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Musculoskeletal aspects of respiratory function in cystic fibrosis: a cross-sectional comparative study

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ABSTRACT

Background: Respiration is an intricate interaction between visceral and musculoskeletal structures. In cystic fibrosis (CF), the airways and lungs are subject to progressive obstruction and destruction. However, knowledge about the musculoskeletal aspects of respiratory function and symptoms is still limited in this patient group.

Methods: In a cross-sectional comparative study, 21 adults with CF enrolled at the Gothenburg CF Centre were matched with 42 healthy controls. The two groups were examined and compared in terms of thoracic mobility, respiratory muscle strength, lung function, and musculoskeletal pain in accordance with a predefined protocol.

Results: Significant differences were observed between the groups in the number of tender points, thoracic excursion, forced vital capacity (FVC), and forced expiratory volume (FEV). The CF group also demonstrated a tendency toward reduced function in other measurements, although these were not statistically significant.

Conclusion: This cross-sectional study revealed that people with CF have reduced thoracic mobility and an increased prevalence of muscular tender points, alongside decreased lung function, compared to healthy controls. These findings stress the need for greater emphasis on the often-overlooked musculoskeletal aspects of CF care, especially as people with CF are living longer and may require more musculoskeletal health support.

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Background

Lung ventilation is determined by the potential for volume and pressure changes in the thorax [1,2]. The respiratory system, which consists of a complex interplay between the visceral and musculoskeletal systems, enables these alterations [2]. In cystic fibrosis (CF), a condition characterised by obstruction of the airways and progressive damage to the lungs, the lung ventilation becomes compromised. Alongside these visceral alterations, stress on the respiratory musculoskeletal system increases, potentially leading to decreased thoracic mobility, muscle fatigue and/or musculoskeletal pain.

The act of breathing can be divided into two forms: costodiaphragmatic and sternocostal [3]. Costodiaphragmatic breathing entails contraction of the diaphragm, which leads to a lowering of the muscle and flattening of its dome. In inspiration, the ribs are lifted through the external intercostal muscles, and the thoracic cage widens in both the sagittal and transversal directions [3–5]. This means that the lower thoracic aperture is kept dilated despite the diaphragmatic contraction, while the diameter of the upper aperture is increased due to the more horizontal position of the ribs. Through the pleural sheets, which are connected to the chest wall, the lungs accompany the chest wall's breathing movements [1,6]. With ageing and in certain diseases, the thorax becomes rigid, causing a shift towards diaphragmatic breathing and a greater involvement of the accessory respiratory muscles [7,8].

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To fully understand the musculoskeletal aspects of respiratory function, it is essential to also consider lung parenchymal mechanics and pleural relationships. The lungs contain strong elastic tissue that prevents the alveolar spaces from caving in. Even though this connective tissue stabilises the lung parenchyma, it is mainly the attachment of the lungs to the inner chest wall that prevents the lungs from collapsing. This viscero-somatic structural interplay ensures functional integrity during breathing [6,9,10]. However, when the lung parenchyma is altered, as in CF, the lung's ability to maintain proper function in terms of compliance and recoil is compromised, resulting in breathing difficulties [6,9].

Concerning people with CF, life expectancy has significantly increased in recent decades [11]. This means, among other things, that more of these individuals are at an age where, as with otherwise healthy people, the prevalence of musculoskeletal conditions and orthopaedic injuries is generally higher [12]. Furthermore, the reduced bone density and osteoporosis that has been reported as common in CF can lead to fractures and postural misalignments such as hyperkyphosis, which exerts additional strain on the respiratory muscles. As people with CF are living longer it is likely that new health challenges will arise, that to a greater extent will expand into the realm of musculoskeletal health. The aim of this study was to investigate musculoskeletal aspects of respiratory function in people with CF and to compare these measures to those of healthy controls in order to better understand the impact of CF on thoracic mobility, respiratory muscle strength, and musculoskeletal pain.

