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RESEARCH ARTICLE

Comparable Systemic Superoxide Dismutase Activity in Advanced Lung Cancer Patients with and without Chronic Obstructive Pulmonary Disease

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Abstract

Introduction: Lung cancer and Chronic Obstructive Pulmonary Disease (COPD) constitute significant global health challenges, primarily driven by shared pathogenic mechanisms, including oxidative stress. Superoxide Dismutase (SOD) is an essential antioxidant enzyme that diminishes reactive oxygen species. This study evaluated the differences in systemic SOD activity among lung cancer patients with and without comorbid COPD. **Materials and Methods:** An analytical cross-sectional study was performed at Ulin Regional Hospital, Banjarmasin, from May to October 2024. Sixty-nine lung cancer patients were enrolled. COPD was diagnosed with post-bronchodilator spirometry in accordance with GOLD criteria. Plasma SOD activity was quantified via spectrophotometric examination. The Mann-Whitney U test was employed to evaluate group differences. **Results:** COPD was 34.78% (n=24) among lung cancer patients, with 84.06% of the total individuals diagnosed with adenocarcinoma, primarily at Stage IV (81.16%). A significant difference in the distribution of COPD severity was identified across the study groups ($p < 0.001$). The median SOD activity in lung cancer patients with COPD was 0.028 IU/ml (IQR: 0.026–0.031), while in those without COPD it was 0.030 IU/ml (IQR: 0.028–0.035). Statistics showed no significant difference in SOD activity across groups ($p = 0.668$). **Conclusion:** Advanced lung cancer patients demonstrated low median SOD activity irrespective of COPD status, with no statistically significant difference identified between the two groups. Due to the study's cross-sectional design and the absence of a healthy control group, these findings should be viewed as an observational reflection of systemic antioxidant levels. These results suggest that factors associated with advanced malignancy may outweigh the oxidative impact of comorbid COPD in this specific population. Routine spirometry screening remains crucial for a comprehensive treatment approach to lung cancer patients.

Keywords: COPD- Lung Cancer- Oxidative Stress- Superoxide Dismutase

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Introduction

Lung cancer and Chronic Obstructive Pulmonary Disease (COPD) are respiratory diseases with considerable global mortality and morbidity [1, 2]. According to Global Burden of Cancer (GLOBOCAN) data from 2020, lung cancer is the second most prevalent cancer and the main cause of death, killing 1.8 million people. In Indonesia, the burden of this disease is substantial, with lung cancer ranking as the third most common type, following breast and cervical cancer [3]. The primary risk factor contributing to the pathogenesis of these diseases is exposure to cigarette smoke or biomass burning products, which induce chronic oxidative stress in lung tissue [4, 5].

Cigarette smoke contains approximately 7,000 distinct chemicals, with at least 69 identified as carcinogenic. These include polycyclic aromatic hydrocarbons and N-nitrosamines [6, 7]. Inhalation of these harmful

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substances triggers the formation of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which can cause massive oxidative damage to Deoxyribonucleic Acid (DNA), lipid peroxidation of cell membranes, and degradation of tumor suppressor proteins [8, 9]. A disparity between its production of free radicals and the body's antioxidant defense mechanisms, such as the enzyme Superoxide Dismutase (SOD), results in oxidative stress that immediately contributes to the initiation and progression of carcinogenesis. Superoxide Dismutase itself plays a crucial role as a first-line endogenous antioxidant enzyme that catalyzes the dismutation of superoxide free radicals into less reactive hydrogen peroxide [9-11].

Clinically, the association between COPD and lung cancer is profound, with reported lung cancer developing up to five times higher in smokers with airflow obstruction than in individuals with a normal level of pulmonary function [5]. The mechanisms of chronic inflammation, airway fibrosis, and pulmonary parenchymal damage in the form of emphysema in COPD are strongly suspected to stimulate rapid cell turnover, abnormal proliferation, and an increased risk of genetic errors [12, 13]. Although the connection of these two diseases through the oxidative stress pathway has been widely discussed at the global level, research on the specific SOD activity profile in the lung cancer population with COPD comorbidities in Indonesia is still very limited. Therefore, this study seeks to examine disparities in SOD activity among lung cancer patients with and without COPD at Ulin Regional Hospital, Banjarmasin, to better understand the role of antioxidant status in this high-risk group.

