# PHYSICAL PREDICTORS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS

**Maged Mohammed Abdrabo[1], Saad Rabie Samra[1], Mohamed Fathy Hassan Habib[1]*, Maha Elsayed Alsadik[1]**

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**Abstract**

Although the six-minute-walk test (6MWT) has been used to predict chronic obstructive pulmonary disease (COPD) exacerbations, additional research is necessary to identify more rapid, simpler tests that are directly associated with exacerbations, such as the five-repetition sit-to-stand (5STS) test and 4MGS test. Moving from sitting to standing is a common activity of daily living. The 5STS has been validated in healthy community-dwelling adults, but data in chronic obstructive pulmonary disease (COPD) populations are lacking.

**Key Words:** COPD, 6MWT, 3 min walking test, STS.

[1]Department of Chest Diseases, Faculty of Medicine, Zagazig University, Egypt

[*]**Corresponding author:** Mohamed Fathy Hassan Habib
[*]Department of Chest Diseases, Faculty of Medicine, Zagazig University, Egypt,
Email: mohammedfhabib2019@gmail.com

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**Introduction.**

Chronic obstructive pulmonary disease (COPD) is a leading cause of mortality and morbidity worldwide. COPD is a major public health problem. Diagnosis and disease progression are mainly classified by lung function, commonly expressed by forced expiratory volume in 1 second (FEV1). Exercise intolerance is a major disability in people with COPD. The disease severely affects their ability to perform activities of daily living and their quality of life (**1, 2**).

Acute exacerbations of COPD are characterized by worsening symptoms, increased ventilatory limitation, and rapid deconditioning. Despite this, evaluation of exercise tolerance during inpatient hospitalization may be necessary. For example, it offers clinicians the opportunity to assess patients' rehabilitation needs, prescribe exercise programs for completion after discharge (particularly for those unable to attend post-exacerbation pulmonary rehabilitation), and to evaluate the potential for re-hospitalization (**3**).

**I -SIX MINUTES WALKING TEST**

The 6MWT is a useful measure of functional capacity, targeted at people with at least moderately severe impairment. It has been widely used for measuring the response to therapeutic interventions for pulmonary and cardiac disease. The new American Thoracic Society guidelines provide a standardized approach for performing the test. Walking tests have been around since the 1960s, when the 12-min walk was popularized by aerobics fitness enthusiast, Kenneth H Cooper, as a quick and easy fitness test. There's a full range of tests that you could perform to assess a patient's functional capacity. The easiest is just a questionnaire or self-report of how much work the patient can do. You might ask, "How many flights of stairs can you climb or how many blocks can you walk?" But patients differ in their ability to recall that kind of information and may overestimate or underestimate their true functional capacity, so objective measurements are usually better than self-reports. Another easy test of fitness is the number of stairs the patient can climb. Many surgeons have said that if the patient can walk up 2–3 flights of stairs, then he or she can survive surgery. The ease of performing a 6-minute walk test falls between stair climbing and testing for exercise-induced asthma **(4).**

The 6-min walk test is a widely used measure of functional exercise capacity in individuals with cardiopulmonary disease. It has advantages over laboratory based tests of exercise tolerance as it more closely resembles the ability to perform activities of daily living and does not require sophisticated equipment **(5).**

The distance walked during the 6-min walking test, the 6-min walk distance (6MWD), shows moderate to good correlation with the peak oxygen uptake measured during an incremental cycle ergometry test in patients with moderate to severe COPD and congestive heart failure (CHF)**(6).**

It is frequently used as an outcome measure in cardiopulmonary rehabilitation and as an assessment tool in the selection of patients for lung surgery **(7).**

Despite the popularity of the 6min walking test in the clinical setting, there is a paucity of 6MWD reference values obtained in healthy subjects. This limits the interpretation of 6MWD in patients and poses problems for clinicians wishing to provide patients with a measure of their expected 6MWD in the absence of disease. The published regression equations for estimating 6MWD in healthy subjects explain between 40% and 66% of the variance in 6MWD using variables such as age, height, weight, sex and health status. However, the equations produce distances that differ by as much as 100m for the same individual, most likely because of the use of different test protocols, that is, different track lengths, test instructions, frequency of encouragement during the test and number of repetitions of the 6MWT **(8).**

