

Original Research Article

DOI: <https://dx.doi.org/10.18203/2320-6012.ijrms20242940>

A comparative assessment of hand grip exercise and 6-minute walk test in chronic obstructive pulmonary disease patients

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Received: 15 August 2024

Revised: 22 September 2024

Accepted: 23 September 2024

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a leading disease often under-discussed and underdiagnosed causing persistent and chronic obstruction of upper airways. Patients not only suffer respiratory dysfunctions but also, peripheral muscle dysfunction and atrophy leading to muscle fatigue, reduced muscle strength, and endurance impacting exercise capacity, physical activity levels, and decreased ability to perform daily tasks. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines highlight the need to enhance functional status through assessments like Hand Grip Strength and a 6-minute walk test. The study aimed at a comparative assessment of these exercises in COPD patients along with spirometry for diagnosis, and grading and to find out their combined advantages in COPD management.

Methods: This cross-sectional study was conducted on 110 patients at the Department of Physiology, King George's Medical University, Lucknow, using a questionnaire, and both tests were performed on COPD patients to determine the effectiveness depending on the severity and spirometry results.

Results: The recruited patients were classified as per GOLD stages in 4 categories, as disease severity increased, functional and exercise capacity was reduced. There was a negative correlation between GOLD stages and 6-minute walk strength, maximum grip strength, and mean endurance time of COPD patients with r-values of -5.672, -6.874, and -5.879 respectively.

Conclusion: COPD patients suffer from functional dysfunctions and exercise limitations, early diagnosis is crucial to limit the severity, and functional tests can play a significant role in determining the health outcomes and improving the quality of life.

Keywords: 6-Minute walk test, Hand grip strength, COPD, GOLD stages, Spirometry

INTRODUCTION

Despite robust research respiratory problems are still the most underdiagnosed and underestimated especially chronic obstructive pulmonary disease (COPD), which

has its relation with both the environment and genetics. COPD is distinguished by persistent and chronic obstruction of the upper airways, with chronic inflammatory reactions triggered by several factors. Elevated levels of inflammatory cells inducing oxidative

stress due to inflammation contribute to several adverse manifestations with a more sedentary lifestyle.¹⁻⁴ People suffering from COPD not only experience respiratory dysfunction but there are several other problems related to this like peripheral muscle dysfunction and atrophy, manifested as fatigue, declined muscle strength, and endurance with cardiac dysfunction, compromised health-related quality of life, leading to exacerbated risk and mortality.⁵⁻⁷ Physiological abnormalities are observed in patients suffering from COPD as muscle function, exercise capacity, and physical activity levels with a notable decrease in the ability to walk or perform tasks like sitting and standing depicting neurophysiological alterations.⁸

The global initiative for chronic obstructive lung disease (GOLD) guidelines highlighted the need to enhance functional status as a primary objective in COPD treatment.⁹ Various assessments can be done to determine muscle strength for example Hand grip strength (HGS) for upper limbs and a 6-minute walk test (6MWT) for lower limbs.¹⁰ There are contrasting views on the predominance of muscle strength in both limbs, interestingly differences in muscle endurance at other anatomical sites are also discovered.¹¹⁻¹³ The 6-minute walking test (6MWT) is widely used in clinical exercise assessment, it is practical, and well-tolerated and reflects the daily life activities that surpass the scope of cardiopulmonary exercise tests, with an addition of hand-grip strength test.¹⁴⁻¹⁸ These tests assess the physical performance of COPD patients along with an insight into daily activities, physical fitness, functional capacity, and changes in peripheral muscle strengths, and serve as monitoring tools to determine the effectiveness of various treatments.^{19,20}

There is more reduced skeletal and respiratory muscle strength in COPD patients in contrast to the general population, and more pronounced weakness is observed in quadriceps muscles compared to the pectoralis major and latissimus dorsi i.e. up to 70% prevalence in chronic lung disease patients. However, the maximal strength of the diaphragm is typically 30-40% lower than those with no disease.²¹⁻²⁶ Hand grip strength, a reliable and cost-effective indicator of overall muscle strength, exhibits correlations with the strength of various other muscle groups, including the quadriceps, upper limb, and respiratory muscles.²⁷⁻²⁹

