British Journal of Hospital Medicine

*Br. J. Hosp. Med. (Lond)* **2026**; 87(8): 57184
https://doi.org/10.31083/BJHM57184

*Article*

# Clinical Significance of the Baseline Six-Minute Walk Test in Patients With Early-Stage Lung Cancer and COPD: Correlations With Pulmonary Function, COPD Severity, Cognitive Function, and Quality of Life

Shuhui Gao[1], Guibin Zhang[2], Deyang Meng[1], Ke Zhang[1], Haixiang Gao[1,*], Li Yan[1,*]

[1]Department of Respiratory Medicine, Hebei Provincial People's Hospital, 050000 Shijiazhuang, Hebei, China
[2]Thoracic Surgery, Hebei Provincial People's Hospital, 050000 Shijiazhuang, Hebei, China
*Correspondence: gaohaixiang0801@163.com (Haixiang Gao); yanlihuxi14@163.com (Li Yan)
Academic Editor: John Alcolado
Submitted: 21 November 2025 Revised: 4 March 2026 Accepted: 30 April 2026 Published: 18 August 2026

**Abstract**

**Aims/Background:** Driven by global industrialization and a rapidly aging population, lung cancer and chronic obstructive pulmonary disease (COPD) increasingly co-occur, posing complex challenges for clinical management. Although the six-minute walk test (6MWT) is a well-established tool for assessing functional status in each condition, its specific role in patients with early-stage lung cancer and comorbid COPD remains unexplored. This study aimed to explore the correlations between the baseline 6MWT results and pulmonary function, COPD severity, cognitive function, and quality of life (QoL) in patients with early-stage lung cancer and comorbid COPD. **Methods:** A retrospective study was conducted, enrolling 215 patients with early-stage lung cancer and COPD admitted to Hebei Provincial People's Hospital between January 2022 and December 2023. Data on patient demographics, baseline 6MWT results (six-minute walk distance [6MWD]), pulmonary function parameters (forced expiratory volume in one second [FEV1], forced vital capacity [FVC], FEV1/FVC ratio), COPD severity grade, cognitive function (Montreal Cognitive Assessment [MoCA] score), and quality of life (St. George's Respiratory Questionnaire [SGRQ] score) were collected from medical records. Patients were dichotomized into High and Low 6MWD groups based on the median 6MWD value. Spearman correlation, univariate analyses, and multivariate logistic regression were used to examine relationships and identify independent factors associated with 6MWD. **Results:** Logistic regression identified age, FEV1, FVC, FEV1/FVC, COPD severity grade, MoCA score, and the dimensions of respiratory symptoms and activity limitation of the SGRQ scores as independent factors influencing 6MWD. Age demonstrated a significant negative correlation with 6MWD ($r_s = -0.666$, $p < 0.001$). FEV1, FVC, and FEV1/FVC were each significantly positively correlated with 6MWD ($r_s = 0.557$, $p < 0.001$; $r_s = 0.139$, $p = 0.041$; $r_s = 0.598$, $p < 0.001$, respectively). A statistically significant difference in 6MWD was observed among patients with different COPD severity levels ($H = 49.283$, $p < 0.001$). MoCA scores showed a significant positive correlation with 6MWD ($r_s = 0.388$, $p < 0.001$). The respiratory symptoms, activity limitation, and impact on daily life scores of the SGRQ were each significantly negatively correlated with 6MWD ($r_s = -0.766$, $p < 0.001$; $r_s = -0.617$, $p < 0.001$; $r_s = -0.245$, $p < 0.001$, respectively). **Conclusion:** The 6MWT results in patients with early-stage lung cancer and COPD demonstrate significant correlations with pulmonary function, COPD severity, cognitive function, and quality of life. Therefore, the 6MWT can be deployed as a comprehensive functional assessment tool in this patient population.

**Keywords:** lung cancer; chronic obstructive pulmonary disease; six-minute walk test; pulmonary function; cognitive function; quality of life

## 1. Introduction

Driven by global industrialization and a rapidly aging population, the incidence rates of both lung cancer and chronic obstructive pulmonary disease (COPD) continue to maintain an upward trend. These conditions frequently coexist and interact, thereby compounding the complexity of clinical management [1,2,3]. COPD, a common respiratory disease characterized by persistent airway inflammation, is not only an independent risk factor for lung cancer. Its chronic inflammatory microenvironment is also thought to interact with multiple mechanisms—including smoking, genetic susceptibility, epigenetic alterations, epithelial-mesenchymal transition, and oxidative stress—to collectively drive the progressive malignant transformation of bronchial epithelial cells, thus promoting the initiation and progression of lung cancer [4,5]. A cross-sectional study involving 11,440 U.S. adults aged 40 and above revealed a significantly higher prevalence of lung cancer among COPD patients compared to non-COPD individuals (3.39% vs. 0.14%), further substantiating this intricate pathophysiological link [6]. In the context of this comorbidity, patients often face a spectrum of complex clinical challenges, including sustained decline in pulmonary function, severely impaired exercise tolerance, increased risk of cognitive im-

**Copyright**: © 2026 The Author(s). Published by IMR Press.
This is an open access article under the CC BY 4.0 license.

**Publisher's Note**: IMR Press stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

pairment, and diminished quality of life (QoL), highlighting an urgent need for targeted functional assessment and comprehensive management strategies.

The six-minute walk test (6MWT) is a simple, safe, and economical submaximal exercise tolerance test routinely used in clinical practice to assess functional status in patients with respiratory diseases [7]. This test provides a composite measure of cardiopulmonary reserve, peripheral muscle strength, and overall endurance. It has been well-established that 6MWT results correlate closely with the degree of airflow limitation, symptom burden, and prognosis in COPD patients [8,9]. Similarly, in lung cancer patients, the 6MWT has demonstrated predictive value for postoperative complications, QoL, and survival outcomes [10,11,12]. Although existing evidence supports the utility of the 6MWT in evaluating single diseases, its application remains unreported in the specific population of patients with early-stage lung cancer and comorbid COPD. Furthermore, emerging research suggests a potential intrinsic link between cognitive dysfunction and limited physical activity in COPD patients [13,14]. As an objective measure of physical capacity, the specific association patterns between the 6MWT and core patient-centered outcomes like cognitive function and QoL in this comorbid population warrant systematic investigation.

Therefore, this retrospective study aimed to analyze baseline 6MWT data from a cohort of patients with early-stage lung cancer and COPD. We sought to comprehensively explore the correlations between the 6MWT results and key clinical parameters, including pulmonary function, COPD severity, cognitive status, and QoL. Critically, while these relationships are recognized in isolated conditions, their interplay and collective impact remain uncharacterized in the comorbid setting of early-stage lung cancer and COPD. This study addresses this gap by providing the first integrated analysis of how a simple functional measure (6MWD) concurrently relates to respiratory, cognitive, and quality-of-life domains in this unique and clinically high-risk population. The findings are expected to elucidate the comprehensive assessment value of the 6MWT in this unique patient group, providing a practical tool for the rapid clinical identification of overall functional impairment and informing the development of tailored intervention strategies.

