



Monaldi Archives for Chest Disease

eISSN 2532-5264

<https://www.monaldi-archives.org/>

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Monaldi Arch Chest Dis 2025 [Online ahead of print]

To cite this Article:

Ertan Harputlu O, Kuran Aslan G, Akıncı B, et al. **Investigation of different field tests in relation to balance, daily living activities, and quality of life in pulmonary hypertension.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2025.3308

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Investigation of different field tests in relation to balance, daily living activities, and quality of life in pulmonary hypertension

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Contributions: OEH, GKA, BA, literature search, data collection, study design, analysis of data, manuscript preparation, review of manuscript; AKB, MI, data collection; GO, data collection, study design, analysis of data, manuscript preparation, review of manuscript. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that there is no conflict of interest.

Ethics approval and consent to participate: the study was approved by the Istanbul University Ethics Committee (number: 2018/285) and conducted by the Helsinki Declaration. Written consent to participate were obtained from all study participants.

Informed consent: written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article. The manuscript does not contain any individual person's data in any form.

Patient consent for publication: not applicable.

Availability of data and materials: data cannot be shared because the informed consent we receive from patients includes a statement saying that their data will not be shared with third parties.

Funding: none.

Acknowledgments: the authors would like to thank David F. Chapman for English editing.

Abstract

Assessment of exercise capacity is useful in monitoring patients and planning a rehabilitation program for subjects with pulmonary hypertension (PH). No study has investigated the relationship of different field tests, except for the six-minute walk test (6MWT), with balance, activities of daily living (ADL), and quality of life (QoL) in subjects with PH. This study aimed to investigate the relationship of different field tests with balance, ADL, and QoL in subjects with PH. This study was a prospective cross-sectional study. A total of 27 subjects who were diagnosed as having PH were included in the study. Field tests were the 6MWT, the Incremental Shuttle Walk Test (ISWT), and the Endurance Shuttle Walk Test (ESWT). Balance assessment was performed using the Timed Up and Go Test (TUG). ADL was evaluated using the London Chest Activities of Daily Living Scale, and QoL was evaluated using emPHasis-10.

TUG was the significant predictor of 6MWD and ISWT walking distance ($\beta=-0.590$, $p=0.001$, $\beta=-0.600$, $p=0.001$). The emPHasis-10 score significantly predicted ESWT time ($\beta=-0.667$, $p<0.001$). Submaximal and maximal exercise capacity were related to balance in subjects with PH, and lower endurance capacity was related to decreased QoL.

This study suggests that submaximal and maximal exercise capacity were related to dynamic balance in subjects with PH, and lower endurance capacity was related to decreased QoL. ISWT can be considered a safe and practical tool to assess maximum exercise capacity.

Key words: six-minute walk test, incremental shuttle walk test, endurance shuttle walk test, pulmonary hypertension.

Introduction

Pulmonary hypertension (PH) is defined as “a pathophysiologic disorder that may involve multiple clinical conditions and can complicate the majority of cardiovascular and respiratory diseases” [1]. PH is a hemodynamic condition defined by a mean pulmonary artery pressure (mPAP) measured at rest >20 mm Hg at a right-sided cardiac catheterization [2]. The symptoms of PH include dyspnea, fatigue, weakness, chest pain and syncope, which are typically effort-induced [3]. Exercise capacity decreases related to these symptoms in the progression of the disease [4]. Therefore, it is important to assess exercise capacity to determine the diagnosis, disease severity, prognosis, and treatment efficacy by taking into account the effort-induced limitations in PH [5]. Exercise capacity in subjects with PH is commonly assessed using the Six Minute Walk Test (6MWT). The 6MWT is a simple, cost-effective, tolerable, and reproducible test [6]. It has been found as an important predictor of quality of life (QoL) and mortality in subjects with PH [7,8]. Although its association with muscle strength and participation in daily living have been well documented, it is not known how body balance influences this test [9-11].

The Incremental Shuttle Walk Test (ISWT) and Endurance Shuttle Walk Test (ESWT) are used to determine exercise capacity in chronic cardiopulmonary conditions [12,13]. It has been demonstrated that ISWT can be administered safely in subjects with PH. Moreover, a limited number of studies reported that this test was sensitive to treatment and a preferable alternative for the assessment of exercise capacity subjects with PH because of its better reflection [14-16]. Accordingly, it is not known whether ISWT or ESWT provide a meaningful clinical outcome regarding functional status or QoL in these patients.

