


Video game-based exercise in children and adolescents with non-cystic fibrosis bronchiectasis: A randomized comparative study of aerobic and breathing exercises

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Abstract

Background: Video game-based systems have been proposed to improve effectiveness and compliance with exercise training in children and adolescents with noncystic fibrosis bronchiectasis (NCFB). This study aimed to investigate the effects of aerobic and breathing video game-based exercises (VGE) on pulmonary function, respiratory and peripheral muscle strength, functional capacity, and balance in children and adolescents with NCFB.

Method: Thirty-nine children and adolescents aged between 8 and 18 years with NCFB were randomly allocated into three groups as “home-based chest physiotherapy group” (CP), “aerobic VGE given in addition to home-based chest physiotherapy group” (CP + aerobic VGE), and “breathing VGE given in addition to home-based chest physiotherapy group” (CP + breathing VGE). All three groups performed chest physiotherapy program twice a day for 7 days per week for 8 weeks. Pulmonary function, respiratory and peripheral muscle strength, functional capacity, and balance were assessed at baseline and after 8 weeks of training.

Results: The improvement in maximum expiratory pressure and balance scores were significantly higher in both CP + aerobic and CP + breathing VGE groups. The significant improvement in maximum inspiratory pressure was greater in the CP + breathing VGE group. The changes in peripheral muscle strength and functional capacity were significantly higher in the CP + aerobic VGE group.

Conclusions: The present study showed that aerobic VGE provides additional benefits in improving peripheral muscle strength and functional capacity, while breathing VGE provides further increase in improving respiratory muscle strength. In addition, both aerobic and breathing VGE were effective in improving balance, but they were not superior to each other.

KEYWORDS

balance, functional capacity, noncystic fibrosis bronchiectasis, peripheral muscle strength, respiratory muscle strength, video game-based exercise

1 | INTRODUCTION

Bronchiectasis not related to cystic fibrosis is defined as noncystic fibrosis bronchiectasis (NCFB) and persistent cough, thick and sticky sputum production, dyspnoea, and fatigue are predominant symptoms of NCFB.^{1,2} Permanent obstruction and impaired gas exchange mechanism in the airways that develop due to chronic inflammation and sputum cause the decrease of respiratory function and respiratory muscle strength.^{3,4} Also, impairment of functional capacity and balance are extrapulmonary manifestations of NCFB.^{4,5}

In current guidelines, it is emphasized that chest physiotherapy and exercise training should be included in the routine treatment to relieve symptoms and improve airway clearance, functional capacity, and quality of life.^{6,7} Poor patient compliance and low rate of participation are principal problems in the exercise programs of patients with chronic respiratory diseases.^{8,9} Video game-based exercise (VGE) is recommended alternative to traditional exercise training, especially in children with chronic respiratory diseases, due to its potential benefits such as increased motivation, interest, and active participation of patients and allowing them to perform exercises entertainingly.^{8,10}

VGE can be used in both aerobic and breathing exercises gaming systems such as “Nintendo Wii Fit Plus” and “Breathing+package” (Breathing Labs).¹¹ The limited number of current studies using these products have demonstrated the additional benefit of VGE compared to traditional exercises^{12,13}; however, no previous study has investigated VGE in children and adolescents with NCFB.

The objective of this study was to investigate the effects of aerobic VGE with “Nintendo Wii Fit Plus” and breathing VGE with “Breathing+ package” which were given in addition to a home-based chest physiotherapy program on pulmonary function, respiratory and peripheral muscle strength, functional capacity and balance in children and adolescents with NCFB.

2 | METHODS

2.1 | Study design

This prospective study was performed as a randomized controlled clinical trial between July 2019 and February 2021. Clinically stable 39 children and adolescents with NCFB aged between 8 and 18 years were included in the study. The inclusion criteria were being diagnosed with bronchiectasis according to clinical history, pulmonary function test (PFT), and high-resolution computed tomography, and having a stable clinical condition which means no exacerbation in the last 4 weeks. The exclusion criteria were being diagnosed with vestibular, neurological, or orthopedic disorders which may affect balance and mobility, having a previous history of lung transplantation, and previous and/or active participation in another supervised exercise training or physiotherapy program.

The children and adolescents were randomly allocated into three groups as home-based chest physiotherapy (CP) group, aerobic VGE

in addition to home-based chest physiotherapy (CP + aerobic VGE) group, and breathing VGE in addition to home-based chest physiotherapy (CP + breathing VGE) group using a numbered series of 39 prefilled envelopes specifying group assignments generated by a computer-based randomization program. The physiotherapist who assessed the children and adolescents was blind to group assignments. Another physiotherapist applied training programs to both groups. All three groups received a home-based CP program twice a day for 7 days per week for 8 weeks. The CP + aerobic VGE group also received “Nintendo Wii Fit Plus”-based aerobic exercise training two times a week for 8 weeks. The CP + breathing VGE group also received “Breathing+package”-based breathing exercise training two times a week for 8 weeks. All children and adolescents were assessed at the beginning and end of the program.