## 2. Methods

### *2.1 Study Participants*

This retrospective study enrolled 215 patients diagnosed with early-stage lung cancer and COPD, who were hospitalized in Hebei Provincial People's Hospital between January 2022 and December 2023.

The inclusion criteria were as follows:

a. Pathologically confirmed primary early-stage lung cancer (clinical stage I–II) meeting the diagnostic criteria for COPD [15].

b. Age >18 years, capable of self-care, and able to independently complete the 6MWT and relevant questionnaires.

c. Availability of complete baseline data required for this study in the medical record system.

The exclusion criteria were as follows:

a. Concurrent severe cardiac, hepatic, or renal dysfunction.

b. History of unstable cardiovascular disease (e.g., myocardial infarction or unstable angina within the preceding month).

c. Limited mobility due to musculoskeletal disorders, neurological diseases, or severe myasthenia.

d. Documented intellectual disability, psychiatric disorders, or severe hearing impairment.

e. Other coexisting active pulmonary diseases (e.g., bronchiectasis, asthma, active tuberculosis).

f. Diagnosis of any other active malignancy.

### *2.2 Method of Measurement*

Data were independently extracted from our hospital's electronic medical record system by two uniformly trained researchers. The collected information included patient demographics (age, sex, body mass index [BMI]), smoking exposure, 6MWT results, pulmonary function parameters, COPD severity grading, lung cancer Tumor-Node-Metastasis (TNM) staging, long-term oxygen therapy, home non-invasive ventilation (NIV) use, cognitive function assessment scores, and QoL assessment scores. All baseline assessments, including spirometry, Montreal Cognitive Assessment (MoCA), and St. George's Respiratory Questionnaire (SGRQ), were performed during the same clinical stabilization period after admission and before the initiation of any anticancer treatment (surgery or chemotherapy).

Six-minute walk test (6MWT) [16]. All patients underwent the test according to a standardized international protocol in a quiet, flat, 30-meter enclosed corridor after admission and before initiation of any surgical or oncological treatment. Specifically, the test was conducted during the preoperative clinical stabilization period for surgical candidates, with a median of 3 days (range, 1–7 days) prior to surgery. For patients scheduled for primary chemotherapy, the test was performed after diagnosis but before initiation of the first cycle, during a period of clinical stability defined as no exacerbation of COPD or other acute cardiopulmonary symptoms in the preceding 4 weeks. Researchers provided detailed instructions beforehand. During the test, patients were encouraged to walk as far as possible in six minutes, at their fastest tolerable pace. They were permitted to slow down or rest if needed, but the timer continued to run. The primary outcome was the six-minute walk distance (6MWD), recorded in meters, which directly reflects the patient's overall exercise tolerance.

Pulmonary function assessment [17]. Spirometry was performed with patients at rest using a MasterScreen Pneumo spirometer (Model No. V-171470, Jaeger Medical, Bavaria, Germany). Key parameters included forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and the calculated FEV1/FVC ratio. A lower FEV1/FVC ratio indicates more severe airflow obstruction.

COPD severity grading. The severity of airflow limitation was graded according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) report [15], which uses a post-bronchodilator FEV1/FVC ratio <0.70 as the threshold for defining persistent airflow limitation. Based on the post-bronchodilator FEV1 percent predicted, severity was graded into four levels: Grade 1 (mild: FEV1 ≥80% predicted), Grade 2 (moderate: 50% ≤ FEV1 < 80% predicted), Grade 3 (severe: 30% ≤ FEV1 < 50% predicted), and Grade 4 (very severe: FEV1 <30% predicted).

Cognitive function assessment. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA) [18]. Developed by Nasreddine et al. [19], this 30-point test assesses eight cognitive domains: visuospatial/executive function, naming, memory, attention, language, abstraction, delayed recall, and orientation. In this study, we applied the standard cut-off score of <26 to indicate potential cognitive impairment. Lower scores indicate greater severity of possible cognitive deficit.

Quality of life assessment. QoL was measured using the St. George's Respiratory Questionnaire (SGRQ) [20]. This instrument contains 50 items distributed across three components: symptoms (8 items, assessing the frequency and severity of respiratory symptoms like cough, sputum, and wheezing), activity (16 items, assessing limitations in daily physical activities due to breathlessness), and impacts (26 items, assessing the comprehensive effect of the disease on overall health status, psychological well-being, and social life). Scores for each component are standardized and presented as percentages ranging from 0 to 100, with a higher score denoting poorer health status and more severe impairment of QoL.

### *2.3 Statistical Analysis*

Statistical analysis was performed using SPSS version 23.0 software (IBM SPSS, Armonk, NY, USA). The Shapiro-Wilk test was performed to assess the normality of continuous data. Data conforming to a normal distribution are presented as mean ± standard deviation, such as FEV1 and FEV1/FVC, and were compared using the independent-samples *t*-test. Data not conforming to a normal distribution, such as age, BMI, and 6MWD, are expressed as medians and interquartile ranges, and were compared using the Mann-Whitney *U* test. Categorical data are expressed as counts and percentages, and were compared by the chi-square test, corrected chi-square test, or Kruskal-Wallis *H* test, as appropriate. Univariate analysis combined with logistic regression modeling was applied to comprehensively identify independent factors influencing 6MWD in patients with early-stage lung cancer and COPD. For correlation analysis between variables, Spearman's rank correlation was employed due to the non-normal distribution of most data, with correlation coefficients expressed as $r_s$. All statistical tests were two-sided, and a $p$-value < 0.05 was considered statistically significant.

## 3. Results

### *3.1 General Information and Clinical Data of Patients*

The general information and clinical data of the enrolled patients are presented in Table 1.

**Table 1. General information and clinical data of enrolled patients.**

| Variable | Value |
|---|---|
| Age (years) | 66.00 (60.00, 72.00) |
| Sex, *n* (%) | |
| Male | 166.00 (77.21) |
| Female | 49.00 (22.79) |
| BMI (kg/m$^2$) | 22.79 (20.53, 24.25) |
| 6MWD (meters) | 447.00 (395.00, 505.00) |
| Smoking exposure (pack-years) | 37.00 (26.00, 50.00) |
| FEV1 (L) | 1.66 ± 0.33 |
| FVC (L) | 3.10 (2.90, 3.45) |
| FEV1/FVC (%) | 52.84 ± 9.35 |
| COPD severity grading | |
| Grade 1 | 26.00 (12.09) |
| Grade 2 | 89.00 (41.40) |
| Grade 3 | 56.00 (26.05) |
| Grade 4 | 44.00 (20.47) |
| Lung cancer TNM staging | |
| Stage I | 122.00 (56.74) |
| Stage II | 93.00 (43.26) |
| Long-term oxygen therapy | |
| Yes | 16.00 (7.44) |
| No | 199.00 (92.56) |
| Home NIV use | |
| Yes | 10.00 (4.65) |
| No | 205.00 (95.35) |
| MoCA score (points) | 24.00 (21.00, 27.00) |
| SGRQ score (points) | |
| Respiratory symptoms | 53.27 ± 11.11 |
| Activity limitation | 49.00 (41.00, 66.00) |
| Impact on daily life | 40.00 (37.00, 45.00) |

Notes: 6MWD, six-minute walk distance; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; MoCA, Montreal Cognitive Assessment; NIV, non-invasive ventilation; SGRQ, St. George's Respiratory Questionnaire; TNM, Tumor-Node-Metastasis.