In COPD patients, low hand grip strength is independently associated with higher risks of exacerbations, particularly among smokers with stable COPD.³⁰ Also, HGS is related to cardiac function and walking distance in individuals with COPD.³¹ The 6-minute walk test (6MWT) is a cost-effective method to evaluate submaximal exercise capacity, and it is also significantly correlated with handgrip force in individuals with stable COPD.^{32,33} In 2016, COPD was responsible for approximately 3 million deaths worldwide with increasing impact, as evidenced by its ranking from the

sixth leading cause of death globally in 1990 to the third leading cause of death in 2016 with a common finding of reduced exercise capacity in COPD patients.^{34,35} The 6-minute walk test (6MWT) can be used to assess functional exercise capacity and serves as an appropriate outcome measure in clinical trials but can be restricted by factors like the patient's condition and available resources.³⁶

The respiratory muscle dysfunction also contributes to dyspnoea and exercise limitations in these patients which are associated with peripheral muscle strength and a major contributor to this is leg fatigue symptom, highlighting the correlation between muscle mass or strength and exercise capacity might be there with a possibility of further research firmly establishing this correlation.^{37,38}

The 6-minute walk distance is a valuable indicator for various daily activities in COPD patients, offering an assessment of the integrated responses of the pulmonary, cardiovascular, and muscular systems in addition to this, it also evaluates functional status, the impact of pulmonary rehabilitation, changes in exercise capacity, and the risk of mortality in COPD patients. The 6-minute walk distance also tends to reduce as the severity of the disease increases thus depicting the role of peripheral muscle weakness or dysfunction in limiting exercise primarily affecting the muscles of the lower extremities.³⁹ Limited findings are present on the muscle function related to upper extremities as these could also be affected if diffuse myopathy is associated with COPD. A study by Gosselink et al, demonstrated reduced hand grip strength (HGS) in COPD patients, additionally, Puhan et al, found that the HGS test was mortality in COPD patients.^{3,40}

When comparing the hand grip exercise and the 6-minute walk test in patients with COPD, both assessments play significant roles in evaluating various aspects of physical function and disease progression. The HGS test primarily focuses on upper extremity strength, providing insights into overall muscle function and potentially correlating with daily activities. Conversely, the 6MWT focuses on assessing functional capacity and endurance, giving information on cardiovascular fitness, and the ability to sustain activities over time. On one hand grip exercise may offer a simpler and more targeted evaluation, the 6MWT provides a broader perspective on overall physical performance.

The choice among these assessments is based on specific goals of evaluation and intervention required for a particular patient. In addition, there is potential for complementary use of these tests in comprehensive COPD management strategies. The current study aims to make a comparative assessment of both these exercises in COPD patients along with spirometry for diagnosis and grading and to find out their combined advantages in COPD management.

METHODS

Study place

This cross-sectional study was conducted at the Department of Physiology, King George's Medical University, Lucknow, U.P., India and patients were recruited from the Department of Respiratory Medicine with ethical clearance from the Institutional Ethics Committee (Ethical approval number: 2129/Ethics/2023).

Study period

The study was conducted in a span of 1 year i.e. February 2023 – March 2024.

Sample size

This cross-sectional study was performed on 110 patients to compare the efficacy of hand grip exercise and the 6-minute walk test to evaluate functional capacity and muscle strength in patients diagnosed with chronic obstructive pulmonary disease (COPD) and 110 control patients for endurance test assessment.

The sample size was calculated based on the overall prevalence of chronic obstructive pulmonary disease (COPD) among the population aged 30 years and above in India, which is 7% using the formula.

The participants were registered using standard inclusion and exclusion criteria.

Inclusion criteria

The study was conducted for a year among patients with stable COPD patients aged 30 years or above, with a duration of illness of more than 2 years.

Exclusion criteria

The study excluded patients with acute exacerbated COPD, unstable angina myocardial infarction during the previous month, and having a heart rate of >120 beats/min, SBP >180 mmHg, and DBP >100 mmHg.

Sampling technique

Simple Random Sampling were used.