We hypothesized that different field tests would vary in their association with dynamic balance, activities of daily living (ADL), and QoL in individuals with PH, and examined whether some tests (e.g., ISWT or ESWT) would better reflect these clinical parameters than the traditionally used 6MWT. Therefore, this study aimed to compare the associations between different field tests (6MWT, ISWT, and ESWT) and clinical outcomes, including dynamic balance, ADL, and QoL in individuals with PH. Investigating which field test best reflects functional performance and QoL in patients with PH may be useful in terms of monitoring the disease and planning a rehabilitation program.

Materials and Methods

This is a cross-sectional study including 27 patients aged 18-80 years with PH (chronic thromboembolic PH $n=5$, idiopathic PAH $n=22$) diagnosed at least 6 months ago at the PH outpatient clinic of Istanbul University Faculty of Medicine, Department of Chest Diseases, between January 2019 and March 2020. Subjects with left heart disease and lung diseases

and/or hypoxemia-induced PH, successful pulmonary endarterectomy, smoking, orthopedic/neurologic disease that could limit exercise testing, participated in any rehabilitation program last year or during the study, uncontrolled cardiovascular disease, and communication problems were excluded. The clinical and demographic data of the subjects were recorded. The study was approved by the Istanbul University Ethics Committee (number: 2018/285) and conducted according to the Helsinki Declaration. Informed consent was obtained from all subjects. The power analysis was performed using G*Power (v3.1.9.4) for a two-tailed correlation test (point biserial model) with an effect size ($\rho = 0.5$), $\alpha = 0.05$, and power = 0.80. The required sample size was calculated as 26 participants [17].

The clinical assessment consisted of obtaining information regarding the subjects' demographics and clinical features, including spirometry values, World Health Organization (WHO) functional classification, PH etiology, mPAP, and pulmonary capillary wedge pressure (PCWP), (from right heart catheterization results), were obtained from medical records.

The balance function was evaluated using the Timed-Up and Go (TUG) test. The subjects were asked to stand up from a chair and walk 3 meters, then turn 180 degrees, walk back to the chair, and sit. A stopwatch was used for the time performance, which was recorded in seconds. It has been indicated that TUG duration is associated with the level of functional mobility [18]. The TUG test is valid and reliable in patients with PH [19].

The 6MWT was applied by following the American Thoracic Society criteria [20]. Subjects were asked to walk as fast as possible at their walking speed for 6 minutes in a 30-meter corridor. Before the test, it was explained to the subjects that if they felt shortness of breath, they could rest and that the rest period was included in the test. Oxygen saturation, heart rate, and blood pressure values were measured at the beginning and end of the 6MWT. Dyspnea and leg fatigue scores were questioned according to the modified Borg scale. The six-minute walk distance (6MWD) was calculated at the end of the test.

The ISWT is a field test consisting of a total of 12 levels in which the walking speed is progressively increased, and subjects walk with maximum performance at the symptom limit. During ISWT, walking speed was determined by an audio signal while the subjects were walking around two cones placed 0.5 meters indented on both sides on a 10-meter flat surface and the test was performed by monitoring the audio signal. The oxygen saturation, heart rate and blood pressure of the subjects were recorded before and after the ISWT. Dyspnea and leg fatigue were questioned according to the modified Borg scale. At the end of the test, the number of completed shuttles was noted in meters. The end of the ISWT was determined in the presence of shortness of breath that prevented the patient from maintaining

the required speed, the patient reached maximal heart rate, and if the patient failed to complete the shuttle after when a bleep from the audio signal [21,22].

ESWT was established as an adjunct to ISWT. The test course is the same as in the ISWT. The maximum capacity of subjects is predicted from a distance walked during the ISWT. The following formula was used to estimate the subjects predicted VO_{2max} (mL/min/kg) = $4.19 + (0.025 \times \text{ISWT distance})$ and the level at which the patient would walk in ESWT was determined using 85% of this value. The ESWT was started at the appropriate level for the patient from the audio file containing 16 different levels. At the beginning of each level, there was a warm-up of 90 sec followed by an audio signal for a maximum of 20 minutes of walking at a constant speed. ESWT continues for a maximum of 20 minutes. The subjects were not informed about the time limitation and were instructed that they could stop walking if they experienced excessive breathlessness. At the end of the test, the duration of walking was recorded in seconds [23].

