

Physiotherapy in cystic fibrosis: a comprehensive clinical overview

Arietta Spinou MSc, PhD

Health, Sports and Bioscience, University of East London, UK

Work address: Arietta Spinou,

Lecturer in Physiotherapy

Health, Sports and Bioscience

Stratford Campus, University of East London

Water Lane, Stratford, E15 4LZ

London, UK

Email: a.spinou@uel.ac.uk

Telephone: +44 (0)20 8223 4520

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1 **Abstract**

2 Physiotherapy remains the cornerstone of cystic fibrosis (CF) management alongside medical
3 treatment. Traditionally, physiotherapy intervention focussed on airway clearance during the
4 clinically stable stage and chest infections. Research evidence consistently supports greater mucus
5 clearance with chest physiotherapy compared to cough alone or no treatment. Various methods and
6 techniques of airway clearance have been developed and investigated, and data suggest that most of
7 them are of similar effectiveness. Nowadays physiotherapy management also extends to other areas,
8 supported by studies and clinical practice. The physiotherapists plan, supervise and follow-up
9 systematic exercise or personalised rehabilitation programs, which, similarly to airway clearance,
10 are recommended in all patients with CF. Furthermore, based on a comprehensive assessment,
11 physiotherapists incorporate the management of accompanying musculoskeletal problems such as
12 back pain and postural disorders, as well as urine incontinence issues. In the era that aims to improve
13 quality of life, it is essential that physiotherapists are aware of specific conditions that might affect
14 the management of CF. Their role is to work alongside and within the CF multi-disciplinary team
15 throughout patient's treatment and consistently support the patient and carers, in particular whilst
16 on clinical pathways of the lung transplantation and palliative care.

17

18 **Keywords:** physiotherapy, cystic fibrosis, airway clearance, chest physiotherapy, exercise.

19 INTRODUCTION

20 Cystic fibrosis (CF) is a recessive genetic disease that affects the patient on multiple systems, with
21 profound manifestations in the respiratory and digestive systems [1]. It is characterised by the
22 mutation and therefore dysfunction of the gene for the cystic fibrosis transmembrane conductance
23 regulator (CFTR). This protein mainly functions as an ion channel, regulating fluid volume on
24 epithelial surfaces via chlorine secretion and inhibition of sodium resorption. In the airways of the
25 patients with CF, dysfunction of the CFTR results in periciliary liquid layer depletion [2]. Clinically,
26 patients with CF present abnormal consistency and high volumes of sputum, cough, dyspnoea,
27 bronchiectasis and weight loss. As the survival of these patients is increasing, it is crucial that health
28 care professionals address symptoms and support individuals in evolving issues developed
29 throughout their life span.

30

31 Physiotherapy is an integral part of the therapeutic management of CF patients, both at the clinically
32 stable stage of the disease and during respiratory infections. In the past, physiotherapy was focused
33 on airway clearance, also known as chest physiotherapy, by teaching or applying methods such as
34 the postural drainage with or without the additional application of manual techniques [3]. Postural
35 drainage of the tracheobronchial tree uses specific gravitational positions to assist mucus
36 mobilisation downwards (towards the mouth) within the airways. Manual techniques (percussions,
37 vibrations and/or shakes) use mechanical forces to assist the detachment of mucus from the airway
38 epithelium and its mobilisation. Nowadays, the choice of airway clearance techniques has been
39 expanded to methods such as the autogenic drainage, the active cycle of breathing techniques
40 (ACBT), the use of positive expiratory pressure (PEP) devices with or without oscillation, and
41 others. Still, modern physiotherapy in CF also includes the assessment of the cardiovascular system
42 and improvement of the patient's fitness level, muscle strength and endurance through exercise, as
43 well as specialised interventions to improve musculoskeletal symptoms of pain, posture and
44 incontinence [4].

45

46 **PHYSIOTHERAPY**

47 **Airway clearance**

48 Patient education, application and monitoring of the airway clearance techniques remain the main
49 physiotherapy treatment for patients with CF [4]. Physiotherapists facilitate the establishment of an
50 individualised airway clearance routine by supporting patients and their families to establish regular
51 regimes during a clinically stable stage and have an escalation plan for disease exacerbations [5].
52 Airway clearance is usually performed on a daily basis and as required. *The selected method applied,*
53 *duration and frequency of each session are tailored to the patient, their general health condition*
54 *and the severity of the disease.* For instance, airway clearance becomes more regular during
55 exacerbations or hospitalisations [6]. Hospitalisations also provide an opportunity for
56 physiotherapists to re-assess the effectiveness of daily airway clearance and provide appropriate
57 feedback and guidance for improving the patient's usual technique prior to discharge.