Before the commencement of the study, all the participants were informed about the purpose and objective of the study along with the detailed procedure to be followed in a language they could understand, and written informed consent was obtained from all the participants in advance. A questionnaire was used to obtain demographic and other clinical/anthropometric details. Spirometry was performed according to the established standard guidelines one as a baseline and another reading after giving Salbutamol (400 mcg), post-

bronchodilator spirometry readings were recorded and results were interpreted with various parameters like forced expiratory volume in 1 second (FEV1) and the ratio of FEV1 to forced vital capacity (FCV), normally, the value of this ratio is around 0.8 or higher. The patients were classified according to the GOLD Guidelines at different stages depicting the severity levels. According to GOLD guidelines, GOLD 1: Mild: $FEV1 \geq 80\%$ predicted. GOLD 2: Moderate: $FEV1 50-79\%$ predicted. GOLD 3: Severe: $FEV1 30-49\%$ predicted. GOLD 4: Very severe: $FEV1 < 30\%$ predicted

After spirometry, the hand grip exercise test was done for each participant using a hand dynamometer (CAMRY ISO 9001 Certified EH101 model), and maximum grip strength and endurance tests were performed. A Six-minute Walk test (6MWT) for a 30 meters (approx 100 feet) distance was performed, which provided a measure of functional exercise capacity.

Statistical analysis

Data was entered in Microsoft Excel and analyzed using statistical software SPSS version 26 (SPSS Inc., Chicago, IL, USA). The continuous variables were evaluated by mean (standard deviation) or range value when required. The dichotomous variables were presented in number/frequency and were analyzed using Chi-square. To compare the means between the two or more groups, analysis by Student t-test was used.

Additionally, ANOVA tests were utilized to compare means across different GOLD stages within COPD patients, with subsequent post-hoc Tukey tests for pairwise comparisons. Furthermore, correlations between GOLD stage and functional tests such as the 6-minute walk test, maximum grip strength test, and mean endurance time were analyzed using the Spearman correlation coefficients (R-values) along with their confidence intervals and corresponding p-values. A p value of <0.05 or <0.001 was regarded as significant.

RESULTS

A total of 110 patients with Chronic Obstructive Pulmonary Disease (COPD) were included in the study based on specific inclusion-exclusion criteria with an equal number of control patients to provide comparative data. This study aimed to explore various anthropometric, functional, and dynamometric parameters to understand their correlation with COPD severity across different GOLD stages.

Anthropometric characteristics and functional spirometry

The table below provides a comparative analysis of patients with chronic obstructive pulmonary disease (COPD) and the control group, with the mean age of the COPD group being slightly higher than the control group.

The Fat-free Mass Index (FFMI) was significantly lower in the COPD group at 21.54 ± 3.25 versus 22.54 ± 3.41 in the controls at $p=0.0350$, which was a significant difference (Table 1). Functional spirometry assessments were only conducted for the COPD group, showing reduced lung function with a forced expiratory volume in 1 second (FEV1) of 52.64%, forced vital capacity (FVC) of 77.48%, and peak expiratory flow (PEF) of 52.84%. The ratio of FEV1/FVC was also observed as notably low at 51.24%, presuming the pulmonary impairment characteristic of COPD (Table 1).

GOLD staging of COPD and distribution of various parameters

The recruited COPD patients were divided into different GOLD stages depending on the severity of the disease. They were classified into 4 categories namely, GOLD 1 (n=15), GOLD 2 (n=49), GOLD 3 (n=33), and GOLD 4 (n=13), with maximum participants within a moderate range of severity.

The trends of age distribution across various GOLD stages were not found statistically significant ($p>0.05$). Some observations depicted an increasing trend while others depicted this in reverse. Gender distribution in different GOLD stages illustrated a significantly marginalized female distribution through various GOLD stages however men were more evenly distributed over the different levels of GOLD categories ($X=0.6630$, $p=0.8819$), indicating no statistical significance among these (Table 2).

Similarly, average height distribution was fairly distributed through the GOLD stages yet no statistical significance was observed ($F=1.474$, $p=0.227$). Contrastingly, average weight showed considerable variation statistically ($p=0.046$), decreasing from 62.99 kg in GOLD 1 to 54.06 kg in GOLD 4, marking a potential impact of COPD severity on body weight (Table 2).

In the same way, BMI decreased with the increasing COPD severity, the reduction could be seen from 24.12 kg/m^2 in GOLD 1 to 20.53 kg/m^2 in GOLD 4, however, the difference was not statistically significant ($F=1.805$, $p=0.151$). The body fat skinfold measurements were estimated using the Durnin and Womersley skinfold formula across various GOLD stages, but the results were also not found statistically significant ($F=1.007$, $p=0.393$). The values for body fat percentage in different GOLD stages of COPD showed a declining trend with 17.50% in GOLD 1 to 13.67% in GOLD 4, although the differences were not statistically significant ($F=1.052$, $p=0.373$) (Table 2).

