Original article

Relationship between serum Sclerostin concentration and 6-minute walking distance and ABE groups in male patients with chronic obstructive pulmonary disease

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Abstract

Objectives: 1) To describe the clinical and paraclinical characteristics of patients with chronic obstructive pulmonary disease (COPD); 2) To investigate serum Sclerostin concentration and its relationship with 6-minute walking distance, symptom groups and ABE groups in patients with COPD.

Materials and methods: Cross-sectional study on 43 male patients with COPD admitted to the Department of Internal Medicine - Endocrinology - Rheumatology, Hue University of Medicine and Pharmacy Hospital, and the Department of Endocrinology - Pulmonology, Hue Central Hospital from July 2024 to June 2025.

Results: The average age of the study group was 62.58 ± 8.05 years. Patients in the study group smoked 34.00 (20.00 - 44.00) pack-years. The proportion of patients in the GOLD I, II, III and IV groups were 2.3%, 55.8%, 27.9% and 14.0%, respectively. 58.1% of patients were in the multiple symptoms group and 41.9% of patients were in the few symptoms group. In addition, the proportions of patients in groups A, B and E were 25.6%, 34.9% and 39.5%, respectively. Serum sclerostin concentration in group E was statistically significantly lower than that in groups A and B ($p < 0.05$). The area under the ROC curve (AUC) of serum sclerostin concentration to identify stage E was 0.774 ($p < 0.001$). With a cut-off point ≤ 6.330 pmol/l, serum sclerostin concentration showed a moderate ability to discriminate stage E with a sensitivity of 88% and a specificity of 69% (95%CI: 0.629 – 0.921). There was a positive correlation between serum sclerostin concentration and 6-minute walk distance ($r = 0.305$, $p < 0.05$).

Conclusion: Serum sclerostin concentration may be a potential biomarker for disease stage and exercise capacity in patients with COPD.

Keywords: *Chronic obstructive pulmonary disease, 6-minute walk distance, ABE stage, sclerostin.*

1. INTRODUCTION

The Wnt signaling cascade is the main regulator of development throughout the animal kingdom, and Wnt is also the main driver of most tissue stem cell types in adult mammals [1]. Sclerostin, a negative regulator of Wnt signaling, is an essential molecule involved in skeletal remodeling and homeostasis. However, sclerostin is not only a component of the skeletal system but is also present in other organs such as cartilage, liver, kidney, heart, and lung [2][3]. By binding to LRP4 and LRP 5/6, sclerostin prevents the formation of the Wnt receptor–LRP5/6–Frizzled receptor complex. β-catenin is phosphorylated and translocated to the proteasome for degradation [4] [5]. Patients with COPD have abnormal regulation of classical and non-classical Wnt signaling pathways [6]. In COPD, the Wnt signaling pathway plays a crucial immunoregulatory role in inflammation and airway remodeling [1]. Research on the role of sclerostin in pulmonary diseases such as pulmonary hypertension, hypoxemia, and COPD has been proposed in recent years [7][8][9][10][11]. Therefore, a hypothesis has been raised that there is a relationship between serum sclerostin levels and clinical and paraclinical factors in COPD. Hence, we conducted this preliminary study with 2 objectives:

1. To describe the clinical and paraclinical characteristics of patients with Chronic Obstructive Pulmonary Disease.

2. To investigate serum sclerostin concentration and its relationship with 6-minute walking distance, symptom groups, and ABE stages in patients with COPD.

2. MATERIALS AND METHODS

2.1. Study subjects: Our study enrolled 43 male patients with COPD admitted to the Department of Internal Medicine - Endocrinology - Rheumatology, Hue University of Medicine and Pharmacy Hospital, and the Department of Endocrinology - Pulmonology, Hue Central Hospital from July 2024 to June 2025.

Inclusion criteria: Patients were diagnosed with COPD according to GOLD 2024 with a combination of a history of exposure to risk factors, appropriate clinical symptoms, and spirometry results with a FEV1/FVC ratio < 0.7 after bronchodilator reversibility test.

