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The Role of Physical Activity and Exercise in Cystic Fibrosis – A Literature Review

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ABSTRACT
Cystic fibrosis (CF) is one of the most widespread genetic disorders worldwide. The disease is caused by a mutation in the CFTR gene, which impairs the transport of chloride and bicarbonate ions across the cell membrane, leading to dysfunction of multiple organ systems - primarily the respiratory and digestive systems. Over the years, the availability of new pharmacological therapies has significantly improved both the quality and length of life in CF patients. Nevertheless, non-pharmacological treatment remains an integral component of the overall therapeutic approach. Physical activity is recommended not only for the general population but is also increasingly recognized for its beneficial effects in patients with various chronic diseases. The multifaceted impact of exercise on the human body is a frequent subject of scientific investigation. With the increasing life expectancy of individuals with CF, there is a growing risk of developing comorbidities, including lifestyle-related diseases, which may lead to overlapping symptoms. In modern clinical practice, cystic fibrosis is not always the direct cause of death in these patients. Therefore, it is crucial to adopt a holistic approach to the health of CF patients. Numerous studies have investigated the role of physical activity and exercise in cystic fibrosis, highlighting both the benefits and limitations imposed by the disease. Positive

outcomes have been reported, including improved physical performance parameters, which contribute to enhanced quality of life and overall functioning. Additionally, exercise has been associated with improved mental health. A key conclusion emerging from these studies is the importance of personalized treatment plans that consider disease severity, physical and economic conditions, and the need to support patient motivation and adherence to exercise regimens.
Keywords: Cystic fibrosis, physical activity, exercise

1. Introduction

Cystic fibrosis (CF) is one of the most common autosomal recessive genetic disorders, with variable prevalence depending on geographic region and ethnic background. It is most frequently observed in Caucasian populations, occurring in approximately 1 in 3,200 live births [1]. The mutation responsible for CF occurs in a gene located on chromosome 7, encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein. This protein is responsible for the transport of chloride and bicarbonate ions, regulated by cyclic AMP and phosphorylation by protein kinase A. To date, approximately 2,000 CFTR mutations have been identified, with the most prevalent being F508del [2]. The mutation may result in a defective CFTR protein and impaired chloride transport or, in severe cases, a complete absence of protein production. The clinical phenotype is highly variable depending on the specific mutation and is also influenced by modifiable environmental factors such as air pollution and tobacco smoke, which further reduce CFTR expression [3]. Due to the diversity in pathophysiology and clinical manifestation, CF is classified into seven categories. CFTR protein is expressed in epithelial cells throughout the body, which explains the multisystem involvement observed in CF. The respiratory system is the most severely affected; patients often present with chronic cough producing thick sputum, dyspnea, and recurrent upper respiratory infections frequently caused by characteristic pathogens such as *Pseudomonas aeruginosa* [4]. Obstruction of the airways by thick mucus leads to chronic inflammation, bronchiectasis, and, in some cases, end -stage lung disease requiring lung transplantation [5].

CF may also result in pancreatic insufficiency, affecting both exocrine and endocrine functions; a significant number of patients develop cystic fibrosis-related diabetes mellitus (CFRD) [6]. Malnutrition and fat-soluble vitamin deficiencies pose additional clinical challenges, contributing to growth disturbances, osteoporosis, and increased risk of fractures. Furthermore, infertility is common in CF patients. Historically, CF was considered a fatal paediatric disease; however, advances in medical science - particularly the discovery of the CFTR protein, first described in 1938 - have enabled the development of novel therapeutic options [7]. Today, newborns undergo routine CF screening, and abnormal results are followed by confirmatory diagnostic tests such as the sweat chloride test and genetic analyses using modern techniques [8,9]. Early diagnosis facilitates more effective treatment. Recently, the development of targeted therapies - classified as CFTR modulators, including correctors, potentiators, and amplifiers - has significantly expanded treatment options [10]. Life expectancy has markedly increased, with the estimated median survival for children born with CF in 2019 in the United States reaching 48.4 years [11]. Consequently, CF is no longer solely a paediatric disease; it now affects a growing adult population, posing new challenges due to increasing multimorbidity, lifestyle-related diseases, and malignancies. To mitigate these effects, it is essential to explore the role of physical activity and exercise in CF management. The World Health Organization recommends at least 150–300 minutes of moderate-intensity or 75–150 minutes of vigorous-intensity physical activity per week, including for individuals with chronic diseases [12].