The mid-upper arm circumference (MUAC) through different GOLD stages of COPD revealed a decreasing trend in circumference as the disease severity progressed. The mean MUAC reduced from $9.63 \pm 2.17 \text{ cm}$ in GOLD

1 to $8.55 \pm 1.37 \text{ cm}$ in GOLD 4, with a statistically significant difference ($F=2.743$, $p=0.0474$), indicating that muscle mass decreased as the severity of the COPD increased, might be reflecting in an overall decline in nutritional status and body composition, more observed in advanced disease stages (Table 2).

Hand grip strength test

Dynamometric parameters of the recruited study groups were done and the results are summarized in the table below (Table 2). The maximum grip strength was found to be considerably low in the COPD group with a mean value of $26.84 \pm 3.48 \text{ kg}$ compared to the control group with a mean value of $33.51 \pm 7.48 \text{ kg}$ with a highly significant difference ($p<0.0001$). Similarly, the average values for 60% of maximum grip and 80% of maximum grip were also significantly lower in the COPD group compared to the control group with average values of $16.52 \pm 3.42 \text{ kg}$ versus $20.84 \pm 5.74 \text{ kg}$ and $22.54 \pm 4.98 \text{ kg}$ versus $28.95 \pm 9.34 \text{ kg}$ for 60% and 80% of the maximum grip, respectively with $p<0.0001$ (Table 3).

Interestingly, the mean endurance time (seconds), was also calculated lower in COPD patients compared to controls with mean values of $23.51 \pm 7.79 \text{ seconds}$ versus $27.84 \pm 6.94 \text{ seconds}$ with $p=0.0003$, suggesting markedly reduced muscle strength and endurance in COPD patients compared to healthy controls (Table 3).

Maximum grip strength, endurance time across GOLD stages in COPD patients

The results of maximum grip strength, recorded in three readings as GRIP 1, GRIP 2, and GRIP 3 were then compared according to GOLD stages and, a consistent decline in the grip strength from less severe to more severe stages with a statistically significant difference was observed. First grip strength, GRIP1 had the highest mean strength at $27.11 \pm 6.77 \text{ kg}$ in the GOLD 1 stage, which decreased further as the GOLD stage increased and the F-statistic was calculated as 4.408 with a p-value of 0.0060 was significant.

GRIP 2 and GRIP 3 also depicted similar patterns in different GOLD categories (Figure 1). The mean of all grips also followed the same pattern i.e. beginning at $28.05 \pm 6.40 \text{ kg}$ in GOLD 1, reducing to $25.47 \pm 5.91 \text{ kg}$ in GOLD 2, $21.55 \pm 4.20 \text{ kg}$ in GOLD 3, and slightly higher value in GOLD 4 ($22.98 \pm 7.77 \text{ kg}$) with F-value 5.077 at a significant p-value of 0.0026 (Table 4).

Almost similar declining patterns were also analyzed when 60% and 80% of mean maximum grip were tabulated across different GOLD stages of COPD, where the reduction was accounted from $16.83 \pm 3.84 \text{ kg}$ in GOLD 1 to $10.79 \pm 4.66 \text{ kg}$ in GOLD 4 for 60% grip strength and 80% grip strength, a decline was observed from $22.45 \pm 5.12 \text{ kg}$ in GOLD 1 to $15.93 \pm 6.21 \text{ kg}$ in GOLD 4, yielding an F-value of 5.081 and 5.094,

respectively for both and a significant p value of 0.0026 (Table 4). Endurance time across different GOLD stages of COPD, recorded at intervals of 2 minutes showed a reduction from an average of 26.31 seconds in GOLD 1 to 20.00 seconds in GOLD 4 for the first interval (Figure 2), and this pattern continued across different intervals with third recoding dropping from 24.15 seconds in GOLD 1 to 18.60 seconds in GOLD 4 (Table 4). These findings unveiled a progressive decline in grip strength with increasing severity of COPD and a declined muscle function along the direction of disease progression due to muscle deterioration.

Six-minute walk test (6MWT)

The observations from 6MWT across different GOLD stages of chronic obstructive pulmonary disease (COPD), demonstrated a significant decline in the walking distance with increasing disease severity. GOLD 1 participants had an average walking distance of 312.19 ± 55.72 meters, which was reduced through stages and a significant drop was reported in GOLD 4 i.e. 207.30 ± 47.96 meters. The results were statistically significant as confirmed by ANOVA with an F-value of 9.176 and a p-value of <0.0001. This marked reduction in walking distance with increasing COPD severity reflected a contraction in physical capacity and respiratory function in patients with COPD (Table 5).

