Bachelor's project

NTNU
Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Neuromedicine and Movement Science

Vilde Marie Qu Nordby,
Alice Emilie Ekeberg Høva,
Frid Ragnhild Ifarnes Tandberg

Improving pulmonary function through exercise training in children with Cystic Fibrosis

BEV2900 - Spring 2021

Bachelor's project in Human Movement Science

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ABSTRACT

Background: Cystic fibrosis (CF) is a progressive autosomal-recessive hereditary disease affecting around 75 000 people worldwide. Recent studies show that exercise can have a positive effect on chronic respiratory disease. The purpose of this review is to investigate the use of exercise training (ET) interventions and its effect on improving pulmonary function in children with CF. **Methods:** Electronic databases such as PubMed and Google Scholar were searched with terms 'CF' and keywords related to 'exercise' and 'pulmonary function'. In terms of inclusion criteria, articles had to be 1) randomized control trials, a sample size consisting of 2) children between 0 - 18 years, with clinically diagnosed cystic fibrosis (non-specified degree of severity) and 3) a form of exercise training intervention. **Results:** Seven randomized controlled trails (RCT) met the inclusion criteria for review. Some of the studies showed slight improvements in pulmonary function, however, no significant changes were located. **Conclusion:** There are still uncertainties associated with the effects ET has on pulmonary function. ET seems to play a beneficial role when it comes to maintaining pulmonary function – future studies need to be conducted.

ABSTRAKT

Bakgrunn: Cystisk fibrose (CF) er en progressiv autosomal-recessiv arvelig sykdom som rammer omtrent 75 000 personer på verdensbasis. Tidligere forskning viser at trening kan ha en positiv effekt på lungesykdommer. Hensikten med denne litteraturstudien var å undersøke bevisene for bruken av ulike treningsintervensjoner for å forbedre lungefunksjonen hos barn med cystisk fibrose (CF). **Metode:** Litteratursøk ble gjort i de elektroniske databasene PubMed og Google Scholar med søkeord ´CF´ og nøkkelord relatert til ´trening´ og ´lungefunksjon´. I forhold til inklusjonskriterier måtte artiklene være 1) randomiserte kontrollerte studier, 2) bestå av et utvalg på barn mellom 0-18 år med klinisk diagnostisert cystisk fibrose (uspesifisert alvorlighetsgrad) og 3) en type treningsintervensjon. **Resultat:** Syv randomiserte kontrollerte studier møtte kvalifikasjonskriteriene for litteraturstudien. Enkelte av studiene viste en liten forbedring i lungefunksjon, men ingen signifikante endringer ble observert. **Konklusjon:** Det er fremdeles usikkerhet knyttet til hvilken effekt trening har på lungefunksjon. Treningsintervensjonene ser ut til å ha en viss effekt på opprettholdelsen av lungefunksjon – flere studier trengs på området.

1. INTRODUCTION

Cystic fibrosis (CF) is a progressive autosomal-recessive hereditary disease affecting around 75 000 people worldwide(1). It is classified as a chronic respiratory disease (CRD), together with chronic obstructive pulmonary disease (COPD), asthma and interstitial lung disease (2). CF is caused by mutations of the cystic fibrosis transmembrane conductance regulator gene (1). This defect results in atypical transport of chloride and bicarbonate across epithelia(3), causing excess mucus production in the lungs, liver, pancreas and reproductive organs. This induces impairment in nutrient absorption, the body´s ability to fight off bacterial infections, and perhaps most importantly, in pulmonary function (2).

The predominant part of morbidity and mortality in CF patients is to a large extent caused by pulmonary disease. In healthy individuals, homeostasis of the airway surface is adequate, enabling the transport of mucus effectively. In CF however, disease causes mucus to accumulate in the lungs, leading to compromised airway lumen, and also contributes to obstructive pulmonary disease. Other physiological defects, such as submucosal gland hyperplasia and thickened mucus secretions are common in CF (1). In children with CF, bronchial obstruction, weakness of respiratory muscles and inflammation in the pulmonary tissue are common – all of result in reduced exercise capacity and cardiorespiratory fitness (2).