Materials and Methods

Study Design

This study used an analytical, cross-sectional design to examine differences in SOD activity comparing lung cancer patients with and without COPD. The research was conducted at Ulin Regional Hospital, Banjarmasin, from May to October 2024, encompassing both inpatients and outpatients.

Individuals were selected according to the specified inclusion criteria: a definitive diagnosis of lung cancer established by histopathological or cytological assessment and the ability to perform the required spirometry maneuvers. Exclusion criteria included individuals with suboptimal functional capacity (Eastern Cooperative Oncology Group [ECOG] score>2), cognitive impairment, or acute medical contraindications that hindered the safe and accurate performance of spirometry maneuvers. The sample size was determined using a power analysis for the difference between two independent means. The selection of a substantial effect size (Cohen's d = 0.8) was based on the assumption that advanced malignancies often entail significant systemic physiological alterations, as shown by previous research documenting substantial antioxidant depletion in these populations. However, we acknowledge that this assumption may be optimistic; if the actual biological difference in SOD activity between lung cancer patients with and without COPD is more subtle (a small or medium effect size), this study may have been underpowered to detect it. A minimum sample size of 56 participants (19 with COPD and 37 without COPD, representing a 1:1.8 ratio) was necessary to attain a statistical power of 80% at a significance level (α) of 0.05. The study successfully enrolled 69 participants (24 with COPD and 45 without), yielding a post hoc power of 87% to detect a large effect size.

Data Collection

Each research participant underwent a standardized clinical assessment, which included an initial anamnesis to gather identity information, smoking status measured by the Brinkman Index, a history of comorbid conditions such as Diabetes Mellitus, Hypertension, and Tuberculosis (TB), and exposure to outdoor and indoor pollutants. Body dimensions, such as weight and height, were assessed to determine the Body Mass Index (BMI). Pulmonary function was objectively assessed utilizing a calibrated Conteq SP100 Spirometer, with subjects performing maneuvers at least 3 times to obtain reliable results, according to the Pneumobile Project Indonesia (PPI) standards. Diagnosis of COPD was established through a bronchodilator test, where 400 mcg of salbutamol was administered via a metered-dose inhaler (MDI) with a spacer, followed by a repeat spirometry examination 15 minutes later to confirm a post-bronchodilator FEV1/FVC ratio of less than 0.70. For the assessment of antioxidant status, 3 mL of venous blood was obtained via the median cubital vein and centrifuged for 8 minutes at 2000 rpm to isolate plasma. SOD activity was then measured using a spectrophotometer at 505 nm at the Biochemistry Laboratory, Faculty of Medicine and Health Science, Lambung Mangkurat University. The research designated lung cancer (with or without COPD) as the independent variable and SOD activity as the dependent variable.

Statistical Analysis

The data were analyzed using SPSS 26. The Kolmogorov-Smirnov test was used to assess normality, indicating that SOD activity data did not follow a normal distribution. As a result, the nonparametric Mann-Whitney U test was employed to examine median differences in SOD activity within lung cancer groups with and without COPD. To improve the clarity of the univariate results, 95% confidence intervals (CI) for median differences and effect sizes (r) were calculated. The Independent T-test was utilized for continuous variables related to demographic and clinical features. Conversely, Chi-Square or Fisher's Exact tests were employed for categorical variables.

To evaluate the independent association between COPD status and SOD activity while controlling for potential confounders, a multiple linear regression analysis was performed. The model included COPD status, smoking intensity (Brinkman Index), and nutritional status (BMI) as independent variables. The regression findings were presented using unstandardized coefficients (β), standard errors (SE), and 95% CIs. All results demonstrate statistical significance if $p < 0.05$.

Results

Patient Characteristics

Table 1 reveals that the study included 69 people with lung cancer, who were an average of 54.74 years old. The majority of individuals were male (71.01%), smokers (63.77%), and underweight (46.38%). Every individual involved in the study was diagnosed with non-small cell lung cancer (NSCLC), primarily adenocarcinoma (84.06%), and was predominantly in advanced stages (Stage IVA: 57.97%; Stage IVB: 23.19%). Hypertension (20.29%), diabetes mellitus (11.9%), and TB (5.80%) were some of the most common comorbidities.

