

Exercise Capacity and Balance in Patients with Anemic and Non-Anemic Chronic Obstructive Pulmonary Disease (COPD)

ความสามารถในการออกกำลังกาย และการทรงตัวใน
ผู้ป่วยโรคปอดอุดกั้นเรื้อรังที่มีและไม่มีภาวะโลหิตจาง

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Abstract

Chronic obstructive pulmonary disease (COPD) is a major public health problem associated with functional decline and reduced quality of life. Anemia is a common comorbidity in COPD and may further worsen physical performance, potentially increasing healthcare utilization and fall risk. The aim was to compare exercise capacity and balance performance among healthy individuals, non-anemic COPD patients, and anemic COPD patients. A cross-sectional study was conducted in 120 participants allocated into three groups: healthy controls (n = 40), non-anemic COPD patients (n = 40), and anemic COPD patients (n = 40). Exercise capacity was evaluated using the six-minute walk test (6MWT), and balance performance was assessed using the Timed Up and Go (TUG) test. Pulmonary function was measured by spirometry. Data were analyzed using one-way ANOVA with Bonferroni post hoc comparisons. The anemic COPD group demonstrated significantly shorter six-minute walk distance and longer TUG completion time compared with both non-anemic COPD patients and healthy controls ($p < .05$). Pulmonary function parameters were significantly lower in both COPD groups compared with controls, but did not differ between anemic and non-anemic

COPD patients. Anemia is associated with additional functional limitations in COPD patients independent of airflow obstruction. Routine screening and integrated management of anemia may improve functional outcomes and support more effective rehabilitation planning in COPD care.

Keywords: *Chronic obstructive pulmonary disease (COPD), anemia, six-minute walk test (6MWT), Timed Up and Go (TUG)*

บทคัดย่อ

โรคปอดอุดกั้นเรื้อรัง (Chronic Obstructive Pulmonary Disease: COPD) เป็นปัญหาสาธารณสุขที่สำคัญซึ่งส่งผลให้สมรรถภาพทางกายลดลงและคุณภาพชีวิตของผู้ป่วยแย่ลง ภาวะโลหิตจางเป็นโรคร่วมที่พบได้บ่อยในผู้ป่วย COPD และอาจทำให้สมรรถภาพทางกายลดลงมากยิ่งขึ้น ส่งผลต่อความสามารถในการทำกิจกรรมในชีวิตประจำวัน รวมถึงเพิ่มความเสี่ยงต่อการหกล้มและการใช้บริการทางสุขภาพ การศึกษามีวัตถุประสงค์เพื่อเปรียบเทียบความสามารถในการออกกำลังกายและการทรงตัวระหว่างบุคคลสุขภาพดี ผู้ป่วย COPD ที่ไม่มีภาวะโลหิตจาง และผู้ป่วย COPD ที่มีภาวะโลหิตจางต่อการจัดการทางคลินิกและระบบบริการสุขภาพ การศึกษานี้เป็นการศึกษาแบบภาคตัดขวาง โดยมีผู้เข้าร่วมจำนวน 120 คน แบ่งเป็น 3 กลุ่ม ได้แก่ กลุ่มบุคคลสุขภาพดี ($n = 40$) กลุ่มผู้ป่วย COPD ที่ไม่มีภาวะโลหิตจาง ($n = 40$) และกลุ่มผู้ป่วย COPD ที่มีภาวะโลหิตจาง ($n = 40$) ประเมินสมรรถภาพการออกกำลังกายด้วยการทดสอบเดิน 6 นาที (Six-Minute Walk Test: 6MWT) และประเมินความสามารถในการทรงตัวด้วยการทดสอบ Timed Up and Go (TUG) การทำงานของปอดประเมินด้วยการตรวจสไปโรเมตรี วิเคราะห์ข้อมูลด้วยสถิติ one-way ANOVA และการเปรียบเทียบรายคู่ด้วย Bonferroni post hoc ผลการศึกษาพบว่ากลุ่มผู้ป่วย COPD ที่มีภาวะโลหิตจางมีระยะทางการเดิน 6 นาที สั้นกว่ากลุ่มผู้ป่วย COPD ที่ไม่มีภาวะโลหิตจาง และกลุ่มบุคคลสุขภาพดีอย่างมีนัยสำคัญทางสถิติ และใช้เวลาในการทดสอบ TUG นานกว่าทั้งสองกลุ่ม ($p < .05$) ขณะที่ค่าการทำงานของปอดของผู้ป่วย COPD ทั้งสองกลุ่มต่ำกว่ากลุ่มบุคคลสุขภาพดีอย่างมีนัยสำคัญทางสถิติ แต่ไม่พบความแตกต่างระหว่างกลุ่มผู้ป่วย COPD ที่มีและไม่มีภาวะโลหิตจาง ดังนั้นภาวะโลหิตจางมีความสัมพันธ์กับข้อจำกัดด้านสมรรถภาพทางกายเพิ่มเติมในผู้ป่วย COPD โดยไม่ขึ้นกับระดับการอุดกั้นของทางเดินหายใจ การคัดกรองและการจัดการภาวะโลหิตจางอย่างเหมาะสมอาจช่วยเพิ่มผลลัพธ์ด้านสมรรถภาพทางกายและสนับสนุนการวางแผนฟื้นฟูสมรรถภาพผู้ป่วย COPD ได้อย่างมีประสิทธิภาพ