Measures of pulmonary function are utilized for prediction of survival in patients with CF, and are also used as markers for disease severity (3). Two of the most common pulmonary tests are forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC). FEV_1 measures the maximum amount of forceful air that can be blown out of the lungs in one second. This measure is the most frequently used tool among physicians to determine the severity of the disease and for following the progression and changes in lung function. FVC, on the other hand, measures the amount of air forced out the lungs after maximal inhalation. This measure is often applied to evaluating lung function and the effectiveness of treatment. Both pulmonary tests are measured by spirometry, an instrument that measures pulmonary air flow (4).

Treatments for CF have gone through major improvements over the last decade. Some of the most renowned treatments are medication, chest physiotherapy, inspiratory muscle training (IMT) and nutrition. Chronic airway infection (a feature of bronchiectasis in people with CF),

is being treated with systemic and/or inhaled antibiotics that contribute to reduce the rate of decline in lung function. Chest physiotherapy is shown to improve clearance of increased airway secretions(5). IMT involves the training of muscles that act to expand the chest in order to take air into the lungs(6). Development of pancreatic enzyme replacement to compensate exocrine pancreatic insufficiency allows higher calories/ high fat diet and improvement in nutritional status(5). The result of interdisciplinary treatment, such as chest physiotherapy in combination with medication and exercise training (ET) seems to influence survival rate, which has increased for patients with CF in the last decades (7). ET is defined as a subset of physical activity that is planned, structured and repetitive and has a final or an intermediate objective of improvement or maintenance of physical fitness (8). There is no existing cure for CF, but ET has become a supplement in the treatment of the disease.

For patients with CF, ET can be used as a part of mucus mobilizing and loosen secretion to increase ventilation in all sections of the lungs and improve breathing, in addition to other treatments. Despite poor lung function, patients with CF can develop good physical capacity through exercise, affecting both survival, because of a slower decrease in lung function, and quality of life (QoL) (9). Evidence shows that ET of the peripheral skeletal muscle is beneficial for patients with CF. With improved oxidative capacity, carbon dioxide production decreases, which in turn reduces the need for breathing, the experience of dyspnea (heavy breathing or shortness of breath) and muscular fatigue(10,11). The different forms of exercise should vary for the different ages. At an early age (5 – 10 years old) ET should consist of motivating and fun activities, implementing various gymnastics and obstacles. After the age of 10, ET can include other forms of activity, such as circle training with different content. It is also recommended that the exercise consists of low- and high intensity training, e.g., as interval training. Scheduled breaks are required during exercise and activity to mobilize mucus, such as specific coughing techniques, or shock techniques and coughing. Activity and exercise should also include exercises for fitness, strength, and mobility, either simultaneously or separately(11).

Recent studies have shown that different types of ET interventions such as endurance training, resistance/ strength training, flexibility and stretching exercises, and Tai Chi have a positive effect on CRD. Flexibility and stretching exercises have helped patients with CRD to increase their work of breathing, which avoids postural impairment that can cause decline in pulmonary function (12). Lan C et al. found that Tai Chi improved pulmonary function and

exercise capacity in patients with COPD compared to standard treatments (13). Another study found that the implementation of aerobic and/ or anaerobic physical exercise training had positive effects on pulmonary function and health-related quality of life (14). Based on the obtained knowledge from the previous mentioned studies, ET can, to some degree contribute to the treatment of the disease. In addition, ET also seems to affect the progression of the disease, and to some extent delay the decline in bodily functions (e.g., pulmonary function). The purpose of this review is to investigate the use of ET interventions and its effect on improving pulmonary function in children with CF.

