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Effects of inspiratory muscle training on postural stability, pulmonary function and functional capacity in children with cystic fibrosis: A randomised controlled trial

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ABSTRACT

Background: Previous research has found conflictive results regarding the benefits of inspiratory muscle training (IMT) for cystic fibrosis (CF) patients. Also, involvement of postural stability is a rising concern in chronic lung diseases but its role in CF patients is poorly understood. Our aim was to investigate the effects of IMT in CF patients as well as analysing the factors which may be related to postural stability.

Methods: Thirty-six children aged between 8 and 18 years with CF were randomly allocated to either "comprehensive chest PT" group (PT) or "IMT alongside comprehensive chest PT" group (PT + IMT). Both groups trained for 8 weeks. Dynamic and static postural stability tests on Biodex Balance system®, spirometry, respiratory muscle strength and 6-min walk distance (6MWD) was assessed at baseline and after 8 weeks of training. Determinants of postural stability was also analysed on baseline values.

Results: Maximum expiratory pressure (MEP) was found to be an independent predictor for overall limits of stability (LOS) score explaining %26 of variance ($R = 0.514$, $p = 0.003$). Overall LOS score, FVC, FEV_1, peak expiratory flow, MEP and 6MWD significantly improved in both groups, with no significant differences between groups. Maximum inspiratory pressure (MIP) also improved in both groups but the magnitude of improvement in MIP was greater in PT + IMT group (38 cmH_2O vs 13 cmH_2O; $p < 0.001$).

Conclusions: Combining IMT with chest PT failed to provide further improvements, except for MIP, suggesting that a comprehensive chest PT program may be individually effective in improving overall LOS score, spirometry, respiratory muscle strength and 6MWD.

Trial registration: www.ClinicalTrials.gov; registration number: NCT03375684.

1. Introduction

Cystic fibrosis (CF) is a genetic disorder affecting multiple organs and systems including lungs, pancreas, liver, gastrointestinal system and reproductive system which rely extensively on exocrine secretion. Lung-related problems are the most important cause of morbidity and mortality in CF patients. Thick and sticky mucus produced in the lungs alters the mucociliary clearance and impairment of pulmonary defence mechanisms makes the lungs susceptible to recurrent infections and chronic airway inflammation [1,2]. Work of breathing is increased [3], and exercise capacity, respiratory and peripheral muscle strengths are reduced in these patients [4–6].

It is stated in the guidelines [7,8] that physiotherapy (PT) approaches such as postural drainage, thoracic expansion exercises, oscillatory devices or physical exercise training for improving airway clearance should be included in the routine treatment of CF [9–12]. Inspiratory muscle training (IMT) is also a well-accepted PT modality and widely used in pulmonary rehabilitation programs [13]. Although it is proved to be effective in improving pulmonary function, respiratory muscle strength and exercise capacity in various diseases [13,14], there is no consensus on the benefits of IMT for CF patients in the literature [15].

Recently, involvement of postural stability has gained a lot of attention as an extra-pulmonary symptom for chronic lung diseases [16]. Possible causes reported for the impairments in postural stability in patients with chronic obstructive lung disease (COPD) include, but are

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not limited to increased work of breathing, hyperinflation, and inspiratory and peripheral muscle weakness [17–20]. It is now recommended to include assessments and rehabilitative approaches for postural stability in the pulmonary rehabilitation programs [13].

Although COPD is extensively studied with respect to the postural stability, studies investigating its role in CF patients are scarce. Still, a relationship between inspiratory muscle strength and postural stability is reported in adult CF patients [21]. Considering this possible relationship between inspiratory muscle strength and postural stability, it is hypothesized that postural stability may also be improved by increasing the inspiratory muscle strength via IMT. So, the aim of this study was to investigate the effects of IMT on postural stability, pulmonary function, respiratory muscle strength and functional capacity as well as analysing the factors which may be related to postural stability in children with CF.