Post-bronchodilator parameters

Post-bronchodilator spirometry values across different GOLD stages of COPD illustrated a progressive decrement in lung function as the severity of the disease increased. The mean values for forced expiratory volume 1 (FEV1) were noted as decreased from 87.77% in GOLD 1 to 24.8% in the GOLD 4 stage with an F-value of 155.25 ($p < 0.0001$). Similarly, Forced Vital Capacity (FVC) declined from 108.15% in GOLD 1 to 52.00% in GOLD 2 depicting a highly significant difference across the stages of COPD ($F=36.440$, $p < 0.0001$) (Table 5).

The ratio of FEV1 to FVC, an indicator of airflow obstruction showed a downtrend from 62.08% in GOLD 1 to 41.97% in GOLD 4 ($F=14.243$, $p < 0.0001$), demonstrating the degradation of pulmonary function associated with advancing stages of COPD, emphasizing the utility of spirometry in monitoring disease progression and severity (Table 5).

Correlation analysis

While evaluating the correlation of COPD GOLD stages with different parameters namely, 6-minute walk strength, maximum grip strength, and mean endurance time of COPD patients using Spearman's correlation, it illuminated a negative correlation of GOLD stages with all three parameters. It meant that as the stages of COPD severity increased, the values of these parameters declined, giving the r-values of -5.978, -6.874, and -5.879

for 6MWT, maximum grip strength, and mean endurance time, which were statistically significant at p values of 0.0007, 0.0003, and 0.0012, respectively at 95% confidence interval (Table 6).

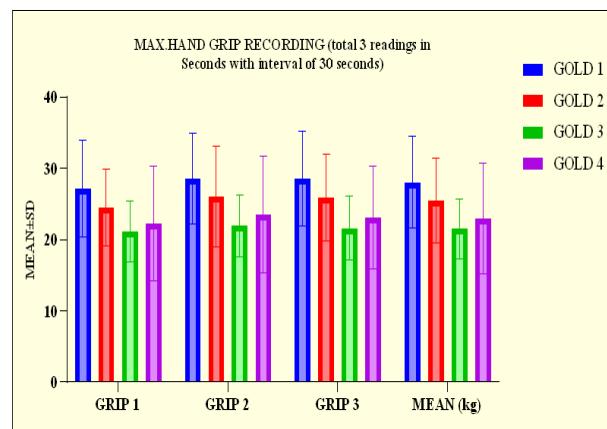


Figure 1: Maximum grip recording across various GOLD stages in COPD patients.

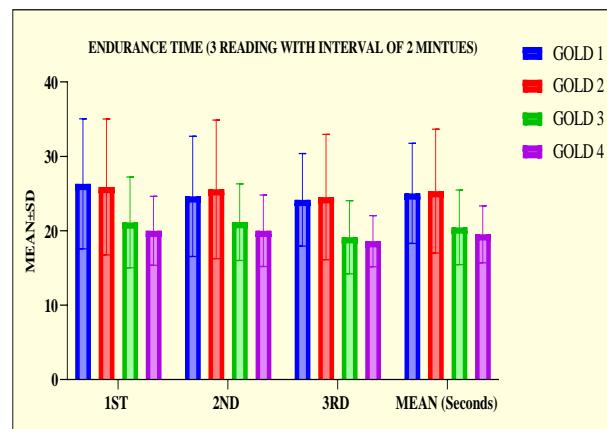


Figure 2: Endurance time (3 readings with 2-minute intervals) across GOLD stages in COPD patients.

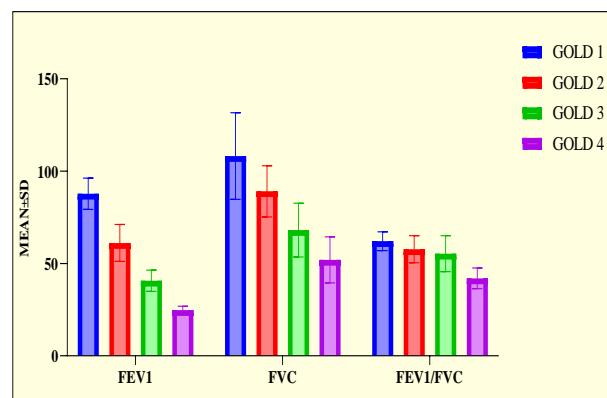


Figure 3: Diagrammatic representation of post-bronchodilator readings across GOLD stages in COPD patients.

