



Original Article

Risks associated with exercise testing and sports participation in cystic fibrosis

Katharina Ruf^{a,*}, Bernd Winkler^a, Alexandra Hebestreit^a, Wolfgang Gruber^b, Helge Hebestreit^a

^a Children's Hospital of the University, University of Würzburg, Germany

^b AHG Klinik für Kinder und Jugendliche, Beelitz-Heilstätten, Germany

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Abstract

Background: Severe adverse reactions (SARs) associated with physical exercise have not been systematically studied in cystic fibrosis (CF).

Methods: Two surveys were conducted to assess the incidence of exercise-related SARs: a caregiver survey asking for complications associated with exercise testing and in-hospital training therapy and a web-based patient survey asking for problems with exercise.

Results: 78 of 107 CF facilities caring for 4208 patients responded to the caregiver survey, 256 patients answered the web-based survey. No SARs were reported for 713 exercise tests. With in-hospital training, the yearly incidence of exercise-related SARs such as pneumothorax, cardiac arrhythmia, injury or hypoglycaemia was <1% each, the respective lifetime incidences reported by the patients were 0.8–6.3%. 67% of the patients reported no SARs with exercise.

Conclusions: Exercise testing is safe in patients with CF. Despite the limitations in quality of data, the incidence of exercise-related SARs appears low in this population.

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Keywords: Cystic fibrosis; Exercise testing; Physical activity; Risks; Adverse reactions

1. Background

Physical activity has become an important component in the treatment of patients suffering from cystic fibrosis (CF). Several studies have shown that these patients benefit from physical exertion in many respects: a higher physical fitness, a slower decline in lung function, and a higher quality of life [1]. As regular exercise seems to be an enjoyable, simple and cheap way to affect the clinical course of CF, patients are encouraged to engage in exercise [2,3]. It has to be kept in mind, however, that CF is an illness that causes pathological changes of pulmonary and cardiac function and may negatively affect the endocrine and musculo-skeletal system (as in CF-related diabetes and osteoporosis) and that therefore exercise might bear certain risks.

Exercise-induced oxygen desaturation has been studied in the past and can easily be assessed and treated [4,5]. Little is

known, though, about other severe health hazards associated with exercise in CF such as pneumothorax, cardiac arrhythmias, hypoglycaemia, and fractures as such adverse reactions to exercise have been underexamined so far.

Hence, the aim of this study was to identify adverse reactions associated with exercise in CF and their incidence. Questionnaires addressing caregivers and patients were employed to include a large sample.

In this study, the term ‘exercise’ is used to describe physical activities as well as sports, as we consider it to summarize best the items asked for in the questionnaires. Furthermore, the term exercise is widely used when referring to any kind of physical activity recommended to patients with CF [2,6–8].

2. Materials and methods

This study comprises two independent studies, in which adverse reactions to exercise were assessed with the help of questionnaires. In the first study that took place in 2005, caregivers of

* Corresponding author. Universitäts-Kinderklinik, Josef-Schneider-Str. 2, 97080 Würzburg, Germany. Tel.: +49 931 201 27101; fax: +49 931 201 27242.

E-mail address: ruf_k@klinik.uni-wuerzburg.de (K. Ruf).

patients with CF were asked to retrospectively report adverse reactions to exercise that had occurred during 2005. A second questionnaire that addressed the patients directly was administered in 2008. Both questionnaires were translated into English and are available as appendices.

The first survey addressing the caregivers took place between April and December 2006. With the help of the German CF foundation (“Mukoviszidose e.V.”), a three-page questionnaire was sent via mail to all German institutions caring for patients with CF, namely 101 German CF centres (university hospitals, non-academic hospitals, and private offices) and to 6 rehabilitation hospitals specialised in the treatment of CF.

From the 107 CF care facilities contacted we obtained answers from 78 facilities (among these 6 rehabilitation hospitals). If caregivers did not respond to the questionnaire, we contacted them via the “Mukoviszidose e.V.” two more times and sent the questionnaire again to enhance the return rate, which finally was 73%. The facilities responding reported data of 4208 patients. 3774 of these patients were seen in CF centres. This sample represents 83% of all patients recorded in the German CF registry for 2005 [9]. 434 patients were treated as in-patients in rehabilitation institutions. Further information regarding patient’s height, weight, and exercise testing data was not included in the survey as the focus lay on capturing adverse reactions.

