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Article

Cardiometabolic Profile Analysis of Patients with COPD-Related Type 2 Respiratory Failure in the Intensive Care Unit

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Abstract: Objectives: Chronic Obstructive Pulmonary Disease (COPD) is a significant cause of morbidity and mortality worldwide and can become complicated by Type 2 respiratory failure. This study aimed to analyze the cardiological and metabolic comorbidities of patients admitted to the Intensive Care Unit (ICU) due to COPD-related Type 2 respiratory failure and evaluate their effects on clinical outcomes. **Methods:** A retrospective analysis was conducted on 258 patients admitted to the Secondary-Level Pulmonary Diseases Intensive Care Unit between January 2022 and January 2024. Patients' demographic data, cardiological and metabolic comorbidities, laboratory parameters, and ICU-related variables were evaluated using statistical analysis methods. **Results:** The most common comorbidities were hypertension (57.0%), congestive heart failure (48.1%), diabetes mellitus (31.4%), and obesity (37.6%). Female patients had significantly higher rates of hypothyroidism, hypertension, obesity, and congestive heart failure compared to males. Patients diagnosed with chronic kidney disease (CKD) had significantly higher cardiothoracic ratios and proBNP levels. ICU length of stay was significantly longer in patients with acute kidney injury (AKI) and coronary artery disease (CAD). Cardiomegaly and obstructive sleep apnea syndrome (OSAS) were more frequently observed in obese patients. Additionally, in COPD patients, a body mass index (BMI) threshold of 25.5 was determined as a cutoff value for radiological cardiomegaly findings with a sensitivity of 69.9% and specificity of 59.5%. Elevated pCO₂ and bicarbonate levels in patients receiving long-term oxygen therapy (LTOT) were associated with advanced-stage COPD. **Conclusion:** Metabolic and cardiological comorbidities significantly impact the clinical prognosis and ICU management of patients diagnosed with COPD and Type 2 respiratory failure. Special attention should be given to monitoring female and obese patients. Future studies should explore how individualized and preventive follow-up and treatment approaches can improve patient outcomes.

Keywords: COPD; type 2 respiratory failure; metabolic profile; intensive care unit; comorbidities; obesity

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive inflammatory lung disease that represents a significant cause of morbidity and mortality worldwide. Type 2 respiratory failure associated with COPD, characterized by hypercapnia and hypoxemia, typically manifests in advanced stages of the disease and often necessitates admission to the intensive care unit (ICU). Analyzing the cardiometabolic profiles and comorbidities of this patient group is crucial for developing more effective strategies for disease management [1,2].

Cardiometabolic profiles, the interplay between respiratory functions, and comorbidities can have a direct impact on the prognosis of COPD patients. Specifically, conditions such as obesity, chronic kidney disease (CKD), acute kidney injury (AKI), diabetes mellitus (DM), hypothyroidism, and anemia can significantly influence clinical outcomes in patients with COPD-related Type 2 respiratory failure. For instance, obesity has been shown to impair respiratory muscle function and increase the need for mechanical ventilation [3,4]. Additionally, DM exacerbates inflammation levels, complicating therapeutic responses and elevating infection risks in COPD patients [5]. Hypothyroidism, by slowing metabolism and reducing energy expenditure, may lead to weight gain and obesity, both of which negatively impact respiratory functions [6]. Anemia, on the other hand, compromises oxygen delivery to tissues, reducing exercise tolerance and exacerbating dyspnea, especially in COPD patients [7].

Furthermore, the coexistence of hypothyroidism and Obstructive Sleep Apnea Syndrome (OSAS) has been reported to further deteriorate respiratory functions in COPD patients and heighten the risk of hypoxemia. This underscores the importance of screening for hypothyroidism in patients with concurrent COPD and OSAS [8].

The impact of these comorbidities, which accompany Type 2 respiratory failure, on ICU length of stay and response to treatment is among the frequently studied topics in the literature. Particularly in cases of hypercapnic respiratory failure, it has been reported that hospital length of stay is significantly influenced by comorbidities and clinical parameters [9]. Furthermore, the interactions between various metabolic conditions and comorbidities clearly complicate clinical management, underscoring the need for individualized approaches and perspectives in this patient group.

