Gait & Posture 78 (2020) 60–64

Contents lists available at ScienceDirect

Gait & Posture

journal homepage: www.elsevier.com/locate/gaitpost

Full length article

Three-axis accelerometer system for comparison of gait parameters in children with cystic fibrosis and healthy peers

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ARTICLE INFO

Keywords:
Cystic fibrosis
Functional exercise capacity
Gait parameters
Accelerometer
Six-minute walk distance

ABSTRACT

Background: Cystic Fibrosis (CF), affecting functional exercise capacity generally measured by submaximal exercise test such as 6min walk test, is a progressive, autosomal recessive and metabolic disorder. Three-axis accelerometers, which are used during gait, are an easy way to assess gait parameters in patients and healthy individuals. Gait parameters were significantly associated with clinical outcomes of COPD. However, the association between gait parameters and clinical outcomes in children with CF is unclear.
Research question: Do clinical outcomes in CF have an important role in determining gait parameters?.
Methods: Twenty-one CF and 21 healthy subjects participated in this case-control study. Body composition was evaluated using Tanita-BC 418. Respiratory and knee extension muscle strengths were assessed. Functional exercise capacity was evaluated using the 6-min walk test (6MWT). Spatiotemporal gait parameters were evaluated using a validated wireless inertial sensing device (G-Sensor, BTS Bioengineering S.p.A., Italy) during the 6MWT and 7-meter gait test.
Results: MIP, the distance of 6MWT, and stride length were significantly lower in the CF group compare to healthy children ($p < 0.05$). Gait speed and functional exercise capacity, cadence and functional exercise capacity, quadriceps muscle strength, FEV1, fat-free mass were found to be correlated in CF patients ($p < 0.05$).
Significance: The aerobic capacity and gait parameters were affected in CF patients with mild disease severity in our study. Clinical outcomes were associated with gait parameters in CF patients. This is the first study to use the 3-axis accelerometer to evaluate functional exercise capacity and gait parameters of CF and healthy children. A three-axis accelerometer can be used to assess functional exercise capacity and gait parameters in CF patients at the clinics.

1. Introduction

Cystic Fibrosis (CF); is a progressive, autosomal recessive and metabolic disease that affects many systems [1]. Systemic inflammation, oxidative stress, the progression of airway obstruction, malnutrition and physical inactivity cause decreased functional capacity [2].

The 6-min walk test (6MWT) is frequently used for functional capacity evaluations, monitoring of effectiveness of interventions, and prognosis by predicting morbidity and mortality in patients with CF [3]. The lack of 6 MWT reference values in children with CF causes limited interpretation of results.

Evaluating and analyzing gait performance is necessary to determine the level of disability in patients or for assessing the effectiveness of a rehabilitation intervention [4]. Previous studies have revealed that decreased gait speed is a strong indicator of poor exercise capacity (6-minute walk distance [6MWD] ≤350m) and short-term mortality in COPD [5]. Gait parameters like gait speed, stride length, and cadence were found to be significantly associated with clinical outcomes of COPD [6]. Okuro et al. [7] found that gait speed could represent overall CF conditions.

Gait is a complex movement that can be assessed not only by gait speed but also by numerous spatiotemporal parameters [8]. Since the

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https://doi.org/10.1016/j.gaitpost.2020.02.018
Received 9 December 2019; Received in revised form 6 February 2020; Accepted 25 February 2020

body center of mass moves in three dimensions during gait, a three-axis accelerometer can evaluate the spatiotemporal parameters, such as speed, cadence, step length, stance phase, swing phase, single support phase, double support phase and pelvic movements [9]. Spatiotemporal gait parameters were assessed using a validated [10] wireless inertial sensing device (G-Sensor, BTS Bioengineering S.p.A., Italy) that was found to be reliable in analyzing gait performance of healthy children [11]. Three-axis accelerometer used during 6 MWT and 7-meter gait tests were generally used to analyze gait parameters during walking in healthy subjects [11], neurological patients [12] and type-2 diabetes [13]. As far as to our knowledge, there is no study evaluating gait parameters with a three-axis accelerometer in CF patients.

The relationship between gait parameters and clinical outcomes in children with CF is unclear. Gait analysis systems were expensive and required a large laboratory environment. Therefore, we aimed to assess gait parameters with a three-axis accelerometer and clinical outcomes in CF patients and healthy controls. Also, it was aimed to determine the relationship between gait parameters and respiratory muscle and quadriceps muscle strength in CF patients.

