Sit-to-stand test in children with bronchiectasis: Does it measure functional exercise capacity?

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ABSTRACT

Background: Similar to six-minute walk test (6MWT), sit-to-stand test (STST) is a self-paced test which elicits sub-maximal effort; therefore, it is suggested as an alternative measurement for functional exercise capacity in various pulmonary conditions including COPD and cystic fibrosis. We aimed to investigate the association between 30-second STST (30s-STST) and 6MWT in both children with bronchiectasis (BE) and their healthy counterparts, as well as exploring cardiorespiratory burden and discriminative properties of both tests.

Methods: Sixty children (6 to 18-year-old) diagnosed with non-cystic fibrosis BE and 20 age-matched healthy controls were included. Both groups performed 30s-STST and 6MWT. Test results, and heart rate, SpO2 and dyspnea responses to tests were recorded.

Results: Univariate analysis revealed that 30s-STST was able to explain 52% of variance in 6MWT (r = 0.718, p<0.001) in BE group, whereas 20% of variance in healthy controls (r = 0.453, p = 0.045). 6MWT elicited higher changes in heart rate and dyspnea level compared to 30s-STST, indicating it was more physically demanding. Both 30s-STST (21.65±5.28 vs 26.55±3.56 repetitions) and 6MWT (538±85 vs 596±54 m) were significantly lower in BE group compared to healthy controls (p<0.01). Receiver operating characteristic (ROC) curve analysis revealed an area under the ROC curve (UAC) of 0.765 for 30s-STST and 0.693 for 6MWT in identifying the individuals with or without BE (p<0.05). Comparison between AUCs of 30s-STST and 6MWT yielded no significant difference (p = 0.466), indicating both tests had similar discriminative properties.

Conclusions: 30s-STST is found to be a valid alternative measurement for functional exercise capacity in children with BE.

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daily activities better than laboratory tests.\textsuperscript{6,11} 6MWT requires no major equipment, however it requires a substantial space (a 30-m corridor) and testing time (above 10 min, considering pre- and post-test resting periods) which may limit its applicability. It is also sensitive to variation in verbal instructions.\textsuperscript{12} 

A growing number of studies present sit-to-stand test (STST) as a time-saving alternative for evaluating exercise capacity in various pulmonary conditions, including COPD,\textsuperscript{13–15} cystic fibrosis (CF),\textsuperscript{16,17} and lung transplantation.\textsuperscript{18} Although STST involves a more specific muscle group compared to 6MWT,\textsuperscript{19} both tests are self-paced and elicit submaximal effort. Ability to perform sit-to-stand maneuver is essential for daily activities and an indicator for mobility related function.\textsuperscript{20} Both STST and 6MWT reflect functional status and this may explain the suggestion of STST as an alternative to 6MWT in the literature. Various STST protocols were implemented in studies which include the repetition of sit-to-stand maneuver in a given period of time or the time required to complete a given number of maneuvers. Most studies use 30-second STST (30s-STST) or 1-minute STST (1min-STST) and include COPD patients. Both 30s- and 1min-STST demonstrate significant correlations with 6MWT.\textsuperscript{13,14} However, these studies solely include adult patients. To our knowledge, there is no study present in the literature that investigate the relationship between STST and 6MWT in children with any pulmonary conditions. Only a single study demonstrates that 1min-STST is valid and reliable alternative to 6MWT for evaluating cardiorespiratory demand in healthy children.\textsuperscript{21} 

Considering the significant relationship between STST and 6MWT in various pulmonary conditions, we hypothesized that 30s-STST may be used to determine functional exercise capacity in a similar manner as 6MWT in children with BE as well. Thus, our primary aim in this study was to investigate the relationship between 30s-STST and 6MWT in both children with BE and healthy controls. We also aimed to compare the cardiorespiratory responses to 30s-STST and 6MWT to each other in order to analyze whether two tests elicit similar cardiorespiratory responses. Also, the discriminative properties of 30s-STST and 6MWT in identifying the subjects with or without BE was compared, and the influence of spirometric variables on test performances were investigated. Lastly, we analyzed the influence of body height on STST performance to be able to discuss the utility of STST in children with shorter stature.