The reference and percentage values for Turkish children and adolescent were used for to calculate body mass index (BMI) z-scores and BMI percentile.¹⁴ Children and adolescents were instructed to keep an exercise and physical activity diary, and it was controlled at every week via telephone calls. Adherence to CP program (%) was defined as the ratio of the completed sessions to total sessions, which was calculated as “(completed sessions)/(total sessions = 112 sessions) multiplied by 100”. On the other hand, compliance with physical activity recommendation (%) was defined as the ratio of the number of days of completed daily physical activity to the number of total days of the program, which was calculated as “(the number of days of completed daily physical activity recommendation)/(the number of total days of the program = 56 days) multiplied by 100”.

The ethics committee of Bezmialem Vakif University approved the study (Protocol number: 06/109), and the study was registered to the ClinicalTrials.gov website (registration number: NCT04038892). The study was conducted on the ethical principles for human research as outlined by the Declaration of Helsinki. Written informed consent was obtained from the parents or the guardians of each child and adolescent.

2.2 | Outcome measures

Participants performed spirometry, maximum inspiratory (MIP) and expiratory (MEP) pressure measurements, knee extensor strength test, 6-min walk test (6MWT), and “Postural Stability Test” (PST), “Limits of Stability Test” (LOST), and “Clinical Test of Sensory Integration of Balance” (CTSIB), respectively.

PFT was performed using a spirometer (COSMED Pony FX; COSMED) according to the guideline of the American Thoracic Society and European Respiratory Society.¹⁵ Forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), FEV₁/FVC, and peak expiratory flow (PEF) were measured. The percentage of predicted spirometry values and their z-scores were calculated according to the GLI 2012 reference standards.¹⁶

MIP and MEP were measured using a mouth pressure meter (MicroRPM; MicroMedical).¹⁷ A maximum value of three efforts that vary less than 5% was recorded for inspiratory and expiratory

pressures. Children and adolescents were allowed to rest for about a minute between the efforts.

The knee extensor muscle strength test was evaluated using a MicroFet2 hand-held dynamometer (Hogan Health Industries Inc.) with the break method. The maximum value of three consecutive measurements was recorded as the knee extensor strength. Subjects were allowed to rest for about a minute between efforts.

The functional capacity was evaluated using 6MWT.¹⁸ The 6MWT is a test found to be valid and reliable for measures of exercise capacity in patients with NCFB.¹⁹ Children and adolescents were instructed to walk as fast as possible between two cones in a 30 m corridor and the walking distance in 6 min was recorded.

PST, LOST, and CTSIB were assessed with the Biodex Balance System (BBS) (Biodex, Inc., Shirley).²⁰ In PST, subjects are instructed to stand still on the platform and the displacement of the center of gravity is quantified for anterior–posterior and medial–lateral axes. PST gives three types of outcome measures: overall stability index, anterior–posterior stability index, and medial–lateral stability index. Higher scores indicate worse postural stability. LOST evaluates the ability to move the center of gravity in desired directions. Subjects are instructed to stand on the platform and lean in eight directions to control the cursor displayed on the screen and try to move the cursor inside the target circles. LOST provides scores for all eight directions as well as an overall score. Higher scores indicate better performance which means better dynamic postural stability. CTSIB is performed on a stable platform and subjects are asked to maintain a stable posture in four different positions: eyes open firm surface, eyes closed firm surface, eyes open foam surface, and eyes closed foam surface. The children and adolescents' oscillations are calculated as the sway index, and higher sway index scores refer to the increase with the disruption of the balance.

2.3 | Interventions

Home-based CP program consisted of diaphragmatic breathing exercise, thoracic expansion exercises, incentive spirometer with Voldyne[®], oscillatory positive expiratory pressure device with Shaker[®], postural drainage with percussions, coughing techniques, and physical activity counseling. Exercises were performed as two sets for five repetitions with the rest intervals of 5–6 tidal breaths between the exercises to avoid respiratory muscle fatigue and hyperventilation. Postural drainage and percussion were performed in 45° Trendelenburg position with the patient lying on front, left, and right sides for 3 min in each position. The duration of one session was 40 min which consisted of 20 min of postural drainage and 20 min of other interventions. Besides home-based CP program, at least 60 min of moderate-intensity physical activity such as walking, dancing, ball games, or simple exercises on a Swiss ball or trampoline daily basis was recommended to each child and adolescent considering their interests to promote physical activity participation. Moderate intensity was described as “Intense enough to make the person feel like he/she is breathing somewhat hard but can still carry on a

conversation” and children and adolescents/parents were instructed to determine the intensity of physical activity accordingly.

Aerobic VGE program consisted of a protocol that included 50 min of “Nintendo Wii Fit Plus” games. The first 10 min consisted of a warm-up period that included three different yoga games (Deep Breathing, Half Moon, and Warrior). The following 30 min consisted of an aerobic training period that included three different aerobic games (Hula Hoop, Basic Step, and Basic Run). To standardize the perceived difficulty level, the games that used in the first 4 weeks have been replaced by more challenging but similar aerobic games (Super Hula Hoop, Advanced Step, and Free Run) in the last 4 weeks. The last 10 min consisted of a cool-down period with the same content as the warm-up period. During the sessions, dyspnea was evaluated using the Modified Borg Scale (MBS), and the rating of perceived exertion was maintained between 4 and 6 points, and moderate aerobic exercise intensity was ensured.²¹

The breathing VGE program consisted of a protocol that included 50 min of “Breathing+ package” games. Breathing+ is a device that detects the flow and duration of expiration through an acoustic microphone and uses maximum exhalation to interact with “breathing games” and “breathing apps” to improve compliance and adherence with pursed lip breathing exercise.²² The first 10 min consisted of a warm-up period that included controlled breathing techniques, and coughing techniques, and intervals. The following 30 min consisted of a breathing training period that included five different breathing games (Balloon, Plane, Wolf, Flowers, and Pluto). To standardize the perceived difficulty level, the games that used in the first 4 weeks have been replaced by more challenging level 2 breathing games in the last 4 weeks. The last 10 min consisted of a cool-down period with the same content as the warm-up period. Similar to aerobic exercise training, dyspnea was evaluated during the sessions and the exercise intensity was kept at similar levels.