2. METHODS

The literature search was carried out using databases PubMed and Google Scholar. The search strategy consisting of the following keywords: (cystic fibrosis) AND (children) AND (exercise) OR (physical activity) AND (pulmonary function) AND (FEV_1) OR (FVC), this led to an initial 2613 results. The search was then limited to randomized controlled trials (RCT) studies only. Based on title, abstract and keywords, 219 articles were retrieved. In terms of inclusion criteria, articles had to be 1) randomized control trials, 2) include children between 0 - 18 years, with clinically diagnosed cystic fibrosis (non-specified degree of severity), 3) measure pulmonary function (FEV_1 and /or FVC), and 4) implement a form of exercise training intervention. In addition, all the articles had to be published in English and had to be conducted on humans. Of 219 retrieved articles, 19 were eligible based on the inclusion criteria. Articles were excluded if only physical activity was performed; and if the training interventions exclusively measured VO_{2peak}, were conducted on one sex, and solely used IMT or medical treatment. Based on these criteria, 14 were excluded from the remaining 19 articles. Two additional studies were retrieved from the Cochrane review; “Physical exercise training for cystic fibrosis”(14). The literature search resulted in seven original articles included for review.

3. RESULTS

Seven articles (2,6,15–19) were included for review, with a total number of 305 participants. Majority of the exercise interventions were supervised by health care professionals, with the exception of two studies (17,19)– where one had a semi-supervised intervention, and the other was unsupervised. Four interventions were performed in-hospital, while the remaining three were conducted at home or where the activity took place (e.g., football practice). Exercise

interventions consisted of different exercise modalities; aerobic, anaerobic and resistance ET (table 1). The studies also used different parameters to determine the effect of the interventions (table 2). Results indicate that ET seems to be beneficial, however, no significant changes were located.

Table 1: Characteristics of the included studies

Articles	IG:CG	M/F	Mean age (years) baseline	Exercise (IG)	Exercise (CG)
Sawyer et al. (15)	10:10	IG= 6/4 CG= 5/5	I= 11.46± 2.45 C= 9.86±2.57	Used a Handheld device w/ a spring tension device*, with a tension of 50-60 % of initial PI_{max}, 30 min/day seven days a week/10 weeks.	Completed the same intervention, at 10 % of initial $PI_{max.}$
Klijn et al. (16)	11:9	-	I= 13.6±1.3 C= 14.2±2.1	Trained two days/week for 12 weeks. Duration: 30- 45 min, it was encouraged to exercise at maximum speed. The training program consisted of eight basic training sessions, repeated every four weeks.	Continued normal daily activities as well as their physiotherapy regime
Santana-Sosa et al. (2012) (2)	11:11	IG= 6/5 CG= 7/4	I= 11±3 C= 10±2	Three times/week for eight weeks. Aerobic training for 20 – 40 min and 'active playing' for 15 min, three circuits of strength exercise (one set, 12 – 15 reps 20 sec duration – no rest between sets). Included chest physiotherapy	Maintaining usual levels of chest physiotherapy sessions
Santana-Sosa et al. (2014) (6)	10:10	IG = 6/4 CG = 6/4	I = 11± 1 C = 10 ± 1	Identical intervention as Santana-Sosa et al. (2012). Included IMT.	IMT
Orenstein et al. (17)	A= 25 S= 28	45%/55%	11.5	Three times/week for one year. A, exercised five min/ session, gradually increasing their exercise to 30 min/ session on a stair-stepping machine. HR 70% of HR_{max}. S, trained on a Nordic Power weight resistance machine to perform lifting exercise.**	No control group
Selvadurai et al. (18)	A=22 R=22 C=22	A = 9/13 R =10/12 C = 9/13	A = 13.2±2.0 R = 13.1±2.1 C = 13.2±2.0	A, had five 30 min sessions/ week on a nonmotorized treadmill at 70 % of HR_{peak}. R, preformed upper and lower limb exercise on a non-isokinetic resistance machine, 10 repetitions on a load 70 % of the prevailing load.	Chest physiotherapy
Schneiderman-Walker et al.(19)	30:35	IG=18/12 CG=20/15	IG=13.4 ± 3.9 CG=13.3 ± 3.6	20 min three times/week aerobic activity of choice- with self-reporting in a diary. In addition, usual schedule for physiotherapy and medication	Maintain regular physical activity, physiotherapy and medication.