Prevalence and Severity of COPD in Lung Cancer

Among the 69 lung cancer patients evaluated, the prevalence of comorbid COPD was 34.78% (24 out of 69). Within the COPD group, airway obstruction severity was evenly distributed across the GOLD grades, with GOLD grades 2, 3, and 4 each accounting for 33.33% of the affected population (Table 1). Statistical analysis revealed a significant association between the distribution of COPD severity and the study groups ($p < 0.001$), confirming that the presence and grades of airway obstruction constituted a major clinical disparity between the lung cancer cohorts (Table 2).

Comparative Analysis of Patient Groups

Table 2 indicates that there were no statistically significant differences in age ($p = 0.132$), gender ($p = 0.587$), and BMI ($p = 0.486$) between lung cancer patients with and without COPD.

Furthermore, a comparative analysis of potential confounders revealed that smoking intensity, as measured by the Brinkman Index, was statistically comparable between the two groups ($p = 0.797$). Regarding clinical management, the distribution of therapy modalities did not differ significantly between the cohorts (chemotherapy vs. targeted therapy; $p = 0.099$).

Superoxide Dismutase (SOD) Activity

Table 3 indicates that the median SOD activity in lung cancer patients without COPD was 0.030 IU/ml (IQR: 0.028–0.035), while in patients with COPD it was 0.028 IU/ml (IQR: 0.026–0.031). A statistically significant difference between the two groups was not found by the Mann-Whitney U test ($p = 0.668$, effect size $r = 0.05$). The data suggest that systemic antioxidant levels are comparably low in advanced lung cancer patients within this cohort, irrespective of concomitant airway obstruction. Figure 1's comparison analysis elucidates this pattern, showing that most patients in both cohorts had SOD activity levels at or below the general median.

The multiple linear regression model demonstrated that COPD status was not an independent predictor of plasma SOD activity ($p = 0.741$) after controlling for smoking intensity (Brinkman Index) and nutritional status (BMI), as shown in Table 4. The low R2 value (0.013) suggests that these clinical factors account for only a small fraction of the variance in SOD levels. It further supports

Table 1. Patient Characteristics

Characteristics (n = 69)	n (%) or Mean ± SD/ Median (IQR)
Age (years)	54.74±10.77
Gender	
- Men	49 (71.01)
- Women	20 (28.99)
BMI (kg/m^2)	18.80±4.09
- Underweight (<18.5)	32 (46.38)
- Normal (18.5–24.9)	29 (42.03)
- Overweight (25.0–29.9)	8 (11.59)
Smoking Status	
- Active smoker	44 (63.77)
Brinkman Index (Mild–Moderate)	28 (70.00)
Brinkman Index (Heavy)	16 (40.00)
- Non-smoker	13(18.84)
- Passive smoker	12 (17.39)
Pollutant Exposure	
- Outdoor pollution	26 (37.68)
- Indoor pollution	14 (20.29)
Comorbidities	
- Tuberculosis	4 (5.80)
- Diabetes Mellitus	8 (11.9)
- Hypertension	14 (20.29)
Histopathology Lung Cancer	
- Adenocarcinoma	58 (84.06)
- Squamous cell carcinoma	11 (15.94)
Staging	
- Stage III	13 (18.84)
- Stage IVA	40 (57.97)
- Stage IVB	16 (23.19)
Metastasis	
- None	13 (18.84)
- Intrapulmonary	32 (46.38)
- Extrapulmonary	24 (34.78)
Lung cancer therapy	
- None	6 (8.70)
- Chemotherapy	36 (52.17)
- Targeted therapy	20 (28.99)
- Targeted therapy and Chemotherapy	7 (10.14)
COPD Comorbidity	
- COPD Presence (COPD +)	24 (34.78)
- COPD Not Present (COPD -)	45 (65.22)
COPD Severity (GOLD Grade)	
- GOLD 2	8 (33.33)
- GOLD 3	8 (33.33)
- GOLD 4	8 (33.33)
Antioxidant Status	
Median SOD Activity (IU/ml)	0.029 (0.010-0.048)

GOLD: Global Initiative for Chronic Obstructive Lung Disease; IQR: Interquartile Range

the hypothesis that the advanced malignancy itself, rather than comorbid respiratory obstruction or smoking history, may have a more prominent association with the observed systemic antioxidant activity. Nonetheless, the very low R2 value (0.013) suggests that this model only explains a minimal fraction of the variability in SOD levels, indicating that other unmeasured factors likely significantly influence the outcomes.