Whereas the caregiver survey mainly focused on adverse reactions during in-hospital exercise, the second survey addressed the patients directly and asked for adverse reactions related to non-supervised exercise at home. This second, anonymous survey addressed patients using a web-based approach and took place in 2008. All German patients with CF were invited to participate by their CF centre, by regional patient groups, and through an announcement in the German CF magazine. Patients were invited no matter whether their institution had taken part in the 2006 caregiver survey or not. Thus, this descriptive study used a convenience sample of patients from Germany whose data are most likely also included in the German CF registry.

The ethics committee of the University Hospital of Würzburg approved this survey which was published on the website <http://www.mukosport.info>. Informed consent was

obtained through ticking consent boxes on the first page of the questionnaire. Participants or their legal guardians consented that they accepted the privacy statement explained on the website; furthermore they agreed to their data being saved and to the analysis of their data for scientific purposes.

2.1. Questionnaires

Both questionnaires employed were developed by KR and HH to specifically assess severe adverse reactions to exercise in patients with CF. For the list of possible adverse reactions, we considered reactions encountered in our own clinical experience [5,10] and from anecdotal reports of other CF clinicians. We selected only adverse reactions which were considered severe and thus clinically relevant. Reliability and validity of the questionnaires were not established. However, we assume that severe adverse reactions would be remembered well.

The caregiver questionnaire assessed complications during exercise testing and in-hospital physical training therapy which had occurred in 2005 in the respective institutions. Specifically, we asked for cardiac arrhythmia, pneumothorax, and hypoglycaemia during exercise testing and these three adverse reactions plus injuries (sprains, contusions, and fractures) during in-hospital physical training therapy. Each institution returned only one questionnaire, which summarized all adverse reactions that had occurred in the respective institution.

The patient questionnaire asked the patient or his or her guardian for actual age, height, weight, FEV1 (in % predicted), and colonization with *Pseudomonas aeruginosa*. Furthermore, the questionnaire asked for the following adverse reactions to exercise which might have occurred anytime in the patient’s past: pneumothorax, injuries, loss of consciousness, and asthma attacks (acute dyspnoea and cough occurring after the end of the exercise) associated with exercise. These questions were worded as closed questions, i.e. patients chose one or more statements out of a list provided. Patients, though, had extra space to specify their adverse reactions and to give additional comments. There was also space to add further severe adverse reactions. Reactions that were additionally reported were hypoglycemia, haemoptoe and arthritis manifesting or significantly worsening during exercise.

Table 1
Incidence of exercise-associated adverse reactions in the caregiver survey (2005).

	Adverse reaction	Number of reported patients for 2005 (% of respective sample)
Exercise testing (n=434 in 29 CF care centres plus n=279 in 5 rehabilitation institutions)	Cardiac arrhythmias	0
	Pneumothorax	0
	Hypoglycemia	0
In-hospital physical training therapy (n=557 in 31 CF centres plus n=338 in 6 rehabilitation hospitals)	Cardiac arrhythmias	1 (0.1%)
	Pneumothorax	0
	Hypoglycemia	4 (0.4%)
	Injuries such as fractures, sprains, contusions	8 (0.9%)

Note: the percentages given were calculated by dividing the number of respective adverse reactions by the total number of patients undergoing exercise testing or by the number of patients participating in in-hospital physical training therapy, respectively.

Table 2
 Patients' characteristics from the online patient survey 2008 in comparison to the respective data in the German CF registry for the year 2008 (14).