IG = Intervention group, CG = Control group, M = Male and F = female, A = Aerobic, S = Strength, R = Resistance, IMT = inspiratory muscle training, HR = heart rate, HR_{peak} = peak heart rate, PI_{max}= maximal inspiratory mouth pressure
* Resistance was increased weekly as long as the child could tolerate it, while taking full breaths for the entire 30 min.
** Number of sets and reps were tailored individually and increased while keeping a HR <55% of HR_{max} (maximum HR)

Table 2: Measures (FEV_1 and FVC) for the included studies

Articles	Interventions	IG		CG		IG		CG	
		FEV_1 (pre)	FEV_1 (post)	FEV_1 (pre)	FEV_1 (post)	FVC (pre)	FVC (post)	FVC (pre)	FVC (post)
Sawyer et al. (15)	IMT (with aerobic measures)	1.71±0.81	1.96±0.86	1.52±0.49	1.41±0.63	-	-	-	-
Klijn et al. (16)	Anaerobic	75.2 ±20.7	-	82.1±19.1	-	-	-	-	-
Santana-Sosa et al. (2012) (2)	Combination of aerobic and strength	1.87±0.24	1.94 ±0.23	1.77 ±0.17	1.87 ±0.15	2.41 ±0.24	2.49 ±0.25	2.29 ±0.19	2.36 ±0.20
Santana-Sosa et al. (2014) (6)	Combination of aerobic, strength and IMT	1.65±0.19	1.74±0.23	1.57±0.26	1.55±0.26	2.23±0.27	2.34±0.29	1.90±0.33	1.85±0.32
Orenstein et al. (17)	Aerobic and strength	A = 91.51±18.34 S = 91.18± 18.07	A = 90.32± 17.92 S = 90.29± 15.82	-	-	-	-	-	-
Selvadurai et al. (18)	Aerobic and resistance	A =56.8±17.9 * R =58.0±16.8	A =6.54± 7.76 R =10.09 ±7.43	57.4±17.3	4.51±6.90	A =70.54 ±17.2 R =73.2± 18.1	A =2.34± 4.62 R =2.45± 4.18	72.7±17.5	2.28±4.22
Schneiderman-Walker et al. (19)	Aerobic	89.2 ±19.5	-1.46 ±3.55	87.9±17.8	-3.47 ±4.93	92.6±15.7	-0.25 ±2.81	90.1 ±12.9	-2.42 ±4.15

Sawyer et al. reported FEV_1/FVC ratio, not included in the table.

Primary outcomes of the included interventions in this review are reported as pulmonary function measures. The following pulmonary function measures were used; FEV_1 and FVC by pre- and posttest (table 2) to make comparisons across the studies. Secondary outcomes were aerobic fitness by change in VO_{2peak}, and QoL measured by two different disease-specific CF questionnaires.

3.1 Primary outcomes: Pulmonary function

FEV_1 and FVC were the most reported measures of pulmonary function (table 2). Most of the studies reported percent change in FEV_1% and/ or FVC, with the exception of two studies that recorded FEV_1 in $L{\cdot}s^{-1}$ or *L/s*. These studies also reported FVC in L and L/min(2,6). Sawyer et al. reported their findings with the FEV_1/FVC ratio (15).

3.1.1 Aerobic

Three studies (17–19)examined the effect of aerobic fitness on pulmonary function. Only one of these studies (17) did not include control group or the measurements of FVC. They all showed a slight decrease in FEV_1 in both groups; however, the control group had a larger decline than the intervention group. The same results occurred in Schneiderman-Walker et al. for FVC, while Selvadurai reported a slight increase from baseline similar to measures obtained in the control group(18,19). The results in table 1 and 2 acknowledge that a short-term aerobic intervention leads to an increase in pulmonary function, this was not found in the long-term interventions.

3.1.2 Strength/Resistance

There is discrepancy amongst the results for strength training and its effect on pulmonary function. Orenstein et al. (17) recorded a slight decrease for FEV_1, while Selvadurai et al. (18) recorded a higher increase in the strength group than the control group for both measures. Both Santana-Sosa et al. (2,6) interventions investigated the combination of strength training and aerobic fitness, and recorder a higher increase in both measures for the intervention group. The combination of strength and aerobic exercise has been shown to have a significant, training-induced increase in pulmonary function. One study reported the opposite (17). Table 2 show an increase of FVC in the control group for two of the combinational interventions. Both of these control groups practiced chest physical therapy during the intervention.