2. Methods

2.1. Study design

A prospective, randomised controlled study was conducted. Between January 2018 and May 2018, thirty-six patients aged between 8 and 18 years in the CF patient registry of a university hospital were included in the study. Inclusion criterion was the diagnosis of CF according to Cystic Fibrosis Foundation Consensus report [22]. In order to obtain a homogeneous sample in terms of severity of the lung disease, only the patients with a forced vital capacity in 1 s (FEV_1) above 70% of the predicted value which is considered mild lung disease according to Cystic Fibrosis Foundation patient registry reports [23] were included. Exclusion criteria were acute exacerbation or hospitalisation history in past month, active participation in another supervised PT program, and diagnosed comorbidities which may affect mobilisation or balance.

After the baseline assessments, linear regression analysis was conducted on baseline values of thirty-six patients who met the inclusion criteria for determining the independent predictors of postural stability among the respiratory parameters. Then, patients were randomly allocated into either comprehensive chest PT group (PT group) or IMT in addition to comprehensive chest PT group (PT + IMT group) using a numbered series of 36 prefilled envelops specifying group assignments generated by a computer-based program. Patients were unaware of their group assignments. The physiotherapist who assessed the patients was blind to group assignments. Another physiotherapist applied training programs to both groups. Both groups received a comprehensive chest PT program twice a day for 8 weeks. PT + IMT group also received IMT twice a day for 15 min. PT + IMT group was instructed to rest for at least 1 h between chest PT and IMT sessions to avoid inspiratory muscle fatigue. For both groups, one session was supervised in the clinic every week, rest of the sessions were performed at home. Patients were instructed to keep a diary for home sessions to improve adherence to exercise program. All patients were assessed again at the end of the program (Fig. 1).

The study was approved by the ethics committee of Bezmialem Vakif University (Protocol number: 54022451-050.05.04) and registered to ClinicalTrials.gov website (registration number: NCT03375684). The study was conducted in accordance with the Helsinki Declaration. A written informed consent was obtained from the parents or the guardians of each patient.

2.2. Outcome measures

Primary outcome measure was the postural stability which was assessed with Biodex Balance System (BBS) (Biodex, Inc., Shirley, NY, USA) using 'Postural Stability Test (PST)' for static postural stability and 'Limits of Stability Test (LOST)' for dynamic postural stability [24]. In PST, subjects are instructed to stand still on the platform and the displacement of the centre of gravity (COG) is quantified for anterior-posterior (AP) and medial-lateral (ML) axes. PST gives three types of outcome measures: overall stability index, AP stability index and ML stability index. Higher scores indicate worse postural stability. LOST evaluates the ability to move the centre 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 a better dynamic postural stability.

Pulmonary function test was performed using a spirometer (COSMED Pony FX; COSMED, Italy) according to the guideline of American Thoracic Society (ATS) and European Respiratory Society (ERS) [25]. Forced vital capacity (FVC), FEV_1, FEV_1/FVC and peak expiratory flow (PEF) were measured and expressed as percentages of the predicted values. Maximum inspiratory (MIP) and expiratory (MEP) pressures were measured using a mouth pressure meter (MicroRPM; MicroMedical, UK) according to the guideline of ATS/ERS [26]. A maximum value of three efforts that vary less than 5% was recorded for inspiratory and expiratory pressures. Patients were allowed to rest for about a minute between the efforts.

Functional capacity was assessed with the 6-min walk test (6MWT) according to the guideline of ATS [27]. Patients were instructed to walk as fast as possible between two cones positioned 30 m apart and the distance walked in 6 min was recorded. Oxygen saturation and heart rate were also measured before and after the test using a pulse oximeter (Beuer oximeter; Beurer GmbH; Germany).