Exclusion criteria: Currently using drugs that affect bone absorption, using oral glucocorticoids within 8 weeks, having diseases that affect bone metabolism, such as primary hyperparathyroidism, diseases that cause hyper or hypocalcemia, fractures due to osteoporosis or trauma, sarcoidosis, cancer, acute renal failure or chronic kidney disease, rheumatoid arthritis, sarcopenia or patients unable to cooperate in participating in the study.

2.2. Research methods

- Study design: Cross-sectional descriptive study.
- After providing informed consent, patients were asked about their medical history and clinical examination by a respiratory specialist.
- Serum sclerostin concentration was measured using a commercially available ELISA kit (Abbexa Ltd., Cambridge, UK) following the manufacturer's instructions. All samples were analyzed in duplicate, and the mean value was used for analysis to minimize measurement variability.
- The 6-minute walk test (6MWT) was performed according to the standardized guidelines of the American Thoracic Society and the ATS/ERS technical standards. Spirometry was performed according to the standardized guidelines of the American Thoracic Society and European Respiratory Society (ATS/ERS 2019).

2.3. Data processing

- Data were entered via Microsoft Excel and processed using SPSS 20.0.
- The distribution of quantitative variables was tested using the Shapiro-Wilk test.
- For quantitative variables with a normal distribution, the mean and standard deviation (X ± SD) were calculated. For quantitative variables with a non-normal distribution, the median and interquartile range were calculated.
- Two means with a normal distribution were compared using the Independent t-test. Two groups with a non-normal distribution were compared using the Mann-Whitney U-test.
- The correlation coefficient r was used to assess the inter-variable relationships. Pearson correlation was applied to continuous variables with a normal distribution. For ordinal or continuous variables that did not follow a normal distribution, Spearman correlation was used.
- The ROC curve was used to evaluate the ability of serum sclerostin to discriminate stage E. The cutoff point, sensitivity, specificity, positive predictive value, and negative predictive value were calculated.
- A p-value < 0.05 was considered statistically significant.

3. RESULTS

3.1. Clinical and paraclinical characteristics of patients with COPD

Table 1. General characteristics of the study group

Characteristics	Value
Average age (years)	62.58 ± 8.05
BMI (kg/m^2)	20.58 (18.75 - 22.49)
Smoking status (pack-year)	34.00 (20.00 - 44.00)
6-minute walking distance (m)	375.12 ± 114.33

The mean age of the study group was 62.58 ± 8.05 years, and the BMI was 20.58 (18.75 - 22.49) kg/m2. Patients in the study group smoked 34.00 (20.00 - 44.00) pack-years, and the average distance walked during the 6-minute walk test was 375.12 ± 114.33 meters.

Table 2. Severity of obstructive airflow obstruction on spirometry and number of exacerbations in the past 12 months

Airflow obstruction severity	n	%
GOLD I	1	2.3
GOLD II	24	55.8
GOLD III	12	27.9
GOLD IV	6	14.0
Number of exacerbations	**n**	**%**
0 - 1	31	72.1
≥ 2	12	27.9
Minimum: 0, maximum: 8		

Patients in the GOLD II group accounted for the majority, with a rate of 55.8% and the GOLD I group had the lowest rate (2.3%). 72.1% of patients had 0 - 1 acute episodes in the past year. 27.9% of patients had 2 or more acute episodes in the past year.

Table 3. Classification of symptom groups and ABE stages

Symptom group	n	Percentage (%)
Severe symptoms (CAT ≥ 10 or mMRC > 1)	25	58.1
Few symptoms (CAT < 10 and mMRC = 0 - 1)	18	41.9
ABE stage	**n**	**Percentage (%)**
A	11	25.6
B	15	34.9
E	17	39.5
Total	43	100

58.1% of patients were in the severe symptom group, and 41.9% were in the few symptom group. The proportions of patients in groups A, B, and E were 25.6%, 34.9% and 39.5%, respectively.