3.2.3 Anaerobic

Only one study investigated the effects of anaerobic ET on children with CF. Klijn et al. (16) looked at the effect anaerobic training could have on both aerobic and anaerobic measures, as well as secondary measures such as FEV_1 of pulmonary function. There were no findings of any significant changes in FEV_1 after the study ended, and therefore did not include posttest measurements in their study.

3.2 Secondary outcomes

3.2.1 Cardiorespiratory fitness

Studies also investigated the effect on VO_{2peak}. Selvadurai et al. (18) reported significant improvements in VO_{2peak} for the aerobic group (21.64 %). The aerobic group also continued to improve their aerobic fitness after discharge. In Klijn et al. (16) the intervention group reported significant improvements in VO_{2peak} (5.2 mL/ min and 5.7% predicted), while the control group showed a significant decrease for VO_{2peak} (-1.5%). In Orenstein et al. (17), VO_{2peak} decreased during the first 6 months, and then increased slightly from 6 months to 12 months. Both Santana-Sosa et al. studies (2,6) assessed VO_{2peak} as one of their primary outcomes. In Santana- Sosa et al. (2012) VO_{2peak} increased significantly with training in the intervention group compared with baseline levels, no significant changes were found in the control group(2). A similar manner were seen in Santana-Sosa et al. (2014)(6).

3.2.2 Quality of life

Quality of life were determined with disease-specific CF questionnaire. Both Santana-Sosa et al. studies (2,6) used a Spanish version of the CF questionnaire Revised (CFO-R) in their assessment of QoL. The Spanish CFO-R was completed differently within the age groups, ranging from; interview for the youngest participants, to completion in writing by themselves. The oldest participants used an age-specific form of the questionnaire, and a parent version was also completed for children over the age of 13. Klijn et al. (16) specified a health related QoL and used the CF questionnaire (CFQ). The CFQ considered the different developmental stages, making it possible to monitor the health status and QoL for CF patients (age six and up).

Klijn et al. (16) reported a significantly higher score in the domain of physical function in the intervention group (70.3±13.8 vs. 88.4±9.0, respectively; $p < 0.001$). No changes were found in the control group or in any other QoL domains. In Santana- Sosa (2012) and (2014), no significant differences in QoL were found in the post- vs. the pre- version of the QoL-questionnaire between the intervention group and control group(2,6). A significant improvement was however found for participants in the intervention group in Santana- Sosa (2012)(2), both studies reported no training induced improvement of QoL, indicating that QoL was not affected by the training intervention.

4. DISCUSSION

To which extent ET affects improvement in pulmonary function cannot yet be established for children with CF. All included studies showed that the intervention group had a greater improvement and maintained a better pulmonary function than the control group. Even though some studies detected a decline in pulmonary function, the intervention group had a lesser decline than the control group.

4.1 Possible risks and considerations concerning ET and testing

Several studies from this review indicate that ET can slow down the decrease in lung function, which can contribute to an increase in physical fitness and QoL (2,19). CF is also, as mentioned, associated with poor pulmonary function resulting in a lower exercise capacity. The changes in pathology for CF patients, also known as advanced lung disease, result in increased dead space ventilation and dynamic hyperinflation, exercise-induced ventilation-perfusion abnormalities, arterial desaturation, and alveolar hypoventilation during exercise. The ventilatory and muscular demands of exercise is therefore constrained for patients with CF. Other risks associated with ET for patients with CF is impairment of the skeletal muscle(20).