Materials and Methods

This study was initiated after obtaining ethical approval (Approval Number:, Date:) from the Ethics Committee of Training and Research Hospital. Patient files of all individuals admitted to the Secondary Level Respiratory Intensive Care Unit between January 2022 and January 2024 were reviewed. A total of 498 patient files were examined. Among these, 401 patients were diagnosed with COPD based on their Pulmonary Function Test (PFT) results and clinical characteristics. Of these patients, 339 were diagnosed with Type 2 respiratory failure according to Arterial Blood Gas (ABG) results and were admitted to the ICU.

Six patients were excluded from the study as they had left the consent box blank in the ICU admission consent form, which routinely includes a section allowing the use of medical information for research purposes. Additionally, 23 patients were excluded due to being transferred to other ICUs for various reasons. Furthermore, 52 patients were excluded as they passed away during their ICU stay. As a result, a total of 258 patients were included in the study (Figure 1).

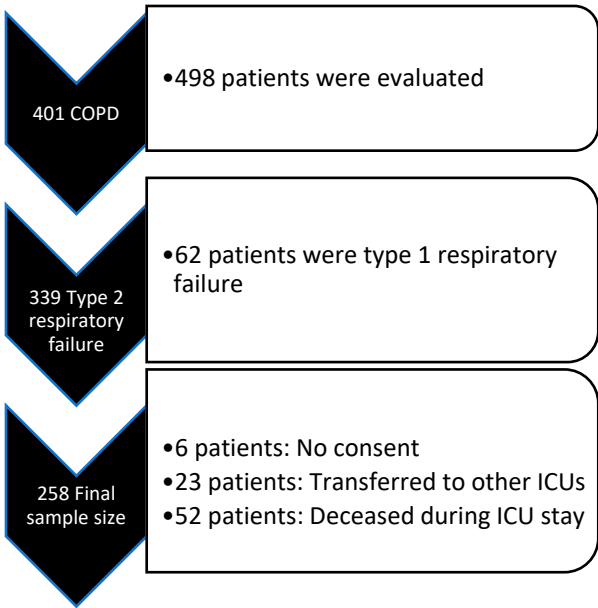


Figure 1. Study design.

Inclusion and Exclusion Criteria

All patients aged 18 years or older, diagnosed with COPD based on Pulmonary Function Tests (PFTs) and clinical findings, diagnosed with Type 2 respiratory failure according to arterial blood gas analysis, and who provided consent for the use of their medical data were included in the study.

Patients were excluded if they:

- Were transferred to another ICU or hospital for any reason after being admitted to the ICU,
- Passed away during their ICU stay for any reason, or
- Did not provide consent for the use of their medical data as indicated on their ICU admission forms.

A total of 258 patients meeting the inclusion criteria were enrolled in the study. Data collected included demographic information such as age, gender, and Charlson Comorbidity Index (CCI), as well as the presence of metabolic, endocrinological, and cardiac diseases, particularly significant comorbidities such as Diabetes Mellitus (DM), Hypertension (HT), Hypothyroidism, Chronic Kidney Disease (CKD), Acute Kidney Injury (AKI), Congestive Heart Failure (CHF), Coronary Artery Disease (CAD), and Obstructive Sleep Apnea Syndrome (OSAS).

Patients’ body mass index (BMI) and cardiothoracic ratios (CTRs) derived from posteroanterior chest X-rays (PA-CXRs) were documented, along with the presence of cardiomegaly determined from these ratios. Laboratory parameters at ICU admission were recorded, including pH, partial carbon dioxide pressure (pCO₂), serum bicarbonate levels, C-reactive protein (CRP), sodium, potassium, magnesium, albumin, pro-brain natriuretic peptide (proBNP), blood urea nitrogen (BUN), creatinine, T4, and thyroid-stimulating hormone (TSH).

CRP and other laboratory results obtained immediately before ICU discharge were also recorded for comparison with admission values. Additionally, whether patients required nutritional support during their ICU stay, were receiving long-term oxygen therapy (LTOT) at home prior to ICU admission, or were anemic based on hemoglobin (HGB) levels (defined as <12 g/dL in men and <11 g/dL in women) at admission was documented.