**Table 2. Univariate analysis of factors influencing 6MWD in patients with early-stage lung cancer and COPD.**

| Variable | High 6MWD group ($n$ = 104) | Low 6MWD group ($n$ = 111) | $\chi^2$/Z/t/H | p |
|---|---|---|---|---|
| Age (years) | 60.00 (53.00, 66.75) | 71.00 (64.00, 76.00) | −8.192 | <0.001 |
| Sex, n (%) | | | 0.773 | 0.379 |
| Male | 83.00 (79.81) | 83.00 (74.77) | | |
| Female | 21.00 (20.19) | 28.00 (25.23) | | |
| BMI (kg/m$^2$) | 22.28 (20.43, 24.26) | 22.97 (20.55, 24.23) | −0.998 | 0.691 |
| Smoking exposure (pack-years) | 36.00 (24.00, 50.00) | 38.00 (27.00, 50.00) | −0.905 | 0.365 |
| FEV1 (L) | 1.83 ± 0.32 | 1.51 ± 0.27 | 7.814 | <0.001 |
| FVC (L) | 3.20 (2.95, 3.52) | 3.00 (2.86, 3.32) | 2.854 | 0.004 |
| FEV1/FVC (%) | 56.98 ± 9.64 | 48.95 ± 7.19 | 6.957 | <0.001 |
| COPD severity grading | | | 30.560 | <0.001 |
| Grade 1 | 21.00 (20.19) | 5.00 (4.50) | | |
| Grade 2 | 53.00 (50.96) | 36.00 (32.43) | | |
| Grade 3 | 20.00 (19.23) | 36.00 (32.43) | | |
| Grade 4 | 10.00 (9.62) | 34.00 (30.63) | | |
| Lung cancer TNM staging | | | 0.074 | 0.786 |
| Stage I | 60.00 (57.69) | 62.00 (55.86) | | |
| Stage II | 44.00 (42.31) | 49.00 (44.16) | | |
| Long-term oxygen therapy | | | 2.029 | 0.154 |
| Yes | 5.00 (4.81) | 11.00 (9.91) | | |
| No | 99.00 (95.19) | 100.00 (90.09) | | |
| Home NIV use | | | 0.048 | 0.827 |
| Yes | 4.00 (3.85) | 6.00 (5.41) | | |
| No | 100.00 (96.15) | 105.00 (94.59) | | |
| MoCA score (points) | 25.00 (23.00, 27.00) | 22.00 (20.00, 25.00) | −4.752 | <0.001 |
| SGRQ score (points) | | | | |
| Respiratory symptoms | 46.05 ± 8.01 | 60.05 ± 9.18 | −11.882 | <0.001 |
| Activity limitation | 44.00 (40.00, 48.00) | 65.00 (50.00, 72.00) | −7.632 | <0.001 |
| Impact on daily life | 39.00 (36.00, 42.00) | 40.00 (37.00, 46.00) | −2.489 | 0.013 |

Notes: 6MWD, six-minute walk distance; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; MoCA, Montreal Cognitive Assessment; NIV, non-invasive ventilation; SGRQ, St. George's Respiratory Questionnaire.

### *3.2 Univariate Analysis of Factors Influencing 6MWD in Patients With Early-Stage Lung Cancer and COPD*

Patients were divided into a High 6MWD group (≥447 m, $n$ = 104) and a Low 6MWD group (<447 m, $n$ = 111) based on the median 6MWD value. Univariate analysis revealed statistically significant differences between the two groups in age, FEV1, FVC, FEV1/FVC ratio, COPD severity grading, MoCA score, and all SGRQ component scores ($p < 0.05$ for all) (Table 2).

### *3.3 Logistic Regression Analysis of Factors Influencing 6MWD in Patients With Early-Stage Lung Cancer and COPD*

Logistic regression analysis was performed with the 6MWD group as the dependent variable (High 6MWD = 1, Low 6MWD = 0). Independent variables included age, FEV1, FVC, FEV1/FVC, COPD severity grading (Grades 1/2 = 0, Grades 3/4 = 1), MoCA score, and the three SGRQ component scores (respiratory symptoms, activity limitation, impact on daily life). The analysis identified age, FEV1, FVC, FEV1/FVC, COPD severity grading, MoCA score, and the dimensions of respiratory symptoms and activity limitation of SGRQ scores as independent influencing factors for 6MWD in this patient population (Table 3).

### *3.4 Correlation Between Age and Baseline 6MWT Results*

As shown in Fig. 1, age was significantly negatively correlated with 6MWD ($r_s = -0.666$, $p < 0.001$).

### *3.5 Correlation Between Lung Function and Baseline 6MWT Results*

As shown in Fig. 2, FEV1, FVC, and FEV1/FVC were significantly positively correlated with 6MWD ($r_s = 0.557$, $p < 0.001$; $r_s = 0.139$, $p = 0.041$; $r_s = 0.598$, $p < 0.001$).

**Table 3. Logistic regression analysis of factors influencing 6MWD in patients with early-stage lung cancer and COPD.**

| Variable | β | S.E. | Wald | $p$ | OR | 95% CI | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower | Upper |
| Age | −0.151 | 0.026 | 33.808 | <0.001 | 0.860 | 0.817 | 0.905 |
| FEV1 | 2.544 | 0.613 | 17.201 | <0.001 | 12.733 | 3.826 | 42.374 |
| FVC | 0.214 | 0.070 | 9.301 | 0.002 | 1.239 | 1.080 | 1.442 |
| FEV1/FVC | 0.122 | 0.020 | 37.271 | <0.001 | 1.129 | 1.086 | 1.174 |
| COPD severity grading | −1.489 | 0.313 | 22.595 | <0.001 | 0.226 | 0.122 | 0.417 |
| MoCA score | 0.222 | 0.049 | 20.683 | <0.001 | 1.249 | 1.135 | 1.374 |
| SGRQ score – Respiratory symptoms | −0.153 | 0.027 | 32.181 | <0.001 | 0.858 | 0.814 | 0.905 |
| SGRQ score – Activity limitation | −0.077 | 0.016 | 22.818 | <0.001 | 0.926 | 0.897 | 0.956 |
| SGRQ score – Impact on daily life | −0.029 | 0.039 | 0.544 | 0.461 | 0.972 | 0.900 | 1.049 |
| Constant | 12.980 | 2.162 | 36.063 | <0.001 | 89.855 | | |

Notes: 6MWD, six-minute walk distance; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; MoCA, Montreal Cognitive Assessment; SGRQ, St. George's Respiratory Questionnaire; CI, confidence interval; OR, odds ratio; S.E., Standard Error.