Methods

Subjects

Sixty children (6 to 18-year-old) diagnosed with BE who were being followed in the division of pediatric chest diseases of a university hospital, and twenty age-matched healthy controls were included in the study. Inclusion criterion for BE group was the diagnosis of non-cystic fibrosis BE. Considering the children with BE may present with a wide spectrum of lung function, the study did not have any clinical criterion for inclusion of BE patients, such as forced expiratory flow in 1 s (FEV1) or forced vital capacity (FVC). This helped obtaining a study sample which represents the BE population more accurately. Exclusion criteria were hospitalization history in past month, diagnosis of other chronic pediatric diseases which may impair exercise tolerance such as cerebral palsy or neuromuscular disease, candidates for lung transplantation and history of lung transplantation. Healthy volunteers were recruited via a notice board in the pediatric chest diseases polyclinics. Volunteers were mostly consisted of the relatives of the BE patients. Inclusion criterion for the healthy control group was not having any diagnosed chronic diseases.

Study design

A prospective, cross-sectional and comparative study was conducted. BE group and healthy controls performed 30s-STST and 6MWT consecutively on the same day. Each participant determined which test to perform first by choosing one of two envelopes specifying 30s-STST or 6MWT. A rest interval of 30 min was given between tests to avoid muscle fatigue. Relationship between STST and 6MWT were explored in both groups. Cardiorespiratory responses to 30s-STST and 6MWT were compared to each other. The ability of 30s-STST and 6MWT in identifying subjects with a disease was explored and discriminative properties of the two tests were compared. Influence of spirometric variables on 30s-STST and 6MWT was analyzed in BE group. Influence of body height on STST performance was also investigated.

The study was approved by the Ethics Committee of Bezmialem Vakif University (Approval number: 18/354) and registered to ClinicalTrials.gov website (registration number: NCT04153448) before the inclusion of first participant. The study was conducted in accordance with the Helsinki Declaration and written informed consents were obtained from both the children themselves and the parents or guardians of each child.

Pulmonary function

Pulmonary function test was performed using a spirometer (Pony FX; COSMED, Italy) according to the guideline of American Thoracic Society (ATS) and European Respiratory Society (ERS).\textsuperscript{22} FVC, FEV1, FEV1/FVC and peak expiratory flow (PEF) were measured and expressed as percentages of the predicted values.\textsuperscript{23}

Sit-to-stand test

The 30s-STST was performed according to the most common protocol described for COPD patients.\textsuperscript{14} A standard, armless chair with a height of 46 cm was used for testing. The chair was stabilized against a wall. Participants were asked to sit on the chair, come forward until their feet are flat on the floor and fold their upper limbs across the chest. Then, they were instructed to stand all the way up until their legs are completely straight and sit back down until their bottom have a clear contact with the chair as fast as possible for 30 s. Patients were not verbally encouraged during testing. Number of completed sit-to-stand repetitions in 30 s was recorded.

Six-minute walk test

The 6MWT was performed according to the guideline of ATS.\textsuperscript{24} The test was applied in a 30-m long corridor and participants were instructed to rest at least for 5 mins on a chair before testing. All participants were informed with the same statements before testing. Every minute during the test, a supervisor verbally encouraged the participants with same phrases and informed them about the time remaining. Participants were allowed to rest during testing but instructed to continue walking as soon as they are able. The distance walked in six minutes was recorded in meters.

