

## Original Article

# The Beneficial Effects of Breathing and Relaxation Exercises on Psychological Status, Sleep, and Quality of Life in Children and Caregivers of Children with Cystic Fibrosis

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### Abstract

**Purpose:** Cystic fibrosis causes high levels of anxiety and depression. Breathing and Relaxation Exercises effectively manage stress in chronic diseases; however, there are no studies on cystic fibrosis. We aimed to investigate changes in children's quality of life, sleep status, and their parents' quality of life and psychological level after exercise. **Methods:** The same psychologist performed exercises for children (n:68) and their families. Cystic Fibrosis Questionnaire-Revised Child and Sleep Questionnaire were administered to the children at baseline and after three months and the Cystic Fibrosis Questionnaire-Revised Parents and other psychological questionnaires were also used for caregivers. **Findings:** There was a significant improvement in depression, anxiety, sleep, and life satisfaction scale scores before and after exercise ( $p<0.05$ ). **Conclusions:** Breathing and relaxation exercises may help to improve depression, anxiety, life satisfaction, and sleep scales for parents of children with cystic fibrosis.

### Key words

Anxiety; Breathing and relaxation exercises; Cystic fibrosis; Depression; Quality of life

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### Introduction

Children with cystic fibrosis (CF) experience recurrent respiratory tract infections, digestion problems, and complex and time-consuming treatment regimens including airway clearance techniques. All these give rise to high distress and numerous psychosocial difficulties in patients decreasing the health-related quality of life (HRQoL) of patients and their caregivers.<sup>1-3</sup>

In addition to the difficulties experienced by the patients, both the emotional stress and sadness of having a child with a chronic disease and the financial burden are additional difficulties for parents. Therefore, it has been determined that parents are at high risk for the development of psychological symptoms and decreased quality of life (QoL).<sup>4</sup> Moreover, most studies examining the impact of CF on parents have found an increased risk for psychological distress and depressive symptoms.<sup>4-6</sup>

Despite remarkable improvements in the management of CF, a higher prevalence of depression and anxiety has been reported in children with CF and their caregivers. An increased frequency of depression and anxiety symptoms has also been reported at our centre.<sup>6</sup> While there are

numerous trials studying the management of mental health issues in patients with CF, only a few include their parents.<sup>7</sup>

Relaxation strategies, such as deep breathing, meditation, and progressive muscle relaxation, have been shown to be effective in stress management in healthy populations and in patients with anxiety and depression.<sup>8,9</sup> Some of these techniques have been studied to improve the HRQoL of children and adults with chronic conditions, including respiratory diseases such as chronic obstructive pulmonary disease and asthma. A randomised controlled study investigating the effect of Buteyko breathing exercises in adults and children with asthma revealed improved QoL scores at three months in the intervention group.<sup>10</sup> Another randomised controlled study showed that breathing exercises decreased anxiety levels and improved sleep quality in mothers of children with special healthcare needs.<sup>11</sup> In addition, during the COVID-19 pandemic, it has become more common to perform these exercises online.<sup>8,9</sup> To the best of our knowledge, no published studies have investigated the effects of breathing and relaxation exercises in children with CF and their caregivers.

In this study, we investigated the effects of breathing and relaxation exercises on the HRQoL and sleep quality of children with CF, as well as on the anxiety and depression levels, sleep quality, and life satisfaction of their parents.

## Materials and Methods

This prospective, single-centre, cohort study was conducted at the Marmara University CF Center between January and May 2021. The aim of the study was explained to the patients and their parents, and all the participants provided written informed consent.

### 1. Intervention

A total of 172 patients, aged 3-12, who were followed up at our centre with a definite diagnosis of CF, were eligible for the study. Invitations were sent to these patients and their parents to participate in the online breathing and relaxation training. Sixty-eight patients and their parents, who had no Internet access problems and who reported that they had time to attend regularly, were included in the study. The participants and their parents were asked to participate in a 12-session online breathing and relaxation training program provided by a designated psychologist. Exclusion criteria were determined according to patient

participation, participation in less than six sessions, and exclusion of parents from the study. Pre-tests were performed on the day of the first session prior to training, and post-tests were performed one week after the 12th training session. The diagram (Figure 1) shows the reasons for withdrawal and the children-parent questionnaires.