Materials and methods

This research was carried out as a single-centre cross-sectional comparative study involving patients from the CF centre at Sahlgrenska University Hospital, Gothenburg, Sweden. This study was approved by the Swedish Ethical Review Authority, case number 2019–02628.

Inclusion and exclusion criteria

The following inclusion criteria were established for the CF group: all eligible adult patients (over 18 years of age) at Gothenburg's CF centre were invited to participate in the study. For the healthy controls, the inclusion criteria were to be matched to the CF group for age and sex. The following exclusion criteria were applied for both groups: participants with orthopaedic, rheumatological or neurological injuries or diseases affecting thoracic mobility were excluded. Participants who were undergoing medical evaluation or who were deemed medically or cognitively unable to participate were also excluded from the study. In addition, no patients had received a lung transplant.

Following the initial data collection from people with CF, a 2:1 ratio of healthy controls ±5 years were included. To recruit participants for the group of healthy controls, social media posts were initially made. Through this, people from varying demographic segments were reached. The recruitment was then completed through direct contact where co-workers and acquaintances of the research team were invited to participate.

Data collection

A total of 21 people with CF who met the inclusion criteria were consecutively included in the study from 2019 to the end of 2022. Recruitment of 42 healthy age- and sex-matched controls commenced in February 2023 and the data collection from this group was finalised in October 2023. Based on a standardised protocol, an evaluation of musculoskeletal respiratory movements, respiratory muscle strength, lung function and musculoskeletal pain was undertaken. The evaluation lasted between 20 and 30 minutes and was performed by one experienced physiotherapist and the first author.

Measurements and instruments

Breathing patterns and thoracic mobility were measured using the Respiratory Movement Measurement Instrument (RMMI) by ReMo, Inc., Keldnaholt, Reykjavík, Iceland [13,14]. For these measurements, the participants were asked to lie supine on a treatment table while six lasers registered the respiratory motions. Thoracic excursion was additionally measured using a tape measure with the patient standing [15,16]. The verbal instruction for these measurements of breathing patterns and thoracic excursion was in accordance with previous research where the participants were asked to 'breathe in/out maximally' and to 'make themselves as big/small as possible' [17]. Respiratory muscle strength was assessed by maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) in accordance with international guidelines [18], using the MicroRPM® by Micro Medical, UK [19]. Forced Vital Capacity (FVC) and Forced Expiratory Volume in One Second (FEV_1) were assessed using the EasyOne™ Frontline spirometer by ndd Medical Technologies, US, which meets international criteria [20,21]. FVC per cent predicted (FVCpp)

and FEV_1 per cent predicted (FEV_1pp) were later used to present the findings. In addition, motion palpation was used to assess joint motion, muscular stiffness, and pain on palpation. These qualitative measurements were guided by a protocol, from which a total score and a score per anatomical region were calculated. This protocol was developed and tested prior to the start of the study but has not yet been published.

Data analysis

All data were coded, organised, and analysed using Microsoft® Excel version 16.78, with results presented as mean, standard deviation (SD), median, and range (min-max). Statistical analyses were conducted using IBM SPSS® version 28. An independent t-test was used to analyse differences between groups in thoracic mobility, respiratory muscle strength, and lung function. The Mann-Whitney U test was employed for assessing differences in musculoskeletal pain. The 95% confidence interval (CI) for mean differences was determined using an independent t-test, with effect size measured by Cohen's d. Additionally, a one-way analysis of covariance (ANCOVA) controlled for body height, BMI, and lung function in the analysis of respiratory muscle strength (MIP, MEP) and thoracic mobility. The threshold for statistical significance was set at $p(\alpha) = 0.05$.

Results

A total of 63 participants were included in the study. The CF group consisted of 21 participants, including 12 females and nine males). The control group included 42 participants, with 24 females and 18 males. Demographic data are displayed in Table 1.