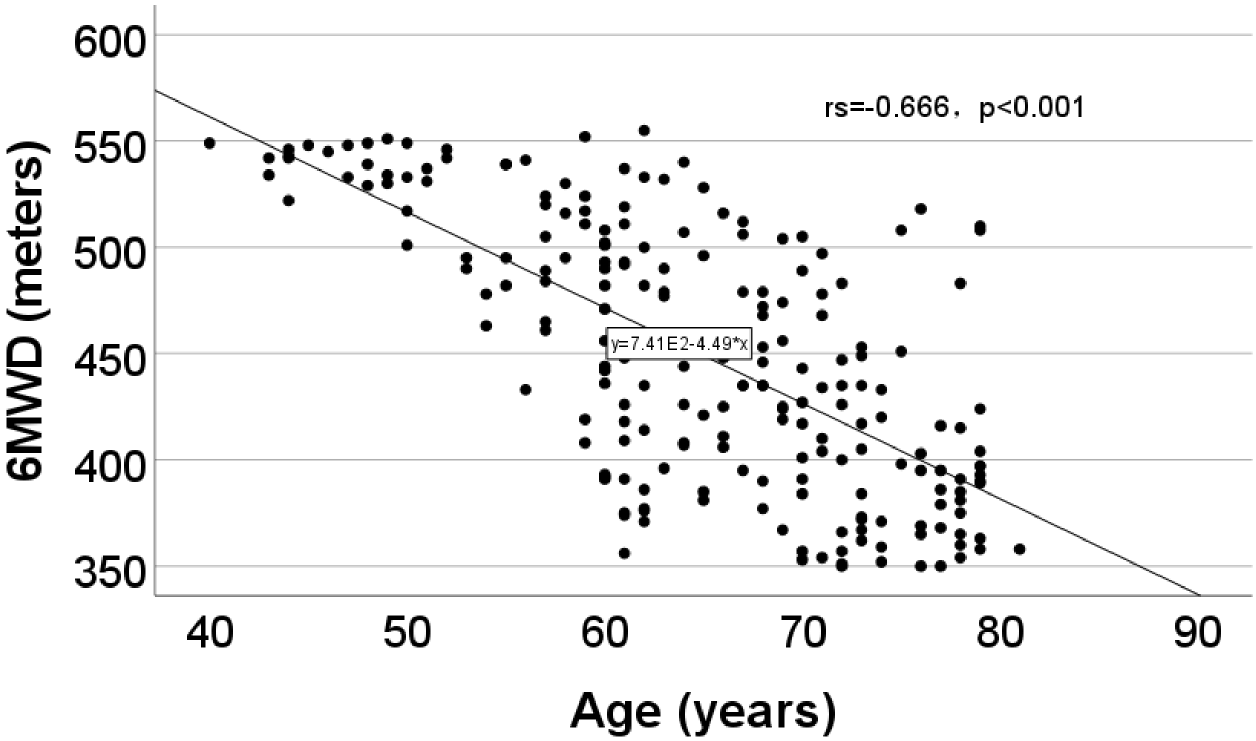


**Fig. 1. Correlation coefficient between age and 6MWD**. Note: The asterisk * stands for the multiplication symbol (×) in mathematical notation. 6MWD, six-minute walk distance.

### *3.6 Correlation Between COPD Severity and Baseline 6MWT Results*

The 6MWD for patients with COPD severity grades 1, 2, 3 and 4 was 517.50 (467.50, 542.00) meters, 459.00 (421.50, 505.00) meters, 426.50 (376.50, 501.25) meters, and 387.50 (368.75, 438.00) meters, respectively. There was a statistically significant difference in 6MWD among patients with different COPD severity levels ($H$ = 49.283, $p < 0.001$).

### *3.7 Correlation Between Cognitive Function and Baseline 6MWT Results*

As shown in Fig. 3, the MoCA score was significantly positively correlated with 6MWD ($r_s = 0.388$, $p < 0.001$).

### *3.8 Correlation Between Quality of Life and Baseline 6MWT Results*

As shown in Fig. 4, the dimensions of the SGRQ—respiratory symptoms, activity limitation, and impact on