The sessions for patients and their parents were conducted separately. Patients and their parents were trained to practice breathing and relaxation techniques according to their age group. Multiple breathing exercises, activities, and relaxation games were taught and practiced during the sessions. Deep breathing exercises and relaxation techniques, such as guided imagery or autogenic training, are provided to parents.<sup>12</sup> The duration of each session was one hour per week. On days without sessions, patients and their parents were encouraged to practice the learned techniques on a daily basis. At the beginning of each session, the participants were asked whether they had performed the exercises in the previous week. An objective scale was not used to assess adherence.

## 2. Measures

This study aimed to evaluate the changes in HRQoL and sleep quality of children with CF as well as the QoL, anxiety, and depressive symptoms of their parents. Assessments were conducted before and after the intervention using the 9-item Patient Health Questionnaire Depression Scale (PHQ-9), 7-Item Generalised Anxiety Disorder Scale (GAD-7), Paediatric QoL Inventory (PedsQL), Cystic Fibrosis Questionnaire-Revised (CFQ-R), Paediatric Sleep Questionnaire (PSQ), Pittsburgh Sleep Quality Index (PSQI), and Adult Life Satisfaction Scale (ALSS).

**2.1. Cystic Fibrosis Questionnaire-Revised (CFQ-R):** The CFQ-R is designed to evaluate the impact on overall health, daily life, perceived well-being, and symptoms of patients with CF.<sup>13</sup> Two validated Turkish versions of the CFQ-R were used in our study to assess the HRQoL of children aged 6-13 years, one completed by the child and the other by the parent (CFQ Child and CFQ-Parent, respectively).<sup>14</sup>

**2.2. Paediatric Quality of Life Inventory (PedsQL):** Varni et al developed the Paediatric QoL Inventory 4.0 (PedsQL), a generic measure for assessing HRQoL in 2- to 18-year-old.<sup>15</sup> This study used the validated Turkish version of the PedsQL to assess HRQoL in children aged to 2-5 years.<sup>16</sup>