Statistical Analysis

The statistical analyses were conducted using IBM SPSS Statistics Version 27 (IBM Corp., Armonk, NY, USA). Categorical nominal data were presented as n (%). Ordinal data or numerical

data that did not follow a normal distribution were presented as median (min-max), while numerical data with normal distribution were expressed as mean $\pm$ standard deviation (SD).

In the patient group, for categorical variables, the chi-square test was applied when all cells contained more than 5 patients; otherwise, Fisher’s exact test was used when at least one cell contained fewer than 5 patients. Numerical data were analyzed using the Student’s t-test if normally distributed or the Mann-Whitney U test if not. The normality of numerical data was evaluated using descriptive statistics, Kolmogorov-Smirnov and Shapiro-Wilk tests, skewness-kurtosis values, histograms, and the proximity of outliers.

For bivariate correlation analyses, Spearman correlation was applied if at least one of the numerical variables was non-normally distributed, while Pearson correlation was used if both variables were normally distributed. Effect sizes were reported using Cohen's d value when significant differences were observed between group means for normally distributed numerical variables.

ROC (Receiver Operating Characteristic) analyses were performed, and the area under the curve (AUC) was presented along with the upper and lower confidence intervals. The cutoff values of ROC curves were reported with their respective sensitivity and specificity percentages.

For all statistical analyses, a 95% confidence interval (CI) was used, and a p-value of <0.05 was considered statistically significant.

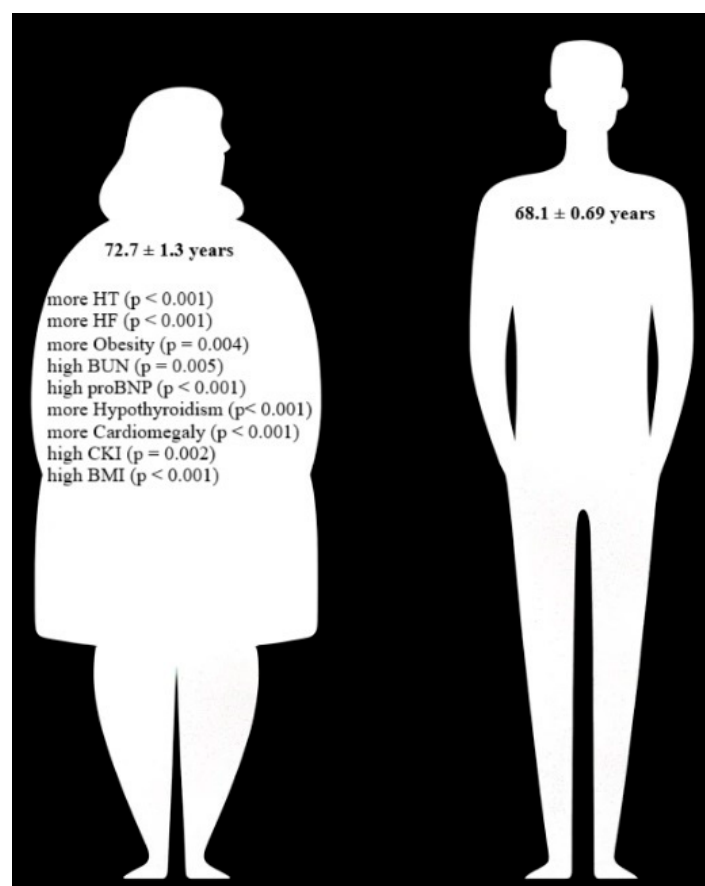
Results

Of the 258 patients included in the study, 167 were male, and 90 were female. The mean age of female patients was calculated as 72.7 ± 1.3 years, while the mean age of male patients was 68.1 ± 0.69 years. Female patients were significantly older than male patients ($p: 0.005$, Cohen’s d: 0.418).