**Purpose**

The original purpose of the six minute walk was to test exercise tolerance in chronic respiratory disease and heart failure. The test has since been used as a performance-based measure of functional exercise capacity in other populations including healthy older adults, people undergoing knee or hip arthroplasty, fibromyalgia, and scleroderma. It has also been used with children. The six minute walk test (6MWT) measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is allowed to self-pace and rest as needed as they traverse back and forth along a marked walkway**(9).**

**Standards and Indications**

The American Thoracic Society Pulmonary Function Standards Committee developed guidelines for the 6MWT in clinical setting .A respiratory therapist working at the Mayo Clinic in Rochester, Minnesota, helped to review the document. The 6MWT was chosen because it is

easier to administer, better tolerated, and better reflects activities of daily living than other walk tests **(4).**

**Uses**

The 6MWT has been used to detect changes following interventions to improve exercise tolerance for healthy older adults as well as people with rheumatic conditions such as knee or hip osteoarthritis and fibromyalgia **(10).**

The 6MWT has been used with a variety of other conditions such as heart failure, chronic obstructive pulmonary disease (COPD) and stroke. It has also been used to predict hospitalization and mortality **(11).**

**Table (1): Lists the indications for the 6MWT**

| |
|---|
| Before-and-After Treatment Comparisons in Lung transplantation, lung resection and Lung volume reduction surgery |
| Pulmonary rehabilitation |
| Drug therapy for chronic obstructive pulmonary disease |
| Pulmonary hypertension |
| Heart failure |
| To Measure Functional Status in Chronic obstructive pulmonary disease |
| Cystic fibrosis |
| Peripheral vascular disease In elderly patients |
| To Predict Hospitalization and Death From heart failure, chronic obstructive pulmonary disease, or pulmonary hypertension |

The most important of which is to measure outcomes before and after treatment in people with moderate to severe heart and lung disease. The 6MWT can also be used to measure functional status and for epidemiologic purposes. A short 6- minute walk distance (6MWD) fairly accurately predicts morbidity and mortality from heart or lung disease **(6).**

**Method**

This is ideally conducted in an enclosed, quiet hallway by a single administrator. However, it is important to note that there are variations among studies in how the test is conducted which affects performance. These variations include the instructions provided to the participant, the number of turns in the course, the frequency and type of encouragement given, and the number of trials performed.

Due to the differing functional statuses of participants, the 6 minute walk test may cause some people to perform at higher exertion levels than others. For patients with moderate to severe heart or lung disease, there are detailed instructions provided by the American Thoracic Society (ATS) which highlight how patients may become out of breath or exhausted and instruct them on taking rest breaks. In contrast, some articles instruct people to walk as quickly as possible. While many studies do not report the exact instructions, most describe the instruction as having participants walk at their usual pace or a comfortable pace and to walk as far as possible. Participants are instructed prior to the test to wear comfortable clothing and shoes and to use their typical walking aid during the test **(12).**

**Walkway length and number of turns in the course:**

The ATS recommends an indoor, 30 meter corridor or walkway with cones placed at the beginning and end of the 30 meter boundary to indicate turns. In the literature, the corridor distance across studies varies which is likely due to the need to use what is readily available. A study in stroke patients suggest the 30 meter length (versus 10 or 20 meter) resulted in the longest distance covered. Although treadmills have been used to conduct the 6MWT, treadmills may underestimated total distance compared to the standard method done in a hallway or exercise room **(13).**

**Use of Encouragement:**

Encouragement is often given and is typically standardized, although it varies in frequency across studies from providing encouragement every 30 seconds to every 2 minutes. Encouragement increases the distance walked and if used, the exact protocol should be reported**(14).**

**Number of Trials Performed:**

Number of trials has been known to increase 6 minute walk distance, with largest improvements seen over the first 3 trials Variation on the tests performed is less than 10% between the first two trials and may reflect true variation in functional capacity. Therefore, one to two practice trials may be useful. In most populations, at least two practice walks should be administered (with adequate time for rest and recovery) prior to recording measurements **(15).**