**2.3. Paediatric Sleep Questionnaire (PSQ):** The PSQ, developed and approved by Chervin et al, is a 22-item

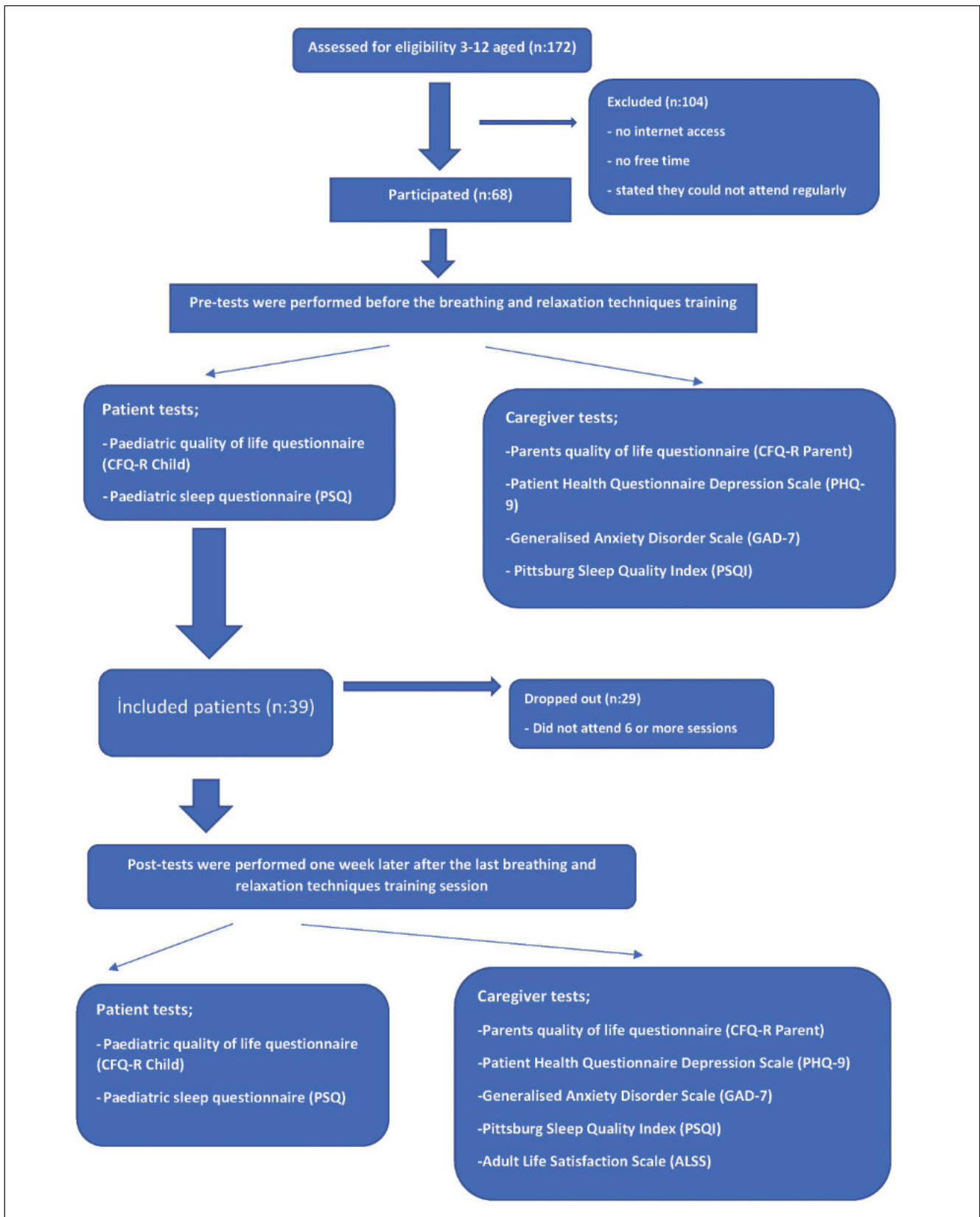


Figure 1. The diagram of withdrawal and recruitment.

questionnaire that was shown to have 81% sensitivity and 87% specificity when a cut-off value of 0.33 was taken for sleep-related respiratory disorders.<sup>17,18</sup>

**2.4. 9-Item Patient Health Questionnaire Depression Scale (PHQ-9):** The PHQ-9 is composed nine depressive symptom items listed in the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV) for depression. Patients were asked to rate the extent of their symptoms that had bothered them during the previous 2 weeks using a 4-point Likert rating scale. The PHQ-9 severity score ranges from 0 to 27. The score ranges for depressive symptom severity in the PHQ-9 were as follows: no symptoms (1-4), mild (5-9), moderate (10-15), and severe (15+) symptoms.<sup>19</sup>

**2.5. 7-Item Generalised Anxiety Disorder Scale (GAD-7):** The GAD-7 is a tool to assess generalised anxiety disorder and comprises seven items representing the DSM-IV symptom criteria for GAD (e.g., "Feeling nervous, anxious or on edge"). Patients were asked to indicate how often, during the last two weeks, they were bothered by each symptom using a 4-point Likert-type rating scale. The GAD-7 severity scores ranged from 0 to 21 (20). The scores for anxiety symptom severity in the GAD-7 results were as follows: no symptoms (1-4), mild (5-9), moderate (10-15), and severe (15+) symptoms.<sup>20</sup>

**2.6. Pittsburgh Sleep Quality Index (PSQI):** The PSQI is a self-rated questionnaire that assesses sleep quality and disturbances over a 1-month time interval.<sup>21</sup>

**2.7. Adult Life Satisfaction Scale (ALSS):** The ALSS consists of 21 items 5-point Likert rating scale measuring the life satisfaction of adults. It was developed for the Turkish population by Kaba et al.<sup>22</sup> The ALSS score ranges from 21 to 105, with higher scores indicating better life satisfaction.