58

59 Table 1 presents the main categories of airway clearance techniques and methods in CF. These can
60 be used in isolation or in combination regimes. Assessment of effectiveness is based on measuring
61 sputum volume or weight, lung function by spirometry, frequency of hospitalisations and quality of
62 life. Airway clearance is extensively supported in the literature when compared to no airway
63 clearance or cough alone [4, 7-9]. A recent systematic review supported a significant increase in the
64 amount of sputum (wet or dry) in the patient groups that applied airway clearance using postural
65 drainage with or without the addition of manual techniques or using PEP, compared to spontaneous
66 cough or not using any technique [7]. The weight of the sputum was higher after the application of
67 the active cycle of breathing techniques compared to the use of the flutter (an oscillating PEP device)
68 or high frequency chest wall oscillation (vest) [10]. The weight of the sputum expectorated was
69 greater after using the PEP mask compared to autogenic drainage, postural drainage positions and

70 their combination, although this difference was short-term (up to one week) [11]. On the other hand,
71 there was no difference in the amount of the expectorated mucus after autogenic drainage compared
72 to the flutter, or between the high frequency chest wall oscillation compared to the autogenic
73 drainage or the PEP mask for longer time-intervals [10, 12].

74

75 Systematic reviews did not show significant differences in the lung function (FEV_1) of adult patients
76 following the use of PEP, when assessed patients prior and immediately after a physiotherapy
77 session or up to 3 months later [7, 10, 11, 13]. Additionally, the lung function did not change after
78 applying the active cycle of breathing techniques in combination with the PEP mask, postural
79 drainage with or without manual techniques, or the high frequency chest wall oscillation [12].
80 However, treatment in children and adolescents that was applied up to one year showed 6% increase
81 in FEV_1 with the use of PEP [13].

82

83 Regarding the hospitalisation frequency, no differences were found for those who practiced the
84 active cycle of breathing techniques compared to the postural drainage with or without manual
85 techniques [12]. The number of hospitalisations, however, was lower for those who used PEP than
86 the patients who used the flutter (5 vs 18 hospitalisations, respectively) [10]. Similarly, fewer
87 patients used intravenous antibiotics from the group that used PEP devices, compared to the group
88 of the high frequency chest wall oscillation [13].

89

90 For the quality of life, there is no difference amongst techniques and devices, such as the postural
91 drainage with or without manual techniques, active cycle of breathing techniques, autogenic
92 drainage, PEP mask, flutter, and cornet [10, 12, 13]. However, patients preferred the PEP mask for
93 long-term use (>1 month), and also preferred seating instead of using postural drainage positions

94 [10, 11, 13]. Autogenic drainage was preferred among children between 12-18 years old, compared
95 to postural drainage in combination with manual techniques [14].

96

97 Important factors for the success of the selected airway clearance plan are the compliance to
98 treatment and patient satisfaction. Factors that increase the rate of compliance are good patient
99 knowledge of the technique and confidence in its application, independence and preference [15, 16].

100 Evidence indicate that patients who receive help, those who produce more sputum, and children
101 with CF whose parents believe in the necessity of treatment are those with higher compliance in
102 airway clearance [17, 18].

103

104 **Airway clearance adaptations**

105 *Mucolytics and other agents*

106 Patients with CF often receive medications that aim to increase the effectiveness of airway
107 clearance, such as nebulised hypertonic saline (3% to 7% NaCl), dornase alpha (DNase), and
108 mannitol. The use of inhaled hypertonic saline (osmotic pressure > 0.9% NaCl) in patients with CF
109 is considered to improve the rheological characteristics of sputum and increase the hydration of the
110 airway epithelium; thus, increase the sputum motility and facilitate the mucus clearance [19]. There
111 is good evidence that the use of hypertonic saline reduces the incidence of respiratory infections,
112 increases FEV₁, and improves the quality of life, although the changes are not maintained in the
113 long term (48 weeks) [20, 21]. During the hospitalisation of patients with CF, hypertonic saline
114 improves the chances of quick return of the lung function (FEV₁) to pre-infectious levels [22]. With
115 regards to timing the hypertonic saline administration, a recent systematic review supports its use
116 before or during the performance of airway clearance, rather than its administration afterwards [23].
117 If the prescribed doses are two, it is recommended to administer one in the morning and one in the

118 evening, and if the patient receives a single dose this is given at a convenient time chosen by the
119 patient [23].

