Original Article

Diagnostic ability of the Timed Up & Go test for balance impairment prediction in chronic obstructive pulmonary disease

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Background: Balance assessment is now recommended by clinical practice guidelines, specific tests have yet to be suggested. The Timed Up and Go (TUG) test is a simple measure of balance status and functional mobility. Nowadays, we need more data of an optimum cut off point of TUG time for detecting balance impairment in patients with chronic obstructive pulmonary disease (COPD). Thus the aim of this study was to evaluate the diagnostic ability relative to balance impairment of the TUG in subjects with COPD.

Methods: The cross-sectional study was conducted in stable COPD patient at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand from November 2015 to October 2017. Balance impairment test was measured using the Berg Balance Scale (BBS), a score of ≤45 indicates balance impairment. The TUG was evaluated using sensitivity, specificity, positive likelihood ratio (LR+), negative likelihood ratio (LR−), Youden's index, and the area under receiver operating characteristic curve (AUROC) from various points of TUG to identify the optimum cut-off point for detecting balance impairment. Multivariable logistic regressions were performed to identify the optimum cut off point of TUG test time for prediction of balance impairment in COPD.

Results: One hundred and eighteen smoking related COPD subjects 86 (72.9% male) with a mean age of 73.5±8.1 years were included in this study. Univariable analysis showed that the AUROC of TUG test to indicate those who had impaired balance was 0.93 [95% confidence interval (CI): 0.88, 0.98]. A cut off point of TUG test time ≥12 seconds had sensitivity, specificity, LR+, LR−, Youden's index, and AUROC of 95.8%, 90.4%, 10.01, 0.05, 86.2, and 0.93 for detecting balance impairment, respectively. Multivariable analysis identified the TUG test time ≥12 seconds was the best predictor of balance impairment in COPD patients with adjusted risk ratio (RR) of 25.2 (95% CI: 1.6, 312.0, P=0.021) and, the AUROC was 0.98 (95% CI; 0.96, 1.00).

Conclusions: Our study indicates the TUG test time ≥12 seconds has a high diagnostic ability for balance impairment prediction in COPD. The result supports a potential role for this simple test to be incorporated into routine COPD assessment to stratify patients' balance.

Keywords: Chronic obstructive pulmonary disease (COPD); balance; movement; falls; validity

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Introduction

Falling is a common problem in elderly people including in subjects with chronic obstructive pulmonary disease (COPD) (1). Previous studies showed the incidence of falling in COPD patients varies from 25.0–31.7% (2,3). Hakamy *et al.* also showed that the incidence of falling in patients with COPD was significant higher than non-COPD subjects (44.9 per 1,000 person-years *vs.* 24.1 per 1,000 person-years) (4). The greater fall risk in COPD patients needs more consideration of modifiable factors. Besides negative effects on mortality and morbidity, falls are linked to poorer overall functional status and quality of life (5). Therefore, reducing the fall risk is very important and assessment of balance impairment in elderly especially in COPD should be addressed (6). Balance impairment should be evaluated in older adults including COPD as a screen for identifying individuals who may benefit from a multifactorial fall risk assessment. Although a balance impairment assessment is now recommended by the guidelines for pulmonary rehabilitation program, specific tests have yet to be suggested (7). A number of tests have been developed to quantitatively measure balance in the elderly population (8). The Timed Up and Go (TUG) test is recommended as a routine screening test for balance impairment and falls in older adults (9). Some studies indicated that the TUG could be used for predicting history of falling and exercise capacity in COPD (10-13). For example, Reynaud *et al.* (13) and Al Haddad *et al.* (11) suggest that a cut-off 11 and 12 seconds could predict fall in patients with COPD, respectively. However, there are few data regarding the cut-off point of the TUG test that could predict balance impairment in COPD patients. Therefore, the aim of this study was to examine the diagnostic ability of the TUG test for identifying balance impairment in COPD.