Thoracic mobility, respiratory muscle strength and lung function

The results are displayed in Table 2. There was no statistical difference between the groups for thoracic mobility during maximum breathing movements, while CF patients had lower thoracic excursion compared to healthy controls ($p = 0.017$). Both expiratory and inspiratory respiratory muscle strength were lower in the CF group as compared to the healthy controls. The mean MIP was decreased by 6.6 cm H_2O in the CF group and the mean MEP was decreased by 11.4 cm H_2O. Neither of these differences was statistically significant ($p = 0.362$ and $p = 0.152$ respectively) when initially analysed. Furthermore, ANCOVA was applied to correct for covariates such as body height, BMI, FVCpp and FEV_1pp, but no statistically significant difference was found between the CF group compared to the healthy control group concerning MIP ($p = 0.620$), MEP ($p = 0.513$), RMMI abdominal level ($p = 0.303$) or thoracic excursion ($p = 0.239$). Nor was any statistically significant effect size over 0.20 found for any of the covariates, except for height in RMMI abdominal ($p < 0.001$; partial ETA square 0.201).

Musculoskeletal pain

A significant difference in the total number of tender points (TPs) was observed between the CF group and

Table 1. Demographic data.

	CF group (*n*=21) *Mean (SD)*	Healthy controls (*n*=42) *Mean (SD)*	*Effect Size (95% CI)*	*p value*
Age in years	34.9 (8.7)	34.8 (9.6)	0.003 (−4.9–4.9)	0.992
Height in cm	170.6 (9.1)	174.4 (10.4)	0.376 (−1.5–9.1)	0.164
Weight in kg	64.4 (12)	72.2 (14)	0.538 (0.6–14.9)	0.034
BMI	21.9 (2.5)	23.6 (3.2)	0.552 (0.0–3.2)	0.044

Table 2. Respiratory characteristics in the CF and healthy control groups.

		CF group (*n*=21) *Mean (SD)*	Healthy controls (*n*=42) *Mean (SD)*	*Effect Size (95% CI)*	*p value*
Thoracic mobility (RMMI) in mm	Upper thoracic	34.2 (10.6)	35.5 (12.5)	0.109 (−5.1–7.7)	0.685
	Lower thoracic	28 (11.7)	30.1 (13.9)	0.156 (−5.0–9.2)	0.561
	Abdominal	25 (8)	28.1 (10.7)	0.306 (−2.3–8.4)	0.257
Thoracic excursion in cm		5.8 (2.1)	7.2 (2.2)	0.659 (0.3–2.6)	0.017
Inspiratory muscle strength (MIP) in cm H_2O		99.1 (27.1)	105.7 (26.7)	0.246 (−7.8–21.0)	0.362
Expiratory muscle strength (MEP) in cm H_2O		122.2 (33)	133.6 (27.6)	0.388 (−4.3–27.2)	0.152
FVCpp		90.3 (18.9)	110.1 (13.1)	1.302 (11.7–28.0)	<0.001
FEV_1pp		70.7 (26.3)	103.6 (13.6)	1.761 (22.9–42.9)	<0.001

Abbreviations: Respiratory Movement Measuring Instrument (RMMI), Maximal Inspiratory Pressure (MIP), Maximal Expiratory Pressure (MEP), Forced Vital Capacity per cent predicted (FVCpp), Forced Expiratory Volume in one second per cent predicted (FEV_1pp).

the healthy controls ($p < 0.001$). Participants from the CF group reported almost five times as many total TPs (median 12.0; IQR 9.0–17.0) compared to the healthy controls (median 2.5; IQR 0.0–5.0). The same trend was found when analysis of the number of TPs in each specific bodily area was conducted (Figure 1).

Discussion

This study was undertaken to identify musculoskeletal aspects of respiratory function in people with CF, and to compare these to a healthy control group. The study indicate that the CF group had more symptoms and impaired function across examined parameters. These findings, particularly regarding musculoskeletal pain, demonstrate a need to pay greater attention to these understudied aspects. Furthermore, recent research indicates that people with CF feel that their pain symptoms are insufficiently managed [22]. The findings of the current study could aid caregivers in developing care strategies for these patients.