2. Methods

2.1. Subjects

This case-control study was carried out with a group of subjects with CF (the CF group) regularly monitored in the Child Health and Diseases unit at the University Hospital of the Dokuz Eylül University from September 2017 to May 2019. Subjects age 7–18 y with a confirmed diagnosis of CF by two altered sweat tests were included in the study. Individuals with acute pulmonary exacerbations and patients receiving long-term oxygen therapy were excluded from the study. The control group (CG) included volunteers between 7 and 18 y old, non-smokers without a previous history of respiratory diseases, and orthopedic problems. This study was approved by the Noninvasive Research Ethics Board of Dokuz Eylül University (decision number: 2017/18–27). All of the subjects or their parents gave written informed consent.

2.2. Assessments

The demographic characteristics of the subjects were recorded. Shwachman scores and sweat test results of the CF group were taken from clinical records. Weight, fat-free mass (FFM) and body mass index (BMI) of the participants were measured using body analyzer (TANITA BC 418 MA, Japan) [14]. Dyspnea perception scores with the modified Borg scale were recorded at rest and activity.

2.2.1. Pulmonary functions

Forced Expiratory Volume in 1s (FEV_1) was measured by spirometry (SensorMedics, 6200 Body Box, Viasys, USA) and also described as a percentage of predicted FEV_1 value [15].

2.2.2. Muscle strength

Respiratory muscle strength was measured using a mouth pressure device (Micro Medical MicroMPM, United Kingdom). Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) measurements were recorded [16]. Quadriceps muscle strength was measured using a digital handheld dynamometer (JTECH, Medical Commander Powertrack II, USA). [17].

2.2.3. Functional exercise capacity

Functional exercise capacity was evaluated using the 6MWT. It was conducted following the American Thoracic Society/European Respiratory Society recommendations [18]. The subjects were instructed to walk as far as possible in 6 min in an enclosed 30 m-long corridor. Standardized encouragement was given once per minute. The maximum distance covered at the end of the test was recorded. The 6MWD was expressed as percentages of the expected values from age and sex (% 6MWD) [19]. During 6MWT, walking distance was measured using a 3-axis accelerometer that was attached to the subject's waist using a semi-elastic belt, covering the L4–L5 intervertebral space [10].

2.2.4. Gait parameters

Spatiotemporal gait parameters were assessed using a validated [10] wireless inertial sensing device (G-Sensor, BTS Bioengineering S.p.A., Italy) that was attached to the subject's waist using a semi-elastic belt, covering the L4–L5 intervertebral space, to acquire the acceleration values for the three anatomical axes. Gait parameters were obtained through analysis of trunk accelerations which have been demonstrated to be reliable in characterizing children's gait patterns [20]. Subjects were asked to walk along a 7-m pathway, at a self-selected speed, as naturally as possible. The weight of the accelerometer was 62 g, with dimensions of 78 × 48 × 20 mm. The collected data, transmitted via Bluetooth to a PC and processed using dedicated software (BTS G-Walk), allowed us to obtain gait parameters like stride length (%), gait speed, cadence (number of steps per minute), stance and swing phase, single support and double support phase.

2.3. Statistics

The statistical evaluation was performed using the SPSS 22.0 statistical software. The data are presented as mean ± SD. Normal distribution was evaluated by the Shapiro-Wilk test. The continuous variables were compared using Student's *t*-test when the assumptions of the parametric tests were met by the data. The variables determined by counting were compared by the Chi-Square test. The height, weight, BMI, and FEV_1 results were expressed as Z scores. Pearson's correlation was performed to detect variables that were correlated. The correlation coefficients (r) between variables were classified as weak (0.26-0.49), moderate (0.50-0.69), high (0.70-0.89) and very high (0.90–1.00) [21]. Statistical significance was set at $p < 0.05$.

Power analysis was performed with the program G*Power 3.1 for the sample size determination with an α of 0.05, effect size of 0.95, and power of 0.88 [7]. The calculated sample size was 42 participants (21 per group).

3. Results

Twenty-one CF patients in the CF group and 21 healthy subjects in CG participated in the study. The mean sweat test result of the CF patients was 103.80 ± 20.77 mEq/L and the mean score of Shwachman was 74.76 ± 11.77. According to the mean Shwachman score, the disease severity of CF patients in our study was mild. Table 1 presents the characteristics and muscle strengths of CF and CG. Gender, age, height, weight, BMI, and FFM were similar in both groups ($p > 0.05$). FEV_1 and MIP were significantly lower in the CF group than CG ($p < 0.05$). There were no significant differences in height Z-score, weight Z-score, BMI Z-score and FEV_1 Z-score between two groups ($p > 0.05$). Dyspnea scores were significantly higher in the CF group than CG ($p < 0.05$). There were no significant differences in MEP and quadriceps strength between the two groups ($p > 0.05$).