Table 1: Basic anthropometric characteristics and functional spirometry among the case and control patients.

Basic anthropometric characteristics and functional spirometry	COPD		Control		P value
	Mean	SD	Mean	SD	
Age (year)	58.38	10.54	57.84	9.48	t=0.3809 p=0.7036
Height	159.84	9.45	161.54	9.87	t=1.244 p=0.2149
Weight	56.84	16.42	57.84	13.54	t=0.4699 p=0.6389
BMI	22.54	6.74	21.54	5.89	t=1.117 p=0.2652
FFMI	21.54	3.25	22.54	3.41	t=2.123 p=0.0350*
Post broncho dilater values	FEV1	52.64	21.54	-	-
	FVC	77.48	18.74	-	-
	PEF	52.84	21.84	-	-
	FEV1/FVC	51.24	10.54	-	-

Where *represents p value<0.05 as significant.

Table 2: Various anthropometric parameters across GOLD stages in COPD patients.

	Gold 1 (n=15)		Gold 2 (n=49)		Gold 3 (n=33)		Gold 4 (n=13)		P value
	N	%	N	%	N	%	N	%	
Age	58.00	10.45	59.54	10.89	60.45	9.93	53.50	10.21	F=1.150 P=0.333
Gender	Female	12	0.00%	0.00%	6	50.00%	5	41.67%	1
	Male	98	15	15.31%	43	43.88%	28	28.57%	12
Height (cm)	161.75	8.83	161.75	8.51	158.10	7.42	161.84	6.53	F=1.474 p=0.227
Weight (cm)	62.99	21.03	58.17	11.65	52.26	9.78	54.06	9.27	F=2.764 p=0.046*
BMI	24.21	8.59	22.25	4.27	20.92	3.77	20.53	2.43	F=1.805 p=0.151
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	P value
Body fat skinfold	1.06	0.02	1.06	0.01	1.07	0.01	1.06	0.01	F=1.007 p=0.393
Body fat %	17.50	9.89	15.82	5.90	14.07	6.86	13.67	6.88	F=1.052 p=0.373
MUAC	9.63	2.17	9.24	1.61	8.38	1.43	8.55	1.37	F=2.743 p=0.0474*

Where *represents p value<0.05 as significant.

Table 3: Dynamometric parameters of the enrolled patients among the case and control groups.

Dynamometric parameters	COPD		Control		P value
	Mean	SD	Mean	SD	
MAX grip (kg)	26.84	3.48	33.51	7.48	t=8.085, p<0.0001*
60% of max grip (kg)	16.52	3.42	20.84	5.74	t=6.466, p<0.0001*
80% of max grip (kg)	22.54	4.98	28.95	9.34	t=6.056, p<0.0001*
Mean endurance time (sec)	23.51	7.49	27.84	6.94	t=4.241, p=0.0003*

Where *represents the p value as significant.

Table 4: Max. hand grip recording, 60% and 80% of maximum grip strength, and endurance time across different GOLD stages in COPD patients.

Parameters	Gold 1 (n=15)		Gold 2 (n=49)		Gold 3 (n=33)		Gold 4 (n=13)		P value	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Max. hand grip recording (total 3 readings in Seconds with intervals of 30 seconds)	Grip 1	27.11	6.77	24.55	5.40	21.11	4.25	22.28	8.04	F=4.408 p=0.0060*
	Grip 2	28.52	6.33	26.05	7.08	21.93	4.39	23.56	8.19	F=4.265 p=0.0071*
	Grip 3	28.51	6.66	25.83	6.09	21.62	4.50	23.11	7.23	F=5.522 p=0.0015*
Mean (kg)		28.05	6.40	25.47	5.91	21.55	4.20	22.98	7.77	F=5.077 p=0.0026*
60%-80% of the mean maximum grip	60%	16.83	3.84	15.28	3.54	12.93	2.52	10.79	4.66	F=5.081 p=0.0026*
	80%	22.45	5.12	20.39	4.74	17.24	3.36	15.39	6.21	F=5.094 p=0.0026*
Endurance time (3 readings with intervals of 2 minutes)	1 ST	26.31	8.73	25.89	9.12	21.13	6.10	20.00	4.62	F=3.474 p=0.019*
	2 ND	24.62	8.09	25.57	9.30	21.16	5.15	20.00	4.81	F=2.840 p=0.042*
	3 RD	24.15	6.22	24.53	8.41	19.13	4.92	18.60	3.44	F=5.154 p=0.002*
Mean (Seconds)		25.02	6.73	25.33	8.33	20.45	5.01	19.53	3.82	F=4.361 p=0.006*

Where *represents the p value as significant.