In female patients diagnosed with COPD and admitted to the ICU with Type 2 respiratory failure, the prevalence of hypothyroidism, hypertension (HT), congestive heart failure (CHF), and obesity was significantly higher compared to male patients. Additionally, Charlson Comorbidity Index (CCI), body mass index (BMI), cardiothoracic ratio (CTR), blood urea nitrogen (BUN), and pro-brain natriuretic peptide (proBNP) values were significantly higher in female patients (Figure 2). In our study, hypertension (HT) and congestive heart failure (CHF) emerged as the most common comorbidities observed in Type 2 respiratory failure associated with COPD (Table 1).

Table 1. Prevalence of Comorbidities in Patients with Type 2 Respiratory Failure Associated with COPD.

Comorbidity	Prevalence (%)
Hypertension (HT)	57.0
Diabetes Mellitus (DM)	31.4
Coronary Artery Disease (CAD)	20.2
Chronic Kidney Disease (CKD)	17.1
Acute Kidney Injury (AKI)	10.9
Congestive Heart Failure (CHF)	48.1
Anemia	25.2
Hypothyroidism	7.8
Obesity	37.6



BMI: Body mass index, BUN: Blood urea nitrogen, CKI: Charlson komorbidity index, HF: Heart failure, HT: Hypertension, proBNP: Pro-B-type natriuretic peptide

Figure 2. comparison of cardiometabolic profiles between genders.

Chronic Kidney Disease, Acute Kidney Failure

Our study data showed that in COPD patients followed up in the ICU with a clinical picture of Type 2 respiratory failure, CKD was associated with a significantly higher cardiothoracic ratio compared to patients without CKD (p<0.001). Moreover, the laboratory values revealed a significantly higher proBNP level at the time of ICU admission (p=0.002). In addition, the incidence of cardiomegaly was significantly higher as determined radiologically (p=0.015). From the metabolic point of view, the BMI of patients with CKD was significantly higher than that of patients without CKD (p=0.023). Regardless of the diagnosis of CKD, patients who were admitted to the ICU with a diagnosis of acute kidney failure in addition to COPD-Type 2 respiratory failure had a significantly longer stay in the ICU (p=0.036).

Congestive Heart Failure

In patients with a diagnosis of CHF, similar to those with a diagnosis of CKD, the values of BMI were significantly higher compared to patients without a diagnosis of CHF (p=0.002). In our study, the presence of CHF was also associated with the impairment of renal functions. Mean values of BUN, creatinine, and potassium upon admission to the ICU were significantly higher in cases with a diagnosis of CHF as compared to those without CHF diagnosis (p<0.001, p<0.001, p=0.021, respectively).

Hypertension

Compared to the group without an active diagnosis of HT, the BMI values of patients with a diagnosis of HT were significantly higher ($p<0.001$). Moreover, BUN, creatinine, and proBNP values upon ICU admission were significantly higher in HT compared with non-HT patients (for all three values: $p<0.001$). Further, in patients with HT, the cardiothoracic ratio was higher with a higher incidence of cardiomegaly and proBNP level (for both values: $p<0.001$). DM constituted the major comorbidity associated with HT ($p<0.001$). Comparing the HT patients admitted to the ICU with non-HT patients, no significant difference could be demonstrated in admission CRP levels. However, a significant difference was noted in the CRP levels measured just before ICU discharge after treatments. Discharge CRP levels among HT patients were significantly higher compared with those without HT ($p=0.021$).

Diabetes Mellitus

Patients with a diagnosis of DM presented with significantly higher ICU admission creatinine levels compared to those without DM ($p=0.003$). Similarly, the incidence of AKI was significantly higher in this patient group ($p=0.007$). Additionally, patients with DM showed a significantly higher prevalence of obesity and CAD ($p=0.003$ and $p<0.001$, respectively).

Hypothyroidism

In the analysis of patients with hypothyroidism as an additional comorbidity or metabolic disease, the only significant and noteworthy finding was the higher incidence of OSAS in patients with hypothyroidism ($p=0.001$). Additionally, radiological evaluations revealed that chest diameters were smaller in patients with hypothyroidism compared to those without ($p=0.025$). This finding may be associated with the higher prevalence of hypothyroidism among female patients.