Table 2 shows the functional exercise capacity and gait parameters in CF and CG. 6MWD, gait speed, and stride length were significantly lower in CF than CG ($p < 0.05$). Cadence, stance phase, swing phase, single support phase and double support phase were similar in both groups ($p > 0.05$).

Table 3 shows the relationship between gait parameters and other outcomes in CF. Cadence was moderate positive correlated with 6MWD (%) and quadriceps strength, moderate negative correlated with FFM ($p < 0.05$). A high positive correlation was found between gait speed and 6MWD(m), 6MWD(%) ($p < 0.05$). Stride length was weak positive correlated with quadriceps strength, moderate positive correlated with

Table 1
Characteristics and muscle strengths of CF and CG.

Characteristics	CF (n = 21)	CG (n = 21)	t/ χ^2	p
Gender			< 0.001	0.999¶
Female	11 (%52.4)	11 (%52.4)		
Male	10 (%47.6)	10 (%47.6)		
Age (years)	12.76 ± 2.77	12.71 ± 3.00	−0.053	0.958†
Height (cm)	148.23 ± 16.63	154.14 ± 17.47	1.122	0.269†
Height Z-score	0.04 ± 0.92	−0.01 ± 0.87	0.154	0.878
Weight (kg)	39.84 ± 15.75	48.8 ± 21.07	1.538	0.132†
Weight Z-score	−0.01 ± 0.95	−0.05 ± 0.87	0.133	0.895
BMI (kg/m^2)	17.35 ± 3.29	19.47 ± 4.12	1.840	0.073†
BMI Z-score	0.02 ± 0.85	−0.03 ± 0.76	0.131	0.896
FFM (kg)	32.55 ± 11.68	39.51 ± 14.62	1.705	0.096†
FEV_1 (L)	1.93 ± 1.04	2.80 ± 1.06	2.666	**0.011**†*
FEV_1 (L) Z-score	−0.01 ± 0.74	−0.02 ± 0.76	0.016	0.987
FEV_1 (%)	78.76 ± 27.51	98.95 ± 11.10	−3.234	**0.003**†*
FEV_1 (%) Z-score	0.01 ± 0.83	0.02 ± 0.85	< 0.001	0.999
MIP (cmH_2O)	65.66 ± 21.50	88.28 ± 18.08	3.689	**0.001**†*
MIP (%)	98.64 ± 34.16	134.17 ± 38.71	3.153	**0.003**†*
MEP (cmH_2O)	87.09 ± 21.42	93.04 ± 16.74	1.002	0.323†
MEP (%)	82.53 ± 23.21	88.34 ± 17.05	0.924	0.361†
Quadriceps Strength (kg)	14.47 ± 5.07	16.81 ± 5.82	1.390	0.172†
Dyspnea at rest	1.57 ± 2.22	0 ± 0	−5.433	**0.002**†*
Dyspnea at activity	4.33 ± 1.70	1.85 ± 1.16	0.098	< **0.001**†*

BMI, body mass index; FFM, Fat Free Mass; FEV_1, forced expiratory volume in one second; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; ¶Fisher Chi-Square test, †Independent samples t test,*p < 0.05, CF: cystic fibrosis; CG: control group.

FFM and FEV_1 (p < 0.05). The stance phase was weak negative correlated with quadriceps strength, moderate negative correlated with FEV_1, weak positive correlated with dyspnea at activity (p < 0.05). The swing phase was weak positive correlated with quadriceps strength, moderate positive correlated with FEV_1 (p < 0.05). The double support phase was weak negative correlated with quadriceps strength and FEV_1 (p < 0.05).

4. Discussion

The aerobic capacity and gait parameters were affected in CF patients with mild disease severity in our study. This is the first study to use the 3-axis accelerometer to evaluate functional exercise capacity and gait parameters of CF and healthy children.

The most commonly used methods for the nutritional status assessment in CF patients are BMI and FFM estimation. In our study, CF patients had lower FFM and BMI, although there was no significant difference from healthy individuals, and our results were similar to the research conducted on CF in assessment of nutritional status [22].

Contrary to the results found in the literature, we found no significant difference in quadriceps muscle strength between CF and healthy subjects. We thought that this is due to the fact that the severity of the disease in CF patients in our study was mild and that BMI and FFM were similar to the healthy group.