3.2. Relationship and correlation between serum sclerostin concentration and symptom groups, ABE stages and 6-minute walk distance in patients with COPD

Table 4. The relationship between serum sclerostin concentrations and symptom groups and ABE stages

Sclerostin (pmol/l)	Median (IQR)	Median (IQR)	p
Symptom groups	**Severe symptoms**	**Few symptoms**	> 0.05
	6.33 (5.55 - 7.00)	6.12 (5.30 - 7.21)	
ABE stage	**A and B**	**E**	**< 0.05**
	6.75 (5.71 - 7.16)	5.71 (5.35 - 6.02)	

There was no statistically significant difference in serum sclerostin concentration between the highly symptomatic and the less symptomatic groups (p > 0.05). Serum sclerostin concentration in group E was statistically significantly lower than that in groups A and B (p < 0.05).

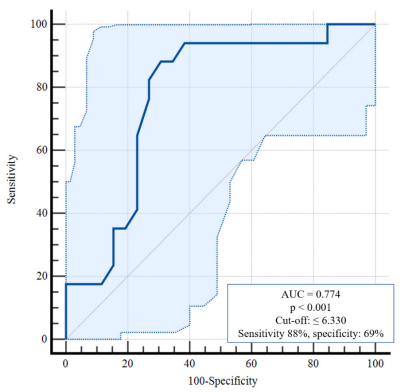

Figure 1. ROC curve of serum sclerostin in predicting ABE stages

The area under the ROC curve (AUC) of serum sclerostin concentration to predict stage E was 0.774 (p < 0.001). With a cut-off point ≤ 6.330 pmol/l, serum sclerostin concentration was able to predict stage E with a sensitivity of 88% and a specificity of 69% (95%CI: 0.629 – 0.921).

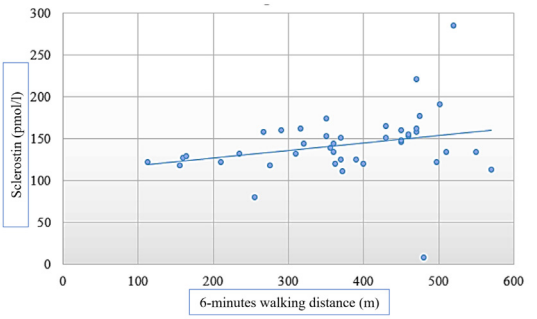

Figure 2. Correlation between serum sclerostin concentration and 6-minute walk distance

There was a positive weak correlation between serum sclerostin concentration and 6-minute walk distance (r = 0.305, p < 0.05).

4. DISCUSSION

4.1. Clinical and paraclinical characteristics of patients with COPD

Our preliminary study was conducted on 43 patients with COPD. The mean age of the study group was 62.58 ± 8.05 years. Patients in the study group smoked 34.00 (20.00 – 44.00) pack-years. The proportion of patients in the GOLD I, II, III, and IV groups in our study was 2.3%, 55.8%, 27.9% and 14.0%, respectively.

GOLD 2024 defines the highly symptomatic group as patients with a CAT score of 10 or mMRC score of 2, and the less symptomatic group as patients with a CAT score of less than 10 and mMRC score of less than 2 [12]. Unlike previous versions of GOLD, since 2017, the ABCD assessment tool has been revised to separate the spirometry results from the ABCD group [13]. In 2023, the ABCD assessment tool was revised to ABE with the combination of groups C and D to form group E [14]. GOLD 2024 and 2025 still apply the ABE stage assessment tool for the diagnosis, management, and prevention of COPD [12][15]. In our study, 58.1% of patients belonged to the highly symptomatic group, and 41.9% of patients belonged to the less symptomatic group. In addition, the proportion of patients in groups A, B, and E was 25.6%, 34.9% and 39.5%, respectively.