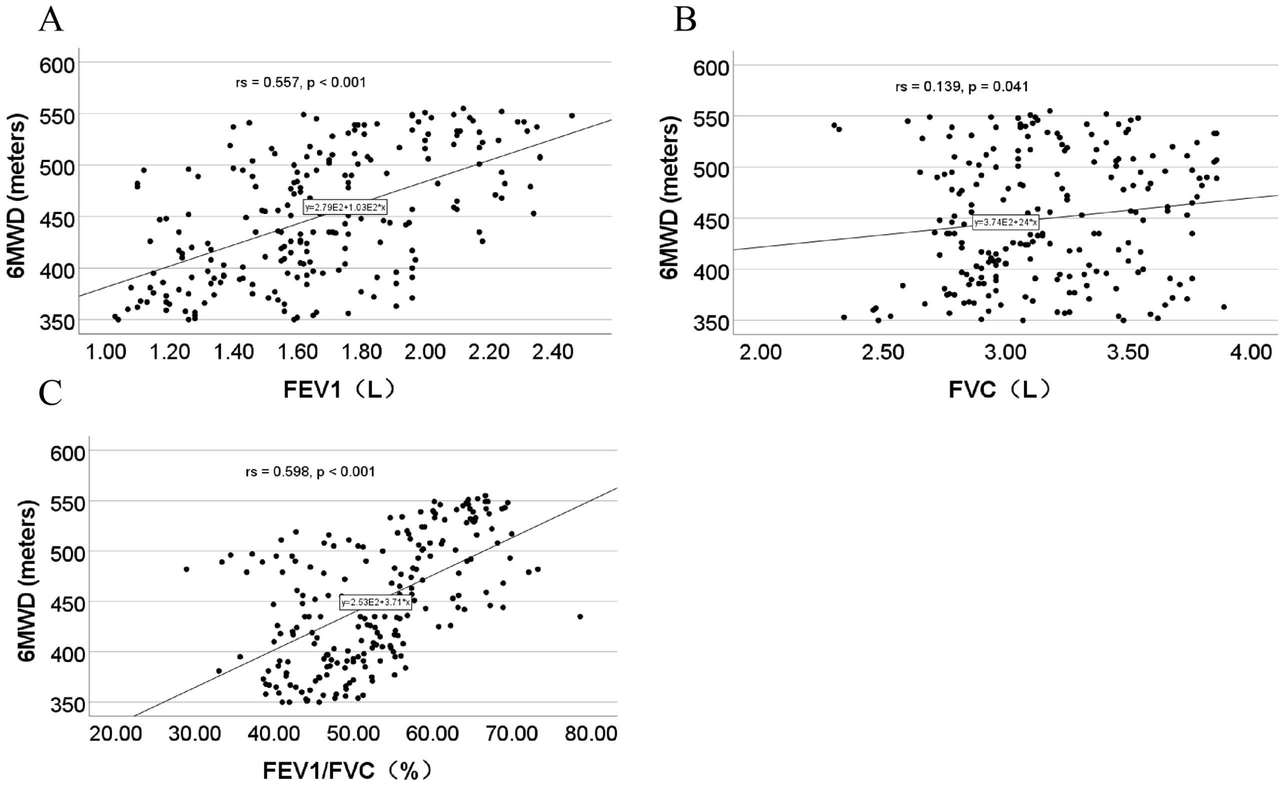


**Fig. 2. Correlation coefficients of 6MWD with FEV1 (A), FVC (B), and FEV1/FVC (C)**. Notes: The asterisk * stands for the multiplication symbol (×) in mathematical notation. 6MWD, six-minute walk distance; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

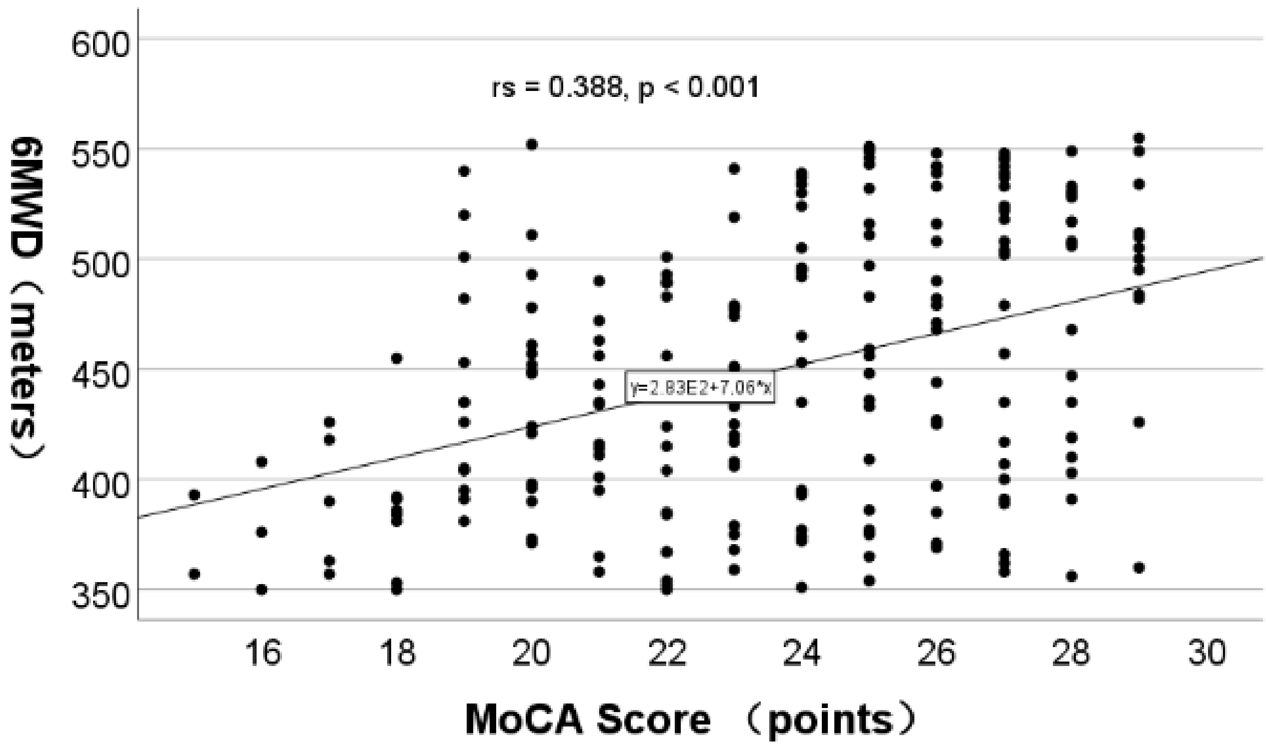


**Fig. 3. Correlation coefficient between MoCA score and 6MWD**. Notes: The asterisk * stands for the multiplication symbol (×) in mathematical notation. 6MWD, six-minute walk distance; MoCA, Montreal Cognitive Assessment.