Coronary Artery Disease

Patients presenting to the ICU with a diagnosis of CAD had significantly higher BUN levels ($p=0.015$). Additionally, ICU length of stay was significantly longer in patients with CAD compared to those without a CAD diagnosis ($p=0.024$).

Anemia

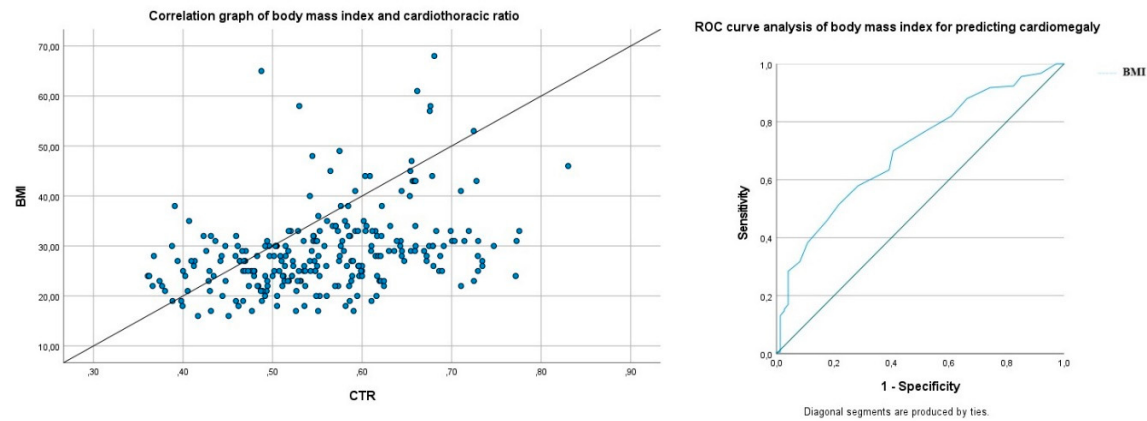
As expected, patients with anemia had significantly higher CKI values ($p<0.001$). Anemic patients were older and had lower albumin, magnesium, and potassium levels, while their TSH and proBNP levels were higher ($p=0.011$, $p<0.001$, $p=0.003$, $p=0.037$, $p=0.008$, and $p=0.03$, respectively). Similar to patients with HT, no significant difference was found in ICU admission CRP levels between anemic and non-anemic patients. However, when comparing CRP levels just before discharge, anemic patients had significantly higher CRP levels ($p=0.039$). A Wilcoxon signed-rank test performed on all patients revealed that among 258 patients, CRP levels decreased in 200, increased in 49, and remained unchanged in 9 patients. Moreover, the decrease in CRP levels was significantly greater than the increase in CRP levels ($p<0.001$). Patients with diagnoses of both HT and anemia stood out with higher discharge CRP levels compared to those with other metabolic conditions or comorbidities.

Obesity

CKI values were significantly higher in obese patients ($p=0.023$). Additionally, these patients had higher ICU admission magnesium and creatinine levels, while their serum bicarbonate levels were lower ($p=0.017$, $p<0.001$, and $p=0.049$, respectively). However, no significant difference was found in admission pH levels compared to non-obese patients. The incidence of cardiomegaly and OSAS was significantly higher in obese patients compared to non-obese patients (for both results: $p<0.001$).

In our statistical analysis evaluating the correlation between BMI and cardiothoracic ratio (CTR) values, a moderately positive significant correlation was identified between the two variables

(Spearman, $p < 0.001$, $r = 0.404$, minimum: 0.293, maximum: 0.504, 95% confidence interval, Figure 3). Subsequently, using a ROC analysis between BMI and the radiological presence of cardiomegaly (cardiothoracic ratio > 0.5), a cutoff value of 25.5 was determined with a sensitivity of 69.9% and a specificity of 59.5% ($p < 0.001$, area under the curve - AUC: 0.704, CI: 0.636-0.771, Figure 3).



BMI: Body mass index, CTR: Cardiothoracic ratio

Figure 3. Correlation graph of body mass index and cardiothoracic ratio, and ROC curve of body mass index for predicting cardiomegaly.