Methods

Study procedures

This cross-sectional study was conducted at a single visit in COPD patient at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai, Thailand from November 2015 to October 2017. Balance tests were measured using the Berg Balance Scale (BBS) and the TUG test. A BBS score of ≤45 indicated balance impairment in this study (14). The demographic and clinical data including age, sex, body mass index (BMI), co-morbidity, lung function, severity of COPD, history of a fall in the previous year using the Elderly Falls Screening Test (EFST) (15), and history of acute exacerbation of COPD (AECOPD) were collected. In addition to the standard assessments at our COPD clinic, the St. George's Respiratory Questionnaire (SGRQ) (16), the Thai version of COPD assessment test (CAT) (17), the modified Medical Research Council (mMRC) dyspnea scale (18), and six-minute walk test (6-MWT) (19) were utilized. Testing was also performed for visual deficits by using the Snellen chart (20) and detection of anxiety or depression using the Thai version of Hospital Anxiety and Depression Scale (HADS) (21). All tests including the BBS, the TUG test, and the single test of 6-MWT were performed by the same well trained physical therapist. The study was approved by the Research Ethics Committee [Institutional Review Board (IRB) approval number: MED-2558-03253, date of approval: 12 October 2015 and filed under Clinical Trials Registry (study ID: TCTR20151015001, date of approval: 15 October 2015). Before enrollment, written informed consent was obtained from all subjects. We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting this cross-sectional study (22).

Study population

One hundred seventy-six COPD patients were screened for eligibility criteria from both clinical and medical record. The inclusion criteria were COPD patients, age ≥60 years, with no history of acute exacerbation for at least three months prior to enrollment. Diagnosis of COPD was based on smoking history of more than ten pack-years and post-bronchodilator (BD) ratio of forced expiratory volume in first second (FEV_1)/ forced vital capacity (FVC) of <0.7 (23). The exclusion criteria were subjects with neurological and musculoskeletal diseases that might affect the balance test were excluded. The subjects who have recently participated in exercise training program prior to study were also excluded.

Spirometry

All subjects were evaluated for lung function using a spirometer (Spiro Master PC, Chest M.I., Inc., Japan). Spirometry was performed according to the standards of American Thoracic Society (ATS)/European Respiratory Society (ERS) (24). Spirometric parameters were collected including FVC, FEV_1, and ratio of FEV_1/FVC. The predicted values were calculated using the Knudson's reference equations (25). However, a correction factor of

0.94 was applied to the FVC and FEV_1 predicted for Thai population (26).

Berg Balance Scale (BBS)

The balance test was measured by a physical therapist using the BBS in all subjects. This test was performed after the patients completed all questionnaires and spirometry. The BBS has more evidence for its psychometric properties than tests such as the Mini- Balance Evaluation Systems Test (BESTest) (7), and that the BBS has been more frequently used in the literature and clinical practice. Therefore, the BBS was selected for using in this study. The BBS includes 14 items for assessment of activities of daily living (ADL) tasks and is considered as the gold standard for testing static and dynamic balance abilities (27). In each task, the scores are classified from 0 (unable) to 4 (independent). The maximum score of 14-task items is 56, the lower score indicates a larger risk of falling and balance impairment. Previous finding suggested a cut-off score ≤45 as the risk of falling in community-dwelling adults (14). Therefore, a cut-off score of BBS ≤45 was defined as balance impairment in our study.

TUG test

The TUG test is a simple and widely used test of balance general mobility (28). The subjects were instructed to sit on an armchair of standard height before standing-up, walk three meters, turn around, walk back to the chair, and sit down on the chair again. The timing of the TUG started when the participant's back lifted off the back of the chair and stopped when their buttocks retouched the seat of the chair. All subjects were instructed to perform the TUG test at their normal regular speed and gait aids were permitted when appropriate. For COPD patients treated with long-term oxygen therapy (LTOT), the test was performed without oxygen flow prescribed for walking. The TUG test was performed three times with a pause between repetitions with the shortest time selected.

Sample size calculation

The sample size of the study was calculated based on the data from the pilot study using the easy ROC: a web-tool for ROC curve analysis Version 1.3.1 (29) which consisted of 25 COPD subjects (twenty non-impaired balance and five impaired balance, ratio of sample size was four). The expected area under receiver operating characteristic curve (AUROC) of TUG test to indicate those who had impaired balance was 0.70. Therefore, at least 75 subjects (60 non-impaired balance and 15 impaired balance) were included in the study (power =0.8 with statistically significant <0.05).