### 3. Statistical Analysis

Statistical analysis was conducted using the IBM® SPSS® Statistics Version 20 software package. For descriptive analysis, normally distributed data are expressed as mean ± SD, while non-normally distributed data are expressed as medians (interquartile range [IQR]). For pre- and post-test comparisons, the paired sample T-test and Wilcoxon signed-rank test were used for normally and nonnormally distributed data, respectively. Statistical significance was set at  $p < 0.05$ .

### 4. Ethical Approval

The Marmara University Medical Faculty Research Ethics Committee approved this study (protocol number 09.2021.669).

## Results

Sixty-eight children and their parents participated in the study, with 39 children completing six or more sessions. The mean age was  $7.7 \pm 2.4$  years, with 46.2% being male. Table 1 displays the clinical characteristics of the participants, 71.8% of whom had pancreatic insufficiency and 2.6% had CF-related diabetes mellitus. None of the participants was taking CFTR modulators or had a history of allergic bronchopulmonary aspergillosis, haemoptysis, or pneumothorax. In the past year, 17.9% of the patients were hospitalised and 69.2% had pulmonary exacerbations.

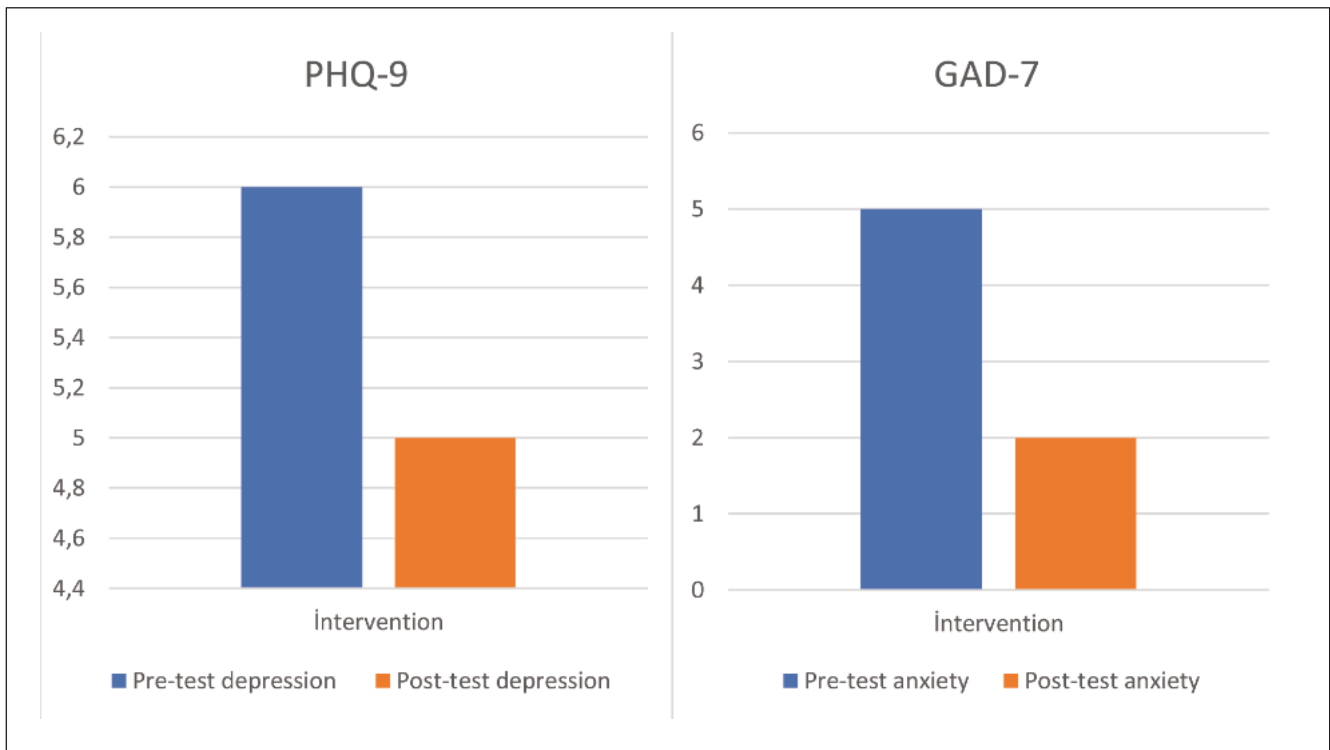
### Anxiety & Depression Symptoms in Parents of Children with CF (GAD-7 and PHQ-9) (n=39)