**Safety Issues and Contraindications:**
As with any physical performance test, technicians should have certification in Basic Life Support. For people with moderate to severe heart disease, additional safety precautions are recommended by the ATS15 including certification in advanced cardiac life support and access to supplies and equipment (such as a crash cart) that would allow for a rapid response to an adverse event. Contraindications for this test as recommended by the ATS include unstable angina in the previous month, myocardial infarction in the previous month, and high blood pressure (resting heart rate of > 120, systolic blood pressure of 180 mm Hg, or diastolic blood pressure >100 mm Hg). The test should be stopped if a person reports chest pain, intolerable shortness of breath, leg cramps, staggering, diaphoresis, or pale/ashen appearance **(16).**

**Training:**
A standard protocol should be followed and each new technician should be trained in test administration and observed several times **(17).**

**Equipment needed**
- A 30meter, pre-measured flat walking area with interval markings every three meters.
- Cones or brightly colored tape to mark boundaries of the course.
- Watch or timer to time 6 minutes.
- Chair available if patients need to rest during testing **(17).**

**Scoring**
Outcomes measured: The primary outcome is the distance covered in meters or converted measure (such as feet) over 6 minutes. To measure functional aerobic capacity or general fitness.
**Interpretation of scores:** A lower score (reflecting less distance covered in 6 minutes) indicates worse function.
**Method of scoring:** Administrator tallies the total distance walked using the pre marked intervals as a guide.
Norms available: The six minute walk distance in healthy adults has been reported to range from 400m to 700m.Age and sex-specific reference standards are available and may be helpful for interpreting 6MWT scores for both healthy adults and those with chronic diseases. However, it is difficult to use normative values because of the differing methods used in studies. An improvement of 54m has been shown to be a clinically important difference in a study of people with chronic lung disease which is similar to the recommended criteria of meaningful clinical change of 50m based on analyses from a sample of 692 community living older adults and individuals who have survived a stroke **(18).**

**Conducting the Test**
When you schedule a walk test, ask the patient to wear comfortable footwear. During the test do not walk with the patient, because even if you walk behind them, it will alter their pace. If the patient is using supplemental oxygen during the walk, don't help push the oxygen tank or the 6MWD will not be the same as if the patient was pushing the tank, as he or she would do at home. In one study the investigators walked 6 people at the same time, which created competition among the study participants, resulting in a 30% larger mean 6MWD than tests in which the patients walked alone **(19).**

**Ensuring Quality**
Follow the published American Thoracic Society guidelines. Using a treadmill or bike on which the patient adjusts the speed and/or the slope, walking with the patient, and using an oval or circular track cannot be used. Standardized phrases for speaking to the patient must be used because the amount of encouragement and enthusiasm given can make a difference of up to 30% in the 6MWD **(4).**
Factors That Influence 6-Minute Walk Distance: (Table 2) lists factors that influence 6MWD. Not surprisingly, short people and women have a shorter stride length and therefore have shorter 6MWDs. Older and heavier subjects usually have reduced muscle mass and, therefore, shorter 6MWDs, as do those who are less motivated or have impaired cognition. Arthritis and other musculoskeletal diseases also decrease the 6MWD **(17).**

**Table (2): Factors That Affect 6-Minute Walk Distance**

| Factors Associated with Shorter 6-Minute Walk Distance: |
|---|
| 1-Shorter height (shorter legs) |
| 2-Old age |
| 3-Higher body weight |
| 4-Female gender |
| 5-Impaired cognition |
| 6-Shorter walking corridor (more turns) |

| |
|---|
| 7-Chronic obstructive pulmonary disease, asthma, cystic fibrosis, interstitial lung disease Angina, myocardial infarction, congestive heart failure, stroke, transient ischemic attack, peripheral vascular disease |
| 8-Arthritis; ankle, knee, or hip injuries; muscle wasting |
| Factors Associated with Longer 6-Minute Walk Distance: |
| 1-Taller height (longer legs) |
| 2-Male gender |
| 3-High motivation |
| 4-Patient has previously performed the test |
| 5-Medication for a disabling disease taken just before the test |

**Variables Measured**

**What variables can be measured in the 6MWT:**

The primary measurement is the total distance walked.