IMR Press

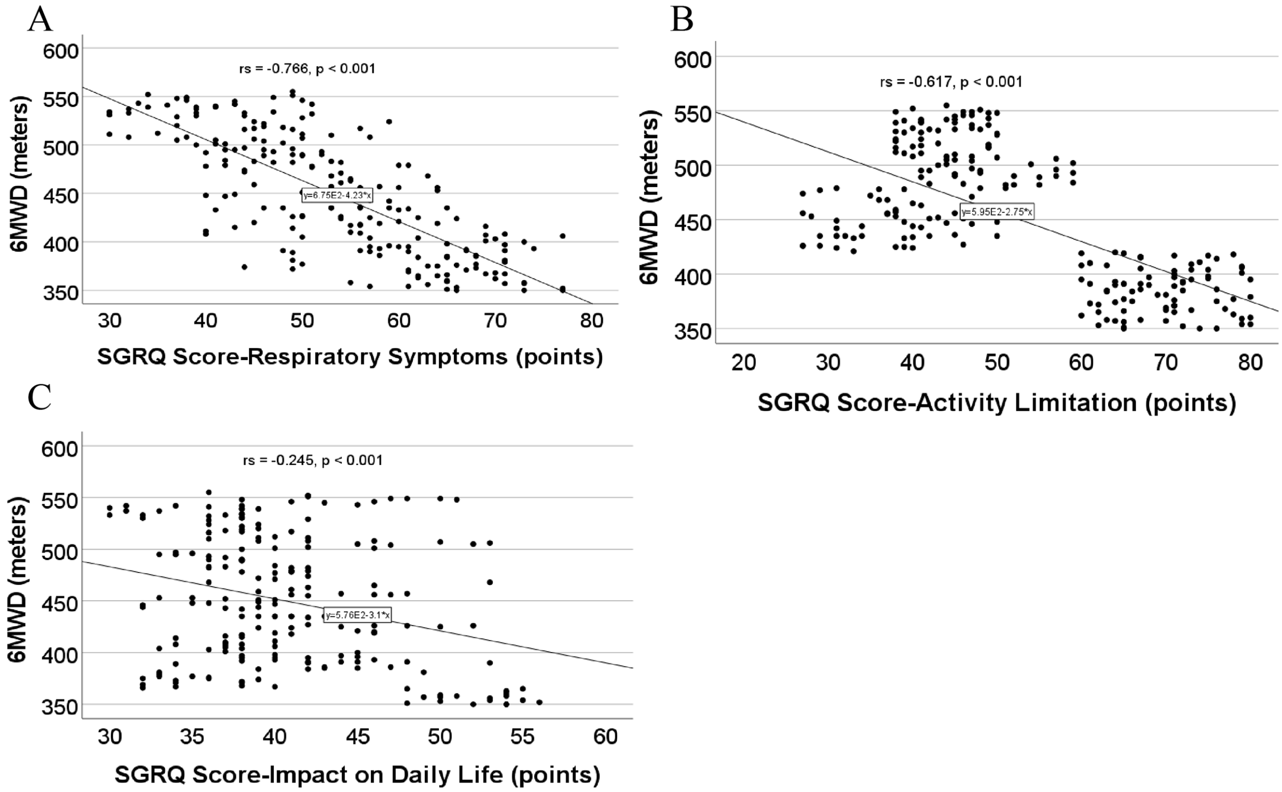


**Fig. 4. Correlation coefficients between the dimensions of the SGRQ (respiratory symptoms, activity limitation, impact on daily life) and 6MWD (A–C).** Correlation coefficients of 6MWD with FEV1 (A), FVC (B), and FEV1/FVC (C). Notes: 6MWD, six-minute walk distance; SGRQ, St. George's Respiratory Questionnaire. Notes: The asterisk * stands for the multiplication symbol (×) in mathematical notation.

daily life—were significantly negatively correlated with 6MWD ($r_s = -0.766$, $p < 0.001$; $r_s = -0.617$, $p < 0.001$; $r_s = -0.245$, $p < 0.001$).

## 4. Discussion

In this study, we retrospectively analyzed the electronic medical records of 215 patients with early-stage lung cancer and comorbid COPD, systematically investigating the multidimensional relationships of their pulmonary function, COPD severity, cognitive function, and quality of life with baseline 6MWT results (6MWD). Our findings indicate that a poorer 6MWT performance was significantly correlated with older age, more severe airflow limitation (reflected by lower FEV1, FVC, and FEV1/FVC values), higher disease severity grades, worse cognitive function (lower MoCA scores), and a poorer quality of life (higher SGRQ component scores). These correlations were further substantiated by univariate and multivariate logistic regression analyses, which confirmed age, pulmonary function parameters (FEV1, FVC, FEV1/FVC), COPD severity, MoCA score, and all SGRQ domain scores as independent factors associated with 6MWD. Although these correlations have been described individually, their convergence and combined strength in patients with coexisting early-stage lung cancer and COPD have not been established. Our findings demonstrate that, in this population, the 6MWT captures a broad spectrum of health impairments, underscoring its distinct utility as a comprehensive assessment tool.

This study demonstrated a significant association between declining 6MWD and increasing age in patients with early-stage lung cancer and COPD, a trend consistent with established clinical understanding. This is likely attributable to age-related physiological declines, including reductions in skeletal muscle fiber count, diminished mitochondrial function, and decreased alveolar elasticity, which collectively contribute to reduced exercise tolerance. Furthermore, the dual pathological burden of lung cancer and COPD may potentiate these age-related mechanisms. We also found significant positive correlations between 6MWD and FEV1, FVC, and FEV1/FVC, with 6MWD showing a decreasing trend as COPD severity worsened. The underlying mechanisms may involve several factors: firstly, dynamic hyperinflation during exercise increases the work of breathing and reduces efficiency; secondly, gas exchange abnormalities leading to hypoxemia can further limit exercise capacity; and finally, persistent systemic inflammation may contribute to dysfunctional muscle metabolism, creating a vicious cycle. This close relationship between the 6MWT and pulmonary function has been widely corroborated in other respiratory conditions. For instance, Hu et al. [21] noted a strong link between 6MWT results and pulmonary function level in patients with interstitial lung disease, while Eksombatchai et al. [22] observed reduced 6MWD in post-Coronavirus Disease 2019 (COVID-19) patients with residual restrictive or obstructive ventilatory defects, particularly among severe cases. Regarding prognostic value, Chen et al. [23] and Zanini et al. [24] respectively confirmed that the 6MWT predicts all-cause mortality in patients with interstitial lung disease and those with low pulmonary function. Similarly, Bae et al. [25] reported correlations of 6MWD and FVC with dyspnea in patients with myositis-associated interstitial lung disease. In a bronchiectasis cohort, Blakney et al. [26] demonstrated that the 6MWT not only reflects symptom severity but also independently predicts mortality.

Concerning cognitive function, our study identified a moderate-to-strong correlation between lower 6MWD and lower MoCA scores. Potential explanations include: first, chronic hypoxemia and systemic inflammation associated with COPD may directly damage cerebrovascular and neuronal integrity. Second, reduced physical capacity may limit social engagement and cognitive stimulation, potentially accelerating cognitive decline, possibly mediated through reduced release of neurotrophic factors. This association is supported by findings from other studies. Wang et al. [27] discovered that 6MWD was linked to working memory and prefrontal cortex activation in older adults with mild cognitive impairment, and Wiley et al. [28] further established a broad connection between walking capacity and global cognition in the elderly. Similar observations have been made in other chronic conditions like stroke and heart failure; for example, Hwang [29] and Pastva [30] reported moderate correlations between 6MWD and MoCA scores in community-dwelling stroke survivors and hospitalized older adults with acute decompensated heart failure, respectively. However, the universality of this relationship remains contentious. Ahn et al. [31], for instance, found no significant correlation between the 6MWT and MoCA in patients with ischemic stroke. Notably, research specifically targeting COPD or lung cancer populations is scarce. Our findings suggest that the relationship between physical capacity and cognitive function may vary across different disease contexts, underscoring the need for more disease-specific investigations.

Regarding quality of life, our results indicated that the 6MWD was significantly negatively correlated with symptoms and activities in the SGRQ score, and weakly but significantly correlated with life impact. This signifies that poorer exercise capacity is closely associated with a worse QoL, suggesting that declining mobility directly restricts daily activities, thereby reducing social participation and potentially increasing feelings of isolation, while possibly heightening sensitivity to respiratory symptoms. Consequently, improving exercise capacity could be a key therapeutic target for enhancing overall QoL in this patient group. This close relationship between functional capacity and QoL is also evident in other chronic respiratory diseases. For example, Yazgan et al. [32] indicated that 6MWT performance in adolescents with multiple sclerosis is influenced by factors like physical capacity, balance, and fatigue, and is related to QoL. Morita et al. [33] also reported that declining walking distance over time, alongside worsening dyspnea, was associated with decreased QoL in patients with non-tuberculous mycobacterial lung disease, echoing our conclusions.