The GAD-7 median scores decreased significantly from 5 (3-9) to 2 (1-6),  $p = 0.001$  (Table 2). At baseline, 48.7% of parents (n=19) had no anxiety symptoms, 28.2% (n=11) had mild anxiety, 12.8% (n=5) had moderate anxiety, and 10.3% (n=4) had severe anxiety. The

**Table 1** Demographic information and medical data of patients

Age (month), mean (SD)	92.5 (29.9)
Male, n (%)	18.0 (46.2%)
Age of diagnosis (month), median (25-75p)	3.0 (2.0-7.0)
FEV1, mean (SD)	94.6 (13.6)
FEV1<80, n (%)	4.0 (10.2)
DeltaF508 homozygous, n (%)	5.0 (12.0)
DeltaF508 heterozygous, n (%)	12.0 (30.0)
Age group	<b>n (%)</b>
36-59 month	5.0 (12.8)
60-72 month	6.0 (15.4)
73-149 month	28.0 (71.8)
Mother's education level	<b>n (%)</b>
Primary school	8.0 (20.5)
Secondary school	6.0 (15.4)
High school	12.0 (30.8)
University	13.0 (33.3)
Father's education level	<b>n (%)</b>
Primary school	7.0 (17.9)
Secondary school	2.0 (5.1)
High school	14.0 (35.9)
University	16.0 (41.1)

FEV1=forced expiratory volume in 1 sec



**Figure 2.** Depression and anxiety scores of parents pre-post breathing and relaxation exercises

**Table 2** Pre and post-test comparison results of parent's PHQ-9, GAD-7, PSQI and ALSS questionnaires

	Pre-test	Post-test	p
<b>Family PHQ-9, median (25-75p)</b>	6.0 (3.0-10.0)	5.0 (2.0-8.0)	<b>0.026*</b>
No symptom, n (%)	15.0 (38.5)	18.0 (46.2)	0.467
Mild, n (%)	13.0 (33.3)	14.0 (35.9)	0.819
Moderate, n (%)	6.0 (15.4)	6.0 (15.4)	1.000
Severe, n (%)	5.0 (12.8)	1.0 (2.6)	<b>0.046*</b>
<b>Family GAD-7, median (25-75p)</b>	5.0 (3.0-9.0)	2.0 (1.0-6.0)	<b>0.001*</b>
No symptom, n (%)	19.0 (48.7)	26.0 (66.7)	0.052
Mild, n (%)	11.0 (28.2)	9.0 (23.1)	0.480
Moderate, n (%)	5.0 (12.8)	3.0 (7.7)	0.317
Severe, n (%)	4.0 (10.3)	1.0 (2.6)	0.083
<b>PSQI, median (25-75p)</b>	6.0 (3.0-8.0)	4.0 (3.0-6.0)	<b>0.041*</b>
<b>ALSS, mean (SD)</b>	69.5 (11.2)	74.0 (10.2)	<b>0.000*</b>

PHQ-9: 9-item Patient Health Questionnaire; GAD-7: 7-item General Anxiety Disorder ; PSQI: Pittsburgh Sleep Quality Index; ALSS: Adult Life Satisfaction Scale

\*p<0.05

moderate-to-severe anxiety rate decreased to 10.3% after the intervention. Depression symptoms also showed a significant decrease, with median PHQ-9 scores decreasing from 6 (3-10) to 5 (2-8),  $p=0.026$ ). At baseline, 38.5% of parents ( $n=15$ ) had no depression symptoms, 33.3% ( $n=13$ ) had mild depression, 15.4% ( $n=6$ ) had moderate depression, and 12.8% ( $n=5$ ) had severe depression. The moderate-to-severe depression rate decreased to 18.1% after intervention.

Baseline PHQ-9 scores showed that 38.5% of parents had no symptoms of depression, 33.3% had mild depression, 15.4% had moderate depression, and 12.8% had severe depression. The prevalence of moderate-to-severe depressive symptoms decreased from 28.2% to 18.1%. Figure 2 displays the depression and anxiety scores of parents before and after the breathing and relaxation interventions.