2.4 | Statistical analysis and sample size

Statistical analysis was conducted using IBM SPSS v.26 (SPSS Inc.). The normality of the distribution of data was analyzed using Shapiro–Wilk Test. The analysis of covariance (ANCOVA), adjusted for the baseline values, was used to compare posttreatment values between groups. Multiple comparison tests were performed to detect the differences among the groups using Bonferroni post hoc tests corrected significance. Categorical variables were compared between groups using χ^2 test. The results were considered significant with p values < 0.05. Complementarily, the effect size was calculated by partial eta-squared (η_p^2) with small, medium, and large effect sizes classified as 0.01, 0.06, and 0.14, respectively.²³ Based on the results of a study in the literature,²⁴ we estimated a sample size of 13 children and adolescents for each group. The sample size calculation was made at 80% power and two-tailed α level of 0.05 with the 0.888 effect size based on comparison of the changes in the 6MWT distance (32.12 ± 48.99 and -8.28 ± 8.12 , respectively) in the experimental group and the control group.

3 | RESULTS

Sixty-four children and adolescents with NCFB were assessed for eligibility. Forty-one children and adolescents were included in this study and randomized. One child each from both CP + aerobic VGE group and CP + breathing VGE group dropped out due to hospitalization because of exacerbation. Thus, 39 children and adolescents completed the study (Figure 1).

There were no significant differences between the demographic and clinical characteristics of all groups ($p > 0.05$). Adherence to CP program (%) was 89.10 ± 13.21 in the CP group, 86.33 ± 11.19 in the CP + aerobic VGE group, and 84.27 ± 24.06 in the CP + breathing VGE group, with no between-groups difference ($p = 0.297$). Compliance with physical activity recommendation (%) was 76.04 ± 22.23 in the CP group, 78.08 ± 20.13 in the CP + aerobic VGE group, and 82.01 ± 19.08 in the CP + breathing VGE group, with no between-groups difference ($p = 0.188$) (Table 1).

Comparison of the pretreatment values in pulmonary function, respiratory and peripheral muscle strength, functional capacity, and balance among all groups are given in Table 2 and there were no significant differences between all groups ($p > 0.05$). Comparison of the posttreatment values, with the ANCOVA test adjusted for the baseline values, among all groups are given in Tables 3 and 4. The significant improvement in MEP was greater in both CP + aerobic VGE and CP + breathing VGE groups compared to the CP group ($p = 0.038$; $p = 0.046$, respectively), whereas the significant improvement in MIP was greater in only the CP + breathing VGE group compared to the CP group ($p = 0.012$). The changes in knee extensor muscle strength and 6MWT distance were significantly higher in the CP + aerobic VGE group compared to both CP and CP + breathing VGE groups ($p < 0.05$). The significant improvements in overall scores of PST and LOS, and composite score of CTSIB, were greater in both CP + aerobic VGE and CP + breathing VGE groups compared to the CP group ($p < 0.05$). The change in fatigue was significantly higher in