Secondary measures can include fatigue and dyspnea, measured with a modified Borg or visual analog scale. Arterial oxygen saturation can also be measured via pulse oximetry, as long as the oximeter is portable and not heavy. However, 3 different pulse oximeters have been used in large epidemiologic studies during the past 10 years, it was found an unacceptably high failure rate, due to motion artifact. For the last 2 studies fourth-generation pulse oximeters were chose specifically designed to compensate for motion artifact. They are reliable for determining the oxygen saturation before and after the 6MWT test, but, cautious in interpreting oxygen saturation readings obtained during exercise should be done **(8).**

**Interpreting the Results**

Ideally, calculation of the predicted distance should be done using equations from a published study of healthy people of the same age group, much like for spirometry tests. Healthy subjects' 6MWDs range from 400 to 700 m. However, the few published studies have all used different methods, and the predicted distances differ by up to 30% between the studies.

A low 6MWD is nonspecific and nondiagnostic (just like a low maximum voluntary ventilation). If the 6MWD is low, thoroughly search for the cause(s) of the impairment. The following tests may then be helpful: pulmonary function, cardiac function, ankle-arm index, muscle strength, nutritional status, orthopedic function, and cognitive function **(17).**

**Improving the 6-Minute Walk Distance**

One good study showed that an improvement of more than 70 m walked was clinically important to the patients. Mean improvements of 70–170 m (12–40% longer 6MWD) have been published for various interventions. Supplemental oxygen for chronic obstructive pulmonary disease and interstitial lung disease was shown to improve 6MWD, despite the extra weight of the ambulatory oxygen source. Lung volume reduction surgery has also been shown to improve 6MWD. In patients with chronic obstructive pulmonary disease, inhaled bronchodilators and rehabilitation programs can increase 6MWD **(20).**

**II- THREE MINUTES WALKING TEST**

The 3 min walking test is a submaximal strength test that is simple and easy to carry out both in the hospital as well as outpatients environment, with a low cost, facilitating the evaluation of the functional capacity of patients with COPD, not very severe patients. Potential use includes evaluation of results after therapeutic treatment: bronchodilator drugs therapy, lung volume surgery, lung transplant and respiratory rehabilitation programs. The results show that a learning effect exists with the 3 and 6 min distances repeated over short periods of time. A good correlation was observed between the distance walked at 3 and 6 min **(21).**

This test has little to no evidence to support its use in the clinic; however, the shorter time frame may be more conducive for children whom are severely limited in their ability to perform exercise for a longer periods of time or children with significant physical impairments whom are unable to ambulate farther distances **(22).**

**III- Five-repetition sit-to-stand**

The sit-to-stand (STS) manoeuvre is a common activity of daily living and is partly dependent on lower limb muscle function and balance (**23).** Variations of the STS manoeuvre have been adapted as functional performance measures, including time taken to perform a given number of STS manoeuvres (**24)** or the maximum number of STS manoeuvres in a given time period, usually 30 or 60 s (**25).**

These have been shown to correlate well with other objective physical performance measures such as Timed Up and Go, gait speed and the 6MWT (**25)** in healthy older community-living populations as well as patients with stroke,

Parkinson's disease and vestibular disorders. The five-repetition STS test (5STS), which measures the time taken to stand five times from a sitting position as rapidly as possible, is the best described STS test in older adults. Normative values (**24)** and data on reliability (**26)** and validity have been well described in healthy older community-dwelling individuals, but there is a paucity of data in COPD populations (**27).**

**Reliability and validity of 5STS in COPD**

Previous data on the STS manoeuvre in patients with COPD are limited to a few studies. **Roig et al. (28)** measured the 5STS in 21 patients with stable COPD and 21 healthy age-matched controls and showed that patients with COPD needed 21% more time to complete the 5STS than controls. However, they were not able to demonstrate any significant relationship between 5STS and knee extensor muscle strength or muscle cross-sectional area as measured by CT, perhaps due to the small sample size.

In a convenience sample of 53 patients with COPD, **Ozalevli et al. (25)** demonstrated a significant relationship between the maximum number of STS manoeuvres performed in 1 min and 6 min walk test and quadriceps muscle strength. The 5STS is also noted to be a single component of the short physical performance battery (SPPB), a standardised objective tool which consistently identifies poor prognosis in community-dwelling older adults.