2.3. Interventions

Comprehensive chest PT program consisted of diaphragmatic breathing exercise, thoracic expansion exercises, incentive spirometer (Triflo®), oscillatory positive expiratory pressure (OPEP) device (Flutter®), postural drainage with percussions, coughing techniques and physical activity counselling. Exercises were performed as two sets for 5 repetitions with the rest intervals of 5–6 tidal breaths between the exercises to avoid respiratory muscle fatigue and hyperventilation. Postural drainage and percussion was performed in 45° Trendelenburg position with the patient lying on front, left and right sides respectively for 3 min in each position. Besides chest PT, at least 60 min of moderate-intensity physical activity such as brisk walking, sports, dancing, ball games or simple exercises on Pilates ball or trampoline on a daily basis was recommended to each patient considering their interests to promote physical activity participation. Moderate-intensity was described as "intense enough to make the child feel like he/she is breathing somewhat hard but can still carry on a conversation [28]" and patients/parents were instructed to determine the intensity of physical activity accordingly.

Inspiratory muscle training was performed using Threshold Inspiratory Muscle Trainer (Philips Respironics, UK) with the intensity of 30% of the MIP value for 15 min, twice a day. Maximum inspiratory pressure was measured weekly when patients came to the clinic for their supervised exercise sessions and the training intensity was adjusted to maintain 30% of the MIP value. Since the repeated measurements of MIP in the PT + IMT group might induce a learning effect on the patient's ultimate MIP performance, MIP value of PT group was also measured weekly.

2.4. Data analysis and sample size

Statistical analysis was conducted using SPSS 20.0 statistical program (SPSS Inc., USA). Normality of the distribution of data was analysed using Kolmogorov Smirnov Test. Linear regression analysis was conducted on baseline measurements of thirty-six subjects for analysing the independent predictors of postural stability among the respiratory parameters. Paired Sample T-test or Wilcoxon Test was used for in-group comparisons and Independent Samples T-test or Mann Whitney *U*