The objective of this paper is to evaluate the impact and implementation principles of physical activity and exercise in patients with cystic fibrosis.

To achieve this, a literature review was conducted using PubMed and Google Scholar databases. Search terms included: “Cystic Fibrosis,” “Cystic Fibrosis Physical Activity,” and “Cystic Fibrosis Exercise.” The inclusion criteria were: open-access articles, published within the last 10 years, in English. Retrieved articles were screened for eligibility based on their titles and abstracts. Study results and conclusions are presented below.

2. Discussion

According to the World Health Organization (WHO), physical activity is defined as any bodily movement produced by skeletal muscles that requires energy expenditure. When this activity is planned, structured, repetitive, and performed for a specific purpose, it is classified as exercise [13]. Two primary types of training are distinguished: aerobic and anaerobic. Numerous scientific studies have demonstrated that engaging in physical activity plays a crucial

role in maintaining health and psychological well-being. Exercise reduces the risk of cardiovascular diseases, type 2 diabetes, and cancer, thereby contributing to a reduction in morbidity and mortality related to these conditions [14]. Enhancing awareness and knowledge about the positive effects of physical activity should be widely promoted in society and implemented from early childhood.

Studies have been conducted to assess the level of physical activity in individuals with cystic fibrosis (CF) compared to healthy populations, with stratification by age group (children and adults). Parameters such as MET (metabolic equivalent of task), MPA (moderate physical activity), and MVPA (moderate-to-vigorous physical activity) were evaluated. The results indicated that individuals with CF are similarly active compared to healthy individuals. However, among younger individuals, there was a noticeable trend toward reduced physical activity, particularly during disease exacerbations and on weekdays [15].

Davies et al. identified physical activity as one of the five essential therapeutic modalities in the management of CF due to its numerous benefits [16]. Positive respiratory outcomes associated with exercise include alleviation of exertional dyspnea and improved exercise tolerance. Due to hyperventilation, mechanical vibrations, altered sputum consistency, and cough stimulation, airway clearance and expectoration of thick mucus—characteristic of CF - are facilitated, thereby slowing the decline in lung function [17]. However, these benefits are often challenging to achieve due to disease-related limitations. Chronic inflammation, frequent recurrent infections, low exercise tolerance, malnutrition, and reduced bone mineral density frequently contribute to physical inactivity and a sedentary lifestyle, which have detrimental consequences [18].

A study conducted in Italy among 85 individuals with CF demonstrated a beneficial effect of regular physical activity on inflammatory markers—interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNFα). These findings suggest that physical activity may act as a modulator of inflammation in CF. Additionally, an increase in adiponectin levels and a decrease in fasting blood glucose were observed [19].

To assess the role of physical activity in CF, multiple clinical endpoints have been studied and compared to values in physically inactive patients. Most interventions lasted 6 months, after which outcomes were assessed; only a few centers extended follow-up beyond this period. Key evaluated parameters included oxygen uptake capacity (VO2, in L/min or mL/min), forced expiratory volume in one second (FEV1, in L or %), and health-related quality of life (HRQoL), assessed via validated instruments or patient self-reports, focusing on physical functioning, respiratory status, and other domains. Some studies also analysed peak work capacity (in watts

or W/kg), functional exercise capacity (6-minute walk test, 6MWT), submaximal exercise tolerance (e.g., time to exhaustion during exercise testing), quadriceps muscle strength (measured via strain gauge sensors or dynamometry), and forced vital capacity (FVC).

Physical activity levels were assessed through subjective patient reports, such as self-completed diaries and questionnaires stratified by exercise intensity, or objectively using devices such as pedometers and accelerometers. The frequency of respiratory exacerbations, including those requiring hospitalization, was also considered, along with the impact on other physiological systems, such as bone mineral density, body mass index (BMI), and glycemic control.