### **Sleep Quality and Life Satisfaction of Parents of Children with CF (n=39)**

Data analysis showed a statistically significant improvement in PSQI and ALSS scores ( $p<0.05$ ) (Table 2).

### **HRQoL of Children with CF**

Patients aged 6-12 years and their parents completed the CFQ-R Child and CFQ-R Parents, respectively ( $n=28$ ). The CFQ-R Child showed significant improvements in

eating disturbances and digestive symptoms after the intervention, whereas CFQ-R Parent showed significant increases in vitality and digestive symptoms. Baseline and post-intervention scores are presented in Table 3.

Mothers of children with CF aged 2-5 years completed the PedsQL questionnaire for toddlers (2-4 years) and young children (5-7 years) ( $n=11$ ). No statistically significant difference was found in the PedsQL pre- and post-intervention scores in this age group.

### **Sleep Quality of Children with CF (n=39)**

There was not any significant difference pre- and post-intervention as the baseline score was  $0.24\pm 0.1$  and post  $0.22\pm 0.13$ ,  $p=0.214$ .

## **Discussion**

The present study revealed that breathing and relaxation training was associated with a significant decrease in anxiety (GAD-7 scores) and depression (PHQ-9 scores) and significant improvement in sleep quality (PSQI) and life satisfaction (ALSS scores) in parents. However, the CFQ-R Child and CFQ-R Parent results showed improvement in only a limited number of domains, and there was no change in the sleep quality of the children.

**Table 3** Results of CFQ-R parent and CFQ-R child questionnaires

	CFQ-R parent (families with children aged 6-12 years) (n=28)			CFQ-R child (6-12 years) (n=28)		
	Pre	Post	p-value	Pre	Post	p-value
	Physical functioning <sup>1</sup>	85.4 (59.4-95.8)	81.2 (68.7-98.9)	0.932	78.5 (66.7-93)	83.3 (73.6-94.4)
Emotional functioning <sup>1</sup>	80 (66.7-91.7)	86.7 (68.3-98.3)	0.238	78.7 (13.9)	86 (13.2)	0.454
Vitality <sup>2</sup>	69.4 (17.6)	78.1 (16.8)	<b>0.038*</b>	NA	NA	NA
School functioning <sup>1</sup>	75 (60.4-83.3)	75 (60.4-91.7)	0.656	NA	NA	NA
Eating disturbances <sup>1</sup>	66.7 (50-100)	100 (37.5-100)	0.683	66.7 (38.9-100)	88.9 (58.3-100)	<b>0.035*</b>
Treatment burden <sup>1</sup>	55.6 (33.3-77.8)	55.5 (33.3-83.3)	0.549	72.2 (18.8)	74.2 (20.1)	0.592
Body image <sup>1</sup>	88.9 (77.8-100)	100 (77.8-100)	0.529	88.9 (80.5-100)	100 (77.8-100)	0.591
Health perception <sup>2</sup>	72.6 (19.5)	76.9 (16.8)	0.156	NA	NA	NA
Weight <sup>1</sup>	100 (33.3-100)	100 (33.3-100)	0.656	NA	NA	NA
Respiratory symptoms <sup>1</sup>	88.9 (79.2-100)	88.9 (66.7-94.4)	0.353	87.4 (83.3-98.61)	87.5 (75-100)	0.875
Digestive symptoms <sup>1</sup>	88.9 (77.8-100)	100 (88.9-100)	<b>0.035*</b>	66.7 (66.7-100)	100 (100-100)	<b>0.003*</b>
Social functioning	NA	NA	NA	47.6 (33.3-60.1)	47.6 (42.8-60.7)	0.354