4.2. Relationship and correlation between serum sclerostin concentration and symptom

group, ABE stage and 6-minute walk distance in patients with COPD

Sclerostin is a glycoprotein encoded by the SOST gene [16]. Although bone cells are the major cellular source of sclerostin, SOST RNA is also expressed in other human and mouse tissues such as cartilage, kidney, heart, liver, epididymis, vas deferens, pyloric sphincter, carotid artery, lung, and parts of the central nervous system [5]. Recently, many studies have shown the relationship of sclerostin to vascular calcification and cardiovascular diseases, endocrine diseases, and other organs [17],[18],[19]. However, the understanding of the role of sclerostin in respiratory diseases, especially COPD, is limited. Worldwide, there have been 2 studies on the concentration and role of serum sclerostin in patients with COPD [7],[11]. In Vietnam, to date, there has been no study examining this issue. Our study showed that serum sclerostin concentration was not related to symptom group but was related to ABE stage. Specifically, serum sclerostin concentration in group E (5.71 pmol/l) was statistically lower than that in groups A and B (6.75 pmol/l, $p < 0.05$). In addition, we also evaluated the ROC curve to find the cut-off point to distinguish between the AB stage and the E stage. The results showed that the area under the ROC curve (AUC) of serum sclerostin concentration to predict E stage was 0.774 ($p < 0.001$). With a cut-off point ≤ 6.330 pmol/l, serum sclerostin concentration showed a moderate ability to discriminate E stage with a sensitivity of 88% and a specificity of 69% (95%CI: 0.629 - 0.921).

In clinical practice, the 6-minute walk test is commonly used to assess changes in the ability to perform physical activities in patients with COPD, with the result recorded as the distance walked in 6 minutes. This test helps assess the effectiveness of treatments such as oxygen therapy, long-term ICS treatment, pulmonary rehabilitation, and lung volume reduction surgery [20]. In addition, the 6-minute walk test is also a factor in the prognosis of disease as well as the prognosis of death in patients with COPD. In patients with moderate to severe COPD, the average distance walked is 283–388 meters, with a range of up to 160–600 meters. Distance walked decreased by 19% (mean 16 m/year) over a 5-year period in patients with stage 3 COPD (FEV1 30–50%), while it decreased by 26% in patients with stage 4 COPD (FEV1 < 30%) [20]. Furthermore, this test helps quantify the degree of disability, establish an exercise program, identify appropriate patient groups for the use of a walker, and record hypoxemia during exercise in patients with COPD [21]. Our study results showed a positive correlation between serum sclerostin concentration and 6-minute walking distance ($r = 0.305$, $p < 0.05$). Our results are also similar to the study of Amado et al., with a positive correlation between serum Sclerostin concentration and 6-minute walking distance ($r = 0.192$, $p = 0.024$) [7].

This study has several limitations. Firstly, the sample size is relatively small, which may limit the statistical power and reduce the generalizability of the findings. Secondly, this was a cross-sectional study; therefore, causal relationships between serum sclerostin concentration and disease severity or exercise capacity cannot be established. Given the cross-sectional design and limited sample size, these findings should be considered exploratory and hypothesis-generating. Finally, the study population included only male patients, which may introduce gender-related bias.

5. CONCLUSION

Serum sclerostin concentration in group E was statistically significantly lower than in groups A and B. Sclerostin demonstrated an acceptable discriminatory ability for identifying group E patients, although further validation in larger studies is required. There was a positive weak correlation between serum sclerostin concentration and 6-minute walking distance, suggesting a potential association with exercise capacity. However, these findings should be interpreted with caution.

Conflict of interest: The authors declare no conflict of interest regarding the research, authorship, and publication of the article.

Ethics: The study was approved by the Ethics Committee of Biomedical Research, University of Medicine and Pharmacy, Hue University, No.: H2024/581.

REFERENCES

1. Liu M, Huo Y, Cheng Y. Mechanistic regulation of Wnt pathway-related progression of chronic obstructive pulmonary disease airway lesions. Int J Chron Obstruct Pulmon Dis. 2023;18:871-880.

2. Biasin V, Obermayer-Pietsch B. Sclerostin, bone morphogenetic protein, Wnt and the lung: a potential role beyond bone metabolism? J Lab Precis Med. 2018;3.

3. Dreyer TJ, Keen JA, Wells LM, Roberts SJ. Novel insights on the effect of sclerostin on bone and other organs. J Endocrinol. 2023;257(2):e220209.