Table 5: 6 Minute walk test and post-bronchodilator results across different GOLD stages in COPD patients.

Parameters	GOLD 1 (n=15)		GOLD 2 (n=49)		GOLD 3 (n=33)		GOLD 4 (n=13)		P value	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
6 MWT (m)	312.19	55.72	293.61	54.52	268.68	52.63	207.30	47.96	F=9.176 p<0.0001*	
Post-broncho dilator	FEV1	87.77	8.52	61.11	10.00	40.71	5.75	24.80	2.10	F=155.25 p<0.0001*
	FVC	108.15	23.45	89.09	13.83	68.13	14.54	52.00	12.44	F=36.440 p<0.0001*
	FEV1/FVC	62.08	5.05	57.77	7.33	55.33	9.74	41.97	5.60	F=14.243 p<0.0001*

Where *represents the p value as significant.

Table 6: Correlation analysis of GOLD stage with 6-minute walk test, max grip strength and mean endurance time of COPD Patients.

Correlation analysis of GOLD stage vs	6 min walk test	Max grip strength test	Mean endurance time
R-values	-5.978	-6.874	-5.879
95% CI	-7.584 to -4.941	-7.845 to -4.875	-6.514 to -3.847
P value	0.0007*	0.0003*	0.0012*

Where *represents the p value as significant.

DISCUSSION

Chronic obstructive pulmonary disease (COPD) is a progressive disorder of the upper respiratory that remains

underdiagnosed for many years, leading to more severe advancements in health conditions and thereby making this one of the leading causes of mortalities worldwide. Despite enormous research, the severity is increasing

manifold creating substantial loss to health and life. The disease increases in severity with its progression and the Global Initiative for chronic obstructive lung disease (GOLD) stages are used for classifying the severity based on the symptoms, exacerbation history, and results of spirometry, ranging from mild (GOLD 1) to very severe (GOLD 4), depicting different level lung function impairment.^{9,41} The results of this cross-sectional study on 110 patients with COPD alongside control subjects, conducted at the department of physiology with the patients recruited from department of respiratory medicine, KGMU, Lucknow reflected the necessity to shift the focus on muscle function, functional capacities, and endurance with different treatment strategies according to the disease severity.⁴²⁻⁴⁴

The differences in age, height, weight, and body mass index (BMI), compared between COPD patients and controls revealed no significant differences, aligning with previous research indicating that these factors might not play a significant role in the disease progression.^{30,45} Contrastingly, the COPD patients exhibited a lower fat-free mass index (FFMI), suggesting alterations in body composition due to muscle wasting and cachexia. Functional spirometry assessments in the COPD group demonstrated reduced lung function, as evidenced by lowered forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), peak expiratory flow (PEF), and reduced FEV1/FVC ratio (Table 1). These findings were consistent with the characteristic airflow limitation and impaired pulmonary function associated with COPD.⁴⁶⁻⁴⁸

The age-wise comparison of COPD as per GOLD stages illustrated no significant differences similarly the gender distribution among COPD patients across various GOLD stages showed more male distribution across the different stages of disease progression compared to the females, aligning with the previous research highlighted gender disparities in COPD prevalence and severity with males at higher risk of disease burden.⁴⁹ Anthropometric characteristics such as height and BMI were not significantly related to COPD severity, as these parameters might not be reliable predictors.