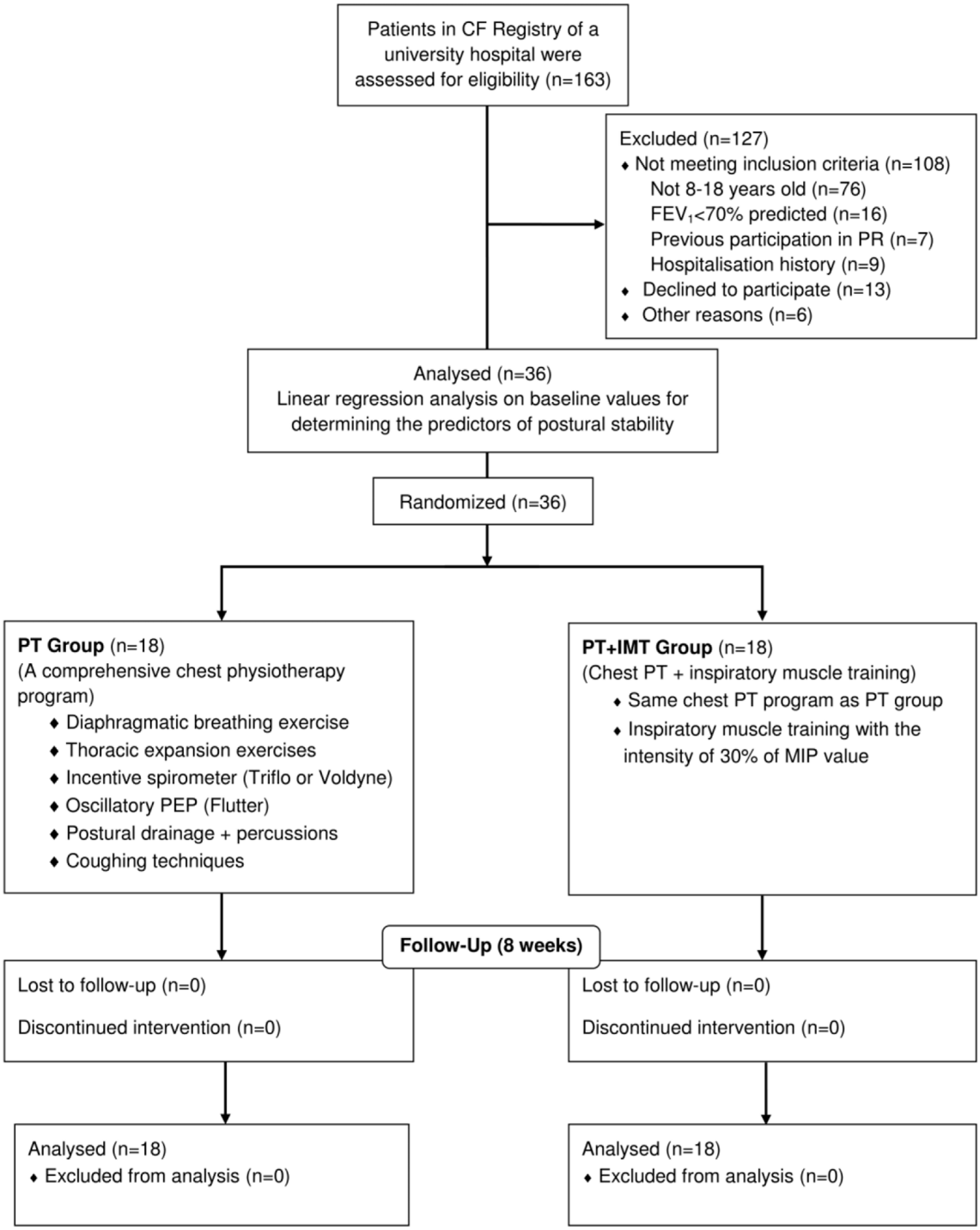

Fig. 1. Flow chart of participants.

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. The results were considered significant with p values < 0.05. We estimated that a sample size of 16 patients for each group would have a power of 80% to detect a minimum clinically significant difference of 54 m [29] of the 6MWT distance which has the highest standard deviation among all variables, with an alpha value of 0.05.

3. Results

One hundred and sixty-three patients in the CF patient registry of a university hospital were assessed for eligibility; total of 127 patients were excluded for not meeting the inclusion criteria or declined to participate. Eighteen patients for each group were included in the study and a total of 36 patients completed the study with no drop-outs. Fourteen of 18 patients in PT + IMT group (78%) and 15 of 18 patients in PT group (83%) completed all training sessions as planned. Adherence to the training program averaged 97.9% ± 4.2% in PT + IMT group and 97.5% ± 5.7% in PT group. Reasons for missing one or more sessions were patient's refusal, family commitments and school exams. No adverse effects were reported during the program.

Baseline characteristics of the groups are presented in Table 1. Linear regression analysis on 36 patients revealed that MEP value was

Table 1
Baseline characteristics of patients.

	PT + IMT Group (n = 18)	PT Group (n = 18)
Gender		
Boys (n)	9 (50%)	8 (44%)
Girls (n)	9 (50%)	10 (56%)
Age (years)	11.66 ± 2.42	10.47 ± 2.03
Age at diagnosis (months)	4.30 ± 2.72	4.18 ± 2.98
Diagnostic test		
Sweat test (n)	15 (83%)	16 (88%)
Sweat chloride concentration (mmol/L)	120 ± 11	113 ± 9
Genetic analysis (n)	9 (50%)	7 (39%)
Body composition		
Body mass index (kg/m^2)	17.65 ± 2.40	17.96 ± 2.49
Muscle mass (%)	33.18 ± 3.20	31.06 ± 3.21
Fat mass (%)	17.19 ± 4.30	19.72 ± 6.35

Data are presented as mean ± standard deviation or n (%).
FVC: forced vital capacity, FEV1: forced expiratory flow in 1 s, PEF: peak expiratory flow, MIP: maximum inspiratory pressure, MEP: maximum expiratory pressure, SI: Stability index, 6MWT: 6-min walk test.

Table 2
Linear regression for prediction of overall postural stability index and overall limits of stability score (n = 36).