The results indicated a trend towards decreased thoracic mobility in people with CF, especially regarding thoracic excursion. Although not statistically significant, the noted thoracic hypomobility can impair pulmonary ventilation and affect non-primary respiratory muscles and joints [7]. Moreover, regional interdependence, where symptom-free areas are proposed to contribute to overall clinical manifestations, may warrant consideration in patient care [23,24]. Regarding the thoracic area, previous studies have shown that isolated thoracic pain is relatively rare, while pain from this anatomical region is reported by approximately 41% of men and 36% of women seeking care for cervical- or low back pain [25]. Consequently, the observed decrease in thoracic mobility in the current study might imply a connection to the marked difference in the number of musculoskeletal TPs between people with CF and the healthy control group.

Respiratory muscle strength was lower in the CF group when compared to the healthy controls in this study. Known factors that can adversely affect the ability to generate respiratory muscle strength include structural skeletal changes, e.g. hyperkyphosis, scoliosis, and/or barrel chest [8,12,26]. Furthermore, increased cytokine levels, vitamin D deficiency, corticosteroids, and generally low muscle activity are all factors that may have a negative effect on muscle tissue and strength in CF [27,28]. In contrast, a study by Dufresne et al. [29], which included 38 adults with CF with mild to moderate systemic inflammation, found that the CF group had a thicker diaphragm and stronger inspiratory muscles compared to a healthy control group of 20 people. Such findings may encourage broader discussions about relative strength in people with CF, i.e. although these patients may exhibit muscle weakness compared to healthy individuals, their fat-free mass and muscle volume

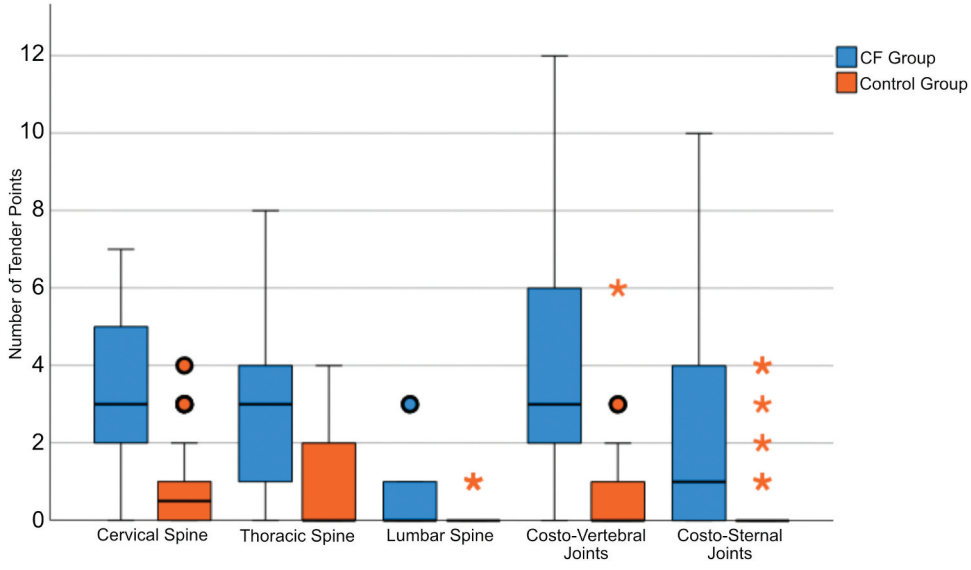

Figure 1. Number of TPs presented in median, interquartile range (IQR) and outliers by the Cystic fibrosis group compared to the healthy controls per anatomical area: **1) cervical Spine**: CF group (3.0; 2.0–5.0) compared to healthy controls (0.5;0.0–1.3) (p <0.001). **2) thoracic Spine**: CF group (3.0; 1.0–4.5) compared to healthy controls (0.0;0.0–2.0) (p <0.001). **3) Lumbar Spine**: CF group (0.0;0.0–1.0) compared to healthy controls (0.0;0.0–0.0) ($p = 0.016$). **4) costo-vertebral Joints**: CF (3.0;1.5–7.0) compared to healthy controls (0.0;0.0–1.0) (p <0.001). **5) costo-sternal Joints**: CF group (1.0;0.0–4.5) compared to healthy controls (0.0;0.0–0.0) (p <0.001). Circles and asterisks represent data points outside the IQR, considered as mild or notably distant outliers respectively.