Age		Height (cm)		Weight (kg)		BMI percentile (0–17 years) BMI (kg/m^2) (> 18 years)		FEV1 (%)		Exercise participation (hours per week)		<i>P. aeruginosa</i> colonization	
		Patient survey	CF registry	Patient survey	CF registry	Patient survey	CF registry	Patient survey	CF registry	Patient survey	CF registry	Patient survey	CF registry
0–5	Male (N=4)	98.8±12.4	n.a.	16.8±5.2	n.a.	64.3±27.3	46.1 ^a N=641	n.a.	n.a.	11.0±11.6	(n.a)	0%	14%
	Female (N=3)	104.7±6.4	n.a.	15.5±2.2	n.a.	18.7±2.5	n.a.	n.a.	n.a.	9.3±3.1	(n.a)	33%	
6–13	Male (N=15)	138.0±9.1	n.a.	31.5±5.5	n.a.	38.7±26.9	34.7 ^a N=1216	94.2±12.0	91.8 ^a N=1179	6.5±5.8	(n.a)	13%	28%
	Female (N=19)	138.9±16.5	n.a.	32.0±11.2	n.a.	34.3±27.9	n.a.	92.6±16.2	n.a.	5.5±3.3	(n.a)	21%	
14–17	Male (N=10)	166.6±12.8	n.a.	50.2±13.1	n.a.	24.3±23.0	33.2 ^a N=641	77.8±14.3	84.2 ^a N=619	5.1±3.7	(n.a)	50%	46%
	Female (N=11)	158.3±8.4	n.a.	50.6±7.4	n.a.	43.9±23.9	n.a.	76.5±21.0	n.a.	3.6±82.4	(n.a)	36%	
> 18	Male (N=81)	176.4±6.8	n.a.	66.6±10.5	n.a.	21.4±3.0	20.7±3.0	62.4±4.2	59.6±29.2	6.2±6.7	(n.a)	79%	68%
	Female (N=113)	164.7±6.0	n.a.	55.4±7.0	n.a.	20.4±3.0	N=2393	61.8±22.2	N=2332	6.8±6.4	(n.a)	78%	

Values are mean±standard deviation or, for *P. aeruginosa* colonization only, percentage of sample.

Abbreviations: n.a. — not available; N — number of patients contributing data.

^a Since the report of the German CF registry used different age ranges for grouping, only means but no standard deviations can be provided.

2.2. Data analysis

Data are presented descriptively as number of reported adverse reactions separately for exercise testing, in-hospital physical training therapy (both taken from the caregiver survey) and lifetime complications of exercise reported by the patients. In the patient survey, group differences between patients with adverse reactions and those without adverse reactions were tested. A Chi-Square test was used to test for differences between male and female patients with regard to the incidence of the various adverse reactions assessed (injury, pneumothorax, asthma attack, haemoptoe and arthritis manifesting during exercise). Mann–Whitney-U-Tests (due to a lack of normal distribution identified with the help of the Kolmogorov–Smirnov test) were used to assess differences between patients with and without an adverse reaction (injury, pneumothorax, asthma attack, haemoptoe and arthritis manifesting during exercise) with regard to age, weight, and FEV1%. Incidence rates relative to the number of exposed patients and – for the data from the patient survey only – relative to 1000 patient years were also calculated.

Data of the online survey was retrieved from the online platform as excel file (Excel, Microsoft); all statistical analysis were performed by SPSS 16.0 (SPSS Inc.).

3. Results

3.1. Caregiver survey

Questionnaires were returned by 72 non-rehabilitation CF centres and 6 rehabilitation centres. In the group of the non-rehabilitation CF centres, exercise testing was performed by 29 institutions (40%). All in all, 434 patients (10%) were tested (213 adults older than 18 years and 221 children). An in-patient physical training therapy was part of the treatment in 31 CF centres (43%), with 557 patients attending the programs, among these 319 adults and 238 children. In the group of the rehabilitation hospitals, 5 of 6 institutions performed exercise testing and tested 279 (64%) of the 434 patients seen in these hospitals, 104 adults and 175 children. All rehabilitation hospitals offered in-patient physical training therapy; 338 patients (78%) participated in respective programs, 101 adults and 237 children.

During exercise testing, no adverse reactions occurred. The incidence of adverse reactions during in-patient physical training therapy was below 1% for each of the assessed complications pneumothorax, hypoglycaemia, injury, and cardiac arrhythmias (Table 1).