Dependent Variable	Independent Variable	R	R^2	p value
Overall PS index	FVC (%)	0.291	0.085	0.106
	FEV_1 (%)	0.216	0.047	0.234
	MIP	0.309	0.095	0.086
	MEP	0.289	0.084	0.108
Overall LOS score	FVC (%)	0.143	0.021	0.434
	FEV_1 (%)	0.347	0.120	0.062
	MIP	0.206	0.042	0.259
	MEP	0.514	0.264	0.003

FVC: forced vital capacity, FEV_1: forced expiratory flow in 1 s, LOS: limits of stability, MIP: maximum inspiratory pressure, MEP: maximum expiratory pressure, PS: postural stability.

the independent predictor for the overall LOST score, explaining 26% of the variance (R = 0,514; p = 0.003). FVC, FEV_1 and MIP values did not have a significant relationship with overall PST or LOST scores ($p > 0.05$) (Table 2).

There were no significant differences between the groups in baseline values of postural stability, pulmonary function, respiratory muscle strength and functional capacity ($p > 0.05$). Effects of the treatments on postural stability, pulmonary function, respiratory muscle strength and functional capacity are shown in Table 3. Overall score of LOST significantly improved in both PT + IMT and PT groups ($p < 0.05$), with no difference between groups. No significant changes were observed in PST results or directional scores of LOST. Both groups also experienced significant improvements in FVC (%), FEV_1 (%) and PEF (%) values in spirometry ($p < 0.01$), with no difference between groups. Regarding the respiratory muscle strength, there was a significant increase in MIP and MEP values in both groups ($p < 0.01$) whereas the magnitude of improvement in MIP value was greater in PT + IMT group compared to PT group (38 cmH_2O vs 13 cmH_2O; $p < 0.001$). Functional capacity indicated by 6MWT walk distance significantly improved ($p < 0.001$) and the amount of oxygen desaturation during 6MWT reduced ($p < 0.05$) in both groups with no differences between groups.

Regarding the physical activity counselling, 10 patients (56%) in PT + IMT group and 9 patients (%50) in PT group reported that they regularly performed at least 60 min of physical activity in most of the days of a week (no between-group difference; $\chi^2 = 0.125$, p = 0.723), rest of the patients did not change their physical activity behaviour.

4. Discussion

In children with CF, MEP value was found to be an independent predictor for the overall LOST score which is a measure of dynamic postural stability. Contrary to literature that reports significant relationship between diaphragm muscle strength indicated by MIP value and postural stability [18,21], we did not detect such a relationship in our sample. Eight-week-long comprehensive chest PT resulted in significant improvements in dynamic postural stability, spirometry, respiratory muscle strength and functional capacity in children with CF. Addition of IMT to chest PT did not yield further improvements, except for MIP value.

In patients with COPD, it is reported that the hyperinflation limits the contribution of trunk to postural stability by forcing the sternum outward and consequently reducing the thoracolumbar spine mobility [17,18]. Hyperinflation may also induce inspiratory muscle weakness by putting a mechanical disadvantage on the diaphragm which is one of the core muscles. When the function of diaphragm is impaired, its motor and sensory contribution to postural stability may also be reduced [18]. Similarly, a significant relationship is reported for MIP value and postural stability measures in adults with CF. Authors stated that a significant hyperinflation was present in almost all patients and this may be the underlying cause for both inspiratory muscle weakness and disturbance in postural stability in a similar manner as in COPD [21]. In children with CF, we did not detect any relationship between MIP value and postural stability measures. Since the mean age of our sample was 11 years and the FEV_1 values were close to normal predicted ranges, it may be presumed that our sample did not have a hyperinflation as pronounced as adults with COPD or CF that might have an influence on thoracolumbar mechanics and this may explain the lack of a relationship between MIP values and postural stability in our study. Besides, due to the complex interactions between the contributing systems, ability of postural control continues to develop until the end of the adolescence period [30] and that may be another explanation for not obtaining the same results which are mainly reported for adults.