Discussion

Patients' Demographic and Clinical Profiles

The average age of patients who were involved in this study was 54.74 years, consistent with numerous epidemiological investigations indicating the highest incidence of lung cancer is observed during the fifth and sixth decades of life, which is closely related to the accumulation of long-term exposure to carcinogens as well as the process of cellular aging or immunosenescence that decreases the body's ability to eliminate malignant cells [14, 15]. The predominance of the male sex (71.01%) reflects the high prevalence of smoking among men in Indonesia, which remains a primary risk factor for pulmonary carcinogenesis [16, 17].

Table 2. Differences in the Characteristics of Lung Cancer Patients with COPD and without COPD

Characteristics	Lung Cancer without COPD (n = 45) (%)	Lung Cancer with COPD (n = 24) (%)	p-value
Age (years, mean ± SD)	53.33±10.51	57.38±10.96	0.132$^{\alpha}$
Gender			0.587$^{\beta}$
- Men	33 (73.33)	16 (66.7)	
- Women	12 (26.67)	8 (33.33)	
BMI (kg/m^2, mean ± SD)	18.65±4.31	19.08±3.71	0.486$^{\alpha}$
Smoking Status			0.057$^{\beta}$
- Active smoker	27 (60.0)	17 (70.83)	
- Non-smoker	12 (26.67)	1 (4.17)	
- Passive smoker	6 (13.33)	6 (25.00)	
Brinkman Index			0.797$^{\beta}$
- Mild–Moderate	16 (59.26)	12 (70.59)	
- Heavy	11 (40.74)	5 (29.41)	
Pollutant Exposure			
- Outdoor pollution	16 (35)	10 (41)	0.795$^{\beta}$
- Indoor pollution	9 (20)	5 (21)	0.584$^{\gamma}$
Comorbidities			
- Tuberculosis History	4 (8.89)	0 (0.00)	0.290$^{\gamma}$
- Diabetes Mellitus	7 (15.56)	1 (4.17)	0.246$^{\gamma}$
- Hypertension	7 (15.56)	7 (29.17)	0.217$^{\gamma}$
Histopathology Lung Cancer			0.736$^{\gamma}$
- Adenocarcinoma	37 (82.22)	21 (87.50)	
- Squamous cell carcinoma	8 (17.78)	3 (12.50)	
Staging			0.260$^{\beta}$
- III	11 (24.44)	2 (8.33)	
- IVA	24 (53.33)	16 (66.67)	
- IVB	10 (22.22)	6 (25.00)	
Metastasis			0.192$^{\beta}$
- None	11 (24.44)	2 (8.33)	
- Intrapulmonary metastasis	18 (40.00)	14 (58.33)	
- Extrapulmonary metastasis	16 (35.56)	8 (33.33)	
Lung cancer therapy			0.099$^{\gamma}$
- None	4 (8.89)	2 (8.33)	
- Chemotherapy	21 (46.67)	15 (62.50)	
- Targeted therapy	17 (37.78)	3 (12.50)	
- Targeted therapy and Chemotherapy	3 (6.67)	4 (16.67)	
COPD Severity			<0.001$^{\gamma}$
- GOLD 2	0 (0.00)	8 (33.33)	
- GOLD 3	0 (0.00)	8 (33.33)	
- GOLD 4	0 (0.00)	8 (33.33)	