Statistical analysis

Results for numerical data were expressed as mean ± standard deviation (SD) or median, interquartile range (IQR). Results with proportion were expressed as frequencies and percentages. Independent sample *t*-tests and Mann-Whitney U Test were used to compare differences between the groups for parametric and non-parametric data, respectively. Fisher's exact test was used to compare the categorical data. To determine the diagnostic ability of TUG for assessing balance impairment, receiver operating characteristic (ROC) curves were constructed by plotting the true positive rate (sensitivity) against the false positive rate (1-specificity) for each scale level of the predictor variables for two dichotomous outcomes (balance impairment and non-balance impairment). The TUG was evaluated using sensitivity, specificity, positive likelihood ratio (LR+), negative likelihood ratio (LR–), Youden's index, and AUROC from various points of TUG to identify the optimum cut-off point. Multivariable logistic regressions were performed to identify the TUG ≥12 seconds as a predictor for balance impairment in COPD when adjusted for other possible confounding factors including age, sex, cardiovascular co-morbidity, history of falling in the previous year, BMI, marital status, impaired visualization, and six-minute walk distance (6-MWD). Results were displayed as adjusted risk ratio (RR) together with a 95% confidence interval (CI) for RR. Statistical significance was accepted at the P value <0.05. All statistical analyses were performed using STATA version 15 (StataCorp., College Station, TX, USA).

Results

One hundred and eighteen COPD subjects were included after excluded 58 subjects due to various reasons including unacceptable spirometry, poor health status, and limited mobility due to neurological disease or musculoskeletal problems that defined by leading to early retirement from work, reduced accumulated wealth and reduced ability to participate in social roles. More details are shown in *Figure 1*. Eighty-six (72.9%) cases were males with a mean

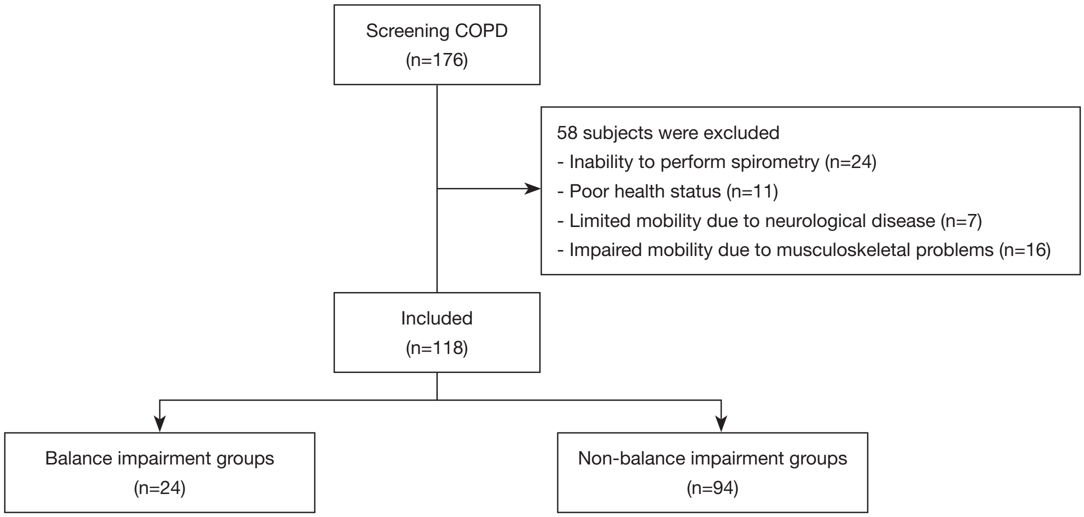

Figure 1 Flow-chart describing the study population. COPD, chronic obstructive pulmonary disease.

age of 73.5±8.1 years. Twenty-four (20.3%) cases were classified with balance impairment defined by the cut-off score of BBS ≤45 and 6 (5.1%) cases had history of falling in the previous year. The baseline characteristics of the balance impairment and non-balance impairment groups are shown in *Table 1*. There was no significant difference between the ratio of FEV_1/FVC, percentage of predicted FEV_1, GOLD classification, visual deficit, inhaled medications, cardiovascular comorbidity, anxiety and depression of subjects in the balance impairment and non-balance impairment groups. However, age, SGRQ score, CAT score, mMRC score, and TUG time in the balance impairment group were significantly higher than non-balance impairment groups. The balance impairment group had a significantly higher frequency of females. Furthermore, the balance impairment group had significantly lower percentage of predicted FVC, BBS score, and six-minute walk distance (6-MWD) compared to the non-balance impairment group.

The sensitivity, specificity, LR+, LR−, and AUROC for each cut-off time of TUG are presented in *Table 2*. The cut-off TUG times of ≥12 seconds represented the highest AUROC (0.93), with sensitivity of 95.8% and specificity of 90.4%, the Youden's index of 86.2 for detection of balance impairment in COPD.