Pleural Effusion

In our patients admitted to the ICU with COPD and Type 2 respiratory failure, the presence of pleural effusion detected radiologically at admission was found to be significantly associated with increased proBNP levels, increased CTR, and longer ICU length of stay ($p = 0.045$, $p = 0.038$, and $p = 0.008$, respectively).

In a multiple linear regression analysis examining factors significantly affecting ICU length of stay, including the presence of pleural effusion, AKI, and CAD, the adjusted R-squared value of the model was determined to be 0.046. This indicates that these three factors collectively explain only 4.6% of the variation in ICU length of stay, which is considered a very low explanatory value.

Long-Term Oxygen Therapy

Among the patients admitted to the ICU, those using LTOT at home had significantly higher pCO_2 and bicarbonate levels at the time of ICU admission compared to non-users ($p = 0.017$ and $p < 0.001$, respectively).

Our patients diagnosed with COPD and admitted to the ICU with Type 2 respiratory failure presented with a variety of overlapping metabolic conditions and comorbidities. While many of our statistical analyses yielded results consistent with medical literature, some findings were striking and noteworthy. We deemed it appropriate to summarize these findings in a table for the study's overview (Table 2).

Table 2. Summary of Metabolic Conditions in COPD-Type 2 Respiratory Failure Patients.

Findings			Evidence-1	Evidence-2	Evidence-3	Evidence-4
Female	patients	have	HT	CHF	Hypothyroidis	Obesity
worse		metabolic	($p < 0.001$) ^{a*}	($p < 0.001$) ^{a*}	m ($p < 0.001$) ^{a*}	($p = 0.004$) ^{a*}
conditions						

CKD patients are overweight and have larger hearts	High BMI Obesity (p=0.023) ^{b*} (p=0.004) ^{a*}	CTR (p<0.001) ^{b*}	Cardiomegaly (p=0.015) ^{a*}	
AKI, CAD, and pleural effusion prolong ICU stay	AKI (p=0.036) ^{b*}	CAD (p=0.024) ^{b*}	Pleural Effusion (p=0.008) ^{b*}	
CHF patients are overweight with impaired RFTs	Obesity (p=0.003) ^{a*}	BUN (p<0.001) ^{b*}	Creatinine (p<0.001) ^{b*}	Admission Potassium (p=0.021) ^{b*}
Anemic patients are older, malnourished, with more comorbidities and inflammation	Age (p=0.011) ^{c*}	CCI (p<0.001) ^{b*}	Discharge CRP (p=0.039) ^{b*}	Low Albumin (p<0.001) ^{c*}
HT patients are overweight, inflamed, and have more heart and kidney dysfunctions	High BMI (p<0.001) ^{b*}	Discharge CRP (p=0.021) ^{b*}	Cardiomegaly (p<0.001) ^{a*}	Creatinine (p<0.001) ^{b*}
DM patients are obese with renal and cardiovascular dysfunctions	Obesity (p=0.003) ^{a*}	AKI (p=0.007) ^{a*}	Creatinine (p=0.003) ^{b*}	CAD (p<0.001) ^{a*}
LTOT users present to the hospital later	High Bicarbonate (p<0.001) ^{b*}	High pCO2 (p=0.017) ^{b*}		

AKI: Acute kidney injury, BMI: Body mass index, CAD: Coronary artery disease, CCI: Charlson comorbidity index, CHF: Congestive heart failure, CKD: Chronic kidney disease, CRP: C-reactive protein, CTR: Cardiothoracic ratio, DM: Diabetes mellitus, HT: Hypertension, LTOT: Long-term oxygen therapy, pCO2: Partial carbon dioxide pressure, RFT: Renal function tests. a: Chi-square test, b: Mann-Whitney U test, c: Student's t-test, *: p<0.05, significant values.

Discussion

This study comprehensively evaluated the effects of accompanying comorbidities and metabolic conditions on clinical outcomes in patients admitted to the ICU with COPD and Type 2 respiratory failure. Our findings largely align with existing literature while presenting some unique and noteworthy results that contribute significantly to the clinical management of this patient group.