<sup>1</sup>Median (25-75p); <sup>2</sup> Mean (SD); \* $p<0.05$

The Studies have shown increased symptoms of anxiety and depression in parents of children with CF compared with the normal population.<sup>6,23</sup> Additionally, psychological symptoms in both children and their caregivers were correlated with reduced lung function, poor compliance to medical treatments, low QoL, frequent hospital admissions, and increased health expenses.<sup>24</sup> These findings illustrate the importance of evaluating depression, anxiety, and other psychological issues among children with CF and their caregivers. International Committee on Mental Health in CF recommends annual screening for depression and anxiety using the PHQ-9 and GAD-7 in children (over 12 years of age and adulthood) and at least one of their caregivers.<sup>24</sup> While numerous trials have studied the management of mental health issues in children with CF, there are only a few for their parents.<sup>7</sup> Fidika et al evaluated the effects of web-based cognitive-behavioral writing therapy on QoL, anxiety, and depression in 23 caregivers of children with CF. The results showed a significant decrease in anxiety and depression symptoms.<sup>25</sup> In another study by Graziano et al, 14 caregivers had a four-session of online cognitive behavioural therapy. The pre- and post-test results showed improvements in stress, anxiety, and depressive symptoms.<sup>9</sup> The current study illustrated significant improvements in the symptoms of anxiety, depression, and sleep quality of parents after breathing and relaxation sessions. These techniques may be considered as interventions to reduce anxiety and depression symptoms in parents of children with CF.

Chronic diseases not only have an impact on patients' sleep quality, but can also affect caregivers. Low sleep quality may be one of the reasons for depression in caregivers. A limited number of studies have investigated sleep quality in parents of children with chronic disorders.<sup>26</sup> Yilmaz et al investigated the sleep quality and anxiety in mothers of children with asthma and CF. They reported higher anxiety levels and lower sleep quality in both asthma and CF groups than in the control.<sup>27</sup> Similarly, Safa et al reported higher anxiety and depression symptoms, and worse sleep quality in mothers of children with CF and asthma.<sup>28</sup> Data on the management of sleep disturbances in the parents of children with CF are scarce. Carr et al studied the effects of Thai Chi exercise on QoL, sleep quality, mindfulness, and health status. In contrast to our study, there were no differences in sleep and QoL before and after the intervention in their study.<sup>29</sup> Our data show that breathing and relaxation techniques improve sleep quality in parents of children with CF. These

techniques may be used to improve sleep quality and to manage sleep problems in this population.

Increased anxiety and depression symptoms in parents of children with chronic diseases have a negative impact on their expectations and hopes in life. Life satisfaction questionnaires measured the content of the participants' lives.<sup>4</sup> Parents of children with CF have lower life satisfaction than parents of the normal population.<sup>4</sup> Limited research has been conducted on the measurement and improvement of life satisfaction in this population. Similar to our study, Graziano et al showed improvements in the life satisfaction of caregivers of children with CF after cognitive behavioural therapy.<sup>9</sup> The present study results showed significant improvements in the life satisfaction scores of parents after breathing and relaxation exercise training. Breathing and relaxation training may improve life satisfaction in addition to psychological symptoms such as anxiety and depression.

Parents of chronically ill children report significantly lower HRQoL and are at a higher risk of psychosocial problems, which may have a negative impact on treatment compliance.<sup>30</sup> Few studies have examined the impact of various exercise interventions on the QoL of parents and children with CF. A study by Carr et al evaluating the effects of Tai Chi exercises in individuals with CF did not find any difference in HRQoL parameters nine months post-intervention.<sup>29</sup> A study by Prem et al evaluating the effects of Buteyko and Pranayama breathing techniques showed improvements in HRQoL with 1-hour training sessions for 3-5 days and instructed to practice the exercises for 15 minutes twice daily for three months duration.<sup>31</sup> Another study evaluating the effects of two months of yoga training on pulmonary function and HRQoL in individuals with CF showed a significant increase in pulmonary function and improvements in the respiratory symptoms subscale of HRQoL. However, there were no significant differences in other HRQoL subscales.<sup>32</sup>

In this study, we investigated the effects of breathing and relaxation exercises on the QoL of children with CF. In the age group of 6-12 years, there were significant positive effects of breathing and relaxation techniques on some HRQoL subscales. These include improvements in eating disturbances and digestive symptoms in the CFQ-R Child results and vitality and digestive symptoms in the CFQ-R Parent results. The number of participants in the 5-7 age group was limited, and no significant difference was found in the PedsQL.