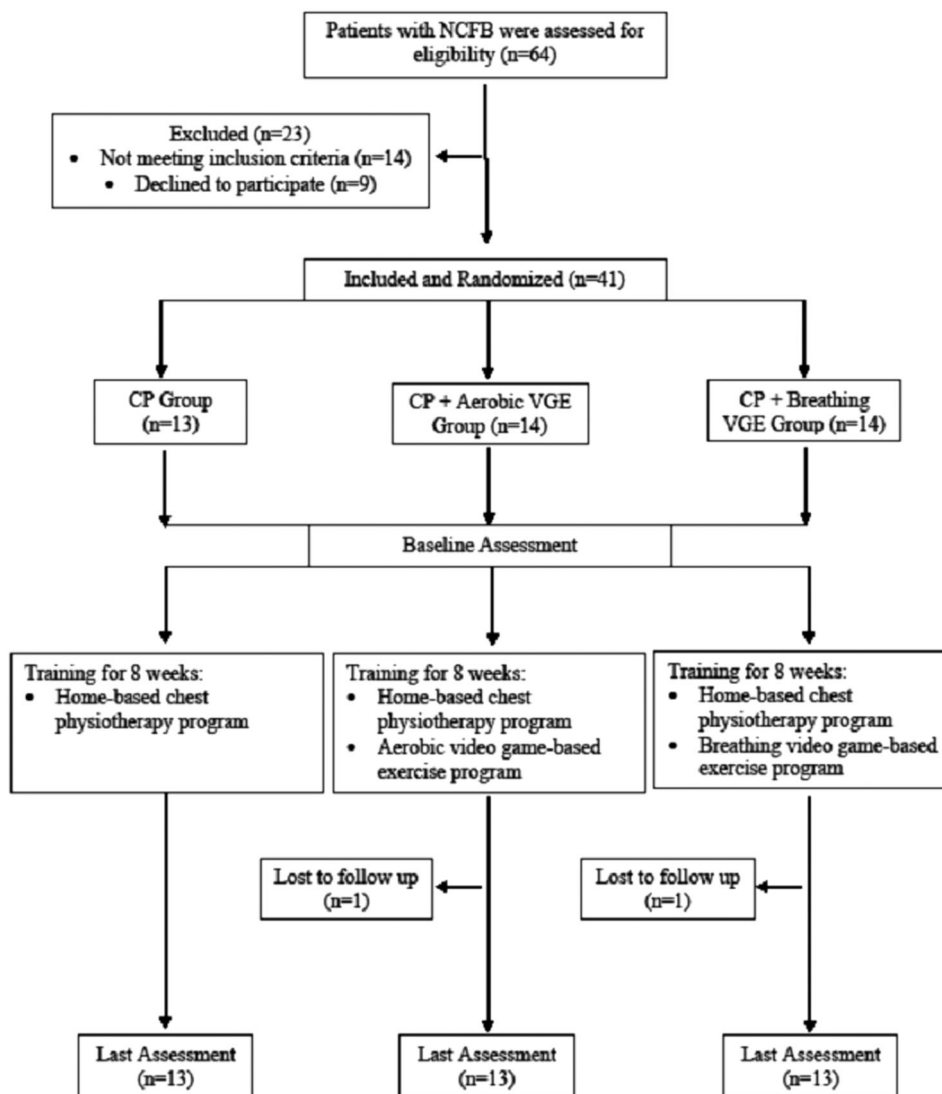


FIGURE 1 Flow chart of the study.

TABLE 1 The demographic and clinical characteristics of groups

	CP group (n = 13)	CP + aerobic VGE group (n = 13)	CP + breathing VGE group (n = 13)	p value
Age (years)	13.46 ± 3.52	13 ± 3.29	11.77 ± 2.83	0.395
Gender				
Girls (n)	7 (53.8%)	4 (30.8%)	7 (53.8%)	0.416
Boys (n)	6 (46.2%)	9 (69.2%)	6 (46.2%)	
Height (cm)	153.23 ± 16.54	149.73 ± 16.05	147 ± 18.92	0.651
Weight (kg)	45.34 ± 13.31	41.48 ± 13.17	38.82 ± 14.01	0.472
BMI (kg/m ²)	18.92 ± 3.38	18.05 ± 2.95	17.34 ± 2.53	0.410
BMI z-scores	0.17 ± 0.54	-0.78 ± 0.93	-0.49 ± 1.26	0.094
BMI percentile				
Poor (<5 percentile)	0 (0%)	0 (0%)	1 (7.69%)	
Ideal (5–85 percentile)	11 (84.61%)	12 (92.30)	12 (92.30)	0.847
Overweight (85–95 percentile)	1 (7.69%)	1 (7.69%)	0 (0%)	
Obese (≥95 percentile)	1 (7.69%)	0 (0%)	0 (0%)	
Etiology				
Idiopathic	5 (38.5%)	6 (46.2%)	4 (30.8%)	
Postinfectious	4 (30.8%)	4 (30.8%)	5 (38.5%)	0.775
Congenital	4 (30.8%)	3 (23.1%)	4 (30.8%)	
Age at diagnosis (months)	110.76 ± 31.99	85.84 ± 40.75	85.38 ± 41.36	0.169
Bronchiectatic lobes				
One lobe	4 (30.76%)	4 (30.76%)	3 (23.07%)	
Two lobes	6 (46.15%)	5 (38.46%)	6 (46.15%)	0.551
Three or more lobes	3 (23.07%)	4 (30.76%)	4 (30.76%)	
Exacerbations ^a	1.92 ± 0.86	1.69 ± 0.85	1.76 ± 0.92	0.795
Adherence to CP program	89.10 ± 13.21%	86.33 ± 11.19%	84.27 ± 24.06%	0.297
Compliance with physical activity recommendation	76.04 ± 22.23%	78.08 ± 20.13%	82.01 ± 19.08%	0.188

Abbreviations: BMI, body mass index; CP, home-based chest physiotherapy.

Note: Data are presented as mean ± SD or n (%).

^aExacerbations in the previous year.

the CP + aerobic VGE group compared to both CP and CP + breathing VGE groups ($p < 0.05$). There was no significant differences between the spirometry values of all groups ($p > 0.05$).

4 | DISCUSSION

The present study demonstrates that relative to home-based CP program and breathing VGE program, aerobic video game-based exercise program resulted in significant improvement in peripheral muscle strength and functional capacity. While both aerobic and

breathing VGE programs were able to provide a higher increase in expiratory muscle strength and balance compared to home-based CP program. Only the breathing VGE program was able to provide a higher increase in inspiratory muscle strength compared to other two groups. Regarding the pulmonary function, there was no difference between the three groups.