α: T-Independent test, β: Chi-Square, γ: Fisher Exact test

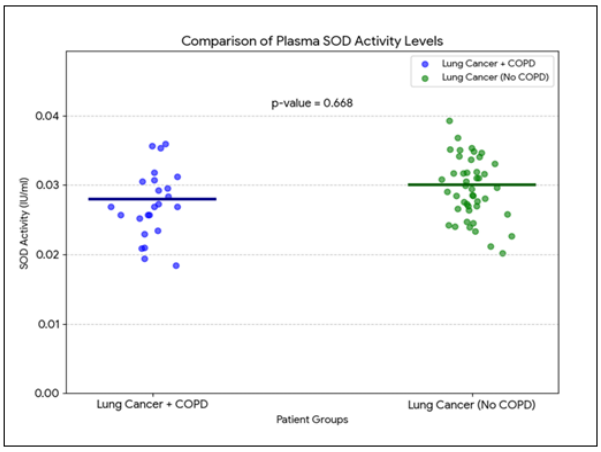


Figure 1. A Comparative Boxplot of Total Plasma SOD Activity in Lung Cancer Patients with and without COPD. The horizontal bars show the median values: 0.028 IU/ml for COPD (+) and 0.030 IU/ml for COPD (-). Statistical analysis revealed a non-significant median difference of 0.002 IU/ml (95% CI: -0.003 to 0.006; p = 0.668), with a small effect size (r = 0.05). This visualization supports the finding that systemic antioxidant levels are comparable across both patient groups.

Histopathologically, the prevalence of adenocarcinoma at 84.06% aligns with the global trend of NSCLC subtypes becoming the most prevalent, surpassing squamous cell carcinoma [18, 19]. Furthermore, the finding that many patients (81.16%) are identified at an advanced stage (Stage IV) underscores the challenges of early detection in this region, often due to non-specific clinical symptoms in the early phase of the disease [20, 21].

Importantly, a comparative analysis of potential confounders revealed no significant differences between lung cancer patients with and without COPD in terms of smoking intensity (Brinkman Index, p = 0.797), nutritional status (BMI, p = 0.486), or treatment modalities (p = 0.099). The balance of baseline characteristics and medication exposures between the study groups is essential, as it reduces the potential for confounding bias in the interpretation of our primary outcome regarding systemic SOD activity.

The Relationship Between COPD and Lung Cancer

The current study identified a 34.78% prevalence of COPD among lung cancer patients at Ulin Hospital, Banjarmasin, the majority of whom were in advanced stages of malignancy (81.16% Stage IV). These findings align with worldwide literature stating that the occurrence of COPD among lung cancer patients ranges from 39% to 53%. Such a strong association reinforces the theory that COPD is not merely a comorbidity but an independent risk factor that significantly increases the likelihood of pulmonary carcinogenesis [22, 23].

The distribution of COPD severity in our cohort was evenly distributed across GOLD grades 2, 3, and 4, with each representing 33.33% of affected participants. It indicates that the airway obstruction in this population was predominantly moderate to very severe. A statistically significant association ($p < 0.001$) confirmed that the distribution of airway obstruction severity constituted a major clinical disparity between the study groups. The chronic inflammation underlying COPD is thought to drive lung structural damage by continuously releasing pro-inflammatory mediators and free radicals, which ultimately trigger genomic instability and promote carcinogenesis [5].

The existence of severe obstructive impairment (GOLD 3 and 4) markedly influences overall therapy. Lung cancer patients with concomitant severe COPD frequently demonstrate diminished tolerance for aggressive therapies such as surgery or radiotherapy. They face a heightened risk of sudden exacerbations during chemotherapy. Consequently, the prompt evaluation of COPD severity using post-bronchodilator spirometry is crucial for formulating effective supportive care plans and enhancing the quality of life for these high-risk patients [24, 25].

Superoxide Dismutase (SOD) Activity and Oxidative Stress Status

Our principal finding, exhibiting no statistically significant difference in plasma SOD activity between lung cancer patients with and without COPD (p = 0.668), was corroborated by multivariate regression analysis, which signified that COPD status was not an independent

Table 3. Differences in SOD Activity Values in Lung Cancer Patients with or without COPD

Variable	Lung Cancer without COPD (n=45)	Lung Cancer with COPD (n=24)	Median Difference (95% CI)	p-value	Effect Size (r)
SOD Activity (IU/ml)	0.03	0.028	0.002	0.668μ	0.05
Median (IQR)	(0.028-0.035)	(0.026-0.031)	(-0.003 to 0.006)		

μ: Mann-Whitney; IQR: Interquartile Range; CI: Confidence Interval.