คำสำคัญ: โรคปอดอุดกั้นเรื้อรัง ภาวะโลหิตจาง การทดสอบเดิน 6 นาที Timed Up and Go

Introduction

Chronic obstructive pulmonary disease (COPD) is a common and preventable respiratory disease characterized by persistent airflow limitation and progressive functional decline (Langefeld, 2024). Beyond pulmonary dysfunction, COPD is increasingly recognized as a systemic condition with extrapulmonary manifestations, including skeletal muscle dysfunction and impaired balance control, which negatively influence quality of life and increase fall risk (Han et al., 2024; Ucgun et al., 2024). In addition, anemia is commonly observed in individuals with COPD and chronic inflammatory conditions (Alisamir et al., 2022).

Anemia in COPD is primarily driven by chronic systemic inflammation, which increases hepcidin levels and disrupts iron metabolism, leading to impaired erythropoiesis (Alisamir et al., 2022). Additional factors such as hypoxemia, oxidative stress, and comorbidities further contribute to reduced hemoglobin levels and diminished oxygen transport capacity (Garcia-Pachon & Padilla-Navas, 2024). Reduced hemoglobin concentration limits oxygen transport capacity, thereby exacerbating fatigue and restricting physical performance (Alisamir et al., 2022). In COPD, where gas exchange is already compromised, anemia may further intensify exercise intolerance and worsen clinical outcomes (Garcia-Pachon & Padilla-Navas, 2024). Aging further compounds these challenges, as declines in muscle mass, strength, and neuromuscular

integration contribute to impaired balance and mobility (Han et al., 2024). Collectively, these factors are strongly associated with an increased risk of falls in individuals with COPD, and the coexistence of COPD and anemia may further amplify functional decline and fall risk. Impairments in postural control and balance have been widely reported in patients with COPD and are associated with an increased risk of falls and functional limitations (Loughran et al., 2020; Ucgun et al., 2024). Structural changes in the respiratory system, reduced muscle strength, and altered neuromuscular control have been proposed as underlying mechanisms contributing to balance dysfunction in this population (Xiang & Luo, 2024). Previous studies using both clinical and laboratory-based assessments have demonstrated reduced balance performance in individuals with COPD compared with healthy controls (Loughran et al., 2020). Balance performance was also inferior in participants with anemia, indicating impairment in postural control. Adequate balance requires integration of sensory input, neuromuscular coordination, and muscle strength, all of which may be compromised in COPD (Xiang & Luo, 2024). Chronic anemia-related hypoxia may further impair neuromuscular function, thereby compromising postural stability and increase fall risk (Loughran et al., 2020). Anemia may further impair postural control and balance in individuals with COPD through multiple physiological mechanisms. Reduced hemoglobin

concentration limits oxygen delivery to skeletal muscles and the central nervous system, thereby compromising neuromuscular function, coordination, and reaction time (Alisamir et al., 2022). Additionally, chronic anemia-related hypoxia may reduce muscle strength and endurance and disrupt proprioceptive and sensorimotor integration, all of which are essential for maintaining postural stability (Han et al., 2024).

