 10 units)	0.77	0.70-0.85	<0.001
Serum iron (per 10 units)	0.79	0.67-0.93	0.006
BMI-based underweight grade (per category)	1.04	0.62-1.73	0.886
Radiological grade (per category)	3.73	2.30-6.04	<0.001

Model diagnostics: apparent AUC=0.945; Brier score=0.092; McFadden pseudo-R²=0.569; Hosmer-Lemeshow p=0.061; maximum VIF=1.75. OR, odds ratio; CI, confidence interval; VIF, variance inflation factor.

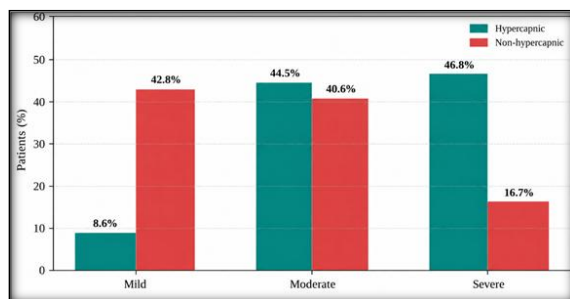


Figure 2: Radiological severity by respiratory-failure group.

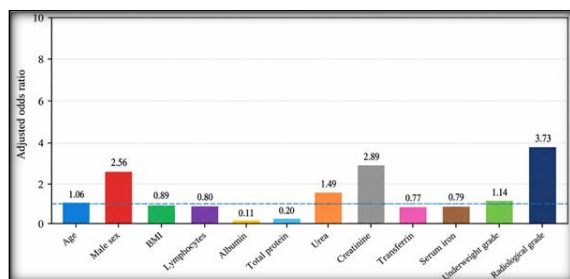


Figure 3: Adjusted odds ratios for hypercapnic respiratory failure

DISCUSSION

This study identified a coherent clinical phenotype among patients hospitalized with AECOPD and hypercapnic respiratory failure: greater nutritional depletion, more severe radiological disease, and poorer short-term treatment response. Hypercapnic patients had lower BMI, lymphocyte count, total protein, albumin, transferrin, and iron, while urea and creatinine were higher. These findings are biologically plausible and align with a meta-analysis in AECOPD showing low serum albumin as a risk marker for acute type II respiratory failure.^[13] The combination of lower albumin and higher urea is also clinically relevant because the blood urea nitrogen-to-albumin ratio has been associated with in-hospital and 90-day mortality during AECOPD.^[14]

The nutritional signal was multidimensional rather than restricted to body weight. COPD may promote inadequate intake, inflammation, increased work of breathing, and loss of fat-free mass, all of which can reduce respiratory muscle reserve. Evidence reviews indicate that appropriately targeted nutritional support can improve energy intake, body weight, and selected functional outcomes in nutritionally depleted COPD populations.^[15] In the present adjusted analysis, lower BMI remained associated with hypercapnia even after accounting for several biochemical measures. This is consistent with a large 2024 dose-response meta-analysis in which underweight status was associated with increased mortality and BMI showed a nonlinear relationship with COPD outcomes.^[16] Importantly, the study's BMI-based underweight grade was only weakly correlated with PaCO₂ and was not independently significant after adjustment, suggesting that continuous nutritional and biochemical variables retained more information than the ordinal category. Radiological severity provided an additional and comparatively strong signal. Increasing radiological grade correlated with PaCO₂ and remained independently associated with hypercapnic respiratory failure. Quantitative CT research has shown that emphysema and air-trapping measures can characterize functional impairment beyond conventional spirometry.^[17] Visual emphysema severity has also been related to GOLD stage and lower BMI, linking structural lung destruction with systemic vulnerability.^[18] In this cohort, severe radiological disease was almost threefold more frequent among hypercapnic patients. Extensive parenchymal destruction and air trapping may increase physiological dead space, worsen ventilation-perfusion mismatch, and reduce ventilatory reserve during an exacerbation, providing a plausible mechanism for the observed association. Short-term outcomes were also less favorable with hypercapnia. Treatment success and clinical

improvement were lower, whereas radiological improvement did not differ significantly. Observational evidence indicates that delayed recognition of acute hypercapnic respiratory failure among COPD patients treated with ward-based noninvasive ventilation is associated with higher in-hospital mortality.^[19] The NIVO study likewise demonstrated that readily available clinical variables can stratify mortality risk among AECOPD patients requiring assisted ventilation.^[20] Together, these findings support early recognition of hypercapnic physiology and systematic assessment of factors that may reflect reduced reserve.

This study has strengths, including a balanced sample size, complete primary data, effect-size reporting, explicit hypercapnia definition, and multivariable analysis with collinearity and model-performance checks. Limitations remain important. The study was single-center and cross-sectional, precluding causal inference. Smoking exposure, spirometric severity, dyspnea scores, inflammatory biomarkers, body-composition measurements, ventilatory-treatment details, length of stay, and mortality were unavailable. The radiological grade and short-term outcome labels lacked prespecified scoring criteria, limiting reproducibility. Apparent model performance was estimated in the same dataset and therefore requires external validation. Prospective studies using standardized nutritional tools, quantitative CT, pulmonary function, and longitudinal outcomes should test whether combined nutritional-radiological assessment improves clinically meaningful risk stratification. This convergence across domains strengthens the internal coherence of findings.

CONCLUSION

Among patients hospitalized with acute exacerbation of COPD and respiratory failure, hypercapnia was associated with a distinct pattern of physiological, nutritional, biochemical, and radiological vulnerability. Compared with non-hypercapnic patients, those with PaCO₂ >45 mmHg had lower pH and PaO₂, lower BMI, reduced lymphocyte count, lower total protein, albumin, transferrin, and serum iron, and substantially greater radiological severity. Treatment success and clinical improvement were less frequent in the hypercapnic group.

The adjusted analysis reinforced the multidimensional nature of this phenotype. Older age, male sex, lower BMI, poorer nutritional and biochemical indices, higher urea, and increasing radiological severity were independently associated with hypercapnic respiratory failure, while radiological severity showed one of the strongest graded associations. The model demonstrated strong apparent discrimination without important multicollinearity, but its performance requires external validation.

These findings support integrating arterial blood gas results with simple nutritional measures and thoracic imaging when characterizing patients admitted with severe COPD exacerbations. Such an approach may help clinicians recognize patients with reduced ventilatory reserve and prioritize monitoring and supportive assessment. Future prospective studies should use standardized nutritional diagnoses, reproducible quantitative or visual CT scoring, spirometric data, and longitudinal outcomes to determine whether this combined assessment improves prognosis or guides treatment decisions.

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