Table 4. Multiple Linear Regression Analysis of Factors Associated with Plasma SOD Activity

Variable	Unstandardized Coefficient (β)	Standard Error	t-statistic	p-value	95% CI
(Constant)	0.054	0.024	2.251	0.028	[0.006, 0.102]
COPD Status (Ref: No COPD)	-0.003	0.009	-0.332	0.741	[-0.021, 0.015]
Brinkman Index (Smoking)	-0.0001	0.0001	-0.101	0.92	[-0.0002, 0.0002]
BMI (kg/m^2)	-0.001	0.001	-0.833	0.408	[-0.003, 0.001]

Dependent Variable: SOD Activity (IU/ml). Model Statistics: R^2: 0.013; Adjusted R^2: -0.032; F-test p: 0.892.

predictor of SOD activity (p = 0.741) when controlled for smoking intensity and BMI. The persistently low median SOD activity in both groups (0.028 vs 0.030 IU/mL) may reflect systemic antioxidant depletion. Biochemically, these data indicate that the endogenous antioxidant defense system is considerably impaired in patients with advanced lung cancer, possibly due to prolonged exposure to elevated amounts of ROS produced by the tumor microenvironment and chronic systemic inflammation. This conclusion aligns with prior research indicating that the substantial oxidative burden in malignancy frequently exceeds systemic neutralizing capabilities [9, 26, 27].

As a result of the fact that there was no discernible difference between the two groups, the 'ceiling effect' hypothesis about oxidative stress was formulated. We hypothesize that in the context of advanced-stage cancer (81.16% stage IV), the magnitude of systemic oxidative burden might reach a threshold where additional pro-oxidant contributions from comorbid COPD could no longer be statistically or biologically distinguishable in this specific study population. This interpretation is currently conjectural and necessitates additional confirmation via longitudinal studies.

Moreover, the potential effects of systemic medicines must be taken into account. In our sample, 91.30% of patients had chemotherapy, targeted therapy, or a combination of both, all recognized as iatrogenic sources of oxidative stress. We propose that the pro-oxidant effects of these medications may have standardized the antioxidant profiles within our study population, thus obscuring baseline disparities in redox status between the COPD and non-COPD groups [28–30].

Our findings are consistent with the findings of Skórska et al. and Ascar et al., who documented substantial decreases in antioxidant enzyme activity in lung cancer patients. Nonetheless, we recognize that the current literature indicates inconsistent SOD activity. Certain investigations, especially those concerning early-stage COPD or treatment-naive cancer patients, have noted a temporary compensatory elevation in SOD activity as an adaptive reaction to initial oxidative damage. The depletion noted in our study likely indicates the advanced clinical profile of our patients, in whom such compensatory mechanisms have been exceeded or depleted [27, 30, 31].

Study Limitations and Clinical Implications

This research identifies some acknowledged limitations that necessitate a prudent interpretation of the results. The cross-sectional methodology unavoidably restricts the capacity to show a conclusive causal link among COPD status, lung cancer progression, and the systemic reduction of SOD activity. As all variables were assessed concurrently, it remains indeterminate whether the observed low SOD levels preceded the onset of these respiratory disorders or were a consequence of the advanced cancer and its corresponding treatments. Moreover, the absence of longitudinal data hinders our understanding of the temporal dynamics of oxidative stress markers as the disease advances.

Secondly, while the study achieved its intended sample size (n=69), we acknowledge the possibility of a Type II error, which could diminish the statistical power to detect modest biological differences between groups. While multiple linear regression was used to adjust for primary confounders, such as smoking intensity (Brinkman Index) and nutritional status (BMI), the model yielded a very low R2 value (0.013). This low coefficient of determination indicates that the selected clinical variables account for only a negligible fraction of the variance in systemic SOD activity. The restricted set of covariates in our model suggests that additional unmeasured biological factors, such as specific tumor mutations, inflammatory cytokines, or nuanced dietary differences, could have a greater impact on redox homeostasis than the clinical parameters examined in this study. Furthermore, the lack of a larger-scale multivariate adjustment and the absence of a healthy control group further constrain our ability to pinpoint the exact drivers of the observed antioxidant levels.