The ADL of the subjects was evaluated using the London Chest Activity of Daily Living (LCADL) which evaluates dyspnea perception in ADL in a simple, practical and comprehensive way. The LCADL, made up of 15 questions in total, consists of four domains: self-care, domestic, physical, and leisure. Each question is scored between 0-5. Higher scores indicate difficulty in performing ADL. There is also a single question that assesses how much ADL is affected by dyspnea perception. The patient answers this question with one of "none", "some" and "a lot" [24,25].

The emPHasis-10 questionnaire was used to evaluate QoL. emPHasis-10 is a short and simple questionnaire that consists of 10 disease-specific questions designed to evaluate the QoL of subjects with PH. The answer to each question is scored between 0-5. Higher scores indicate a lower QoL [26,27].

Protocol

All assessments were completed on the same day. Subjects rested between each assessment for complete muscle recovery and to eliminate subjective symptoms such as dyspnea and leg fatigue. Balance was assessed using the TUG before the field tests. All field tests were performed in the same order by the same physiotherapist who was experienced in pulmonary rehabilitation—first, 6MWT; second, ISWT; and last, ESWT. There was a rest period of at least 30 minutes between tests. All patients had previously performed the 6MWT as they were followed up in the clinic. The 6MWT and ISWT were performed twice due to the learning effect as suggested [20,21]. The ESWT was performed once because it was performed in the same setup as the ISWT. The LCADL scale and emPHasis-10 were

completed as an interview by the same physiotherapist during the resting periods of the field tests.

Statistical analysis

Data was evaluated using the Statistical Package for the Social Sciences (SPSS V.21) program for Windows. Descriptive statistics are expressed as frequency, mean, and standard deviation. The normal distribution of data was analyzed using the Shapiro-Wilk test. Intercorrelations among parameters were computed using Spearman correlation analysis. Correlation coefficients (r) were considered as poor: 0.26-0.49, moderate: 0.50-0.69 and high: 0.70. Multiple linear regression analysis was performed to determine the multivariate influence of the predictors (TUG, QoL and ADL) of 6MWT, ISWT, ESWT test performances. The adjusted R^2 was used to explain the total variance. A p -value of < 0.05 was considered statistically significant for all tests.

Results

A total of 54 subjects with PH were screened for eligibility in terms of the inclusion criteria. Twenty-seven subjects were not included for the following reasons: PH associated with left heart disease ($n = 5$), lung diseases and/or hypoxemia-induced PH ($n = 6$), smoking ($n = 5$), successful pulmonary endarterectomy operation ($n = 4$), follow-up less than 6 months ($n = 3$), unwillingness to participate in the assessment session ($n = 4$). Twenty-seven subjects (21 females, 6 males) were enrolled in the study (Figure 1). Subjects did not use supplemental O_2 during the tests. No adverse effects related to the assessments were reported by the subjects during the study.

The mean age of the subjects was 47.74 ± 12.26 years. Five subjects were diagnosed as having chronic thromboembolic PH and 22 subjects had idiopathic PAH. The mean disease duration of subjects was 38.85 ± 29.63 months and the mPAP was 43.56 ± 18.15 mmHg based on the right heart catheterization results. According to the WHO PH functional classification, 20 subjects were Class II and seven subjects were Class III (Table 1).

Table 2 presents the 6 MWT, ISWT and ESWT test results and balance, ADL, and QoL of the subjects. There was a moderate negative correlation between the 6MWD and the TUG test ($r = 0.614$, $p = 0.001$). A moderate negative correlation was found between ISWT walking distance and TUG test ($r = -0.604$, $p = 0.001$), LCADL ($r = -0.430$, $p = 0.025$) and emPHasis-10 ($r = -0.401$, $p = 0.038$). There was a strong negative correlation between ESWT walking time and emPHasis-10 ($r = 0.658$, $p < 0.001$) (Table 3).