In patients with COPD, who already exhibit muscle dysfunction, reduced physical activity, and balance impairment, the presence of anemia may further exacerbate these deficits, leading to greater instability and an increased risk of falls (Loughran et al., 2020). Despite these potential interactions, limited evidence has directly examined the combined impact of anemia on balance performance in individuals with COPD. Therefore, comparing balance and functional mobility between anemic and non-anemic individuals with COPD may provide important insights into the role of anemia as a contributing factor to postural instability and fall risk in this population.

Reduced exercise capacity observed in the anemic COPD group may be attributed to impaired oxygen delivery to working muscles. Anemia decreases hemoglobin availability, limiting oxygen transport and increasing fatigue during physical activity (Alisamir et al., 2022). In patients with COPD, who already experience

ventilatory limitation and impaired gas exchange, this reduction in oxygen availability may further restrict exercise tolerance (Garcia-Pachon & Padilla-Navas, 2024). Age-related physiological decline may further explain these findings. Older adults with COPD often present with reduced muscle mass, impaired proprioception, and delayed motor responses (Han et al., 2024). The coexistence of anemia may amplify these age-related changes, leading to greater impairments in balance and mobility. From a clinical perspective, these findings highlight the importance of comprehensive assessment of anemia in individuals with COPD. Early identification and management of anemia, combined with targeted pulmonary rehabilitation and balance training, may improve functional outcomes and reduce fall risk (Loughran et al., 2020).

From a clinical perspective, early identification and management of anemia, alongside targeted balance and pulmonary rehabilitation interventions, may help reduce fall risk and improve functional outcomes in this population. Therefore, the present study aimed to compare exercise capacity and balance performance among healthy individuals, non-anemic COPD patients, and anemic COPD patients. Understanding these differences may provide important insights for clinical assessment and rehabilitation planning in individuals with COPD.

Research Methodology

1. Study Design

This study employed a cross-sectional analytical design to examine functional outcomes among individuals with COPD.

2. Participants and sample size

The sample size estimation was performed using G*Power (version 3.1), assuming a medium effect size ($f = 0.25$), an alpha level of 0.05, and a desired power of 0.80 for a one-way ANOVA with three groups. Based on these parameters, the required total sample size was 159 participants. However, due to practical constraints, 120 participants were included in the present study. Patients diagnosed with COPD were classified into anemic and non-anemic groups based on hemoglobin levels obtained from medical records. A total of 120 participants were recruited and categorized into three groups: healthy controls ($n = 40$), non-anemic COPD patients ($n = 40$), and anemic COPD patients ($n = 40$). Diagnosis of COPD was established according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. (Langefeld, 2024). According to the World Health Organization criteria (World Health Organization, 2023), anemia was defined as a hemoglobin level <13.0 g/dL in men and <12.0 g/dL in women. Accordingly, the non-anemic COPD group was required to have hemoglobin levels within or above these thresholds, whereas the anemic COPD group was defined by hemoglobin levels below these

cut-off values. The healthy control group was defined as individuals without a history of chronic respiratory disease, anemia, or significant comorbidities, and with normal pulmonary function as confirmed by spirometry (World Health, Organization, 2024).

3. Pulmonary Function Assessment

Pulmonary function was assessed using standardized spirometry performed in accordance with the guidelines of the American Thoracic Society (ATS) and European Respiratory Society (ERS). Forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), percent predicted FVC, percent predicted FEV_1 , and the FEV_1/FVC ratio were obtained to characterize airflow limitation and pulmonary function status (Graham et al., 2019). Spirometry measurements were used primarily to confirm disease severity and comparability between COPD groups.