Cardiorespiratory responses

Heart rate, pulse oxygen saturation ($\text{SpO}_2$) and dyspnea level were recorded before and immediately after each test. Heart rate and $\text{SpO}_2$ were measured using a pulse oximeter (Beurer oximeter; Beurer GmbH, Germany) connected to the index finger. During 6MWT, $\geq$4% decrease in $\text{SpO}_2$ was considered significant desaturation, while $<4$% decrease was considered normal.\textsuperscript{25} Dyspnea was rated on the Modified Borg Scale. The anchors were ‘0’ for no dyspnea and ‘10’ for maximum dyspnea.\textsuperscript{26}
Statistical analysis and sample size

Statistical analysis was conducted using SPSS 20.0 statistical program (SPSS Inc., USA). Distribution of data was analyzed using Kolmogorov-Smirnov test, histograms and QQ-plots. Paired Sample T-test or Wilcoxon Test was used for within-group comparisons and Independent Samples T-test or Mann Whitney U test was used for between-groups comparisons depending on the distribution properties of the data. Categorical variables were compared between groups using Chi-square Test. A univariate linear regression was conducted to analyze the relationship between 30s-STST and 6MWT for each group. Receiver operating characteristic (ROC) curve analysis was conducted to detect the ability of 30s-STST and 6MWT in identifying subjects with or without BE, and areas under the ROC curve (AUC) of 30s-STST and 6MWT were compared using Hanley-McNeil method.27 Influence of spirometric results and resting cardiorespiratory variables on 30s-STST and 6MWT, and the relationship between body height and STST performance was analyzed using Pearson correlation analysis. The results were considered statistically significant with p values < 0.05.

Our primary aim in this study was to investigate the relationship of 30s-STST with a well-accepted functional exercise capacity measure, i.e. 6MWT using correlation analysis to determine whether STST yields results in parallel with 6MWT. For this reason, sample size calculation for the study was based on the correlation coefficient that is expected to be detected between STST and 6MWT. Unfortunately, there was no study present in the literature that investigated the relationship between STST and 6MWT in BE to determine a possible correlation coefficient for our study. However, correlation coefficients ranging from 0.470 to 0.750 were reported for the relationship between STST and 6MWT in COPD.13 Similarly, correlation coefficient of 0.660 was reported for the relationship between STST and another exercise capacity measure which is VO2peak of cardiopulmonary exercise test (CPET) in CF.16 Therefore, we hypothesized to detect a significant relationship between 30s-STST and 6MWT with a correlation coefficient of at least 0.350 in BE. Accordingly, sample size was determined as 60 subjects to detect this relationship with 95% confidence level and 80% power.28

Results

Demographics and clinical characteristics of participants are shown in Table 1. BE group and healthy controls had similar characteristics in terms of gender, age, body mass index, resting heart rate and dyspnea. Resting SpO2 were significantly lower in BE group compared to healthy controls. Most common cause for BE was infection. BE group had a minor airflow obstruction indicated by FEV1 and PEF, which were 76% and 73% of the predicted values, respectively.

Univariate linear regression analysis revealed that 30s-STST was able to explain 52% of variance in 6MWT and there was a strong relationship between 30s-STST and 6MWT (r = 0.718, p < 0.001) in BE group. Similarly, 30s-STST explained 20% of variance in 6MWT and significantly correlated to 6MWT (r = 0.453, p = 0.045) in healthy controls (Fig. 1). 30s-STST was found to be an independent predictor for 6MWT in both BE group and healthy controls, which indicates a strong association between those two measures. Pearson correlation analysis revealed that spirometric or resting cardiorespiratory variables did not have a significant relationship with 30s-STST or 6MWT (p > 0.05) in BE group. Pearson correlation analysis also revealed that body height had a 'positive' weak correlation with 30s-STST (r = 0.343; p = 0.007) in BE group, and 'positive' but insignificant correlation in healthy controls (r = 0.360; 0.119).

Results of 30s-STST and 6MWT, and cardiorespiratory responses to each test are shown in Table 2. Variance in 30s-STST and 6MWT results for each group are shown in Fig. 2. 30s-STST was able to discriminate between BE group and healthy controls, similar to 6MWT.

Results of both 30s-STST and 6MWT were significantly lower in BE group (p < 0.01). BE group had higher desaturation of SpO2 during both 30s-STST and 6MWT, compared to healthy controls (p = 0.02). Changes in heart rate and dyspnea level were similar in both groups during 30s-STST and 6MWT. Within group comparisons revealed that 6MWT elicited higher changes in heart rate, SpO2 and dyspnea level in BE group and, heart rate and dyspnea level in healthy controls compared to 30s-STST, indicating that 6MWT was more physically demanding than 30s-STST.