Conversely, the results for weight distribution across stages of GOLD suggested a potential association between COPD severity and body composition. The mean values of skinfold thickness indicated a decreasing trend in thickness with disease severity progression, however, the results were not statistically significant. These findings indicated changes in the body composition associated with COPD severity, but these changes were not robust enough statistically (Table 2).^{13,50,51}

The analysis of body fat skinfold measurements across different GOLD stages of COPD severity revealed relatively consistent mean values across stages of COPD, indicating similar body fat percentages regardless of

disease severity displaying extreme variability, reflecting complex interactions between age, disease severity, and individual physiological responses. These results highlighted the multifaceted nature of COPD and its effect on body composition, emphasizing the need for personalized approaches in disease management accounting for variations in nutritional status and body composition (Table 2). The assessment of MUAC (mid-upper arm circumference), revealed a significant decline in muscle mass progressively from GOLD 1 to GOLD 4 ($p=0.0474$), emphasizing lowered circumference with increasing severity of COPD (Table 2). These findings implied the importance of assessing nutritional status and body composition in COPD patients, as the results of MUAC reflected muscle wasting and nutrition deprivation in the advanced stages of the disease, a need to implement interventions to address malnutrition, preserving muscle mass could be beneficial in managing COPD progression and improving health outcomes.^{4,14,51,52}

The assessment of maximum hand grip strength in COPD patients across various GOLD stages had a consistent decline with disease progression (Table 3,4) and, the results were statistically significant indicating a progressive reduction in muscle function with increasing disease severity. Patients in the GOLD 1 stage, had the highest mean grip strength, which gradually declined in GOLD 2, GOLD 3, and GOLD 4 stages, suggestive of a declining trend in muscle strength as COPD advanced (Figure 1).

These results emphasized the importance of assessing muscle function in COPD patients, as reduced grip strength may be worsened with disease severity.⁵³⁻⁵⁵ These findings enlightened the need to strategize specific interventions to preserve muscle strength and function to improve health-related outcomes. The observations of hand grip strength at 60% and 80% of the mean maximum grip, revealed a consistent decline in muscle strength with disease advancements and depicted reduced functional capacity (Table 4).^{30,54} The endurance times were recorded at intervals of two minutes consistently reduced from GOLD 1 to GOLD 4 across various intervals with statistically significant results (Figure 2). The overall mean endurance time also significantly declined across various GOLD stages, indicating worsening physical capacity and reduced ability to sustain physical activity with advancing COPD.^{11,56,57}

The results from the 6-minute walk test (6MWT), observed across different GOLD stages in COPD patients had progressively declined walking distance (Table 5), aligning with the existing literature on the functional impairment associated with the disease. Studies highlighted that reduced exercise capacity is a hallmark feature of COPD progression, with 6MWT serving as a reliable measure of the functional status and prognosis of such patients.^{17,22} The post-bronchodilator spirometry findings aligned with existing literature that suggested a

reduction in lung function across different GOLD stages of COPD (Figure 3). Meier et al, Celli et al, reported similar patterns of FEV1 and FVC reductions, correlating with disease severity, underscoring the utility of spirometry in assessing COPD progression.^{58,59} The correlation analysis demonstrated the impact of COPD severity on functional performance as evidenced by negative correlations between GOLD stages and parameters like 6 MWT, maximum grip strength, and mean endurance time (Table 6). This study aligned with the previous study by Spruit et al, which demonstrated a strong relationship between lung function impairment and reduced exercise capacity in COPD patients.³⁹

The overall findings of this study emphasized the clinical significance of spirometry along with the maximum hand grip strength test and the six-minute walk test in assessing disease severity, accentuating the importance of functional assessments in managing COPD patients' physical limitations and quality of life. These findings revealed significant differences in muscle strength, endurance, and body composition, emphasizing the systemic impact of the disease and delineating the importance of early diagnosis, timely interventions, and targeted management strategies to recede functional alterations in COPD patients. This study can contribute to addressing pulmonary as well as extra-pulmonary manifestations of the disease and improving the health outcomes and quality of life for individuals living with this highly debilitating condition and contribute to reducing the undue burden of this disease, both in Indian scenarios as well as globally.

There is limited generalizability of these findings due to the relatively smaller sample size and not enough changes can be assessed in this type of study design along with the probability of selection bias.

CONCLUSION

This study highlights the need to conduct large-scale studies for improved generalizability, and should be performed at various centers to increase the representativeness of the study population. Other factors like socioeconomic factors, lifestyle, and environmental exposure must also be assessed to address health disparities in affected populations. This study contributes valuable evidence to the existing literature on COPD, guiding clinical practice and informing future research prospects aimed at improving outcomes and quality of life for individuals living with this debilitating condition.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kumar T, Verma D, Singh S, Bajpai M, Srivastava A, Rao A. A comparative assessment of hand grip exercise and 6-minute walk test in chronic obstructive pulmonary disease patients. *Int J Res Med Sci* 2024;12:3768-78.