4. Exercise Capacity Assessment

Functional exercise capacity was evaluated using the six-minute walk test (6MWT), administered according to standardized guidelines (Holland et al., 2014). Participants were instructed to walk at a self-selected pace along a standardized walkway for six minutes, aiming to cover the maximum possible distance. The six-minute walk distance (6MWD) was recorded as the primary indicator of exercise capacity. Heart rate and peripheral oxygen saturation were measured at rest and immediately following test completion to reflect physiological responses to functional exertion.

5. Balance Assessment

Balance performance and functional mobility were assessed using the Timed Up and Go (TUG) test. The TUG test evaluates the time required for a participant to rise from a seated position, walk a short distance, turn, return, and sit down, reflecting dynamic balance and mobility relevant to daily activities (Mesquita et al., 2020). The TUG test has been widely used in older adults and individuals with chronic conditions to identify balance impairment and fall risk (Loughran et al., 2020).

6. Statistical Analysis

Data were analyzed using descriptive and inferential statistics. Continuous variables are presented as mean $\pm$ standard deviation. Comparisons among groups were performed using one-way analysis of variance (ANOVA) with Bonferroni post hoc tests. Categorical variables, including sex distribution, were analyzed using the chi-square test. Statistical significance was set at $p < .05$. All analyses were

conducted using standard statistical software.

6. Ethical Approval:

All participants were clinically stable at the time of enrollment and provided written informed consent prior to participation. This study protocol has been approved by the Human Research Ethics Committee of Saint Louis College, Bangkok, Thailand. (E. 061/2568)

Results

1. Participant Characteristics

There were no significant differences among the three groups in age, sex distribution, body weight, height, or body mass index ($p > .05$). Hemoglobin concentration was significantly lower in the anemic COPD group compared with the other groups ($p < .05$). Pulmonary function parameters were significantly reduced in both COPD groups compared with healthy controls, with no significant differences between anemic and non-anemic COPD patients (Shown in Table 1).

Table 1. Participant characteristics and pulmonary function parameters among three groups

Variables	Healthy controls	Non-Anemic COPD	Anemic COPD	<i>p</i> -value
Age (years)	71.45 $\pm$ 4.16	71.40 $\pm$ 5.67	71.88 $\pm$ 5.00	.069
Sex (M/F)	20/20	20/20	20/20	1.000 ^a
Weight (kg)	56.05 $\pm$ 4.30	55.65 $\pm$ 6.76	55.38 $\pm$ 7.41	.075
Height (cm)	161.18 $\pm$ 6.72	160.21 $\pm$ 7.36	160.88 $\pm$ 6.29	.085
BMI (kg/m ²)	20.95 $\pm$ 1.95	20.82 $\pm$ 2.04	20.89 $\pm$ 2.13	.560
Hemoglobin (g/dL)	15.16 $\pm$ 0.88	15.08 $\pm$ 0.78**	11.38 $\pm$ 0.61*	.001

Table 1. (Cont.)

Variables	Healthy controls	Non-Anemic COPD	Anemic COPD	p-value
Pulmonary Function				
FEV ₁ (%predicted)	97.33 ± 8.15	47.82 ± 10.01	46.65 ± 14.22*	.025
FVC (%predicted)	94.88 ± 7.45	70.97 ± 14.44	68.35 ± 12.12*	.026
FEV ₁ /FVC (%)	83.66 ± 2.56	50.77 ± 7.66	52.28 ± 13.85*	.004

Data are presented as mean ± standard deviation unless otherwise indicated.

p* < .05 vs. control group *p* < .05 vs. non-anemic COPD

^a Sex distribution was analyzed using the chi-square test.

2. Exercise Capacity

Six-minute walk distance differed significantly among the groups (*p* < .001). Anemic COPD patients demonstrated the shortest walking distance, followed by non-anemic COPD patients, whereas healthy controls achieved the greatest distance (Shown in Table 2).