3.2. Patient survey

In total, data from 256 patients (146 females) aged 0 to 65 years (mean age 26 years), with an FEV1 between 10 and 125% predicted (on average 68%) and a mean reported engagement in exercise of 3.6 hours per week became available. Among the 256 patients (representing 5% of the patients reported to in the German CF registry in the year 2008), 46 (18%

Table 3
Participants' engagement in different activities reported in the patient survey (2008).

Activity	Number of participants' replies (n=403)	% of all participants' replies (n=403)
Endurance activities (e.g. running, cycling, swimming, and walking)	166	41.2
Team Sports (e.g. soccer, volleyball, and handball)	51	12.6
Individual Sports (e.g. tennis, yoga, gymnastics, dance, martial arts, and rowing)	93	23.1
Fitness centre/weight training	93	23.1

Note: Patients had the possibility to report more than one activity. In order to create the table, the patients' answers were clustered into the above four categories. Some patients mentioned more than one activity within a category. In order to create the percentages, these multiple activities within a category were seen as one only. In total, 46 patients (18% of all patients included in the survey) did not report any activities.

of the study sample) did not engage in any exercise. 168 patients were chronically colonized with *P. aeruginosa*. The population responding to the survey was thus on average somewhat older than the average patient in the German registry (19.1 years in the registry vs. 25.9 years in the survey) and had a slightly worse lung function (FEV1: 72.4% in the registry vs. 67.8% in the survey). In our experience, the reported sports participation is relatively representative for German patients. Hebestreit et al. [11] found an average time spent in vigorous physical activity of

4.3 h per week in their study population. The patients' characteristics of the web-based survey are presented in Table 2.

The engagement in the different activities reported by the patients is summarized in Table 3. The activities reported have been clustered into four categories: endurance, team sports, individual sports, and fitness centre/weight training. In Table 3, examples for each category are provided.

171 of the 256 responding patients (67%) had not encountered any serious problem during exercise. The adverse reactions that were reported by the patients are summarized in Table 4. In total, 85 patients reported adverse reactions associated with exercise. The most common adverse reaction was an asthma attack (22% of all patients in the survey), followed by injury (6%), pneumothorax (4%), and loss of consciousness (1%). Adverse reactions not specifically asked for in the survey but reported by the patients were arthritis worsening with exercise (4%), haemoptoe (3%), and hypoglycaemic events associated with exercise (1%). Pseudomonas colonization and a low FEV1 were associated with asthma attacks while high age was a risk factor for pneumothorax (Tables 4 and 5). Female patients were more likely to report arthritis manifesting or worsening during exercise (Tables 4 and 5).

4. Discussion

As regular exercise is a recommended treatment for patients with CF and increasingly established as an important component of CF therapy, this study intended to gain an insight into

Table 4
Characteristics of patients with and without exercise-associated adverse reactions anytime in life reported in the patient survey 2008.