An important finding is that MEP value was found to be an independent predictor for dynamic postural stability in our study. MEP measurement reflects the combined effect of abdominal and internal intercostal muscles, and the elastic recoil of the lungs and the chest wall [26]. But, since the largest contribution is made by the abdominal muscles, it is plausible to consider MEP value mainly as a measure of abdominal muscle strength. Abdominal muscles play an important role in stabilization of the lumbopelvic region and become active as movement occurs in the trunk or extremities. When in a standing position, recruitment of abdominal muscles for preparing the spine for perturbations is faster compared to sitting position [31] and this indicates the importance of abdominal muscles particularly in postural tasks in the standing position which is in fact the ability of dynamic postural stability. Also, overall LOST score improved in both groups even though no specific training for balance or posture was applied to patients in our study. Improvement in LOST score may be attributed to increase in the MEP value (possible explanations for how MEP value increased will be discussed further in this section) and this supports the relationship between dynamic postural stability and abdominal muscle strength. To our best knowledge, this is the first study to investigate the determinants of static and dynamic postural stability in children with CF. Since a poor postural stability is a key modifiable risk factor for falls and fall-related injuries [32], assessments and therapeutic approaches for postural stability have great importance in the management of chronic diseases. Considering the evident interaction between expiratory muscle strength and dynamic postural stability in our study, it may be presumed that as the respiratory muscle function of these patients deteriorate; ability of postural stability may be affected as well. In such cases, IMT may be utilized as a therapeutic approach for postural stability considering its benefits on the respiratory muscle function.

It is advocated in the guidelines that chest physiotherapy is an

Table 3
Effects of treatments on postural stability, pulmonary function, respiratory muscle strength and functional capacity.

	PT + IMT Group (n = 18)				PT Group (n = 18)				Between groups difference
	Before Treatment	After Treatment	In-group Change (Δ)	P value	Before Treatment	After Treatment	In-group Change (Δ)	P value	
Postural Stability Test									
Overall SI	2.31 ± 0.93	2.19 ± 1.22	−0.16 ± 1.07	0.658	2.39 ± 0.80	2.21 ± 0.83	−0.17 ± 0.38	0.086	0.968
Anterior/ posterior SI	2.11 ± 0.97	2.04 ± 1.17	−0.06 ± 1.03	0.791	2.12 ± 0.99	2.03 ± 1.06	−0.09 ± 0.19	0.070	0.924
Medial/lateral SI	0.85 ± 0.36	0.71 ± 0.37	−0.17 ± 0.38	0.137	1.06 ± 0.86	0.97 ± 0.69	−0.08 ± 0.32	0.309	0.463
Limits of Stability Test (0–100)[a]									
Overall Score	44.24 ± 11.89	52.25 ± 15.77	8.01 ± 8.13	0.001	42.83 ± 10.37	47.44 ± 7.62	5.88 ± 8.71	0.034	0.480
Forward DS	58.63 ± 18.51	64.37 ± 18.70	5.74 ± 10.05	0.370	51.41 ± 17.54	56.19 ± 16.34	4.75 ± 7.32	0.109	0.752
Backward DS	51.38 ± 15.76	55.19 ± 16.54	3.85 ± 14.48	0.790	47.38 ± 13.12	52.38 ± 15.98	5.00 ± 11.91	0.114	0.696
Left DS	53.99 ± 16.20	59.38 ± 18.79	5.39 ± 8.62	0.052	47.32 ± 12.76	50.13 ± 14.19	2.75 ± 10.47	0.240	0.692
Right DS	49.68 ± 13.66	54.99 ± 21.96	5.30 ± 16.63	0.220	46.08 ± 12.64	50.88 ± 13.58	4.81 ± 11.07	0.104	0.922
Pulmonary Function									
FVC (%)	87.13 ± 13.66	90.47 ± 12.72	3.88 ± 3.46	0.002	88.91 ± 13.97	92.06 ± 14.05	3.13 ± 3.18	0.001	0.833
FEV_1 (%)	79.36 ± 13.67	82.93 ± 12.21	3.63 ± 4.39	0.006	78.69 ± 15.91	82.38 ± 15.50	3.69 ± 4.42	0.005	0.968
PEF (%)	78.38 ± 17.37	90.56 ± 18.11	12.63 ± 10.07	< 0.001	73.84 ± 20.94	87.71 ± 19.20	13.50 ± 12.55	< 0.001	0.829
Respiratory Muscle Strength									
MIP (cmH_2O)	67.74 ± 12.42	98.86 ± 13.20	37.63 ± 8.21	< 0.001	71.29 ± 15.44	84.23 ± 14.32	12.94 ± 8.25	< 0.001	< 0.001
MEP (cmH_2O)	91.78 ± 13.45	99.03 ± 17.06	7.28 ± 7.51	0.002	86.14 ± 17.76	91.88 ± 15.83	5.75 ± 6.21	0.002	0.534
Functional Capacity									
6MWT distance (m)	561 ± 45	603 ± 57	42.88 ± 20.65	< 0.001	544 ± 62	584 ± 64	40.20 ± 26.2	< 0.001	0.936
Resting SpO_2 (%)	97.56 ± 1.01	97.71 ± 0.88	0.15 ± 0.33	0.104	97.69 ± 0.79	97.88 ± 0.80	0.19 ± 0.40	0.083	0.756
SpO_2 change during test (%)	−1.86 ± 1.31	−0.66 ± 0.70	1.21 ± 1.27	0.002	−2.13 ± 1.66	−1.13 ± 0.71	1.00 ± 1.36	0.010	0.659