120

121 Dornase alpha (DNase) is a recombinant human deoxyribonuclease that reduces sputum viscosity
122 by selectively hydrolysing the large extracellular DNA molecules contained in the mucus into
123 smaller structures, thereby increasing the potential for its elimination [24]. This drug is administered
124 via a jet-nebuliser device and has been shown to reduce the incidence of respiratory infections,
125 increase respiratory function, and improve quality of life [24]. With regards to timing its
126 administration, it appears that using DNase before or after airway clearance does not have any
127 difference in improving lung function (FEV₁ and FVC) or patient's quality of life [25, 26]. In clinical
128 practice, physiotherapy often follows the proposed guidelines of the pharmaceutical company to
129 perform airway clearance 30 minutes after the DNase administration [27].

130

131 Inhaled mannitol is a naturally occurring sugar alcohol which enhances osmosis, causing mucus
132 hydration [28]. Inhaled mannitol is administered as dry powder (capsules) using an inhaler. As
133 demonstrated by two 26-week multi-centre studies with a total number of 600 participants with CF,
134 inhaled mannitol improves the respiratory function of patients but does not improve their quality of
135 life [29, 30]. Although its use usually precedes airway clearance in clinical practice, there is no
136 research data to compare different timings of administration.

137

138 ***Haemoptysis***

139 Haemoptysis is a major change in the patient's clinical presentation and may be life-threatening. The
140 physiotherapy assessment should include questions about sputum description and reference to
141 current or past haemoptysis episodes. Active frank haemoptysis (>100-1000 ml haemoptysis in 24
142 hours or 48 hours) is treated exclusively medically, e.g. with bronchial embolisation of the arteries

143 or thoracic surgery, while the airway clearance treatment is temporarily discontinued [31, 32]. In
144 moderate or low haemoptysis, physiotherapists, in collaboration with the medical team, decide
145 whether or not it is appropriate to continue airway clearance using clinically reasoning. If the
146 treatment is appropriate and safe to continue, then the active cycle of breathing techniques or
147 autogenic drainage is often selected over other techniques.

148

149 ***Pneumothorax***

150 Spontaneous pneumothorax is a common complication in patients with CF. It is associated with a
151 reduction in pulmonary function and 50-90% chance of recurrence [32, 33]. If the pneumothorax
152 occurs for the first time and it is small, then it can be treated conservatively with oxygen supply
153 [34]. In patients continuing airway clearance, it is suggested to liaise with the medical team for
154 adding humidification to the oxygen supply and ensuring adequate analgesia for the duration of the
155 treatment sessions [35]. In the case of large pneumothorax (>2 cm between parietal pleura and
156 visceral pleura) or recurrent pneumothorax, chest drainage is performed using thoracic catheters,
157 while patients might get pleurodesis in resistant cases [34]. Positive pressure devices such as PEP,
158 flutter and acapella are contraindicated in the presence of pneumothorax [34]. Regarding physical
159 activity, patients need to be engaged with moderate activities but should avoid bearing weights over
160 2 kg or strenuous aerobic exercise for a period of two to six weeks after the complete drainage of
161 the pneumothorax [34].

162

163 **Exercise**

164 Exercise is an integral part of the comprehensive physiotherapy intervention for patients with CF
165 [36]. American College of Sports Medicine guidelines advocate 3-5 sessions of moderate exercise
166 per week, with the aim to adopt exercise as a way of living [37]. Benefits of specific exercise
167 modalities in cystic fibrosis are yet to be identified in methodologically strong studies [38]. Despite

168 research interest, evidence has not established the effectiveness of inspiratory muscle training on
169 this group of patients, therefore this is currently not routinely incorporated in the CF treatment. In
170 the clinical setting, the assessment of patients with CF uses simple and cost-effective exercise field
171 tests, such as the 6-minute walk test (6MWT) and the incremental shuttle walk test (ISWT), whilst
172 the level of dyspnoea is assessed using the Borg dyspnoea scale [39].