Three separate multiple linear regression models were conducted to determine the predictors of the 6MWD, ISWT walking distance, and ESWT walking time as dependent variables

where TUG, LCADL, and emPHasis-10 score were entered as independent variables. In the first model, ($F(3,23) = 8.329, p = 0.001$), TUG was the only significant predictor of 6-MWD accounting for 45.8 % of the variance ($\beta = -0.590, p = 0.001, B = -25.83$). In the second model ($F(3,23) = 9.308, p < 0.001$), TUG was the only significant contributor to 48.9% of the variance explained in the significant regression for ISWT walking distance ($\beta = -0.600, p = 0.001, B = -40.37$). In the last model ($F(3,23) = 7.843, p = 0.001$), the emPHasis-10 score was the only significant predictor of ESWT walking time for 44.1 % of the variance ($\beta = -0.667, p < 0.001, B = -26.1$).

Discussion

The present study investigated the relationship between three different field tests and balance, ADL, and QoL. Our results showed that balance was a predictor of both submaximal and maximal exercise capacity in subjects with PH. Additionally, lower maximal exercise capacity was associated with restricted ADL and QoL, and lower endurance capacity was related to decreased QoL.

It is known that exercise training significantly improves exercise capacity subjects with PH [28]. Therefore, it is important to assess exercise capacity before subjects are included in rehabilitation programs. In this study, exercise capacity in subjects with PH was evaluated using three different field tests. The 6MWT is the most used field test in assessing the exercise capacity of patients with PH [6]. The use of ISWT and ESWT is not as common as the 6MWT [29]. In our study, the ISWT and ESWT were used safely in subjects with PH without any negative events.

Irisawa et al. [15] investigated the efficacy of the ISWT in clinical practice in subjects with PH ($n=19$). They reported the mean ISWT walking distance as 359.4 ± 151.6 m and mean 6MWD as 432.7 ± 78.4 m. In the present study, the mean 6MWD was found similar (418.59 ± 59.67 m); however, the mean ISWT was shorter (265.19 ± 91.75 m) than in previous studies which may due to different PH etiologies of the subjects. The balance-functional mobility status of our subjects ($TUG = 8.63 \pm 1.36$ sec) was similar to those of previous studies conducted on subjects with chronic obstructive pulmonary disease (COPD) ($TUG = 8.87 \pm 3.20$ sec) [30]. In this study, regression analysis revealed that balance-functional mobility was a predictor of both submaximal and maximal exercise capacity. Subjects need to walk faster to cover more distance during these tests. Therefore, this result may be relevant to the nature of these tests. Especially in the ISWT, good balance control is essential because of the shorter course (10-m-long) and progressively increasing speed. We found that the 6MWD increased by 25.8 m and ISWT walking distance increased by 40.3 for each 1-second decrease in the TUG test. Our findings were similarly reported in individuals with

interstitial lung disease. Zamboti et al. [31] stated that these tests reflect similar functional components such as mobility, balance and exercise capacity. Similarly, Montgomery et al. [32] showed that TUG performance was associated with 6MWT in healthy old individuals and emphasized that this relationship was linked to physical determinants such as lower limb muscle strength and body composition. A study comparing static and dynamic balance and balance confidence in healthy subjects and patients with PAH reported that although static balance performance was preserved, and patients with PAH had reduced dynamic balance performance and balance confidence compared with healthy controls without a significant history of falls [11]. Specific research on balance training in patients with PH is limited. Balance assessment is more common in patients with COPD [33,34]. There is a growing body of research supporting the benefits of balance training for people with COPD, and it has been reported that targeted balance training provides the greatest benefit in improving balance [35]. As a clinical implication of this finding, subjects with a decreased walking distance in the 6MWT or ISWT may be assessed in respect of balance-functional mobility. The association between submaximal and maximal exercise capacity and balance in our study suggests that it may be beneficial to include balance training in PR programs for patients with PAH and how to implement it.

It is known that contributions to ADL are affected by effort-related symptoms in subjects with PH [36,37]. Okumus et al. [37] reported a significant correlation between ADL (as measured using the Nottingham Extended Activity of Daily Living Index) and the 6MWD (mean 6MWD = 342.9 ± 113 m). In our study, we found that ADLs measured with LCADL were only related to ISWT. This difference may have originated from the difference between the mean 6MWDs of the study populations or using different ADL scales. It may also be thought that ISWT reflected the limitations in contribution to ADL better than 6MWT because the ISWT is not a time-based test. However, regression analysis showed that LCADL was not a predictor of ISWT walking distance.