The TUG test demonstrated excellent overall accuracy relative to the balance impairment inpatients with COPD with an AUROC of 0.93 (95% CI: 0.88, 0.98) (*Figure 2*).

After adjustment for the possible confounding factors including age, sex, cardiovascular co-morbidity, history of falling in the previous year, BMI, impaired visualization, and exercise performance. Multivariable analysis showed that the TUG test time ≥12 seconds was the best predictor of balance impairment in COPD patients with adjusted RR of 25.2 (95% CI: 1.6, 312.0, P=0.021) (*Table 3*) and the AUROC was 0.98 (95% CI: 0.96, 1.00) (*Figure 3*).

Discussion

Falling and balance impairment in COPD are concerning issues. The previous studies showed a high proportion of falling in COPD patient (46%) (13,30) which were higher than our study (5.1%). The lower rate of falling of COPD patients in our study may be due to there were more family members' supports and assist their daily activities than those in western countries as a large family type is common in Thai society. Therefore, the elderly persons have their relatives helping them on various activity daily living e.g.; housework, gardening, and shopping. Therefore, when the physical activity in COPD patients was reduced, the chance of falls is also reduced.

A balance assessment such as the TUG test is an integrated assessment of physical function, which consists of balance and gait speed (28). Our study demonstrated that the TUG test showed a high sensitivity, specificity, and AUROC for correct detection of balance impairment in COPD. Our study also showed that the TUG time was 6.6 seconds longer in COPD patients with balance impairment than non-balance impairment. This finding was higher when compared to the data from previous studies

Table 1 Demographics of smoking related COPD patients with and without balance impairment

Characteristics	Balance impairment (n=24)	Non-Balance impairment (n=94)	P value
Age (median, IQR)	81.0 (73.5–85.3)	72.0 (65.0–78.3)	<0.001
Sex (male)	9 (37.5)	77 (81.9)	<0.001
BMI (kg/m^2) (median, IQR)	19.2 (15.5–21.4)	21.3 (18.5–24.0)	0.025
Spirometry results (median, IQR)			
Post-bronchodilator FEV_1/FVC	59.9 (49.0–65.8)	55.3 (47.6–62.1)	0.275
Post-bronchodilator FVC (%)	76.6 (55.7–85.4)	83.6 (69.2–100.1)	0.039
Post-bronchodilator FEV_1 (%)	57.5 (36.9–68.9)	60.3 (44.9–70.4)	0.377
SGRQ total score (median, IQR)	44.5 (35.7–55.3)	37.8 (16.9–53.2)	0.036
CAT score (median, IQR)	14.0 (11.3–19.3)	9.0 (5.0–15.3)	0.002
mMRC scale, median (IQR)	3.0 (2.3–3.0)	2.0 (1.0–2.0)	<0.001
TUG (second) (median, IQR)	15.7 (13.8–18.8)	9.1 (7.8–10.8)	<0.001
6-MWD (meter) (median, IQR)	131.0 (68.0–232.3)	345.0 (289.8–420.0)	<0.001
Berg Balance score (median, IQR)	37.5 (32.0–41.8)	53.0 (49.0–55.0)	<0.001
Percent of Berg Balance Score =56 points	0 (0.0)	9 (9.6)	0.201
History of fall in the previous year	4 (16.7)	2 (2.1)	0.047
History of AECOPD in the previous year	8 (33.3)	20 (21.3)	0.274
Impaired visualization	4 (16.7)	8 (8.5)	0.261
GOLD classification			0.057
A	2 (8.3)	30 (31.9)	
B	9 (37.5)	25 (26.6)	
C	0 (0.0)	5 (5.3)	
D	13 (54.2)	34 (36.2)	
Inhaled COPD medication			0.820
LABA or LAAC	5 (20.8)	20 (21.2)	
Combination of ICS and LABA	9 (37.5)	37 (39.4)	
Triple therapy (ICS + LABA + LAAC)	10 (41.7)	37 (39.4)	
Cardiovascular disease comorbidities	8 (33.3)	27 (28.7)	0.803
LTOT used	3 (12.5)	6 (6.4)	0.385
Anxiety	1 (4.2)	2 (2.1)	0.498
Depression	4 (16.7)	6 (6.4)	0.117
Gait aids used	6 (25.0)	0 (0.0)	<0.001

6-MWD, six-minute walk distance; AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BMI, body mass index; CAT, COPD Assessment Test; FEV_1, forced expiratory volume in first second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; ICS, inhaled corticosteroids; IQR, Inter quartile range; LAAC, long acting anticholinergic; LABA, long acting beta2-agonists; LTOT, long term oxygen therapy; mMRC, modified Medical Research Council; SGRQ, St. George's Respiratory Questionnaire; TUG, Timed Up and Go.