In terms of testing this specific study population, Gulmans et al. acknowledge several factors that can be challenging. Their study accentuates that children are under continuous development, resulting in changes in lung function, rate of progression of the disease, and physical growth(21). On the other hand, both Orenstein et al. (17) and Selvadurai et al.(18) emphasize the importance of testing on children with CF. For instance, to assess the severity of the illness, in addition to other important information such as cardiorespiratory status and QoL(18). Exercise capacity testing among patients with CF are also good predictors for functional status, as well as a good estimate of survival (22), and should therefore be implemented. All the interventions included in this review were approved by an ethics committee to ensure the safety and well-being of the participants.

Even though exercise causes potential risks for patients with CF, it still seems to work beneficially in terms of preventing the known decline and deterioration of the lungs – which can postpone the need for invasive operations. ET can also have positive effects on social aspects such as higher self-esteem and well-being, as well as bodily functions (mucus clearing, and strength in respiratory muscles), that in return will make the patients more

equipped in terms of independence. It is generally recommended that patients with CF follow the guidelines set for physical activity and ET. Having said that, they are pre-disposed to chronic bacterial infections, that may lead to more severe respiratory viral infections (23). Santana-Sosa et al. (2012) were one of several studies in this review that conducted the ET with only one supervisor and one subject to minimize the risk of infection(2).

4.2 Exercise intervention

Results from the aerobic interventions showed a slight increase in pulmonary function parameters (FEV_1 and FVC). Orenstein et al. (17) performed three separate measurements of FEV_1 during the intervention period, showing a slight decrease the first six months. During the following months FEV_1 increased, indicating that the duration of the intervention may play an essential role. In Schneiderman- Walker et al.(19) the intervention and control group had a slight decline in both parameters. Then again, the decline was still smaller in the intervention group, suggesting that the aerobic exercise may have had an effect. In contrast, Selvadurai et al. (18) reported a slight increase in both parameters. Increases in the aerobic group from baseline were similar to the results obtained in the control group, indicating that supplementary treatment is more likely the cause of improvement. Nevertheless, the exercise in this group caused other improvements, related to VO_{2peak}, QoL and activity levels in general.

For studies combining strength- and aerobic exercise, two showed significant training-induced results of pulmonary function increase (18,19). However, the results in Selvadurai et al. (18) were only recorded in the daily activity levels of a subgroup one month after discharge. Because this was just a small portion of the intervention group, especially the aerobic group, it is not certain that it can be representative for the whole group. Other studies reported the opposite (2,16,17). In terms of strength training alone, Orenstein et al. (17) showed a slight decrease in FEV_1. Selvadurai et al. (18) reported a significant increase in FEV_1 in the intervention group compared to the control group, indicating exercise was of importance. Even though a slight increase in FVC were recorded, it was not of significance. This may indicate that strength training alone is not directly correlated to an increase in pulmonary function. However, changes in muscle strength were found – suggesting that it may still be of importance, especially in regard to bronchial drainage and expectoration of sputum(18).Only one study, performed by Klijn et al. (16) conducted an anaerobic intervention program, showing improvement in both anaerobic and aerobic outcome

parameters. Among these, VO_{2peak} had significant improvement in the intervention group, but no significant results were found in terms of pulmonary function, which was also the case for the rest of the included studies.

Based on the findings in this review, exercise seem to have a greater influence on cardiorespiratory fitness, rather than pulmonary function. A study conducted by Pianosi et al. (24) suggests that measures of FEV_1 does not comprehend the entirety of the functional assessment, instead this can be delivered by measurements of VO_{2peak}. FVC also partake in assessing the effectiveness of treatment, yet it is excluded from several of the included studies. On the basis of this, it is conceivable that more studies would benefit from measuring FVC. Evidence has also shown that QoL correlates better with changes in VO_{2peak} than changes in pulmonary function. Still, changes in pulmonary function may contribute to a small change in QoL. Exercise tests in children with CF is there for needed to reflect the overall impact of the disease on the patients QoL(17,18).