	<i>P. aeruginosa</i> colonization	Age (years) Mean±SD [range]	Gender m = male f = female	FEV1 (%) Mean±SD [range]	Weight (kg) Mean±SD [range]	Incidence per 1000 patient years
Pneumothorax ^a	Yes N=10	7 (70%) 34.8±18.9 [18–44]	4 m, 6 f	61.9±23.3 [21–93]	54.2±15.4 [12–95]	0.15%
	No N=246	161 (68%) 25.6±11.2 [0–65]	106 m, 140 f	68.2±24.8 [10–125]	56.5±10.4 [44–77]	
Injury ^a	Yes N=16	11 (69%) 26.8±9.0 [11–41]	6 m, 10 f	69.6±25.3 [22–105]	53.9±15.5 [12–95]	0.39%
	No N=240	157 (65%) 25.9±11.4 [0–65]	104 m, 136f	67.8±24.8 [10–125]	59.4±9.5 [41–77]	
Asthma attack (acute shortness of breath and cough occurring after exercise) ^b	Yes N=56	43 (77%) 28.4±8.8 [11–49]	22 m, 34 f	58.5±25.3 [14–115]	53.7±16.0 [12–95]	0.84%
	No N=200	125 (63%) 25.2±11.8 [0–65]	88 m, 112f	70.4±24.1 [10–125]	56.4±11.9 [16–82]	
Arthritis manifesting during exercise ^b	Yes N=9	8 (89%) 30.3±11.1 [11–43]	1 m, 8 f	57.2±12.8 [40–73]	54.2±15.4 [12–95]	0.14%
	No N=247	160 (68%) 26.0±11.2 [0–65]	109 m, 138f	68.3±25.0 [10–125]	55.9±10.7 [34–73]	
Haemoptoe ^b	Yes N=8	7 (88%) 30.1 (7.2) [20–44]	4 m, 4 f	69.3±20.8 [22–105]	54.1±15.4 [12–95]	0.12%
	No N=248	161 (68%) 25.8 (11.3) [0–65]	106 m, 142f	69.0±24.9 [10–125]	61.3±4.8 [53–37]	
Hypoglycemia ^b	Yes N=2	1 28, 31	1 m, 1 f	72, 89	56, 69	0.03%
Loss of consciousness ^a	Yes N=2	2 27, 31	1 m, 1 f	70, 75	54, 77	0.03%

^a The survey asked specifically for these severe adverse reactions occurring during or shortly after exercise.

^b These severe exerciserelated adverse reactions were additionally reported by the patients.

Table 5

Risk factors for severe adverse reactions to exercise in patients with CF. The table shows probability (p)-values of a type 1 error when assuming a significant difference between patients with and patients without a severe adverse reaction with respect to gender, *P. aeruginosa* colonization, age, FEV1, and weight based on Chi-Square- and Mann–Whitney-U-test statistics.

	Gender p-value ^a	<i>P. aeruginosa</i> colonization p-value ^a	Age (years) p-value ^b	FEV1 (%) p-value ^b	Weight (kg) p-value ^b
Pneumothorax ^c	0.847	0.776	0.008	0.500	0.839
Injury ^c	0.648	0.186	0.767	0.640	0.143
Asthma attack ^c	0.529	0.047	0.067	0.002	0.221
Arthritis manifesting during exercise ^d	0.049	0.135	0.217	0.137	0.776
Haemoptoe ^d	0.683	0.186	0.246	0.966	0.079

Bold data are those *p*-values which are significant.

^a Chi-Square-test.

^b Mann–Whitney-U-test.

^c The survey asked specifically for these severe adverse reactions occurring during or shortly after exercise.

^d These severe exercise-related adverse reactions were additionally reported by the patients.

possible serious risks of exercise for CF patients. We tried to cover a large number of patients in order to identify problems with a low incidence.

The yearly incidence of cardiac arrhythmias during exercise testing and in-patient physical conditioning in our caregiver survey was 0–0.1% and matches that of the healthy population [5,12,13] but appears far lower than recently reported for CF patients [5]. This latter discrepancy may reflect an unawareness of caregivers with respect to exercise-induced cardiac arrhythmias resulting in less ECG recordings during exercise tests and thus a low detection rate.

More than 10% of all patients with CF suffer from a CF-related diabetes mellitus and even more from an impaired glucose tolerance [14]. Although there are reports on hypoglycaemic episodes in patients with CF [15] the role of exercise as trigger of symptomatic hypoglycaemias has not been explored. We found an incidence of exercise-induced symptomatic hypoglycaemia in 0.4% of all patients represented in our caregiver survey and 0.8% in the patient survey. These numbers are low compared with the 20% incidence of hypoglycaemias with loss of consciousness reported by patients with CF-related diabetes [16] even if the prevalence of this condition among the CF population is assumed to be only 10% and thus somewhat less than that reported for German patients [14]. This may be due to a certain underreporting in the web-based survey as we did not explicitly ask for hypoglycemia but relied on the patients to mention it in the additional space for further severe adverse reactions.