Table 2 Discriminative property TUG cut-off points for balance impairment in smoking related COPD

TUG cut-off (second)	Sensitivity (%)	Specificity (%)	LR+	LR−	AUROC	Youden's index
≥10.0	100.0	60.6	2.54	0.00	0.80	60.6
≥10.5	100.0	70.2	3.36	0.00	0.85	70.2
≥11.0	95.8	76.6	4.09	0.05	0.86	72.4
≥11.5	95.8	83.0	5.63	0.05	0.89	78.8
≥12.0	95.8	90.4	10.01	0.05	0.93	86.2
≥12.5	87.5	90.4	9.14	0.14	0.89	77.9
≥13.0	79.2	93.6	10.63	0.23	0.86	72.8
≥13.5	79.2	93.6	12.40	0.22	0.86	72.8
≥14.0	75.0	95.7	17.63	0.26	0.85	70.7
≥14.5	66.7	96.8	20.89	0.34	0.82	63.5
≥15.0	58.3	98.9	54.83	0.42	0.79	57.2
≥15.5	54.2	98.9	50.92	0.46	0.77	53.1
≥16.0	45.8	98.9	43.08	0.55	0.72	44.7
≥16.5	41.7	98.9	39.17	0.59	0.70	40.6
≥17.0	39.2	98.9	39.17	0.59	0.70	38.1

AUROC, area under receiver operating characteristic curve; COPD, chronic obstructive pulmonary disease; LR+, positive likelihood ratio; LR−, negative likelihood ratio; TUG, Timed Up and Go.

(range from 1.4–4.3 seconds) which might be explained by the higher age of subjects in our cohort (10,30,31).

To the best of our knowledge, this is the first study that shows the ability of TUG to identify COPD subjects with balance impairment. A previous study suggested that the BBS test is valid, reliable, and valuable in identifying the fall status in COPD patients (32). Moreover, the gap of knowledge was highlighted in a recent systematic review on the simple balance test such as TUG test in COPD (7). Thus, we explored the role of TUG for detection of balance impairment in this specific population. Our result indicates that the TUG test demonstrated excellent overall accuracy in prediction of balance impairment with high AUROC of 0.93 (95% CI: 0.88, 0.98). Moreover, multivariable analysis showed that the TUG ≥12 seconds was the best predictor of balance impairment in COPD patients with adjusted RR of 25.2 (95% CI: 1.6, 312.0, P=0.021) and the AUROC of TUG test time ≥12 seconds to indicate those who had impaired balance was 0.98 (95% CI: 0.96, 1.00). Therefore, we suggested a cut-off value of TUG ≥12 seconds as an indicator of balance impairment in this population. This threshold showed discriminative ability to identify subjects with balance impairment with high sensitivity (95.8%), specificity (90.4%), and AUROC (0.93). These results were similar to the previous findings (11-13). However, these studies used different outcomes including history of falling and exercise capacity. Previous studies published by Al Haddad *et al.* (11) and Reynaud *et al.* (13) suggested that the TUG test was found to predict falling with TUG of ≥12 seconds (sensitivity, specificity, and AUROC =74%, 74%, and 0.77, respectively) and ≥11 seconds (sensitivity and specificity =93% and 74%, respectively). Another studies indicated that the TUG could be used for a measure of physical performance (10,12). They showed that the TUG could be used as an excellent diagnostic ability to predict the exercise capacity (10,12). Cut-off values of TUG ≥11.2 seconds (AUROC =0.86) and ≥8.42 seconds (AUROC =0.826) corresponded to 350 and 360 meters of 6-MWDs, respectively (10,12). Applicably, in clinical practice, COPD patients whose TUG time was ≥12 seconds should receive any early interventions to prevent subsequent complications related to balance impairment or falling.