Third, excluding those patients exhibiting an ECOG performance status exceeding 2 was a necessary methodological choice to ensure the accuracy of the COPD diagnosis using post-bronchodilator spirometry. Patients with elevated ECOG scores often exhibit significant weakness and fatigue, making it technically challenging to achieve reliable, consistent spirometric outcomes in accordance with GOLD criteria. While this decision may restrict the generalizability of our research results to the most debilitated lung cancer populations, this criterion was essential to prevent misclassification bias.

Fourth, the study could not account for all factors impacting redox homeostasis, such as exogenous antioxidant supplements or herbal remedies. However, given the heterogeneity in treatment exposure, where 91.30% of participants received pro-oxidant systemic therapies, and the high prevalence of malnutrition (46.38% underweight), it is hypothesized that minor exogenous intake was insufficient to counteract the systemic oxidative burden. Fifth, the assessment of SOD was restricted to total plasma activity. The lack of data on individual SOD isoforms (SOD1, SOD2, SOD3) and other markers, such as Malondialdehyde (MDA), constrains a more detailed mechanistic analysis of the specific redox pathways implicated.

Finally, the use of a large effect size for sample size calculation may have overestimated the expected biological disparity between the two groups. This method aligns with the observation of significant systemic alterations in advanced disease; however, it limits the research's capacity to detect subtler or moderate variations in SOD activity that may be clinically significant.

Notwithstanding these constraints, the findings possess considerable clinical significance. The significant prevalence of COPD (34.78%) in lung cancer patients, many of whom demonstrate moderate to severe airway obstruction (GOLD 2-4), highlights the imperative for comprehensive respiratory evaluation. Screening for COPD through post-bronchodilator spirometry should be integrated as a routine component of the diagnostic evaluation for all lung cancer patients to optimize treatment tolerance and prevent exacerbations during

chemotherapy [32, 33].

Furthermore, the observed systemic antioxidant depletion, regardless of COPD status, suggests that advanced malignancy creates a state of oxidative stress that may require specialized supportive care. Additional longitudinal investigations are required to validate the prognostic significance of SOD activity and to examine whether antioxidant-based supportive interventions could improve clinical outcomes in this high-risk group.

In conclusion, the findings in this study indicate no statistically significant difference in systemic SOD activity between advanced lung cancer patients with concomitant COPD and those without. The persistently low antioxidant levels reported in both groups suggest that factors such as advanced disease stage, systemic inflammation, and multimodal therapies could potentially obscure the oxidative consequences associated with COPD in this population. Although SOD activity showed no variation, the significant prevalence of COPD (34.78%) in this group highlights the urgent necessity for regular post-bronchodilator spirometry monitoring to guarantee thorough clinical management and enhance supportive care for lung cancer patients.

Declarations

Funding

No specific funding was received for this study.

Clinical trial registration

Not applicable.

Conflicts of interest/Competing interests

The authors declare that they have no conflicts of interest.

Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding authors upon reasonable request.

Code availability

The custom code was used.

Authors' contributions

HH, IV, and FY contributed to the conception, design, and final drafting of the manuscript. IV, HH, EK, AA, MI contributed to data collection and analysis. HH, IV contributed to the primary drafting of the manuscript. HH, FY supervised the study. All authors approved the final version for submission.

Ethics approval

This study was approved by the Ethics Committee of Ulin Regional Hospital, Banjarmasin, with approval number 88/VI-Research Reg/RSUDU/24.

Consent to participate

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from all participants for the publication of anonymized data in accordance with ethical guidelines.

Originality Declaration for Figures

All figures included in this manuscript are original and have been created by the authors specifically for this study. No previously published or copyrighted images have been used. The authors confirm that all graphical elements, illustrations, and visual materials were generated from the data obtained in the course of this research or designed uniquely for this manuscript.

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Declaration on generative AI and AI-assisted technologies in the writing process

AI was used to improve the clarity and grammatical accuracy of the manuscript. The authors confirm that no original data were fabricated or manipulated using AI tools.

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