4. Lewiecki EM. Role of sclerostin in bone and cartilage and its potential as a therapeutic target in bone diseases.

Ther Adv Musculoskelet Dis. 2014;6(2):48-57.

5. Omran A, Atanasova D, Landgren F, Magnusson P. Sclerostin: from molecule to clinical biomarker. Int J Mol Sci. 2022;23(9):4751.

6. Qu J, Yue L, Gao J, Yao H. Perspectives on Wnt signal pathway in the pathogenesis and therapeutics of chronic obstructive pulmonary disease. J Pharmacol Exp Ther. 2019;369(3):473-480.

7. Amado C, García-Unzueta M, Agüero J, Martín-Audera P, Fueyo P, et al. Associations of serum sclerostin levels with body composition, pulmonary function, and exacerbations in COPD patients. Pulmonology. 2024;30(6):512-521.

8. Lee J, Cho DH, Min HJ, Son YB, Kim DH, et al. Higher sclerostin is associated with pulmonary hypertension in pre-dialysis end-stage kidney disease patients: a cross-sectional prospective observational cohort study. BMC Pulm Med. 2024;24(1):78.

9. Wang XM, Liu H, Li JY, Zhang Y, Chen L, et al. Rosamultin attenuates acute hypobaric hypoxia-induced bone injuries by regulation of sclerostin and its downstream signals. High Alt Med Biol. 2020;21(3):273-286.

10. Genetos DC, Toupadakis CA, Raheja LF, Wong A, Yellowley CE, et al. Hypoxia decreases sclerostin expression and increases Wnt signaling in osteoblasts. J Cell Biochem. 2010;110(2):457-467.

11. Tsukamoto M, Mori T, Nakamura E, Okada Y, Fukuda S, et al. Chronic obstructive pulmonary disease severity in middle-aged and older men with osteoporosis associates with decreased bone formation. Osteoporos Sarcopenia. 2020;6(4):179-184.

12. GOLD. Global strategy for prevention, diagnosis and management of COPD: 2024 report. Fontana (WI): Global Initiative for Chronic Obstructive Lung Disease; 2024.

13. Liao YX, Chen YH. Twenty years of changes in the disease assessment method of the Global Initiative for Chronic Obstructive Lung Disease. Chin Med J (Engl). 2020;133(17):2098-2103.

14. Sharma M, Joshi S, Banjade P, Ghamande SA, Surani S. Global initiative for chronic obstructive lung disease (GOLD) 2023 guidelines reviewed. Open Respir Med J. 2024;18:e18743064279064.

15. Venkatesan P. GOLD COPD report: 2025 update. Lancet Respir Med. 2025;13(1):e7-e8.

16. Veverka V, Henry AJ, Slocombe PM, Ventom A, Mulloy B, et al. Characterization of the structural features and interactions of sclerostin: molecular insight into a key regulator of Wnt-mediated bone formation. J Biol Chem. 2009;284(16):10890-10900.

17. Jaśkiewicz Ł, Chmielewski G, Kuna J, Stompór T, Krajewska-Włodarczyk M. The role of sclerostin in rheumatic diseases: a review. J Clin Med. 2023;12(19):6248.

18. Golledge J, Thanigaimani S. Role of sclerostin in cardiovascular disease. Arterioscler Thromb Vasc Biol. 2022;42(7):e187-e202.

19. Alramah T, Cherian P, Al-Khairi I, Abu-Farha M, Thanaraj TA, et al. Evaluating the correlation of sclerostin levels with obesity and type 2 diabetes in a multiethnic population living in Kuwait. Front Endocrinol. 2024;15:1392675.

20. Jenkins SC. 6-Minute walk test in patients with COPD: clinical applications in pulmonary rehabilitation. Physiotherapy. 2007;93(3):175-82.

21. Ghofraniha L, Dalir Sani Z, Vakilian F, Khajedalooyi M, Arabshahi ZJ. The six-minute walk test (6MWT) for the evaluation of pulmonary diseases. J Cardiothorac Med. 2015;3(2):284-287.