A systematic review of studies conducted across various centers concluded that engaging in physical activity for at least 6 months is likely to improve exercise capacity in CF patients, measured as VO2 max. However, differences in pulmonary function and quality-of-life indicators compared to inactive patients were minimal or not statistically significant [17].

Rowbotham et al. investigated whether physical exercise could replace airway clearance therapies (ACTs) [20], which are a cornerstone of CF treatment, facilitating airway clearance and mucus expectoration [21]. Conventional chest physiotherapy (CPT) is the oldest ACT technique. Other methods include the active cycle of breathing technique (ACBT), autogenic drainage (AD), and oscillating positive expiratory pressure (OPEP). The selection of an appropriate method should consider patient capability, preference, and available resources [22,23]. Given the considerable time and financial burden associated with ACT, patients and their families often seek alternative methods, including physical activity [24]. In some studies, nearly half of the patients admitted to skipping ACT when engaging in physical exercise [25].

Sputum composition was compared between patients who exercised and those relying solely on ACT, but results were inconclusive and of low evidentiary strength to determine whether ACT could be replaced by exercise. The most optimal solution appears to be a combination of both approaches, with continued promotion of physical activity and further scientific research in this area.

Pancreatic insufficiency and the development of cystic fibrosis-related diabetes (CFRD) are among the extrapulmonary manifestations of CF [26]. Research from the United Kingdom revealed that, in 2018, 30% of CF patients over the age of 10 were being treated for CFRD [27]. The pancreas is thus one of the earliest organs affected, and diabetes significantly reduces quality of life and increases mortality. Due to the importance of this issue, studies have examined the correlation between the presence of CFRD and reduced aerobic capacity during exercise, as well as pulmonary function parameters. Findings indicated lower physical fitness (VO2 max) and FEV1 values in patients with CFRD compared to those without diabetes [28].

It has been shown that physical training can improve insulin sensitivity in adults with CF, stabilizing blood glucose levels and mitigating both hyperglycemia and reactive hypoglycemia [29].

The nervous system has also been a focus of recent research. Elce et al. explored the effects of physical activity on cognitive function in individuals with CF [30]. CFTR protein expression has been observed in neurons, although its function in these cells remains unclear. Furthermore, CFTR expression levels have been correlated with cerebral artery wall tension, suggesting a role in regulating cerebral blood flow [31]. CF patients more frequently experience depression and anxiety, and children with CF report reduced sleep compared to healthy peers. These abnormalities correlate with low BMI and compromised respiratory function. CF children also exhibit poorer performance in executive function, memory, attention, and deficits in logical, conceptual, and abstract thinking. These symptoms are likely associated with hypoxia, as they are also observed in other chronic conditions, such as asthma [32].

Numerous studies have shown that physical activity contributes to mental well-being and has preventive effects against depression, anxiety disorders, and potentially sleep disturbances [33]. Furthermore, it supports brain health and cognitive functioning. Structured and regularly performed exercise promotes neuroplasticity, which plays a crucial role in learning, memory, brain repair, and development [34]. Although direct effects of physical activity on cognitive function in CF have not yet been fully elucidated, its multifaceted benefits suggest its potential utility in addressing the neurological challenges faced by these patients. Further research is warranted to establish conclusive evidence.

Patients with cystic fibrosis (CF) face a greater number of barriers to engaging in physical activity compared to the healthy population. These factors can be categorized as physical (e.g., dyspnoea, weakness, infections) and psychological (e.g., lack of motivation, fear of exercise, stress). In a study conducted by Dillenhoefer et al., patients were divided into two groups—active and inactive—based on completed questionnaires. It was observed that individuals in the inactive group encountered a greater number of limitations in undertaking physical activity. These individuals more frequently cited physical limitations rather than psychological ones. This may be attributed to a more severe disease course in this group, necessitating more time for treatment and rehabilitation, consequently making physical activity more difficult to incorporate [35].