Table 2. Exercise capacity, cardiorespiratory responses, and balance performance among the three groups

Variables	Healthy controls	Non- anemic COPD	Anemic COPD
Exercise capacity			
6MWD (meters)	477.31 ± 47.12	370.42 ± 48.55*	290.12 ± 66.53*
Cardiorespiratory responses			
Resting HR (beats/minute)	72.76 ± 9.03	83.44 ± 10.01	91.94 ± 9.27*
HR immediately after 6MWT (beats/minute)	99.10 ± 14.20	114.06 ± 9.42	125.35 ± 10.01
Resting peripheral oxygen saturation (SpO ₂) (%)	99.35 ± 0.99	96.35 ± 2.32	95.65 ± 2.57
SpO ₂ immediately post-test (%)	96.65 ± 2.62	90.06 ± 0.11**	84.82 ± 2.69*
Balance performance			
Timed Up and Go (seconds)	17.90 ± 0.23*	18.60 ± 0.73*	29.50 ± 0.69*

Data are presented as mean ± standard deviation.

p* < .05 vs. control group *p* < .05 vs. non-anemic COPD

3. Cardiorespiratory Responses

Heart rate after the 6MWT was highest in the anemic COPD group, while post-exercise oxygen saturation was significantly lower compared with the other groups ($p < .05$).

4. Balance Performance

Timed Up and Go performance was significantly impaired in anemic COPD patients compared with non-anemic COPD patients and healthy controls ($p < .001$), indicating poorer balance and mobility.

Discussions

The present study demonstrated that individuals with COPD and concomitant anemia exhibited significantly lower exercise capacity and poorer balance performance compared with both non-anemic COPD patients and healthy controls. Despite similar levels of pulmonary function between the COPD groups, the presence of anemia was associated with shorter six-minute walk distance and longer TUG completion time, suggesting additional functional limitations beyond airflow obstruction alone.

Importantly, beyond statistical significance, the magnitude of these differences indicates potential clinical relevance. The observed reduction in six-minute walk distance may reflect a meaningful decline in functional exercise capacity, which has been associated with increased morbidity and reduced quality of life in patients with COPD. Similarly, prolonged TUG performance suggests clinically relevant impairment in

dynamic balance and mobility, which may increase fall risk and limit independence in daily activities. Therefore, the differences observed between groups are likely not only statistically significant but also clinically meaningful.

From a physiological perspective, these impairments can be explained by reduced oxygen delivery to skeletal muscles and the central nervous system. Decreased hemoglobin levels limit oxygen transport and cellular energy production, leading to reduced muscle strength, endurance, and motor unit recruitment (Alisamir et al., 2022). In addition, impaired cerebral oxygenation may reduce cortical processing speed and neuromuscular coordination, resulting in delayed reaction time and compromised sensorimotor integration (Garcia-Pachon & Padilla-Navas, 2024).

The reduced exercise capacity observed in the anemic COPD group, as reflected by the 6MWT, may be attributed to impaired oxygen transport and early onset of muscle fatigue. Decreased hemoglobin levels limit oxygen delivery to working muscles, thereby reducing aerobic capacity and endurance. At the cellular level, insufficient oxygen availability impairs mitochondrial oxidative phosphorylation, leading to reduced ATP production and increased reliance on anaerobic metabolism. This results in early muscle fatigue, reduced force generation, and diminished exercise tolerance. In patients with COPD, who already experience ventilatory limitation and impaired gas exchange,

the additional burden of anemia may further compromise oxygen availability and exacerbate fatigue during physical activity (Alisamir et al., 2022; Loughran et al., 2020).

Although some studies have reported inconsistent findings, these discrepancies may be explained by differences in anemia severity, compensatory physiological mechanisms, and variability in study design. Mild anemia may not produce sufficient physiological disruption to affect functional outcomes, whereas more severe anemia is likely to result in clinically detectable impairments. Taken together, the present findings suggest that anemia is a clinically relevant and potentially modifiable factor influencing neuromuscular function, reaction time, and functional performance in individuals with COPD. These results support the inclusion of anemia screening and targeted rehabilitation strategies in the comprehensive management of this population.