The AUC calculated for 30s-STST and 6MWT revealed that both tests had discriminative values for identifying the individuals with or without BE (p < 0.05). 30s-STST had an AUC of 0.765 [95% CI: 0.658–0.871] and 6MWT of 0.693 [95% CI: 0.576–0.808]. Comparison between AUCs of 30s-STST and 6MWT yielded no significant difference (difference between areas: 0.072; standard error of difference: 0.0989; p = 0.466), indicating that both tests had similar discriminative properties (Fig. 3).

Discussion

Our study demonstrates that there was a significant association between 30s-STST and 6MWT in children with BE, which supports the convergent validity of 30s-STST for evaluating functional exercise capacity in this population. A significant association between 30s-STST and 6MWT was also present in healthy controls, but it was weaker than that obtained from children with BE. Similar to 6MWT, 30s-STST was also able to discriminate between BE patients and healthy individuals, suggesting that 30s-STST is sensitive to significant differences in functional exercise capacity. Both tests had similar discriminative properties in identifying individuals with or without
the disease. Heart rate, SpO₂, and sensation of dyspnea responses to 30s-STST was lower than those to 6MWT and it suggests that 30s-STST would be safer to perform for evaluating functional exercise capacity in children with BE in terms of cardiorespiratory responses. We also observed that spirometric variables have no significant influence on 30s-STST and 6MWT performance in children with BE.

Although STST is widely adopted to measure functional status in elderly population, a growing body of evidence supports its implication in various diseases. COPD is the most common disease among pulmonary conditions in which STST has been applied. Several studies have also included CF patients. STST protocols vary in these studies including 5-repetition STST (5xSTST), 30s-STST and

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<td><strong>Comparison of test results and cardiorespiratory responses of 30s-STST and 6MWT.</strong></td>
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<td><strong>Bronchiectasis (n = 60)</strong></td>
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<tr>
<td>Test result (repetitions or m)</td>
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<tr>
<td>Δ Heart rate (beats/min)</td>
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<td>Δ SpO₂ (%)</td>
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Abbreviations: 30s-STST, 30s sit-to-stand test; 6MWT, 6-min walk test.
Δ Change in the variable during testing.
* Significant between-groups difference (p<0.01).

Fig. 1. Scatter plot for the relationship between STST and 6MWT in bronchiectasis and healthy controls.

Fig. 2. Variance in STST and 6MWT results in bronchiectasis and healthy controls.
1-min STST. In COPD patients, it was demonstrated that 6MWT significantly correlates to 5xSTSST (r = 0.50815), 30s-STST (r = 0.44015, 0.52815 and 0.65015) and 1min-STST (r = 0.40016, 0.48015 and 0.75015). In CF patients, relationship between 1min-STST and CPET was investigated by two studies and significant correlations were observed between 1min-STST and VO2peak, with correlation coefficients of 0.66016 and 0.62717 respectively. These studies suggest that STST is a valid tool to evaluate exercise capacity to an extent. In our study, we demonstrated a significant correlation between 30s-STST and 6MWT, with a correlation coefficient of 0.718. Our findings seem to be in consistent with those derived from COPD patients, but it should be interpreted carefully since our sample consists of children.

Peripheral muscle strength has a significant impact on functional exercise capacity for children with BE and had similar AUCs, thus, it becomes more relevant as the testing duration of STST increases. Cardiorespiratory burden of STST will approach to that of 6MWT. Supporting this, Aguilaniu et al.36 demonstrated that a three-minute-long STST (3min-STST) elicits SpO2 and heart rate responses similar to those obtained in 6MWT in COPD patients. However, they also observed that fatigue level was significantly higher after 3min-STST compared to 6MWT. It therefore makes us assume that increasing the duration of STST to meet the cardiopulmonary demand of 6MWT would not be reasonable since the individual’s physical performance in STST may be limited by leg fatigue, rendering the test less reliable to detect functional exercise capacity. Considering the evident relationship between 30s-STST and 6MWT in BE, COPD and healthy individuals, we concluded that 30s-STST may be used to evaluate functional exercise capacity, without the need of increasing the duration of the test. In addition, the lower cardiopulmonary responses in 30s-STST suggest that performing 30s-STST would be safer compared to 6MWT.