We found a lifetime incidence of pneumothoraces of about 4% in our patient survey. This is in line with Flume [17] who reported an incidence of 3.4% spontaneous pneumothoraces in a population of 965 patients with CF. The patients with pneumothorax in our population had a FEV1 ranging from 21% to 93% predicted and older age but not FEV1 was the only detectable risk factor. Five of the ten patients gave explanations for the situations when the pneumothorax occurred. All 5 patients reported that the pneumothorax occurred after a period of infection while coughing with exercise. Hence, at least 50% of the pneumothoraces reported in our survey were associated with cough, which may or may not have been exercise-induced.

Concerning exercise-related injuries, we found a yearly incidence of 0.9% during a supervised in-hospital physical

training therapy and an overall lifetime incidence of 6.3% in the patient survey. This seems extremely low in comparison to epidemiological studies on sports injuries in children and adolescence [18–20]. Based on the low incidence of injuries, CF-related osteoporosis did not seem to cause exercise-related fractures. A possible explanation for this low incidence is that CF patients may participate in less injury-prone activities or may exercise less vigorously than healthy people. Another reason for the low incidences of reported injuries in our surveys could be a recall bias, as minor injuries may not be remembered well and might, thus, have been underreported.

The limitations of our study certainly are that both surveys are subject to recall and participation bias. Minor adverse reactions may not be recalled at all, especially as we asked for any event during the patient's lifetime in the patient survey. This sometimes very long time span may have led to a certain underreporting of adverse reactions. However, we specifically asked for severe adverse reactions which are usually remembered well. Another limitation of the study design is the fact that neither of the questionnaires has been validated. Furthermore, we cannot exclude that some questions might have been ambiguous for some participants. Finally, the sample size of the patient survey was relatively small. Thus, especially rare risks may not have been discovered in this latter survey and the incidence rates reported have a large confidence interval.

In order to gain further insight in severe adverse reactions associated with exercise, new methods of reporting adverse reactions need to be developed and established in order to identify patients at risk. The data of our study, though, suggests that exercise testing is safe in patients with CF when conducted under controlled conditions by trained personnel. Although there are a variety of possible adverse reactions in this population, the incidence appears low for both in-hospital physical training and physical activities and exercise during daily life.

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Appendix A

Survey 2005

1. institutional information

- private office, university hospital, non-university hospital, rehabilitation hospital
- number of patients care for in 2005:
 - Patients 18 years and older: _____
 - Patients younger than 18 years: _____

2. complications during exercise testing

- Are you conducting exercise tests in your institution?
 - yes ○ no
- If yes, how many patients underwent an exercise test in the year 2005?
 - Patients 18 years and older: _____
 - Patients younger than 18 years: _____

Type of complication	Number of patients
Pneumothorax	
Cardiac arrhythmia	
Hypoglycaemia (symptomatic and measured)	

3. complications during in-hospital supervised training therapy

- Has your institution offered in-hospital supervised training therapy during exercise- and physiotherapy (endurance training, weight training)?
 - yes ○ no
- If yes, how many patients took part in the training therapy in the year 2005?
 - Patients 18 years and older: _____
 - Patients younger than 18 years: _____

Type of complication	Number of patients
Pneumothorax	
Cardiac arrhythmia	
Hypoglycaemia (symptomatic and measured)	
Injuries (strains, contusions, fractures)	

Survey 2008

- Please enter your age: _____
- Please check the box whether you're male or female:
 - female ○ male
- Please enter your current FEV1 in % predicted: _____
- Are you chronically colonized by *Pseudomonas aeruginosa*?
 - yes ○ no
- How many hours per week do you engage in physical activity and sports (e.g. soccer, running, dancing): _____h/week
- What kind of physical activity and sports did you participate in during the last month?
 - Activity / Sport 1: _____
 - Activity / Sport 2: _____

- Activity / Sport 3: _____
- Activity / Sport 4: _____
- Activity / Sport 5: _____
- Did you ever encounter severe adverse reactions during physical exertion?
 - No severe adverse reactions
 - pneumothorax
 - asthma attack (cough and shortness of breath occurring after the end of exercise)
 - unconsciousness
 - injury
 - any other problem: _____
- If applicable, please specify the symptoms and the situations of the adverse reactions you reported: _____

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