There is no time limit for exercises that would change

the HRQoL. Our participants had 1-hour training sessions every week for 12 weeks, with instructions to practice daily. The duration of the study and the unspecified time for the patients to perform daily exercises may be one of the reasons why our results did not show a significant improvement in HRQoL. Longer and regular daily practices in daily life can lead to more meaningful changes in QoL. In addition, it has been previously reported that patients with better lung function have better HRQoL.<sup>33</sup> In our study group, most participants had normal respiratory function (mean FEV1, 94.6%). Therefore, breathing and relaxation exercises may not have a significant effect on HRQoL scores.

The prevalence of sleep disorders in adults with CF is high; however, few studies have evaluated sleep disorders in children with CF.<sup>34</sup> Qualitative studies using questionnaires showed a high prevalence of sleep disturbances; however, the results of polysomnography (PSG) studies have been contradictory.<sup>34</sup> Additionally, there is limited data in the literature on the management of sleep disturbances with psychological interventions. A study by McNamara et al, which evaluated yoga in children with CF, did not show any significant improvements in sleep disturbances.<sup>35</sup> Carr et al did not observe any improvements in lung function, health status, QoL, sleep, or mindfulness after a Tai Chi exercise regimen.<sup>29</sup> Considering the inconsistencies between patient-reported outcome measures of sleep and PSG in the literature, the PSQ may be insufficient to measure sleep quality, and evaluation with PSG might be more beneficial in addition to the PSQ. In our study, we evaluated the change in sleep quality of children with CF after breathing and relaxation exercises, and the results did not show any significant differences in PSQ scores pre- and post-intervention.

Breathing and relaxation exercises offer several advantages. Our CF patients, who could not meet together physically due to infection control measures, except during the pandemic, came together online with these exercises and had the opportunity to meet their peers with CF.

This study has some limitations. First, there was no control group to compare the effects of breathing and relaxation exercises in patients with CF. A control group consisting of children with CF and their caregivers who did not receive the intervention would have been appropriate for this study. However, participants stated that the intervention helped decrease their anxiety and stress levels. Second, the sample size for the training group was small. In particular, due to the limited number of participants

between 2-5 years, the PedsQL results were not appropriate for statistical analysis. To the best of our knowledge, this is the first study to evaluate breathing and relaxation techniques in children with CF and their caregivers.

## Conclusions

Online programs have found a wider place during the COVID-19 pandemic in the treatment of chronic diseases and seem appropriate for CF patients, as group treatments cannot be applied because of infection transmission. In addition, the increase in the survival of children with CF with improved treatment has made supportive interventions for psychological problems necessary for both children and their caregivers. In conclusion, our study showed significant improvements in anxiety/depression symptoms and sleep quality in parents of children with CF after breathing and relaxation exercise training. The results were not conclusive owing to the small sample size. Attributing these positive results to the effect of exercise will require a randomised controlled trial or a waiting-list control group design. Breathing and relaxation techniques may be added to supportive intervention methods that are efficient and easily applicable for children with CF and their caregivers.

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## Declaration of Interest

The authors declare no conflict of interest.

## Author Contribution

Mine Kalyoncu performed the questionnaires, collected the data, performed the statistical analysis and wrote the manuscript. Cansu Yilmaz Yegit, Burcu Uzunoglu, Gamze Tastan performed the questionnaires, collected the data, performed the statistical analysis. Muruvvet Yanaz and Aynur Gulieva performed the questionnaires, collected the data. Almala Pinar Ergenekon and Huseyin Hakan Mursaloglu performed the statistical



analysis and wrote the manuscript. Zuhale Yerlikaya contributed to the conception of the study and administered the Breathing and Relaxation Exercises. Yasemin Gökdemir performed study design, conceptualisation and statistical analysis, wrote the manuscript and supervised the whole study process. Ela Erdem Eralp performed study design, conceptualisation and statistical analysis, wrote the manuscript and supervised the whole study process. Fazilet Karakoc wrote the manuscript and supervised the whole study process. Bulent Karadag performed study design, conceptualisation and statistical analysis, wrote the manuscript and supervised the whole study process.

All authors read and approved the final manuscript.

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