In our study, female patients were older and had a higher prevalence of comorbidities such as HT, CHF, obesity, and hypothyroidism compared to males, indicating a higher metabolic burden in this group. The detection of higher CTR and proBNP levels in females supports these findings. The literature also corroborates that female patients tend to have an increased burden of comorbidities with aging [10,11].

Anemic patients in our study exhibited significantly higher CCI, proBNP, and TSH levels, alongside lower albumin and magnesium levels. Although not the main focus of our study, the metabolic profile observed in anemic patients suggests the presence of anemia of chronic disease. These findings highlight the association of anemia of chronic disease with metabolic dysfunction (such as euthyroid sick syndrome) and cardiovascular burden. Existing literature reports that anemia adversely affects respiratory functions and increases cardiac stress levels in chronic diseases like COPD [12]. Anker et al. emphasized that elevated proBNP levels in anemic patients are a significant

marker of cardiovascular risk [13]. Additionally, the significantly higher CRP levels observed in anemic patients before discharge indicate the persistence of chronic inflammation, which can be linked to the systemic effects of anemia in COPD patients.

Chronic kidney disease (CKD) and acute kidney injury (AKI) were common comorbidities in our study, significantly influencing clinical outcomes. Increased CTR, proBNP levels, and the frequency of cardiomegaly in patients with CKD reveal the relationship between renal dysfunction and cardiovascular burden. Literature suggests that CKD is associated with left ventricular hypertrophy and cardiomegaly [14]. AKI was observed to significantly prolong ICU stay, consistent with prior studies showing that AKI increases mortality and morbidity in COPD patients [15].

HT is a common and impactful comorbidity in COPD patients, affecting ICU parameters. Our study found that patients with HT had higher proBNP levels, CTR, and cardiomegaly rates, indicating an increased cardiovascular risk. DM was significantly associated with obesity and AKI prevalence. Literature indicates that the coexistence of HT and DM increases the risk of cardiovascular and renal complications in COPD patients [16].

The association of pleural effusion with proBNP levels and CTR suggests that this finding may be explained by cardiac dysfunction and fluid overload. Additionally, the prolongation of ICU stays in patients with pleural effusion reflects a more complex clinical course in this group [17]. The significantly higher pCO₂ and bicarbonate levels in LTOT users further support that these patients are in advanced stages of COPD. This may also indicate that aggressive correction of hypoxia in LTOT users could contribute to hypercarbia and metabolic compensation through respiratory center suppression due to chronic hypercarbic desensitization. A simpler explanation could be that LTOT is prescribed for more severe COPD patients. The literature also emphasizes that LTOT is associated with chronic hypoxemia and hypercapnia [18].

Obesity is a critical factor that increases cardiovascular and metabolic burden in COPD patients. Our study found that obese patients had higher frequencies of cardiomegaly and OSAS, underscoring the importance of a multidisciplinary approach in this group. Clinical dietitians play a vital role in managing these patients. Proper nutritional management could improve both respiratory parameters and cardiovascular risk in this group. Additionally, the increased frequency of OSAS in patients with hypothyroidism may be explained by the effects of hypothyroidism on respiratory functions [19]. We observed that an increased BMI in COPD patients with Type 2 respiratory failure was associated with an increased risk of cardiomegaly, with a cutoff value of 25.5. Considering that this cutoff aligns with the overweight threshold in standard classifications, we emphasize the need for strict weight monitoring during routine follow-ups to prevent increased cardiac risk in this patient group.

Strengths and Limitations of the Study

This study is significant for its detailed examination of the effects of comorbidities on ICU processes in COPD and Type 2 respiratory failure patients. However, the retrospective design and single-center setting limit the generalizability of the findings.

Conclusion and Recommendations

Our study highlights the critical role of comorbidities in the clinical management of patients with COPD and Type 2 respiratory failure. Conditions such as anemia, HT, DM, CKD, CHF, and obesity necessitate closer monitoring and treatment during ICU care. Controlling systemic inflammation is particularly crucial in anemic and hypertensive patients. Future studies should aim to validate these findings in larger patient groups and explore the underlying mechanisms of these comorbidities in greater detail.

Conflict of Interest: The authors declare no conflicts of interest.

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