The SPPB has been studied in a single cohort of relatively young COPD patients with milder disease, demonstrating lower scores compared with age-matched healthy controls and associations with lung function, body composition and increased risk of disability (**29).**

**Responsiveness of 5STS in COPD**

As the STS manoeuvre is related to lower limb muscle function and reflects an important activity of daily living, previous training studies in patients with COPD have used this as an outcome measure. However, due to the heterogeneity of the population and interventions and the small sample sizes, data regarding the responsiveness of the STS in COPD have been inconsistent. **Kongsgaard et al. (30)** randomised elderly men with COPD to 12 weeks of resistance training or control. There was no significant improvement in the number of STS manoeuvres completed in 30 s in either group, although only six patients completed resistance training.

**Advantages and limitations of the 5STS in COPD**

There are obvious advantages to the 5STS as an assessment tool in COPD.

- First, it is quick to perform (all patients completed the test within 2 min) and the data suggest there is no learning effect. This contrasts with the 6MWT and the ISW, both of which require repeat walks with adequate rest between tests (usually 30 min).
- Second, the 5STS is cheap to perform with easily available equipment (chair and stopwatch).
- Third, the test requires only limited space, which makes it feasible in most healthcare settings including the home setting. **(31)**

The major limitation to the test is the presence of a 'floor' effect, with up to 15% of patients unable to attempt or complete the test. Hence, the 5STS may have increased value as a functional outcome measure in better functioning patients. Other simple functional outcome tests, such as the habitual gait speed over 4 m, (**32)** or a battery of physical performance measures, such as the SPPB, (**33)** may be more appropriate for more poorly functioning individuals.

The 5STS may be particularly useful as a functional outcome tool in certain healthcare settings, such as the outpatient clinic or home setting, where space and equipment may be at a premium. Another potential use for the 5STS is as a stratification tool. Patients unable to complete the 5STS had grossly reduced exercise capacity and considerable quadriceps weakness, and the 5STS could be used as a simple bedside or clinic assessment tool to identify significantly impaired walking capacity or lower limb weakness. For example, the risk of mortality increases markedly when ISW falls below 170 m; using receiver-operator characteristic curves plotted for their cohort, the 5STS had a C-statistic (area under the curve) of 0.82 to identify an ISW below 170m(**34).**

**IV- Four meter gait speed**

Usual gait speed measured over 4 metres (4MGS) has been recommended as a potentially useful marker of multi systemic wellbeing in community-dwelling older adults. A slow 4MGS is a consistent risk factor for disability, cognitive impairment, nursing home admission, falls, cardiovascular and all cause mortality in older adults who report no functional limitation. Moreover, It is reliable, and quick to perform (**35).**

4MGS is also an established marker of exercise capacity in the elderly and has been shown to correlate with other measures of function. An expert working group identified the 4MGS as the most appropriate functional test for interventional trials in frail older adults (**36).**
A slow gait speed in the elderly is typically defined as a walking speed less than 0.8 meters per second, which corresponds to a reduction in the median life expectancy for most ages. Most studies of 4MGS have been in community dwelling older adults, a proportion of whom would likely have respiratory disease. However, the 4MGS has not been validated specifically in a COPD population. The use of a reliable, validated and easy to perform assessment tool to evaluate functional performance and predict adverse outcomes in COPD is attractive. Although field walking tests such as the six minute walk and incremental shuttle walk are well validated, they show learning effect and require space that limits widespread use in some clinical settings (**37).**

**Method**
Although gait speed has been reported over a variety of distances, most investigators currently believe that 4 metres is optimal for a field test, balancing a distance short enough to be feasible in most clinical settings, but long enough to ensure measurement accuracy. Test-retest reliability for 4MGS is better than that reported over an 8 feet course and as reliable as over 6 metres (**38).**

A 4-metre course has also been shown to be feasible in 90% of households allowing the possibility of using the 4MGS as a tool in community or homebased studies. It is important to note that reliable 4MGS measurements can be made even by non-professional staff and good reliability has been shown in frail patients or those with cognitive dysfunction (**38).**

**Significance of the findings**
The 4MGS as a single item tool has not been previously reported in COPD. **Roig et al**. **(28)** reported self-selected gait speed in 21 COPD patients over a 5 metre course, demonstrating a 20% reduction in speed compared with age matched controls.