Strength and limitation of this study

This study has strengths that should be considered. To

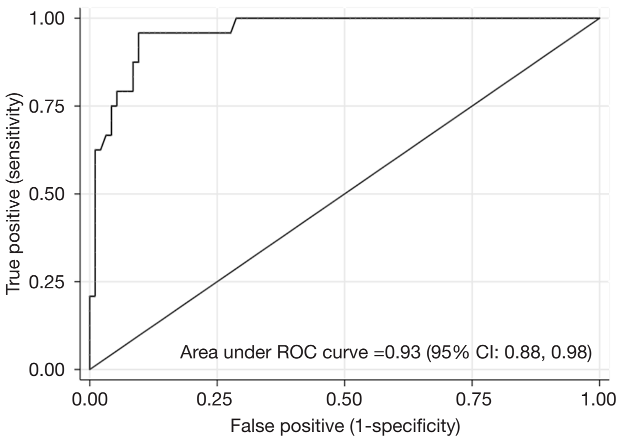

Figure 2 Receiver operating curve of the TUG for detecting balance impairment in smoking related COPD patients. COPD, chronic obstructive pulmonary disease; ROC, receiver operating characteristic curve; TUG, Timed Up and Go.

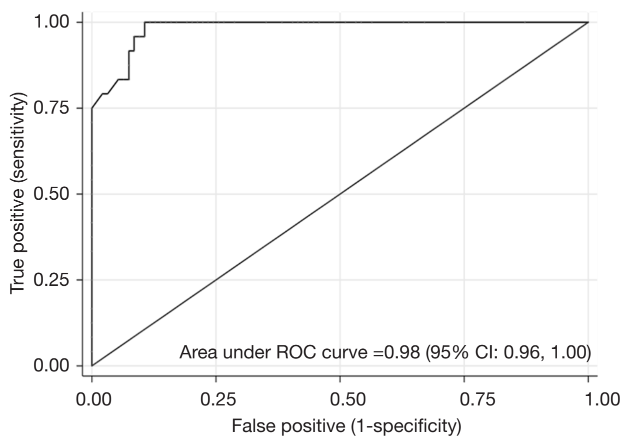

Figure 3 ROC of the TUG ≥12 second form multivariate analysis for detecting balance impairment in COPD patients. COPD, chronic obstructive pulmonary disease; ROC, receiver operating characteristic curve; TUG, Timed Up and Go.

Table 3 Multivariable analysis for identifying the TUG ≥12 seconds as a predictor for balance impairment in COPD patients

Risk factors	Adjusted risk ratio	95% CI	P value
TUG ≥12 seconds	25.2	1.6–312.0	0.021
6-MWD <300 meters	3.1	0.4–28.0	0.303
Cardiovascular co-morbidity	1.8	1.0–3.2	0.043
Sex: female	1.5	0.8–2.6	0.186
History of falling in the previous year	1.3	0.9–1.9	0.171
BMI <18.5 kg/m^2	1.3	0.9–1.9	0.163
Age ≥70 years	1.2	0.7–2.0	0.520
Impaired visualization	1.1	0.6–1.8	0.776
Marital status: married	0.9	0.6–1.5	0.838

6-MWD, six-minute walk distance; BMI, body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease; TUG, Timed Up and Go.

the best of our knowledge, this is the first study that identifies the TUG as a predictor for BBS-diagnosed balance impairment in COPD. However, this study has some limitations. Firstly, a healthy control group was not included in this study. Therefore, age-, sex-matched controls should be included to determine whether the TUG time differs in comparison with healthy elderly. Secondly, some baseline characteristics including age, sex, QOL, dyspnea score, exercise capacity, and cardiovascular comorbidity between balance impairment and non-balance impairment were different. Thus, the results of this study should be interpreted with caution. Thirdly, this is single-center study. The cut-off time of TUG for detecting balance impairment in COPD may be different in other clinical practices. Further research is needed to confirm these results. Fourthly, we used only the BBS for detecting balance impairment in COPD since the literature is rather clear on this subject on the fact that a multifactorial analysis e.g.; Performance-Oriented Mobility Assessment, the 30-Second Chair Stand test, the Mini-Balance Evaluation Systems Test (BESTest) and the 4-Stage Balance test must be cooperated with the BBS test (7,33,34).

Conclusions

Our study indicates the TUG test time ≥12 seconds has a high diagnostic ability for balance impairment prediction in COPD. The result supports a potential role for this simple test to be incorporated into routine COPD assessment to stratify patients' balance.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jtd.2020.03.47). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by the Research Ethics Committee [Institutional Review Board (IRB) approval number: MED-2558-03253, date of approval: 12 October 2015 and filed under Clinical Trials Registry (study ID: TCTR20151015001, date of approval: 15 October 2015). Before enrollment, written informed consent was obtained from all subjects.

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