may be adequate, but their muscular output may still be limited due to structural constraints. In addition, a previous study on people with CF at the CF centre in Gothenburg showed no patient group-specific anatomical change or thoracic configuration with ageing [30]. Similar to the findings on thoracic mobility, these findings represent aspects of musculoskeletal health that need monitoring due to the demographic shift that is currently being seen in this patient group [11,31]. Regarding lung function, the results from this study were consistent with already well-established knowledge regarding the progressive nature of the disease on lung structure and function and will therefore not be discussed further at this time.

Besides lung function, musculoskeletal pain was found to be the most noticeable difference observed between the two groups. The number of TPs reported by the CF group was nearly five times that of the control group. This finding may result from continuous coughing, ongoing self-care, or periods of reduced activity associated with exacerbation. The pain can also indicate stress and strain that manifests in the musculoskeletal system due to impaired lung function. These results concur with recent patient reports [22] and underline the importance of a continued and even expanded biopsychosocial perspective for people with CF. Regarding musculoskeletal health, interventions aimed at improving thoracic mobility, strengthening respiratory muscles, and managing muscle and joint pain can facilitate activity and exercise. As the average age of people with CF increases, so will the challenges of managing typical age-related musculoskeletal conditions, and it will be necessary to explore how these can best be managed. As also highlighted in previous research [12,31,32], this will probably require new and multidisciplinary approaches.

In terms of strengths and limitations, this study provides a thorough overview of the musculoskeletal respiratory characteristics in people with CF, largely due to applying a wide range of different measurements. However, it should be noted that while most of the applied measurement methods are well-established, manual palpation is still a potential source of inaccuracy. Previous research has indicated that the intra-rater reliability for manual palpation is reasonably good, whereas the inter-rater reliability is poor [33–36]. Therefore, the authors recommend applying this method in accordance with a standardised procedure whenever possible and ensuring that the same tester performs these tests. A further limitation is the relatively small sample size of 21 participants in the CF group, which may affect the ability to detect statistically significant differences in some variables. Despite this and given the rarity and severity of the disease, combined with the data collection coinciding with the COVID-19 pandemic, the research team is ultimately satisfied regarding the number of people with CF that participated in the study. It is also important to acknowledge that the design of the study does not allow for conclusions regarding causal relationships. The provided results should therefore primarily be interpreted as hypothesis-generating and as laying the foundation for future research.

Finally, highly effective modulator treatments (HEMT) had not yet been approved in Sweden at the time of our study. There were only two patients in the CF group with access to these therapies for compassionate reasons. The CF landscape is changing with these effective new therapies. With less production of sticky sputum, diminished inflammatory and infectious symptoms, and less need for cumbersome airway physiotherapy and repeated antibiotic courses, the demands on the musculoskeletal respiratory system should also decrease.

Conclusion

This cross-sectional study emphasises significant impairments in thoracic mobility, an increased number of musculoskeletal tender points, and reduced respiratory muscle strength in people with CF compared to healthy controls. These findings stress the critical need to focus on the currently underexplored musculoskeletal components more thoroughly in CF. Furthermore, this study underscores the importance of continued research in this domain to enhance our understanding and improve treatment approaches for these critical aspects of CF care.

Ethical considerations

This research project was carried out in accordance with the ethical principles for medical studies involving humans, which were established at the 18th World Medical Association General Assembly in Helsinki. All participants in this study took part voluntarily and all data collected was treated with confidentiality. The participants were free to discontinue their participation in the study at any time and without giving a reason. All participants received written and oral information regarding the study and gave written consent to their participation.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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Authors' contribution

All authors conceived the idea for the study and contributed to the design and concept. NSS and MFO managed the data collection. All authors constructed the manuscript, and all have read and approved the manuscript.

Data availability statement

Data will be available upon request.

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