**Ilgin and colleagues (39)** described significant associations between gait speed and lung function parameters and health related quality of life in COPD, although gait speed was calculated from six minute walk distance rather than from a short course. **Andersson et al. (40)** showed high test retest reliability when measuring walking speed in 49 COPD patients, although the 30 meter course may limit generalisation of the findings.

**Evans et al. (41)** demonstrated the validity of self paced walking and the responsiveness to pulmonary rehabilitation in 37 COPD patients. Interestingly, although the test was performed in an enclosed, temperature controlled 250 meter flat corridor. 4MGS correlates significantly to health outcome measures commonly used in COPD. The 4MGS is also noted to be a single component of the short physical performance battery (SPPB). Previous data on the SPPB in COPD have been described in a single cohort, demonstrating lower (worse) SPPB scores in COPD patients compared with age matched healthy controls, and an association between increased lean to fat ratio and preserved lung function with higher SPPB scores. This cohort was restricted to ages between 40-65 years and tended to have milder disease 30% of patients were in the now defunct GOLD stage 0(**29).**

The 4MGS is quicker to perform, and previous studies have shown that the 4MGS has similar associations and predictive abilities to the SPPB. The 4MGS had been frequently used in epidemiological studies of older adults due to its ease and speed of use. It has been shown to predict health status, functional decline, institutionalization, onset of disability and mortality (**42).**

Other investigators have used gait speed as a functional outcome measure, and expert working groups (including representatives from the Food and Drug Agency) have identified the 4MGS as the most appropriate functional test for interventional studies in frail older adults and sarcopenia (**43, 44).**

The 4MGS has potential as an assessment tool in COPD. It is quick to perform, and cheap. Walking is familiar to the vast majority of adults, and the test is easy to understand the 4MGS has been shown to be highly reliable even in people with cognitive dysfunction. Furthermore, it requires little space, and the operator does not require any specialist training. These properties mean that the 4MGS could be adopted in almost any clinical environment (even at the bedside, or in primary care) (**45).**

4MGS is reliable in COPD with excellent test retest reliability. This is significant, particularly as current field tests of exercise capacity show learning effect and some, like the six minute walk test, require a 30 metre course. Evidence of

concurrent validity was demonstrated by showing significant associations with exercise capacity, health status and dyspnoea. By stratifying COPD patients according to 4MGS, the "slow walking speed" clinical phenotype exhibited significant deficits in exercise capacity, increased dyspnoea and poor health status in comparison to those with preserved walking speed. Interestingly, despite large differences in these outcome measures (that exceeded the commonly agreed minimum clinically important differences), there was no significant difference in FEV1 %predicted between the groups. Although 4MGS was shown to correlate negatively with age and BMI, it is unlikely that these were significant confounding factors for results given that there were still large differences in ISW %predicted (which corrects for age and BMI). Furthermore, 4MGS was not simply a reflection of comorbidity burden; no or very weak relationships was showed between 4MGS and validated comorbidity indices **(37).**