Poor adherence to treatment is a common and challenging clinical problem, particularly in children and adolescents with chronic and lifelong diseases.²⁵ Goodfellow et al.²⁶ found that 49% of children and adolescents with cystic fibrosis had low adherence to CP. In our study, adherence to CP program was relatively high and

TABLE 2 Comparison of the pretreatment values in pulmonary function, respiratory and peripheral muscle strength, functional capacity, and balance among groups

	CP group (n = 13) Pretreatment	CP + aerobic VGE group (n = 13) Pretreatment	CP + breathing VGE group (n = 13) Pretreatment	p value
FVC (% pred)	82.41 ± 14.70	73.11 ± 42.30	78.90 ± 37.60	0.593
FVC z-score	-1.51 ± 1.33	-1.86 ± 2.51	-1.65 ± 1.48	0.484
FEV ₁ (% pred)	78.31 ± 13.63	65.49 ± 50.18	76.60 ± 20.33	0.417
FEV ₁ z-score	-1.77 ± 1.09	-1.96 ± 2.10	-2.03 ± 2.62	0.104
FEV ₁ /FVC (%)	92.28 ± 10.44	90.33 ± 14.51	95.09 ± 29.40	0.195
FEV ₁ /FVC z-score	-0.82 ± 0.98	-0.94 ± 2.66	-0.21 ± 0.44	0.316
PEF (% pred)	74.92 ± 41.07	61.04 ± 39.30	62.00 ± 04.12	0.094
PEF z-score	-1.85 ± 1.88	-2.51 ± 1.71	-2.40 ± 0.79	0.290
FEF ₂₅₋₇₅ (% pred)	62.29 ± 41.18	57.71 ± 47.08	58.90 ± 44.25	0.658
FEF ₂₅₋₇₅ z-score	-1.79 ± 1.90	-2.04 ± 1.41	-1.93 ± 1.29	0.382
MIP (cm H ₂ O)	69.38 ± 22.94	73 ± 18.96	55.92 ± 13.67	0.065
MEP (cm H ₂ O)	57.84 ± 19.68	68.23 ± 25.84	49.30 ± 14.99	0.078
Knee Extensor Strength (kg)	31.76 ± 8.86	30.53 ± 9.72	27.80 ± 7.00	0.493
6MWT distance (m)	556.07 ± 69.69	585.07 ± 74.43	559.07 ± 52.22	0.477
ΔSpO ₂ (%)	0.46 ± 0.96	-2.00 ± 3.08	0.00 ± 2.00	0.055
ΔDyspnea (MBS)	1.34 ± 1.31	2.30 ± 1.54	1.38 ± 1.19	0.062
ΔFatigue (MBS)	1.80 ± 1.88	2.61 ± 1.50	2.26 ± 1.80	0.166
PST/overall	0.29 ± 0.12	0.37 ± 0.12	0.39 ± 0.14	0.143
PST/anterior/posterior	0.20 ± 0.10	0.25 ± 0.05	0.22 ± 0.05	0.295
PST/Medial/Lateral	0.20 ± 0.11	0.26 ± 0.10	0.26 ± 0.09	0.343
LOST/Overall	44.69 ± 8.11	38.92 ± 14.56	36.61 ± 12.51	0.226
LOST/Forward	58.07 ± 22.88	49.84 ± 26.12	50.15 ± 19.21	0.588
LOST/Backward	49.84 ± 15.97	40.53 ± 20.31	39.53 ± 20.81	0.330
LOST/Left	46.84 ± 8.23	47.61 ± 10.82	46.53 ± 15.37	0.972
LOST/Right	51.76 ± 17.39	48.07 ± 15.53	48.23 ± 16.53	0.813
CTSIB/Eyes open firm surface	0.99 ± 0.45	1.04 ± 0.72	1.09 ± 0.57	0.906
CTSIB/Eyes closed firm surface	1.28 ± 0.37	1.49 ± 0.73	1.72 ± 0.99	0.326
CTSIB/Eyes open foam surface	1.54 ± 0.53	1.72 ± 0.69	2.01 ± 0.85	0.246
CTSIB/Eyes closed foam surface	3.01 ± 0.56	3.38 ± 1.11	3.16 ± 1.09	0.918
CTSIB/Composite score	1.75 ± 0.43	1.81 ± 0.49	2.11 ± 0.77	0.252

Note: Data are presented as mean ± SD.

Abbreviations: 6MWT, 6-min walking test; CTSIB, clinical test of sensory integration of balance; FEF₂₅₋₇₅, forced mid-expiratory flow between 25% and 75%; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; LOST, limits of stability test; MBS, modified Borg scale; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure; PEF, peak expiratory flow; PST, postural stability test.