In a study by Hurley et al., involving interviews with patients regarding their barriers, motivators, preferences, and perceived outcomes related to exercise, the most common reason for inactivity was reported as a lack energy, followed by external factors such as weather, and

then issues related to self-confidence during exercise (self-awareness and perceived ability) [36]. Motivation emerged as a key driver for exercise engagement, both intrinsic—often rooted in positive previous experiences with physical activity—and extrinsic, such as encouragement from peers or healthcare providers. Mood regulation following physical activity was cited as a motivating factor by the more active group. Another important finding was the preference for exercising at home rather than in gyms or CF treatment centers. This is understandable, as home-based activity may positively influence feelings of low perceived competence, self-consciousness, and mitigate time- and weather-related barriers.

An important responsibility of physicians and physiotherapists is to educate and encourage patients to engage in regular exercise. However, studies conducted in Canada have shown that exercise testing and training programs are underutilized in CF centers due to issues with funding, time constraints, and limited personnel. Addressing these barriers is essential for improving the quality of care [37].

It is necessary to consider in more detail how best to utilize physical activity in CF care, given the abundance of existing scientific studies, modern treatments, and technological advancements. A significant challenge is the increasing life expectancy of CF patients and the emergence of a new generation of patients who are healthier than ever before. A major innovation in treatment has been the introduction of CFTR modulators. Studies have shown that patients taking these new medications engaged in physical activity more frequently, participated in team sports, and derived greater enjoyment compared to patients not using modulators [38]. As health improves, there is a risk that exercise may be perceived as less essential to treatment, potentially leading to sedentary behavior, caloric excess, and obesity—trends already observed in the general population. Therefore, it is crucial to promote physical activity from an early age. In children, regular exercise not only benefits neuromuscular and cardiopulmonary function but also supports a sense of “normalcy,” which can lead to increased value placed on physical activity and the formation of long-term healthy habits into adulthood.

In pediatric populations, growing attention is being paid to integrated neuromuscular training (INT), which includes a wide range of activities such as strength training along with exercises that develop agility, coordination, and speed. Its primary goal is the proper development of muscle mass and improved sports readiness [39]. In CF patients, INT may provide additional benefits, as this group often experiences delayed growth, low body mass, and delayed puberty, which can contribute to reduced neuromuscular skills and poorer body image compared to healthy peers. Early intervention in sport development may help mitigate these disadvantages

and enable children to "catch up" with their peers. Researchers emphasize that this is especially important in girls, as their participation in physical activity is lower and, due to hormonal differences, they tend to have less muscle strength than boys [40].

Another area of focus in research is the selection of the most suitable type of exercise. Aerobic training is most commonly recommended by clinicians, as it improves cardiac output, aids in mucus clearance, and reduces the sensation of breathlessness. A frequent challenge, particularly among previously sedentary patients, is boredom and a sense of wasted time during aerobic workouts. Therefore, it is emphasized that aerobic exercise should be tailored to patient preferences, enjoyable, and implemented as a long-term intervention.

In a study by Reuveny et al., the effects of high-intensity interval training (HIIT) were evaluated, during which patients cycled at 70% of their maximum heart rate (HRmax) with 60-second breaks at 35% intensity. After eight weeks, the VO_2max kinetics during low-intensity steady-state cycling, as well as the tolerance threshold during high-intensity cycling, were compared between the intervention and control groups. The intervention group showed a shortened time to reach VO_2max and prolonged time to exhaustion. These outcomes are favorable, as they indicate more efficient oxygen delivery to tissues and prolonged aerobic capacity, thereby reducing the risk of hypoxia, anaerobic byproduct accumulation, and enhancing training capacity. These physiological benefits may translate into improved "functional capacity" during daily activities, increasing exercise tolerance and overall quality of life in CF patients [41].