Systemic pathophysiologic changes in subjects with PH result in decreased exercise capacity. Decreased exercise capacity plays an important role in decreased QoL in PH [7]. However, this relationship has not been investigated using different field tests other than the 6MWT. In contrast to previous findings [7], QoL was correlated with ESWT and ISWT but not with 6MWD in our study. Moreover, we found that QoL was a predictor of ESWT walking time. To our knowledge, this is the first study to use the ESWT as a field test in subjects with PH. The mean duration in the ESWT was 771.70 ± 335.56 sec, which is twice as long as the duration in the 6MWT. On the other hand, it has been reported that the ISWT showed a better correlation with peak oxygen consumption (VO_2) and VO_2 at the anaerobic threshold [15]. Assessment of QoL is important because it is associated with prognosis and survival

subjects with PH [38]. Adding the ESWT may be considered in clinical assessments, especially in subjects with a relatively better 6MWD. Moreover, endurance exercise-based pulmonary rehabilitation programs could be preferred with the aim of increasing QoL.

This study has some limitations. The sample of the study population was relatively small. We focused on dynamic-functional mobility because it is compatible with ADL, but the static balance status of the subjects was not investigated.

Our results support those in previous studies [39] that reported that exercise programs can improve endurance capacity and QoL. In the present study, it was found that dynamic balance was a significant reflector predictor of submaximal and maximal walking distance. The addition of balance exercises to rehabilitation programs may be beneficial for individuals with PH.

Clinical implications

The results of this study provide some evidence regarding the use of the 6MWT, ISWT, and ESWT tests and their relationship with dynamic balance, ADL, and QoL in subjects with PH. The relationship between submaximal and maximal exercise tests and balance performance highlights the need for balance assessment when planning patient evaluation and rehabilitation programs. In addition, the association between lower endurance capacity and reduced QoL suggests that it may be beneficial to include endurance interventions in exercise programs. Assessment with different field tests may contribute to the development of more effective rehabilitation programs for patients with PH.

Conclusions

This study suggests that submaximal and maximal exercise capacity were related to dynamic balance in subjects with PH, and lower endurance capacity was related to decreased QoL. The effect of exercises for balance added to rehabilitation programs should be investigated with further studies. The results of this study also highlight the clinical importance of including balance assessment in PH. Given the significant relationship between balance and functional capacity, the inclusion of balance training, which is widely used in COPD rehabilitation, may also benefit patients with PH. In addition, the relationship between endurance capacity and quality of life suggests the inclusion of endurance training in PH rehabilitation programs. No adverse events occurred in any of the field tests. The ISWT may be a safe and practical tool for assessing maximal exercise capacity in patients with PH, especially when cardiopulmonary exercise testing is not available.

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Table 1. Demographics and clinic characteristics of patients.

	Data (n=27)
Age (years)*	47.74±12.26
Sex [#]	
Female	21 (77.8 %)
Male	6 (22.2 %)
BMI (kg/cm ²)*	28.03±5.48
Etiology [#]	
IPAH	22 (81.5 %)
CTEPH	5 (18.5 %)
WHO Functional Class [#]	
Class II	20 (74.1 %)
Class III	7 (25.9 %)
Spirometry Values	
FEV1 (% pred)	83.04±22.37
FVC (% pred)	83.81±21.54
FEV1/FVC (%)	96.19±13.03
DLCO (%)	62.48±24.64
Dyspnea level (Modified Borg Scale)*	0.07±0.38
Basal SpO ₂ (%) [*]	95.81±4.33
Disease Duration (month)	38.85±29.63
Mean Pulmonary Artery Pressures (mmHg)*	43.56±18.15
Pulmonary Capillary Wedge Pressure (mmHg)	12.19±3.54

*Mean±Standard deviation, [#]n(%). N, number; IPAH, idiopathic pulmonary arterial hypertension; CTEPH, chronic thromboembolic pulmonary hypertension; WHO, World Health Organization; BMI, body mass index.