TABLE 3 Comparison of the posttreatment values in pulmonary function, respiratory and peripheral muscle strength, and functional capacity among groups

	CP group (n = 13)		CP + aerobic VGE group (n = 13)		CP + breathing VGE group (n = 13)		Intra-group post hoc p value					
	Posttreatment		Posttreatment		Posttreatment		CP versus CP + aerobic VGE		CP versus CP + breathing VGE		CP + aerobic VGE versus CP + breathing VGE	
FVC (% pred)	85.78 ± 13.53	83.34 ± 23.36	83.34 ± 23.36	91.44 ± 22.30	91.44 ± 22.30	0.308	0.214	0.308	0.214	0.157		
FVC z-score	-1.22 ± 1.15	-1.47 ± 2.03	-1.47 ± 2.03	-0.51 ± 1.90	-0.51 ± 1.90	1.000	0.094	1.000	0.094	0.060		
FEV ₁ (% pred)	83.28 ± 15.30	79.27 ± 20.53	79.27 ± 20.53	89.35 ± 28.29	89.35 ± 28.29	0.452	0.311	0.452	0.311	0.190		
FEV ₁ z-score	-1.62 ± 1.25	-1.71 ± 1.71	-1.71 ± 1.71	-0.99 ± 2.40	-0.99 ± 2.40	1.000	0.277	1.000	0.277	0.106		
FEV ₁ /FVC (%)	93.35 ± 9.90	97.20 ± 18.62	97.20 ± 18.62	91.12 ± 11.46	91.12 ± 11.46	0.601	0.662	0.601	0.662	0.347		
FEV ₁ /FVC z-score	-0.77 ± 1.15	0.42 ± 4.57	0.42 ± 4.57	-1.01 ± 1.46	-1.01 ± 1.46	0.096	0.533	0.096	0.533	0.057		
PEF (% pred)	77.42 ± 20.53	75.18 ± 14.82	75.18 ± 14.82	78.95 ± 32.23	78.95 ± 32.23	0.303	1.000	0.303	1.000	1.000		
PEF z-score	-1.73 ± 1.10	-1.80 ± 2.02	-1.80 ± 2.02	-1.69 ± 1.46	-1.69 ± 1.46	0.449	0.704	0.449	0.704	0.411		
FEF ₂₅₋₇₅ (% pred)	65.92 ± 24.42	65.00 ± 31.67	65.00 ± 31.67	66.79 ± 22.16	66.79 ± 22.16	0.576	0.190	0.576	0.190	1.000		
FEF ₂₅₋₇₅ z-score	-1.72 ± 1.26	-1.85 ± 1.70	-1.85 ± 1.70	-1.66 ± 1.19	-1.66 ± 1.19	0.622	1.000	0.622	1.000	1.000		
MIP (cm H ₂ O)	74.76 ± 25.61	82.61 ± 21.91	82.61 ± 21.91	67.61 ± 17.71	67.61 ± 17.71	0.391	0.012	0.391	0.012	0.395		
MEP (cm H ₂ O)	65.53 ± 21.67	83.76 ± 33.90	83.76 ± 33.90	66.00 ± 19.99	66.00 ± 19.99	0.038	0.046	0.038	0.046	0.977		
Knee extensor strength (kg)	32.28 ± 9.02	35.46 ± 10.45	35.46 ± 10.45	27.93 ± 7.01	27.93 ± 7.01	<0.001	1.000	<0.001	1.000	<0.001		
6MWT distance (m)	581.15 ± 64.78	639.07 ± 72.09	639.07 ± 72.09	595.53 ± 54.09	595.53 ± 54.09	<0.001	0.216	<0.001	0.216	0.014		
ΔSpO ₂ (%)	1.15 ± 1.46	-1.46 ± 2.14	-1.46 ± 2.14	1.00 ± 1.58	1.00 ± 1.58	0.010	1.000	0.010	1.000	0.012		
ΔDyspnea (MBS)	1.26 ± 0.97	1.57 ± 1.28	1.57 ± 1.28	1.03 ± 0.98	1.03 ± 0.98	1.000	1.000	1.000	1.000	1.000		
ΔFatigue (MBS)	1.19 ± 0.75	2.61 ± 1.44	2.61 ± 1.44	1.15 ± 1.28	1.15 ± 1.28	0.031	1.000	0.031	1.000	0.009		

Note: Data are presented as mean ± SD. Abbreviations: 6MWT, 6-min walking test; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; FEF₂₅₋₇₅, forced mid-expiratory flow between 25% and 75%; PEF, Peak expiratory flow; MBS, modified Borg scale; MEP, maximal expiratory pressure; MIP, maximal inspiratory pressure.