The focus on early-stage (stage I–II) lung cancer patients, though narrowing the generalizability of results to advanced stages, is justified by key methodological and clinical reasons. Patients at this stage generally have a lower systemic tumor burden and are treatment-naïve to major cancer therapies such as chemotherapy or radiotherapy, both of which independently impair functional capacity, cognition, and quality of life. Studying this treatment-naïve cohort, therefore, minimizes these confounding effects, enabling a clearer examination of the relationship between 6MWT performance and comorbid COPD status. Furthermore, the preoperative period in early-stage disease represents a critical window for prehabilitation. Establishing functional baselines and their correlates in this specific population provides directly applicable evidence for guiding preoperative risk stratification and informing tailored rehabilitation protocols to optimize surgical outcomes and recovery.

This study has several limitations. First, as a single-center, retrospective analysis, it is susceptible to selection and information bias. Second, our observational dataset did not include detailed information on the use of respiratory medications, such as long-acting muscarinic antagonists, long-acting β2-agonists, or inhaled corticosteroids. As these medications can significantly modulate lung function, symptom burden, exercise capacity, and QoL scores, their unrecorded effects represent a potential confounding factor. Third, the study population was restricted to patients with early-stage lung cancer and COPD; whether the findings are generalizable to lung cancer patients across broader disease stages requires validation. Fourth, and most critically, the cross-sectional and descriptive nature of this study precludes any causal inference. We cannot demonstrate whether incorporating the 6MWT into standard assessments would alter therapeutic decisions, postoperative risk stratification, or ultimately improve patient outcomes. Fifth, the MoCA and SGRQ, being subjective instruments, are potentially influenced by patient mood, educational background, and social desirability bias. Furthermore, the absence of longitudinal follow-up data, such as survival, postoperative complications, or long-term functional trajectories, significantly weakens the direct clinical implications of our findings. Sixth, multicollinearity may exist among the independent variables included in our regression models; therefore, future studies should employ techniques such as principal component analysis to better disentangle the independent clinical contributions of these measures. Finally, potential confounding factors, such as nutritional status and psychological state, were not accounted for in the analysis, which might influence 6MWT results and the observed associations. Therefore, future prospective multicenter studies with a longitudinal design, incorporating hard clinical endpoints and evaluating the utility of 6MWT in guiding specific management strategies, are warranted to further validate these findings and establish its actionable clinical value.

## 5. Conclusion

In summary, the 6MWT is a simple, low-cost functional assessment tool that provides a composite measure of respiratory function, physical capacity, and daily living status in patients with early-stage lung cancer and COPD. Integrating this test into routine clinical assessment could facilitate rapid identification of patients at higher risk of functional impairment and inform the development of personalized management strategies, including targeted breathing exercises and physical rehabilitation programs.

## Key Points

• The baseline six-minute walk test (6MWT) results correlate with pulmonary function, COPD severity, cognitive status, and quality of life in early-stage lung cancer patients with COPD.

• A shorter walking distance is strongly associated with poorer health-related quality of life.

• Better exercise capacity is linked to higher cognitive function scores in these patients.

• The baseline 6MWT serves as a practical, comprehensive functional assessment tool for this distinct patient population.

## Availability of Data and Materials

All data included in this study are available from the corresponding authors upon reasonable request.

## Author Contributions

SHG and GBZ designed the research study and wrote the first draft. SHG, GBZ and KZ performed the research. SHG, DYM, HXG and LY analyzed the data. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

This study utilized data from our hospital following approval by the Institutional Ethics Committee of Hebei Provincial People's Hospital (Approval No. 2026-LW-011). All participants provided written informed consent before completing the questionnaires. The study procedures adhered to the Declaration of Helsinki, guaranteeing the confidentiality and anonymity of all participants.


## Acknowledgment

Not applicable.

## Funding

This study was supported by the Medical Scientific Research Project of Hebei Provincial Health Commission (Grant No. 20220907) and the Medical-Research-Enterprise Collaborative Innovation Special Project of Hebei Province (Grant No. LH20250246).


## Conflicts of Interest

The authors declare no conflicts of interest.

## References


[1] Qiao P, Sheng P, Liu H, Liang H. Chronic Obstructive Pulmonary Disease and Lung Cancer: A Meta-Analysis of Risk Association. International Journal of Chronic Obstructive Pulmonary Disease. 2025; 20: 3269–3277. https://doi.org/10.2147/COPD.S539213

[2] Lin M, Huang Z, Chen Y, Xiao H, Wang T. Lung cancer patients with chronic obstructive pulmonary disease benefit from anti-PD-1/PD-L1 therapy. Frontiers in Immunology. 2022; 13: 1038715. https://doi.org/10.3389/fimmu.2022.1038715

[3] Yu Z, Xie G, Qin C, He H, Wei Q. Effect of postoperative exercise training on physical function and quality of life of lung cancer patients with chronic obstructive pulmonary disease: A randomized controlled trial. Medicine. 2024; 103: e37285. https://doi.org/10.1097/MD.0000000000037285

[4] Qi C, Sun SW, Xiong XZ. From COPD to Lung Cancer: Mechanisms Linking, Diagnosis, Treatment, and Prognosis. International Journal of Chronic Obstructive Pulmonary Disease. 2022; 17: 2603–2621. https://doi.org/10.2147/COPD.S380732

[5] Xu W, Zhu J, Li L, Li D, Du R. The Prognostic Role of Chronic Obstructive Pulmonary Disease for Lung Cancer After Pulmonary Resection. The Journal of Surgical Research. 2022; 275: 137–148. https://doi.org/10.1016/j.jss.2022.01.014

[6] Chen H, Hu XB, Zhou J, He CY, Wang K, Yi Q. Association of chronic obstructive pulmonary disease with risk of lung cancer in individuals aged 40 years and older: A cross-sectional study based on NHANES 2013-2018. PLoS ONE. 2024; 19: e0311537. https://doi.org/10.1371/journal.pone.0311537

[7] Agarwala P, Salzman SH. Six-Minute Walk Test: Clinical Role, Technique, Coding, and Reimbursement. Chest. 2020; 157: 603–611. https://doi.org/10.1016/j.chest.2019.10.014

[8] Ferté JB, Boyer FC, Taiar R, Pineau C, Barbe C, Rapin A. Impact of resistance training on the 6-minute walk test in individuals with chronic obstructive pulmonary disease: A systematic review and meta-analysis. Annals of Physical and Rehabilitation Medicine. 2022; 65: 101582. https://doi.org/10.1016/j.rehab.2021.101582