Another important form of exercise is resistance training, which unlike aerobic activity, promotes gains in strength and muscle mass. This is particularly relevant for CF patients, who often experience muscle atrophy due to chronic inflammation and corticosteroid use, which may contribute to myopathy and structural and metabolic alterations in skeletal muscles. These patients frequently report increased dyspnea, fatigue, and impaired mucus clearance, which further discourage physical activity. Introducing strength training can break this vicious cycle. In a study by Sosa-Pedreschi et al., the effects of a once-weekly, hour-long resistance training session over eight weeks were assessed by measuring muscle strength and body composition in CF patients [42]. Results showed increased leg muscle strength, which positively correlates with lung function and overall physical fitness [43], highlighting the clinical relevance of muscular strength improvement. The study also reported a reduction in fat mass and an increase in lean body mass. Similar improvements in muscle strength were observed in a pediatric study conducted by Donadio et al. Additionally, the potential of neuromuscular electrical stimulation

(NMES) as an adjunct to improve strength was investigated, though no significant improvements were observed [44].

In the era of modern technology, it is also worthwhile to consider the role of telemedicine in promoting physical activity among individuals with CF. The daily routines of CF patients are often shaped by rehabilitation, medical appointments, and physical exercise. A partial solution may lie in remote monitoring and information delivery via mobile applications or video consultations [45, 46]. This approach gained traction during the COVID-19 pandemic, which accelerated the development of remote methods. Several of the aforementioned studies were conducted online to ensure optimal patient safety. Specialized exercise programs utilizing interactive video games have also been developed to encourage and motivate patients to move while remaining at home in an enjoyable and accessible way [47]. Furthermore, wearable devices, such as smartwatches, can track steps, heart rate, and oxygen saturation during exercise to monitor physical activity. However, there are certain risks associated with telemedicine, including potential technical issues, patient withholding of information, or reduced trust in healthcare providers. These methods should therefore be used cautiously, and as technology continues to evolve rapidly, further research in this area is necessary.

3. Conclusion

Physical activity plays a crucial role in the treatment of cystic fibrosis (CF). While it affects multiple physiological systems, the majority of research has focused on the respiratory system due to its being the primary site of symptom manifestation and functional impairment. Studies indicate that various forms of exercise contribute to improved physical capacity in CF patients and assist in airway clearance. Additionally, beneficial effects on glucose metabolism and the nervous system are of particular importance, especially in the context of increased life expectancy in this population.

The mental health benefits of physical activity should also be emphasized, given the rising prevalence of psychiatric disorders globally. Another key factor is the early introduction of physical activity, as it not only yields the most significant improvements in aerobic capacity but also shapes long-term attitudes toward exercise, fosters a healthy lifestyle, encourages social integration, and may help delay the onset of lifestyle-related diseases later in life.

The introduction of CFTR modulators, while groundbreaking, should not lead to reduced engagement in physical activity or diminish its value as a component of CF management. Clinicians must take a systemic view of the patient, recognizing physical activity as one of the

simplest and most accessible therapeutic tools. By integrating various therapeutic approaches, it is possible to significantly enhance quality of life in this population.

Comprehensive care in CF treatment centers should be based on interdisciplinary collaboration between the patient and specialists, including physicians, physiotherapists, dietitians, exercise professionals, and psychologists. The literature highlights the importance of individualized treatment plans tailored to the patient's preferences, age, sex, and perception of the disease. In the context of physical activity, one must also consider time availability, motivation, and existing limitations. Given the transformative impact of new treatments and technological advancements, the role of physical activity in CF care must continue to be explored, and further research is essential to address these evolving variables.

Disclosure

Author's contribution

Conceptualization: Anna Bieniasz and Anna Zdziebło; methodology: Katarzyna Zdziebło; software: Maria Sitko check: Dominika Stolarczyk, Martyna Biernacka and Aleksandra Bąk; formal analysis: Igor Biernacki and Katarzyna Zdziebło; investigation: Anna Bieniasz and Katarzyna Agopsowicz; resources: Katarzyna Blicharz and Igor Biernacki; data curation: Martyna Biernacka; writing-rough preparation: Anna Zdziebło; writing- review and editing: Maria Sitko and Katarzyna Agopsowicz ; visualization: Aleksandra Bąk; supervision: Katarzyna Blicharz; project administration: Dominika Stolarczyk

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