TABLE 4 Comparison of the posttreatment values in balance among groups

	CP group (n = 13)		CP + aerobic VGE group (n = 13)		CP + breathing VGE group (n = 13)		Intra-group post hoc p value			
	Posttreatment		Posttreatment		Posttreatment		CP versus CP + aerobic VGE	CP versus CP + breathing VGE	CP + aerobic VGE versus CP + breathing VGE	
PST/Overall	0.25 ± 0.09	0.18 ± 0.12	0.21 ± 0.09	0.16 ± 0.07	0.25 ± 0.11	0.17 ± 0.08	0.035	0.040	1.000	$p = 0.044$ $\eta_p^2 = 0.198$
PST/Anterior/Posterior	0.21 ± 0.11	0.18 ± 0.12	0.12 ± 0.07	0.16 ± 0.07	0.13 ± 0.06	0.13 ± 0.06	0.002	0.025	0.920	$p = 0.002$ $\eta_p^2 = 0.303$
PST/Medial/Lateral	0.18 ± 0.12	0.18 ± 0.12	0.16 ± 0.07	0.16 ± 0.07	0.17 ± 0.08	0.17 ± 0.08	0.041	0.046	1.000	$p = 0.041$ $\eta_p^2 = 0.182$
LOST/Overall	45.38 ± 8.40	45.38 ± 8.40	51.15 ± 17.23	51.15 ± 17.23	49.38 ± 12.39	49.38 ± 12.39	<0.001	<0.001	1.000	$p < 0.001$ $\eta_p^2 = 0.432$
LOST/Forward	59.00 ± 23.00	59.00 ± 23.00	62.15 ± 24.53	62.15 ± 24.53	58.92 ± 1.91	58.92 ± 1.91	0.040	0.051	0.697	$p = 0.039$ $\eta_p^2 = 0.207$
LOST/Backward	51.84 ± 16.28	51.84 ± 16.28	61.15 ± 23.09	61.15 ± 23.09	55.38 ± 20.71	55.38 ± 20.71	0.006	1.000	0.062	$p = 0.003$ $\eta_p^2 = 0.281$
LOST/Left	49.69 ± 12.61	49.69 ± 12.61	61.53 ± 12.69	61.53 ± 12.69	55.46 ± 10.89	55.46 ± 10.89	0.007	0.269	0.394	$p = 0.009$ $\eta_p^2 = 0.219$
LOST/Right	53.30 ± 17.28	53.30 ± 17.28	67.15 ± 18.69	67.15 ± 18.69	58.53 ± 16.42	58.53 ± 16.42	<0.001	0.144	0.111	$p = 0.001$ $\eta_p^2 = 0.336$
CTSIB/Eyes open firm surface	0.93 ± 0.41	0.93 ± 0.41	0.55 ± 0.55	0.55 ± 0.55	0.89 ± 0.45	0.89 ± 0.45	0.018	1.000	0.101	$p = 0.016$ $\eta_p^2 = 0.210$
CTSIB/Eyes closed firm surface	1.24 ± 0.37	1.24 ± 0.37	1.18 ± 0.70	1.18 ± 0.70	1.40 ± 0.72	1.40 ± 0.72	0.119	0.263	1.000	$p = .090$ $\eta_p^2 = 0.129$
CTSIB/Eyes open foam surface	1.51 ± 0.71	1.51 ± 0.71	1.17 ± 0.88	1.17 ± 0.88	1.65 ± 0.71	1.65 ± 0.71	0.010	0.268	0.568	$p = 0.012$ $\eta_p^2 = 0.222$
CTSIB/Eyes closed foam surface	2.92 ± 0.72	2.92 ± 0.72	2.92 ± 0.86	2.92 ± 0.86	2.38 ± 0.76	2.38 ± 0.76	0.602	0.005	0.128	$p = 0.006$ $\eta_p^2 = 0.255$
CTSIB/Composite score	1.72 ± 0.49	1.72 ± 0.49	1.52 ± 0.50	1.52 ± 0.50	1.68 ± 0.58	1.68 ± 0.58	0.029	0.037	1.000	$p = 0.048$ $\eta_p^2 = 0.184$

Note: Data are presented as mean ± standard deviation.

Abbreviations: CTSIB, clinical test of sensory integration of balance; LOST: limits of stability test; PST, postural stability test.

there was no difference between the groups. Although physical activity has been shown to improve functional capacity, quality of life, and pulmonary function parameters in patients with cystic fibrosis,²⁷ studies showing the results of a regular physical activity program in children and adolescents with NCFB are limited.²⁸ It was stated that the compliance with physical activity is quite low, especially in pediatric and young adult population.²⁷ In the present study compliance with physical activity recommendation was slightly higher in the CP + breathing VGE group, but there was no difference between the groups. Consequently, we concluded that neither adherence to CP program nor compliance with physical activity recommendation did not contribute to the differences of the improvements between the groups.

One study by Dassios et al.²⁹ found significant improvement in MIP and MEP in children with cystic fibrosis. The authors stated that aerobic exercise training provides an increase in skeletal muscle strength which is included with high levels of evidence in current guidelines and that they assumed that increase in respiratory muscle strength is a normal response because respiratory muscles have similar structural features as skeletal muscles. In our study with the contribution of possible similar mechanisms, the increase in MEP in the CP + aerobic VGE group was found significantly higher than in the CP group. Likewise, Mandal et al.³⁰ found a significant increase in MEP in the patients with bronchiectasis, who performed strengthening and aerobic exercises in addition to OPEP treatment compared to the control group.³⁰ There are a limited number of studies on the pursed lip breathing exercise, which is also the basis of the "Breathing + package" in our study. Nield et al.³¹ compared the effects of pursed lip breathing exercise compared to the expiratory muscle training and control groups and found a statistically higher increase in MIP in the pursed lip breathing exercise group in patients with COPD. Authors have speculated that pursed lip breathing exercise reduces expiratory tidal volume by creating repetitive and intense forced expiration. This mechanism may help us to understand the increase of MIP and MEP in the CP + breathing VGE group. Incentive spirometry provides a visual aid that encourages patients to achieve maximum deep inspiration, forced expiration, and effective coughing.³² Paiva et al.³³ achieved training to improve MIP with an incentive spirometer and they assumed that an incentive spirometer may encourage the respiratory muscles to work more intensely and with resistance. The significant improvement in respiratory muscle strength in the CP + breathing VGE group may be also explained by features of visual feedback, deep inspiration, and forced expiration of the Breathing+ device similar to the incentive spirometer.