Exercise capacity of patients with BE is impaired by altered pulmonary mechanics, inefficient gas exchange, decreased muscle mass and sedentary lifestyle.3,4,6–8 VO2peak is demonstrated to be lower in both adults24 and children with BE25,26 compared to healthy individuals. However, studies comparing 6MWT of BE to healthy controls are rather limited. Ozalp et al. demonstrated that adults with BE has significantly lower 6MWT distance compared to their healthy counterparts, and this impairment in functional exercise capacity is associated with reduced respiratory and peripheral muscle strength.

Peripheral muscle strength has a significant influence on both 6MWT7 and STST13,19,32 and this may also help explaining the relationship between these two tests. However, in order to consider 30s-STST as a valid instrument for evaluating functional exercise capacity, it is also expected to be sensitive to differences between patients and healthy individuals besides just having a significant relationship with 6MWT. It is demonstrated that COPD patients had a significantly lower sit-to-stand repetitions in 1min-STST compared to healthy counterparts.15,39 Despite involving the smallest effort among all STSSST, 5xSTSST is found to be able to differentiate between patients and healthy controls, as well.40,41 Parallel to findings obtained from COPD patients, children with BE performed significantly lower sit-to-stand repetitions compared to healthy individuals (21.66 vs 26.55; p<0.001) in our study. Both 30s-STST and 6MWT were able to discriminate patients from healthy individuals, which supports the known-group validity of 30s-STST. Also, in our study, ROC curve analysis revealed that both 30s-STST and 6MWT were able to adequately identify the individuals with or without BE and had similar AUCs, indicating that they had similar discriminative properties. We did not encounter a similar study comparing the discriminative properties of two tests in the literature, however, Morita et al.14 explored whether 5xSTSST, 30s-STST and 1min-STST are able to discriminate between COPD patients with poor and preserved functional exercise capacity evaluated by 6MWT. It was
demonstrated that both tests have similar AUCs (ranging between 0.710 and 0.850), indicating that they have similarity in predicting functional exercise capacity. This study further supports our findings regarding the association between 30s-STST and 6MWT, and the discriminative properties of 30s-STST.

In our study, we did not detect a significant relationship between spirometric variables and 30s-STST. Literature has conflicting results regarding this relationship. Several studies state that there is no significant association between FEV₁ and STST performance, indicating that FEV₁ is not a good predictor for functional status in COPD patients, whereas others report the opposite. FEV₁ may not be able to adequately explain the ventilatory limitation during a physical effort and this may help explaining inconsistent findings. This assumption is supported by study of Foglio et al. which states that FEV₁ is not a predictor for exercise performance in patients with chronic airway obstruction. On the other hand, our BE sample had a relatively milder impairment in spirometric parameters and this may help explaining lack of a relationship between FEV₁ and physical performance measures, as well. Since the BE is a multidimensional and etiologically diverse condition, it is not possible to determine disease severity and its reflection on the general health status with a single parameter, including spirometric variables such as FEV₁ or FVC. To this end, composite disease-specific prognostic indices have been developed to help the evaluation of these patients such as Bronchiectasis Severity Index (BSI). BSI attributes points according to age, body mass index, FEV₁, exacerbation frequency, prior hospitalization, presence of chronic bacterial colonization, radiological extension, type of bronchiectasis and degree of dyspnea for classifying the severity of BE. It is shown that these composite scores reflect exercise performance and physical impairment better compared to spirometric results alone. Researchers exploring exercise performance in these patients may benefit from including such composite scores in their studies.