173

174 Exercise can theoretically assist airway clearance through the kinetic forces and vibrations generated
175 within the airways, but it cannot substitute for the formal airway clearance [40]. When compared to
176 airway clearance techniques, moderate aerobic exercise leads to less mucus expectoration [41].
177 Also, exercise as a single agent does not increase cough immediately after its completion, although
178 it improves the subjective ease of sputum clearance [42]. Clinically, exercise is mainly used
179 additionally to airway clearance, as a means to improve the exercise capacity of the patient and is
180 usually performed before the implementation of airway clearance.

181

182 **Exercise considerations**

183 *Musculoskeletal and postural issues*

184 Back and thoracic pain are frequently reported in patients with CF, although they do not have an
185 effect on lung function [43, 44]. Higher thoracic kyphosis is associated with lower lung function,
186 but nowadays it is more uncommon compared to a few years ago [45]. Low bone density and
187 osteopenia is also a common issue in patients with CF [46, 47]. Counselling and appropriate exercise
188 programs from physiotherapists can potentially address and improve these postural and structural
189 issues [36].

190

191 *Urinary incontinence*

192 Surveys show that urinary incontinence in patients with CF is reported in 30% to 68% of women or
193 girls and 5% to 16% of men or boys [48-51]. The dynamic pressure created during coughing is
194 potentially a key mechanism of CF urinary incontinence, although it may not be the only one [52].
195 Coughing, sneezing, laughing and spirometry are among the activities that trigger urinary
196 incontinence incidents [53]. Incontinence worsens during respiratory infections and has been
197 associated with poorer quality of life and higher anxiety and depression scores [51, 54, 55].
198 Assessing incontinence using screening tools and clarifying questions should be an integral part of
199 the CF physiotherapy assessment, regardless of gender [56]. Physiotherapy treatment of urinary
200 incontinence includes counselling and specialised training involving pelvic floor exercises, such as
201 Kegel exercises [55, 57, 58].

202

203 ***Diabetes mellitus***

204 Diabetes mellitus is associated with CF and is the most common comorbidity of the disease,
205 occurring in up to 20-50% of adult patients [59-61]. This comorbidity requires the co-operation of
206 the physiotherapists with the endocrine team, especially for the patients who require insulin therapy
207 [62]. Additionally, the presence of diabetes mellitus needs to be considered in the physiotherapy
208 plan, mainly in the exercise prescription and performance. In this case, the proper scheduling of the
209 meal times or insulin intake is essential.

210

211 **Quality of life**

212 Over time and as the CF severity and symptoms progress, the quality of life of patients is
213 deteriorating. Females with CF often report poorer quality of life compared to their male age-
214 matched peers [63]. Although the correlation between lung function and quality of life is weak to
215 moderate, patients with better lung function report higher quality of life [54]. Also, the presence of

216 *Pseudomonas aeruginosa* and frequent respiratory infections appear to have a negative impact on
217 the quality of life of patients [54].

218

219 Researchers and clinicians can use a number of validated questionnaires for the assessment of
220 quality of life in people with CF. Those include: generic questionnaires or questionnaires for a
221 specific disease symptom, such as the Short Form-36 (SF-36) and the Leicester Cough
222 Questionnaire, respectively [64, 65]; disease-specific questionnaires, such as the Manchester
223 Questionnaire, the Cystic Fibrosis Questionnaire-Revised and the Cystic Fibrosis-Quality of Life
224 [64, 66-69]; and questionnaires for babies and children of young age, such as the Modified Parent
225 Cystic Fibrosis Questionnaire-Revised [70].

226

227 **Special considerations**

228 *Long term oxygen therapy and non-invasive ventilation*

229 A recent systematic review in patient with CF did not show long-term benefits from the long-term
230 oxygen therapy, in survival, respiratory function or cardiovascular health, although it showed
231 improved school or work attendance rates [71]. When oxygen is administered during exercise only,
232 it helps to improve oxygenation, reduces the feeling of dyspnoea and increases the duration of the
233 exercise [71, 72]. However, supplemental oxygen during exercise in patients with initially low
234 arterial oxygen values appears to cause hypercapnia in the short term (PCO₂ up to 16 mmHg) [71].
235 Also, oxygen therapy during sleep improves oxygenation, but is accompanied by small hypercapnia
236 [71]. The use of supplemental oxygen should follow the established clinical guidelines that are based
237 on hypoxia (PaO₂ ≤55 mmHg or 60 mmHg) and the presence of clinical symptoms [73].