It has been reported that two basic mechanisms may be responsible for muscle strength loss in chronic respiratory diseases. The first one is the intrinsic structure changes in the muscle secondary to chronic corticosteroid use and systemic inflammation, and the second one is the deterioration of the ventilation-perfusion rate, the inability to meet the oxygenation, and other metabolic needs of the muscles during contraction.³⁴ As stated in a recent review, the fact that the pulmonary rehabilitation program was applied together with strength and aerobic training as recommended in the guidelines

in most studies of bronchiectasis may be a limiting factor to show the effect of aerobic exercise on peripheral muscle strength.³⁵ The significant increase in knee extensor strength observed in the CP + aerobic VGE would be more likely attributable to increases in recruitment and coordination of motor units or increases in muscle cross-sectional area. While aerobic exercise may increase the myoglobin content and the volume and size of mitochondria, these adaptations improve aerobic performance and endurance. Such adaptations have little impact on torque production or contractile properties of skeletal muscle based on principle of training specificity.³⁶

An important finding is that the aerobic VGE program provided a higher increase in functional capacity compared to the home-based CP program and the breathing VGE program. Del Corral et al.²⁴ achieved significant improvement in 6MWT distance in the aerobic VGE group compared to the control group in children with cystic fibrosis. Similarly, Gomes et al.³⁷ compared the effect of the aerobic VGE program with the exercise training on treadmill in children with asthma and found that the significant increase in the aerobic VGE group was lower than the increase in the treadmill group. Likewise, Sutanto et al.³⁸ stated that the aerobic VGE program significantly improved the 6MWT distance value in patients with COPD. Considering these three studies, which are similar to the methodology and findings of our study, it is seen that aerobic VGE is compatible with traditional approaches. Both the increase in peripheral muscle strength in the aerobic VGE group and the physiological changes in aerobic training which were mentioned in these studies such as the improvement of cardiovascular metabolism, perfusion, and ventilation, increase in maximum oxygen consumption and heart rate which may be related to the our results. Additionally, reduction in fatigue is known as an adaptive response to aerobic exercise in children with cystic fibrosis and NCFB.²⁷ Similarly, it was found that the aerobic VGE program provided a higher decrease in fatigability compared both breathing VGE and CP programs in the present study. Accordingly, we think that the decrease in fatigue in the CP + aerobic VGE group may have played a role in the better development of functional capacity.

As the literature mostly focused on research on balance in adults with COPD, there is a lack of knowledge about these issues in children and adolescents with NCFB. Due to the limited number of studies in children and adolescents with NCFB, the guidelines do not yet include recommendations for the evaluation and treatment of balance; however, the importance of balance in patients with COPD is clearly stated in current guidelines.³⁹ Rutkowski et al.⁴⁰ stated that aerobic VGE provided a significant improvement in the Timed Up and Go test, which evaluates dynamic balance in patients with COPD. Cho et al.⁴¹ also found a significant increase in the pediatric balance scale in the aerobic VGE group in children with cerebral palsy. In light of these studies, possible mechanisms of aerobic VGE in improving balance; it has been explained as the increase in peripheral muscle strength, the development of motor strategies required for rapid and safe postural changes, and the equal distribution of body weight to the lower extremities by the development of body symmetry

perception. Significant improvements were obtained in overall scores of PST and LOS, and composite score of CTSIB in the CP + aerobic VGE group in the present study. These findings support the previous research and we think that similar mechanisms may have played a role. Although to the best of our knowledge there is no study investigating the effect of breathing VGE on balance, Zeren et al.⁴² found that MEP was an independent predictor for the overall LOST score in children with cystic fibrosis. The authors stated that the MEP is a parameter that reflects the abdominal muscle strength which plays an important role in providing dynamic balance. Similarly, Develi et al.⁴³ determined that the dynamic balance improved with core stabilization training in patients with asthma and reported that the increase in MIP and functional capacity may have played a role. Considering these results, the enhancement of overall scores of PST and LOS and composite score of CTSIB may also benefit from the increase in MIP, MEP, and 6MWT distance in the CP + breathing VGE group.

The study is limited by the lack of a control group that did not perform any CP program. Our second limitation is that VGE is known to be an entertaining approach, we did not use any enjoyment scale. With the lack of literature on the use of VGE for pulmonary rehabilitation, the future undertaking of certain research directions may be imperative to establish its efficacy.

5 | CONCLUSION

In conclusion, to the best of our knowledge, our study is the first study to investigate the effect of aerobic and breathing VGE in children and adolescents with NCFB. While significant improvement was achieved in balance scores in both VGE groups, home-based CP program failed to improve balance scores. Improvement in peripheral muscle strength was achieved only with the CP + aerobic VGE program. Our findings suggest that aerobic VGE is important for further increase in peripheral muscle strength and functional capacity; breathing VGE is also important for further increase in respiratory muscle strength as an alternative to respiratory muscle training in children and adolescents with NCFB.

AUTHOR CONTRIBUTIONS

Hikmet Ucgun: data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); resources (equal); writing—original draft (equal). **Hulya Nilgun Gurses:** methodology (equal); project administration (lead); resources (lead); supervision (lead); writing—original draft (equal); writing—review & editing (lead). **Meltem Kaya:** data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); writing—original draft (equal). **Erkan Cakir:** investigation (supporting); methodology (supporting); resources (supporting); supervision (supporting); writing—review & editing (supporting).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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