The observed impairment in balance and mobility may be explained by reduced oxygen delivery to skeletal muscles and the central nervous system in individuals with anemia. Decreased hemoglobin levels limit oxygen transport and cellular energy production, resulting in reduced muscle strength, endurance, and motor unit recruitment, which are essential for postural control (Alisamir et al., 2022). In addition, chronic hypoxia may impair cortical processing speed and neuromuscular coordination, leading to delayed reaction time

and reduced motor responsiveness (Garcia-Pachon & Padilla-Navas, 2024). These mechanisms may partly explain the prolonged Timed Up and Go performance observed in the anemic COPD group.

Balance performance was also inferior in participants with anemia, indicating impairment in postural control. Adequate balance requires effective integration of sensory input, neuromuscular coordination, and sufficient muscle strength, all of which may be compromised in individuals with COPD (Xiang & Luo, 2024). Chronic anemia-related hypoxia may further impair neuromuscular function and contribute to reduced postural stability and delayed motor responses (Alisamir et al., 2022). When combined with physical inactivity and muscle weakness commonly observed in COPD, these factors may substantially increase the risk of functional mobility limitations and falls (Loughran et al., 2020).

Age-related physiological decline may further explain the observed differences between groups. Older adults with COPD frequently present with sarcopenia, reduced proprioceptive acuity, and delayed motor responses, all of which contribute to impaired balance and mobility (Han et al., 2024). The presence of anemia may further exacerbate these age-related changes through reduced oxygen delivery and neuromuscular dysfunction, leading to greater impairments in functional performance (Alisamir et al., 2022). These findings highlight

the importance of considering anemia as a clinically relevant and potentially modifiable factor influencing functional performance in older individuals with COPD. Taken together, the present findings highlight the potential role of anemia as an additional and potentially modifiable factor influencing neuromuscular function, balance performance, and fall risk in individuals with COPD. These results underscore the importance of incorporating anemia screening and targeted interventions, including exercise and balance training, into comprehensive management strategies for this population.

From a clinical perspective, the results emphasize the need for comprehensive assessment of anemia in patients with COPD, particularly in those with reduced exercise capacity or balance deficits. Early identification and appropriate management of anemia, combined with targeted exercise and balance training, may enhance functional outcomes and reduce fall risk in this population (Alisamir et al., 2022; Loughran et al., 2020). Clinical implications for physical therapists should consider anemia as a modifiable factor influencing exercise tolerance and balance in COPD. Individualized exercise prescription, close monitoring during rehabilitation, and incorporation of balance training may optimize outcomes, particularly in patients with anemic COPD. From a health service management perspective, these findings highlight the importance of integrating anemia screening into routine clinical assessment for patients with

COPD. Early identification of anemia may facilitate timely intervention and individualized rehabilitation strategies. Incorporating multidisciplinary approaches involving physicians, physical therapists, and nutrition specialists may further improve functional outcomes and reduce fall risk among older adults with COPD.

Limitations and future research

Several limitations should be acknowledged. First, the cross-sectional design limits the ability to establish causal relationships between anemia and functional impairment. Second, the study did not assess potential confounding factors such as nutritional status, inflammatory markers, or habitual physical activity, which may influence exercise capacity and balance. Finally, the sample size was relatively modest and participants were recruited from a single setting, which may limit generalizability. Future longitudinal and interventional studies are warranted to determine whether treatment of anemia can improve functional outcomes in patients with COPD.

Conclusions

In conclusion, anemia is associated with significantly reduced exercise capacity and impaired balance performance in individuals with COPD, independent of pulmonary function status. These findings highlight the importance of considering hemoglobin status during functional assessment and rehabilitation planning. Routine screening and appropriate management of

anemia may contribute to improved functional outcomes and reduced fall risk in patients with COPD.

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