238

239 Non-invasive ventilation (NIV) is used in patients with CF on respiratory failure, hypoventilation
240 during sleep, as well as a bridge to lung transplantation [3]. For patients with severe clinical

241 presentation where airway clearance causes fatigue and high levels of dyspnoea, NIV can be used
242 to assist airway clearance [74]. The use of NIV during the physiotherapy session facilitates mucus
243 expectoration and reduces the sensation of dyspnoea during the treatment compared to other
244 techniques particularly for patients with low lung function [75]. However, the long-term effects of
245 NIV on airway clearance need further investigation [76].

246

247 *Paediatric population*

248 Choosing a treatment plan for children with CF is based on age, clinical presentation and certain
249 social criteria [77]. There is no agreement on the most appropriate starting age for airway clearance.

250 A proposal for early disease management (pre-symptomatic) is to carefully monitor the clinical
251 presentation of children and adopt an active treatment plan following the onset of symptoms [78].

252 At young ages, where the child can not follow instructions and cooperate, assisted autogenic
253 drainage or PEP devices with a child mask can be used. Physiotherapists are also responsible for
254 educating the child's parents or carers for appropriate evaluation of the child's symptoms and
255 treatment implementation as required [79]. Postural drainage with tilt (head-down positions) is no
256 longer advised for babies, as it has been shown to increase the gastroesophageal reflux [80].

257

258 As children grow older, they can more actively participate in their treatment. Children over 3 years
259 old can also use an airway clearance game, the bubble PEP. This is a positive-pressure breathing
260 home-made device, where children are encouraged to generate soap bubbles by breathing out
261 through a small plastic tube and into a bottle of soapy water [81]. According to the UK Cystic
262 Fibrosis Foundation, at the age of 6 years or more, the use of nebulised hypertonic saline can be
263 initiated in combination with airway clearance [82]. Also, at all ages, activity games and
264 engagement with exercise are encouraged and used, for instance racing, trampolines and exercises
265 using a gym ball [83].

266

267 *Palliative care*

268 CF is a disease that limits life expectancy and requires discipline and consistency to many hours of
269 daily treatment. As a result, its psychological impact should not be ignored [84]. If patients are in
270 respiratory failure and in lung transplantation list, pulmonary rehabilitation is the treatment priority,
271 alongside the aim to relieve symptoms. Working in line with the patient's wishes is very important,
272 particularly during the palliative care stage. Airway clearance of less active patient participation (eg.
273 postural drainage), massage and some dyspnoea relieving positions could be applied during this
274 stage, if they provide comfort to the patient [85].

275

276 **CONCLUSIONS**

277 CF management is highly demanding, mainly aiming to the reduction and treatment of chest
278 infections, improvement of quality of life and increase of life expectancy. Physiotherapy is an
279 integral part of the patient's daily treatment routine, and additionally to airway clearance other
280 important issues should be addressed. International clinical guidelines suggest access to specialised
281 physiotherapy care both during a clinically stable stage of the disease and during respiratory
282 infections. At the clinically stable stage, patients should be evaluated by physiotherapists every 3-6
283 months to re-evaluate and optimize their treatment plan. During respiratory infections,
284 physiotherapy interventions are intensified according to the clinical presentation. Although in CF
285 airway clearance is the cornerstone of physiotherapy treatment, physiotherapists work beyond the
286 respiratory system and play an important role in the management of other issues, mainly using
287 individualised exercise programmes. The exercise programmes need to be tailored to patient-related
288 needs and issues, such as pain, diabetes and incontinence. This way, the patient-centred and
289 individualised treatment follows the international standards and clinical guidelines.

Table 1. Common airway clearance techniques and methods.

Airway clearance techniques
Postural drainage
Manual techniques
Active circle of breathing techniques (ACBT)
Autogenous drainage (AD)
Positive expiratory pressure (PEP) devices (PEP mask, Pari-PEP, etc)
Positive expiratory pressure (PEP) devices with oscillation (flutter, acapella, cornet, etc.)
Intermittent Positive Pressure Breathing (IPPB)
High frequency chest wall oscillation (HFCWO) or vest
Non-invasive mechanical ventilation (NIV)
Aerobic exercise

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