4.3 Location and supervision

Four studies completed interventions in-hospital and the remaining three were completed at home. A home- based intervention can be useful for this patient group, in the way that it may create a safe and active environment and promote patterns of physical activity. However, this is not appliable for all patient groups, as severity of the disease may vary. The home-based interventions (15,17,19) were either unsupervised or semi-supervised by parents or healthcare professionals. In contrast to the reviewed home-based interventions, all the in- hospital interventions were supervised. Supervised interventions are presumably motivating for high compliance, and also allow closely monitoring of the patients (19). Even so, the home-based interventions who reported compliance also had a relatively high compliance, maybe because they used different strategies for ensuring it. This was the case for Schneiderman-Walker et al(19). This resulted in a significant protective effect on the decline of FVC. Orenstein et al. (17) on the other hand, observed a low compliance with no change in pulmonary function. The in-hospital interventions also have disadvantages. For instance, they can lead to invalid results for the control group, caused by the deconditioning effect of inactivity and bedrest. Selvadurai et al. (18) detected this effect where their control group had a slight reduction from baseline measures but improved over the one month after hospital discharge. A significant improvement in lung function was also the case, for the intervention group (18). For studies

with longer duration a supervised exercise intervention seems to be beneficial, on the evidence of less compliance and a higher validity.

4.4 Short term vs. long term intervention

Previous research has suggested that pulmonary function decline can be affected by short-term supervised training programs. This was indicated on behalf of the changes in FEV_1 and FVC. Most of the studies included in this review only investigated the short-term effects that ET had on pulmonary function. In later years investigators at The Hospital for Sick Children found that a 2-year study period is required to detect long-term changes in pulmonary function, for mild to moderate impaired patients with CF(25). In a long-term study, patients are able to overcome or at least attenuate the declining effect that CF has on lung volumes (6,18). This corresponds with the findings in this review. Neither of the interventions (short-term or long-term) showed any significant differences in pulmonal function. Although, Schneiderman-Walker et al. (19) found in their long-term study that ET might help the decrease in pulmonary function over time. There is no clear agreement to which study length gives the best results on changes in pulmonary function, further studies should be conducted.

4.5 methodological limitations

The implementation of ET as an additional supplement in CF treatment is relatively new, which may be why there are limitations in CF related research. A reoccurring challenge related to this review was the comparison of results, due to the different and in some cases missing measurements of pulmonary function – Klijn et al. (16) did not include values for FEV_1 and FVC after the intervention, and Sawyer et al. (15) only measured FVC in ratio to FEV_1 at the pre- and post-intervention testing. The task of the control groups varied between maintaining regular physical activity and/or only perform physiotherapy (table 1), this can make it difficult to determine if actives conducted by the controls could influence the insignificant increase in pulmonary function for the intervention groups. Time spent in sedentary is thought to increase for those who were in-hospital compared with those who conducted the interventions at home. This can be problematic in terms of the total time in activity, which can be a contributing factor to the increase in pulmonary function. It is also worth mentioning that most of the studies included, used pulmonary function as an additional measure combined with other aspects of the disease – such as malnourishment, QoL, and not as their only measurement.

Variation in sample size, exercise modalities, duration and pulmonary function measures can cause systematic and/or random errors of the study design. A way to reduce random errors is to increase the sample size. However, there are some challenges connected to the severity and progression of the disease, that can make it difficult to increase this study population. As mentioned, variation in duration makes it difficult to conclude the long-term effects of exercise on pulmonary function, only two studies in this review excided an intervention period over 12 months(17,19). Several studies also included combination of different exercise modalities, making it difficult to determine what kind of exercise contributes to an increase in pulmonary function (2,6,18). In terms of IMT, there are limited specification on how it was preformed, this makes it difficult interpret in which way it increased/maintained pulmonary function in addition to other treatment. QoL was measured using different questionnaires, but it is not included in all the studies.

5. CONCLUSION

There are still uncertainties associated with the effects of ET on pulmonary function. Based on the findings in this review, ET seems to play a beneficial role when it comes to maintaining pulmonary function – although none of the included studies recorded any significant improvement. This can be due to methodological limitations of the study design, as mentioned earlier. Articles of this review found that short-term ET interventions can contribute to a greater pulmonary function. Future studies should include a larger sample-size, longer duration of the intervention including a longer follow-up time – to better evaluate the long-term effects ET has on pulmonary function.

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