**References:**


1. **Agustí, A., Vogelmeier, C. and Faner, R. (2020)** 'COPD 2020: changes and challenges', *American Journal of Physiology-Lung Cellular and Molecular Physiology*. American Physiological Society Bethesda, MD, pp. L879–L883.
2. **Adeloye, D., Song, P., Zhu, Y., *et al.* (2022)** 'Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis', *The Lancet Respiratory Medicine*, 10(5), pp. 447–458.
3. **Osadnik, C. R., Borges, R. C., McDonald, C. F., *et al.* (2016)** 'Two 6-minute walk tests are required during hospitalisation for acute exacerbation of COPD', *COPD: Journal of Chronic Obstructive Pulmonary Disease*, 13(3), pp. 288–292.
4. **Guimarães GV, Bellotti G, Bacal F. (2002).** Can the cardiopulmonary 6-Minute Walk Test Reproduce the Usual Activities of Patients with Heart Failure? Arq Bras Cardiol; 78:557-60.
5. **Ubuane, P. O., Animasahun, B. A., Ajiboye, O. A. et al. (2018).** The historical evolution of the six-minute walk test as a measure of functional exercise capacity: A narrative review. Journal of Xiangya Medicine, 3(3), 40.
6. **Agarwala, P., & Salzman, S. H. (2020).** Six-minute walk test: clinical role, technique, coding, and reimbursement. Chest, 157(3), 603-611.
7. **Vitale, G., Sarullo, S., Vassallo, L. et al. (2018).** Prognostic value of the 6-min walk test after open-heart valve surgery: experience of a cardiovascular rehabilitation program. Journal of Cardiopulmonary Rehabilitation and Prevention, 38(5), 304-308.
8. **Gibbons WJ, Fruchter N, Sloan S, Levy RD. (2001).** Reference values for a multiple repetition 6-minute walk test in healthy adults older than 20 years. J. Cardiopulm. Rehabil; 21: 87 – 93.
9. **Li, L., Cheng, S., Wang, G., et al. (2019).** Tai chi chuan exercises improve functional outcomes and quality of life in patients with primary total knee arthroplasty due to knee osteoarthritis. Complementary Therapies in Clinical Practice, 35, 121-125.
10. **Joo, Y. B., Lee, K. B., Sul, B. et al. (2022).** Effect of resistance exercise on serum leptin levels in a prospective longitudinal study of women patients with rheumatoid arthritis. Arthritis Research & Therapy, 24(1), 1-9.
11. **Mudge S, Stott NS. (2009).** Timed walking tests correlate with daily step activity in persons with stroke. Archives of physical medicine and rehabilitation; 90(2):296-301.
12. **Lord S, Menz H. (2002).** Physiologic, psychologic, and health predictors of 6-minute walk performance in older people. Archives of physical medicine and rehabilitation; 83(7):907-11.
13. **Olper L, Cervi P, De Santi F. et al. (2011).** Â Validation of the treadmill six-minute walk test in people following cardiac surgery.Â Phys Ther; 91(4):566-76.
14. **Pinna GD, Opasich C, Mazza A. et al. (2000).** Reproducibility of the six-minute walking test in chronic heart failure patients. Statistics in medicine; 19(22):3087-94.
15. **Wu G, Sanderson B, Bittner V. (2003).** The 6-minute walk test: how important is the learning effect? The American heart journal; 146(1):129-33.
16. **ATS statement. (2002).** guidelines for the six-minute walk test. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. Am J Respir Crit Care Med; 166(1):111–117.
17. **Enright P. (2003).** The six-minute walk test. Respiratory care.; 48(8):783-5.
18. **Perera S, Mody S, Woodman R, Studenski S. (2006).** Meaningful change and responsiveness in common physical performance measures in older adults. Journal of the American Geriatrics Society; 54(5):743-9.
19. **Roomi J, Johnson MM, Waters K. et al. (1996).** 4-Respiratory rehabilitation, exercise

capacity and quality of life in chronicairways disease in old age. Age Ageing; 25(1):12–16.