Data are reported as mean ± standard deviation.
DS: Direction score, FVC: forced vital capacity, FEV_1: forced expiratory flow in 1 s, PEF: peak expiratory flow, MIP: maximum inspiratory pressure, MEP: maximum expiratory pressure, SI: stability index, 6MWT: 6-min walk test.
[a] Scores of forward-left, forward-right, backward-left, backward-right directions were not reported. No significant differences were detected for in-group or between group comparisons ($p > 0.05$).

essential component of maintenance therapy of CF for achieving airway clearance and none of the PT techniques is found superior to another [7,8]. In a review comparing the acute effects of various chest PT techniques to spontaneous coughing [9], only one study reported a post-session increase in FEV_1 and FVC values (up to 7% and 3%, respectively) favouring chest PT. Another review which examines the effects of oscillatory devices [11], no significant increase was reported for any of the spirometric values. Similarly, a review investigating the effects of various breathing exercises [10] reports no significant variations for FEV_1, FVC or PEF. Despite being statistically insignificant, an increase in FVC up to 1.6% and FEV_1 up to 3.8% is still reported in various studies in the aforementioned reviews. It is stated that a possible explanation for achieving improvements in the spirometric values to an extent may be the mechanical effect resulting from the mucus that has been removed from the airways via chest PT techniques. In our study, none of the patients had participated in supervised PT programs before and they have not been performing chest PT techniques on a regular basis. Primary complaints of patients were the excessive amount of phlegm and frequent coughs in daily life before included in the study. Families stated that in the first two weeks of the training program, their children expectorated 'tremendous' amount of sputum during the sessions but it decreased in the following weeks. It seems that the long-term accumulation of mucus in the absence of regular airway clearance techniques in our sample vastly benefited from the chest PT program, especially in the acute period. In accordance with the literature, we think that the increase of %4 in FVC and FEV_1 values in both groups may be attributed to the mechanical effect of the removal of the mucus from the airways and the fact that our patients had not performed chest PT on a regular basis in the past may also have enhanced the effects of the program on the spirometric values. In the literature, studies generally investigated the effects of a single modality or compare one technique to another. Most of these studies failed to achieve significant improvements in spirometric values. In our study, we implemented a comprehensive chest PT program consisted of several modalities including breathing exercises, incentive spirometer, OPEP device, drainage techniques and physical activity counselling. Significant improvements we achieved in the spirometric values may also be attributed to the combined effect of these modalities which suggests such comprehensive programs may provide further benefits on spirometry.

Addition of IMT to a comprehensive chest PT program did not provide further improvements except for MIP value in our study. In the literature [15], there is no evidence to suggest that IMT is either beneficial or not in CF patients but it is found to be effective in improving inspiratory muscle strength. Since the inspiratory muscles are morphologically and functionally skeletal muscle, they will respond to training in a similar way as any skeletal muscle when the appropriate physiological load is applied [33]. Considering that the IMT specifically targets the inspiratory muscles, it is not surprising to achieve further improvements in the MIP value of PT + IMT group in our study. Literature suggests that IMT may be applied to CF patients with significant respiratory muscle weakness.