[9] Gao B, Wang S, Zhao L, Liao H, Qumu S, Wang P, et al. Characteristics and Quality of Life of Patients with COPD with Different Degrees of Exercise-Induced Desaturation on Six-minute Walk Test. International Journal of Chronic Obstructive Pul-

monary Disease. 2025; 20: 2381–2391. https://doi.org/10.2147/COPD.S513089
[10] Ferreira V, Minnella EM, Awasthi R, Gamsa A, Ferri L, Mulder D, et al. Multimodal Prehabilitation for Lung Cancer Surgery: A Randomized Controlled Trial. The Annals of Thoracic Surgery. 2021; 112: 1600–1608. https://doi.org/10.1016/j.athoracsur.2020.11.022
[11] Lee H, Kim HK, Kang D, Kong S, Lee JK, Lee G, et al. Prognostic Value of 6-Min Walk Test to Predict Postoperative Cardiopulmonary Complications in Patients With Non-small Cell Lung Cancer. Chest. 2020; 157: 1665–1673. https://doi.org/10.1016/j.chest.2019.12.039
[12] Wesolowski S, Orlowski TM, Kram M. The 6-min walk test in the functional evaluation of patients with lung cancer qualified for lobectomy. Interactive Cardiovascular and Thoracic Surgery. 2020; 30: 559–564. https://doi.org/10.1093/icvts/ivz313
[13] Tsai CL, Chang WP, Lin YK, Ho SC, Lin YH. Physical frailty related to cognitive impairment and COPD exacerbation: A cross-sectional study. Respiratory Medicine. 2023; 208: 107129. https://doi.org/10.1016/j.rmed.2023.107129
[14] Rozenberg D, Reid WD, Camp P, Campos JL, Dechman G, Davenport PW, et al. Translating the Interplay of Cognition and Physical Performance in COPD and Interstitial Lung Disease: Meeting Report and Literature Review. Chest. 2024; 166: 721–732. https://doi.org/10.1016/j.chest.2024.05.027
[15] Patel N. An update on COPD prevention, diagnosis, and management: The 2024 GOLD Report. The Nurse Practitioner. 2024; 49: 29–36. https://doi.org/10.1097/01.NPR.0000000000000180
[16] ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. American Journal of Respiratory and Critical Care Medicine. 2002; 166: 111–117. https://doi.org/10.1164/ajrccm.166.1.at1102
[17] Miller MR, Hankinson JA, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. European Respiratory Journal. 2005; 26: 319–338. https://doi.org/10.1183/09031936.05.00034805
[18] Luo J, Yang W, Liu Y, Ji H, Li X, Bai J, et al. Construction and evaluation of nomogram for risk prediction of cognitive impairment in chronic obstructive pulmonary disease comorbidity. BMC Psychology. 2025; 13: 273. https://doi.org/10.1186/s40359-025-02516-3
[19] Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society. 2005; 53: 695–699. https://doi.org/10.1111/j.1532-5415.2005.53221.x
[20] Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. Respiratory Medicine. 1991; 85: 25–31; discussion 33–37. https://doi.org/10.1016/s0954-6111(06)80166-6
[21] Hu ZW, Gao L, Yu Q, Jin Z, Liu JH, Lian YY, et al. Use of 6-minute walk test for assessing severity of interstitial lung disease: an observational study. Sarcoidosis, Vasculitis, and Diffuse Lung Diseases: Official Journal of WASOG. 2023; 40: e2023013. https://doi.org/10.36141/svdld.v40i2.13991
[22] Eksombatchai D, Wongsinin T, Phongnarudech T, Thammavaranucupt K, Amornputtisathaporn N, Sungkanuparph S. Pulmonary function and six-minute-walk test in patients after recovery from COVID-19: A prospective cohort study. PLoS ONE. 2021; 16: e0257040. https://doi.org/10.1371/journal.pone.0257040
[23] Chen C, Kolbe J, Paton JFR, Fisher JP. Clinical utility of the Borg dyspnoea score in 6-minute walk tests in interstitial lung disease: A systematic review. Respiratory Medicine and Research. 2024; 85: 101103. https://doi.org/10.1016/j.resmer.2024.101103
[24] Zanini U, Luppi F, Kaur K, Anzani N, Franco G, Ferrara G, et al. Use of 6-minute walk distance to predict lung transplant-free survival in fibrosing non-IPF interstitial lung diseases. Respirology (Carlton, Vic.). 2024; 29: 387–395. https://doi.org/10.1111/resp.14669
[25] Bae SS, Markovic D, Saygin D, Sullivan D, Yamaguchi K, Moghadam-Kia S, et al. Associations between 6-minute walk distance and physiologic measures and clinical outcomes in myositis-associated interstitial lung disease. Rheumatology (Oxford, England). 2025; 64: SI79–SI87. https://doi.org/10.1093/rheumatology/keae477
[26] Blakney RA, Ricotta EE, Follmann D, Drew J, Carey KA, Glass LN, et al. The 6-minute walk test predicts mortality in a pulmonary nontuberculous mycobacteria-predominant bronchiectasis cohort. BMC Infectious Diseases. 2022; 22: 75. https://doi.org/10.1186/s12879-022-07054-6
[27] Wang P, Si Y, Cai Z, Jiang W, Xin X, Li S, et al. The relationship between grip strength, 6 minute walking distance and working memory in older adults with mild cognitive impairment: an fNIRS study. BMC Geriatrics. 2025; 25: 437. https://doi.org/10.1186/s12877-025-06080-8
[28] Wiley E, Noguchi KS, Moncion K, D'Isabella N, Shkredova DA, Fang H, et al. The association between global cognitive function and walking capacity in individuals with broad ranges of cognitive and physical function: Are there sex differences? Frontiers in Rehabilitation Sciences. 2022; 3: 960437. https://doi.org/10.3389/fresc.2022.960437
[29] Hwang S, Woo Y, Kim KH, Ki KI. Effects of falls experience on cognitive functions and physical activities in community-dwelling individuals with chronic stroke. International Journal of Rehabilitation Research. Internationale Zeitschrift Fur Rehabilitationsforschung. Revue Internationale De Recherches De Readaptation. 2013; 36: 134–139. https://doi.org/10.1097/MRR.0b013e32835b667e
[30] Pastva AM, Hugenschmidt CE, Kitzman DW, Nelson MB, Brenes GA, Reeves GR, et al. Cognition, Physical Function, and Quality of Life in Older Patients With Acute Decompensated Heart Failure. Journal of Cardiac Failure. 2021; 27: 286–294. https://doi.org/10.1016/j.cardfail.2020.09.007
[31] Ahn SY, Lee NG, Lee TH. Relation of exercise capacity to comprehensive physical functions in individuals with ischemic stroke. NeuroRehabilitation. 2021; 48: 375–383. https://doi.org/10.3233/NRE-201630
[32] Zenginler Yazgan Y, Vural P, Ormen R, Akinci B, Tarakci E, Guler S, et al. Six-Minute Walk Performance and Related Factors in Pediatric-Onset Multiple Sclerosis. Journal of Child Neurology. 2022; 37: 351–358. https://doi.org/10.1177/08830738211072701
[33] Morita A, Yagi K, Asakura T, Namkoong H, Sato Y, Ogawa T, et al. Longitudinal significance of six-minute walk test in patients with nontuberculous mycobacterial pulmonary disease: an observational study. BMC Pulmonary Medicine. 2023; 23: 247. https://doi.org/10.1186/s12890-023-02528-y