20. **Redelmeier DA, Bayoumi AM, Goldstein RS. Et al. (1997**). Interpreting small differences in functional status: The Six Minute Walk test in chronic lung disease patients. Am J Respir Crit Care Med; 155(4):1278–1282.
21. **Koraa, E. E. A., Ali, E. R., & Elshaer, T. K. (2020).** Three minutes walking test in correlation to six minutes walking test in COPD patients. QJM: An International Journal of Medicine, 113(Supplement_1), hcaa043-001.
22. **Pan AM, Stiell IG, Clement CM. et al. (2009).** Feasibility of a structured 3-minute walk test as a clinical decision tool for patients presenting to the emergency department with acute dyspnea. Emerg Med J; 26(4): 278-282.
23. **Bohannon RW. (2009).** Body weight-normalized knee extension strength explains sit-to-stand independence: a validation study. J Strength Cond Res;23:309–11.
24. **Bohannon RW. (2006).** Reference values for the five-repetition sit-to-stand test: a descriptive meta-analysis of data from elders. Percept Mot Skills;103:215–22.
25. **Ozalevli S, Ozden A, Itil O. et al. (2007).** Comparison of the sit-to-stand test with 6 min walk test in patients with chronic obstructive pulmonary disease. Respir Med;101:286–93.
26. **Bohannon RW. (2011).** Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults. J Strength Cond Res;25:3205–7.
27. **McCarthy EK, Horvat MA, Holtsberg PA. et al. (2004).** Repeated chair stands as a measure of lower limb strength in sexagenarian women. J Gerontol A Biol Sci Med Sci;59:1207–12.
28. **Roig M, Eng JJ, MacIntyre DL. et al. (2011).** Deficits in muscle strength, mass, quality, and mobility in people with chronic obstructive pulmonary disease. J Cardiopulm Rehabil Prev;31:120–4.
29. **Eisner MD, Iribarren C, Blanc PD. et al. (2011).** Development of disability in chronic obstructive pulmonary disease: beyond lung function. Thorax ; 66: 108–114.
30. **Kongsgaard M, Backer V, Jorgensen K. et al. (2004).** Heavy resistance training increases muscle size, strength and physical function in elderly male COPD patients—a pilot study. Respir Med;98:1000–7.
31. **Jones SE, Kon SS, Canavan JL, et al. (2013).**The five-repetition sit-to-stand test as a functional outcome measure in COPD. Thorax. 68(11): 1015–1020.
32. **Kon SS, Patel MS, Canavan JL. et al. (2012).** Reliability and validity of the four metre gait speed in COPD. Eur Respir J. Published Online First: 6.
33. **Latham NK, Mehta V, Nguyen AM. et al. (2008).** Performance-based or self-report measures of physical function: which should be used in clinical trials of hip fracture patients? Arch Phys Med Rehabil;89:2146–55.
34. **Ringbaek T, Martinez G, Brondum E. et al. (2010).** Shuttle walking test as predictor of survival in chronic obstructive pulmonary disease patients enrolled in a rehabilitation program. J Cardiopulm Rehabil Prev;30:409–14.
35. **Hirabayashi, R., Takahashi, Y., Nagata, K. et al. (2020).** The validity and reliability of four-meter gait speed test for stable interstitial lung disease patients: the prospective study. Journal of Thoracic Disease, 12(4), 1296.
36. **Kon, S. S., Canavan, J. L., Nolan, C. M. et al. (2014).** The 4-metre gait speed in COPD: responsiveness and minimal clinically important difference. European Respiratory Journal, 43(5), 1298-1305.
37. **Kon, S. S. C., Patel, M. S., Canavan, J. L., *et al.* (2013)** 'Reliability and validity of 4-metre gait speed in COPD', *European Respiratory Journal*, 42(2), pp. 333–340.
38. **Mun˜oz-Mendoza CL, Caban˜ero-Martı´nez MJ, Milla´n-Calenti JC. et al. (2011).** Reliability of 4-m and 6-m walking speed tests in elderly people with cognitive impairment. Arch Gerontol Geriatr; 52: e67–e70.
39. **Ilgin D, Ozalevli S, Kilinc O. et al. (2011).** Gait speed as a functional capacity indicator in patients with chronic obstructive pulmonary disease. Ann Thorac Med; 6: 141–146.
40. **Andersson M, Moberg L, Svantesson U. et al. (2011).** Measuring walking speed in COPD: test-retest reliability of the 30- metre walk test and comparison with the 6-minute walk test. Prim Care Respir J; 20: 434–440.
41. **Evans RA, Hill K, Dolmage TE. et al. (2011).** Properties of self-paced walking in chronic respiratory disease; a patient-goal orientated assessment. Chest; 140: 737–743.
42. **Abellan van Kan G, Rolland Y, Andrieu S. et al. (2009).** Gait speed at usual pace as a predictor of adverse outcomes in community-dwelling older people. An International Academy on Nutrition and Aging (IANA) Task Force. J Nutr Health Aging; 13: 881–889.
43. **Goodman AD, Brown TR, Edwards KR. et al. (2010).** A phase 3 trial of extended release

oral dalfampridine in multiple sclerosis. Ann Neurol; 68: 494–502.

44. **Cruz-Jentoft AJ, Baeyens JP, Bauer JM. et al. (2010).** Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing; 39: 412–423.
45. **Nolan, C. M., Maddocks, M., Maher, T. M. et al. (2018).** Phenotypic characteristics associated with slow gait speed in idiopathic pulmonary fibrosis. Respirology, 23(5), 498-506.