Literature has also conflicting results regarding the benefits of IMT on spirometric values. Enright et al. state that training intensities of > 20% of MIP value are required to significantly improve pulmonary function and report significant improvements in FVC and total lung capacity (TLC) of CF patients with the IMT at the intensity of 80% of MIP value compared to controls [34]. Similarly, Sawyer et al. were also able to achieve significant increases in vital capacity (VC) and TLC values with the intensity of 60% of MIP [35] but, De jong et al. failed to provide benefits for any of the spirometric values with the intensity of 40% [36]. Santa-Sosa et al. also failed to improve spirometric values with IMT at 40% of MIP despite combining IMT with the 'whole body' aerobic exercise training [37]. There is no consensus on the exercise intensity of IMT for CF patients. Intensity of 30% of MIP is found to be the minimal threshold for IMT in patients with COPD [14], but still no

dose-response relationship was reported for training intensity and that means higher intensities may not guarantee further benefits. Reid et al. states that the CF patients may benefit from IMT during the later stages of their disease when they develop a more pronounced respiratory muscle weakness and/or hyperinflation [38]. This assumption may explain why Enright et al. [34] achieved significant improvements in spirometric values and other similar studies did not. Baseline predicted values of FEV_1 and FVC in their study were 64% and 53%, respectively and the severity of lung deterioration in their patients may have enhanced the benefits of IMT on the spirometric values. This may also explain our lack of improvement in the spirometric values via IMT since the patients in our study had almost normal predicted values on spirometry at baseline.

An interesting finding is that the MEP value also increased in both groups in our study despite no training was applied for expiratory muscles. This may be attributed to the neural conditioning effect which results from the repeated exposures to same tasks. Neural conditioning improves the neuromuscular recruitment pattern, and consequently provides improvements in the muscle strength [39]. Patients in both groups performed maximum inspiratory and expiratory manoeuvres repeatedly during the exercises in chest PT program and this may have induced neural conditioning effect both for MIP and MEP values in our study.

Although we did not apply a structured physical exercise program to our patients, 53% of the patients increased their physical activity participation through the physical activity counselling component of our PT program. Physical activity guideline for CF [28] states that even if a structured physical exercise program is not implemented, habitual physical activity may still provide health benefits which suggests that the improvements in functional capacity in our sample may be partly attributed to physical activity participation. Functional capacity may also benefit from the improvement of FEV_1 in our sample. Exercise limitation in CF is multifactorial but bronchial obstruction plays a major role. FEV_1 is reported to be a predictor for exercise capacity in these patients [40]. Considering the interaction between exercise tolerance and airway obstruction, improvements in FEV_1 and airway clearance may also contribute to functional capacity in our study. Similar to spirometry results, IMT did not yield further improvements in functional capacity either, suggesting that a comprehensive chest PT program may be individually efficient in improving functional capacity.

Since the pulmonary function test is not an adequate method for assessing the airway clearance, main limitation of our study was the lack of objective assessments for airway clearance such as radioactive tracer technique or lung clearance index. Also, we were not able to measure sputum wet weight on a regular basis since the PT program was mainly applied at home by patients' parents.

In conclusion, MEP value was found to be an independent predictor for overall score of LOST indicating a possible interaction between expiratory muscle strength and dynamic postural stability. Eight-week-long comprehensive chest PT program provided significant improvements in dynamic postural stability, spirometry, respiratory muscle strength and functional capacity in children with CF. Addition of IMT to chest PT did not yield further improvements except for inspiratory muscle strength. IMT may be applied selectively to CF patients with significant respiratory muscle weakness but there was insufficient evidence to support its routine implementation. But, considering the natural history of the disease, it may be potentially useful in attenuating the decline in the inspiratory muscle function later in life.

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