Table 2. The exercise capacity, balance, ADL, and QoL of patients

	Data (n=27)
6 MWT	
6 Minute Walking distance (m)*	418.59±59.67
Δ SpO ₂ (%)	5.19±6.36
Δ Modified Borg Dyspnea (0-10)	2.3±1.77
Δ Modified Borg Leg Fatigue (0-10)	1.37±1.47
ISWT	
ISWT Walking distance (m)*	265.19±91.75
Δ SpO ₂ (%)	7.19±6.65
Δ Modified Borg Dyspnea (0-10)	2.26±1.22
Δ Modified Borg Leg Fatigue (0-10)	1.56±1.39
ESWT	
ESWT Walking Time (sec)*	771.70±335.56
Δ SpO ₂ (%)	7.30±6.99
Δ Modified Borg Dyspnea (0-10)	1.41±1.30
Δ Modified Borg Leg Fatigue (0-10)	1.22±1.15
TUG (sec)*	8.63±1.36
LCADL Score (0-75)*	19.67±4.24
emPHasis-10 Score (0-50)*	16.81±8.58

*Mean±Standard deviation. N, number; 6 MWT, six-minute walk test; ISWT, incremental shuttle walk test; ESWT, endurance shuttle walk test; TUG, timed up and go test; LCADL, London chest activity of daily living scale.

Table 3. Relationship between field tests and balance, ADL, and QoL scores

	6 MWD	ISWT walking distance	ESWT walking time
TUG	$p = 0.001$ $r = -0.614$	$p = 0.001$ $r = -0.604$	$p = 0.261$ $r = -0.264$
LCADL	$p = 0.191$ $r = -0.305$	$p = 0.025$ $r = -0.430$	$p = 0.235$ $r = -0.278$
emPHasis-10	$p = 0.363$ $r = -0.215$	$p = 0.038$ $r = -0.401$	$p < = 0.001$ $r = -0.658$

6 MWD, six-minute walking distance; ISWT, incremental shuttle walk test; ESWT, endurance shuttle walk test; TUG, timed up and go test; LCADL, London chest activity of daily living scale.

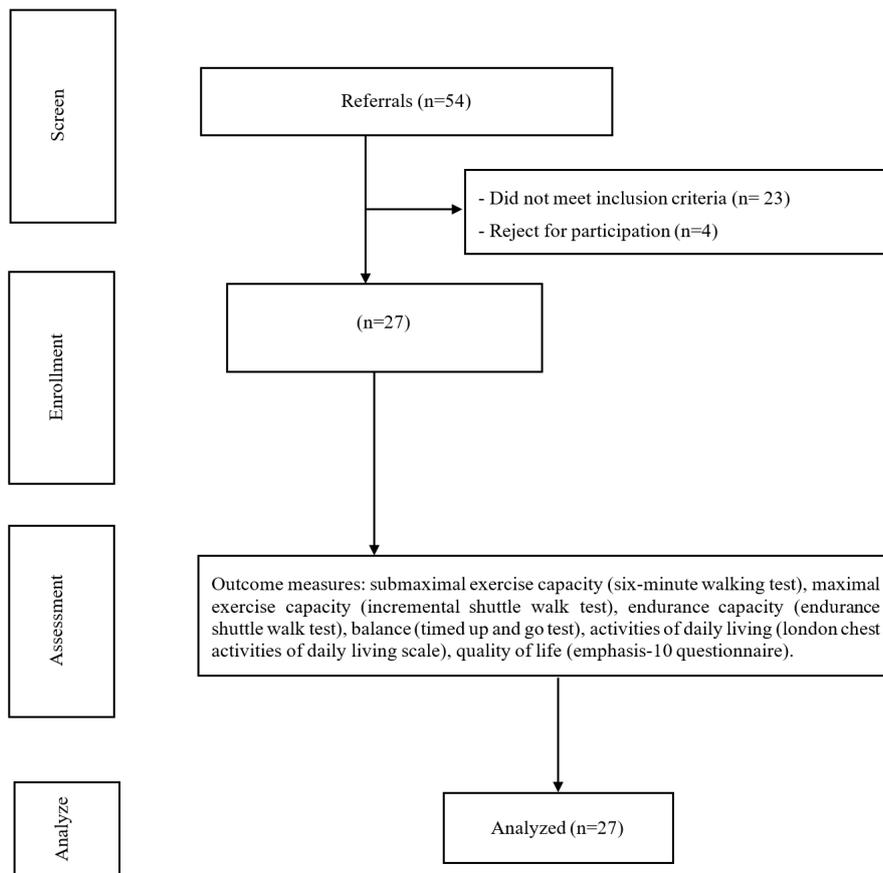


Figure 1. Flowchart of the study.