Protocol for STSTs include a standard chair with a fixed height, i.e. 46 cm. In order to not modify the well-adopted protocol, we used the same chair in our study as well. Height of the chair is not seen as a major concern in studies including adults. However, using a standard chair in a population including children may raise concerns. It may be assumed that children with shorter stature will have to cover a much smaller distance to complete a sit-to-stand maneuver compared to taller children, which may give shorter children an advantage, independent from the actual physical performance. However, for this assumption to be justified, there would be a ‘negative’ correlation between body height and STST repetitions, i.e. shorter children would perform higher STST repetitions. In our study, we detected ‘positive’ correlations between body height and sit-to-stand repetitions in both BE group and healthy controls, which may indicate that shorter stature does not necessarily provide an advantage in STST performance. From another perspective, it may also be assumed that taller individuals will have to cover a much longer distance to complete a sit-to-stand maneuver compared to shorter individuals, which is not generally considered as a major concern for this test either. A study by Gurses et al. reports that body height does not correlate to neither of 10s-, 30s- or 60s-STST performances in young adults. Although the correlations were statistically insignificant, it is still evident that body height and STST performances have a ‘positive’ relationship (with correlation coefficients of 0.381, 0.270 and 0.275, respectively) which supports our assumptions. Considering study samples will include both shorter and longer subjects, these individual differences in height may not have a major impact on the average of STST performance of the sample. We also think that adjusting the seat height of the chair by using blocks with various heights or other mechanisms to achieve a knee angle of 90° for every individual in an attempt to standardize the test may not be logistically possible either. Even if it is, doing so will contradict using this test for its practicality.

**Clinical implications**

Guidelines recommend evaluating exercise capacity in both the children and the adults with BE, since it helps identifying physical impairment in daily life that would not be predicted by diagnostic tests. Therapeutic approaches for BE should not focus only on preserving lung function or improving the symptoms such as cough or sputum production, but also on improving physical impairment in daily life which is shown to be quite common in these patients. Including field tests such as 6MWT in the management of BE helps addressing this physical impairment. But space and time requirements of 6MWT may limit its utilization, especially during a busy clinical practice. In such instances, 30s-STST may be utilized for addressing functional exercise capacity and possible physical impairment, as well as evaluating the effects of therapeutic approaches on exercise capacity.

**Limitations**

Despite reporting novel findings with clinical relevance, we had some limitations in the present study. We were not able to measure peripheral muscle strength in our sample. Studies demonstrate that STST is dependent on lower limb strength, suggesting an involvement of anaerobic metabolism in STST performance. Yet, the relationship between STST and 6MWT suggests an involvement of aerobic metabolism as well. Such studies should include both the measurement of lower limb strength and 6MWT, and explore which metabolism is involved to what extent in STST performance. This may help better explaining the association between STSTs and physical performance measures. Also, literature suggests that impairment of physical activity is common in obstructive airway diseases, including both the children and the adults with BE. It is shown that physical activity level is one of the strongest correlates of exercise capacity in these patients. Studies investigating the exercise capacity should also include the assessments of sedentary behavior and physical activity. Comparing the correlations of physical activity level with different physical performance measures may help demonstrating the similarities between those measures. In addition, sit-to-stand performance of an individual also depends on coordination skills (i.e., balance) and core stability, and future studies including the evaluation of these aspects of STST may provide insights in this context. Despite our findings suggest that 30s-STST has a value in evaluating functional exercise capacity in children with BE, the association between 30s-STST and 6MWT in BE samples including adults and elderly should also be investigated to be able to generalize the utility of 30s-STST to general BE population.

**Conclusion**

A significant association is present between 30s-STST and 6MWT in both children with BE and their healthy counterparts. 30s-STST and 6MWT have similar discriminative properties in identifying individuals with or without the disease, which strengthen the association between two tests. In addition, cardiorespiratory burden of 30s-STST is lower compared to 6MWT, which suggests that 30s-STST is relatively safer to perform. It is important to note that our findings do not necessarily imply 30s-STST and 6MWT are interchangeable, instead both tests provide results in parallel with each other when performed with the purpose of evaluating functional exercise capacity. In conclusion, 30s-STST is found to be a valid, space- and time-saving alternative measurement for functional exercise capacity in children with BE.

**Declaration of Competing Interest**

The authors have no conflict of interests to declare.
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