In a study investigating respiratory muscle strength in CF, the CF group had significantly lower MIP and MEP than the healthy group [23]. In a study, no significant difference was found between MIP and MEP values between CF and healthy individuals [3]. Divangahi et al. [24] found that calcium malabsorption due to CFTR deficiency and diaphragmatic dysfunction due to pulmonary infections caused early muscle weakness in the diaphragm in CF patients. In our study, only MIP was affected in CF patients.

In studies investigating functional exercise capacity using 6MWT in CF, the CF group had significantly lower 6MWD than the healthy group [3,25]. Troosters et al. [26] found that exercise capacity was maintained if the percentage of 6MWD was above 82 %. In a study, it was found that VO2max values are unchanged and in normal range in mild CF patients undergoing cardiopulmonary exercise testing [27]. Although the percentage of 6MWD in CF patients in our study is within normal range, it is lower than healthy individuals, indicating that 6MWD can be used relatively as well as laboratory tests evaluating functional capacity in mild CF patients. Okuro et al. [7] found that the CF group had a significantly lower gait speed than the CG. In our study, CF patients had significantly lower gait speed than healthy individuals.

There are no reference values for 6MWD in children with CF. Therefore, the use of different parameters provides additional information to evaluate and interpret the functional exercise capacity of CF patients. However, since gait analysis in the clinics has traditionally been limited to the use of subjective scales or assessment tools, an easy-to-use, convenient, and portable system is required for gait evaluation.

Table 2
Functional exercise capacity and gait parameters in CF and CG.

Variables	CF (n = 21)	CG (n = 21)	t	p
6MWD (m)	556.06 ± 80.12	645.21 ± 94.93	4.206	**0.002**†*
6MWD (%)	83.92 ± 12.70	96.39 ± 11.73	3.440	**0.002**†*
Gait speed (m/sn)	1.85 ± 0.38	2.21 ± 0.50	2.596	**0.013**†*
Cadence (steps/min)	135.45 ± 21.88	134.48 ± 21.00	−0.146	0.884†
Stride length (%)	49.26 ± 1.60	50.24 ± 1.35	−2.131	**0.039**†*
Stance phase (%)	60.45 ± 4.26	61.17 ± 4.49	0.534	0.596†
Swing phase (%)	39.21 ± 3.61	38.82 ± 4.49	−0.313	0.756†
Single support phase (%)	39.57 ± 3.35	40.89 ± 5.01	1.000	0.323†
Double support phase (%)	10.62 ± 3.21	10.24 ± 3.86	−0.344	0.733†

All values are expressed as mean ± SD. 6MWD; 6-minute walk distance; †Independent samples t test, *p < 0.05; CF: cystic fibrosis; CG: control group.

Table 3
Correlations between gait parameters and other outcomes in CF.

Variable	6MWD[a] (m)	6MWD[a] (%)	Quadriceps[a] Strength (kg)	FFM[a] (kg)	FEV_1[a] (L)	Dyspnea at activity[a]
Cadence (steps/min)	0.379	**0.559***	**0.524***	**−0.598***	−0.385	0.186
Gait speed (m/sn)	**0.719***	**0.730***	−0.023	−0.055	−0.152	0.193
Stride length (%)	0.364	0.257	**0.470***	**0.510***	**0.533***	0.042
Stance phase (%)	0.058	0.245	**−0.462***	−0.374	**−0.529***	**0.440***
Swing phase (%)	−0.092	−0.274	**0.484***	0.412	**0.540***	−0.413
Single support phase (%)	−0.105	−0.263	0.341	0.330	0.382	−0.259
Double support phase (%)	0.114	0.296	**−0.436***	−0.380	**−0.473***	0.359

6MWD; 6-minute walk distance; FFM, Fat Free Mass; FEV1, forced expiratory volume in one second; [a] r-value; *$p < 0.05$; CF: cystic fibrosis.

Accelerometers, which are used during gait, are an easy way to assess gait parameters in patients and healthy individuals because of their small size and wireless features (i.e. Bluetooth) [11]. The acceleration system required <5 min to measure and calculate the target gait parameters. Therefore, accelerometer-based gait analysis could be an alternative to gait analysis methods currently used in the routine clinical setting.

A three-axis accelerometer was found to be reliable in evaluating the spatiotemporal parameters in healthy adults and children [11]. In terms of validity, it has been found that cautious interpretation is needed for temporal parameters based on final foot contact (stance, swing and single/double support phase) [11]. In our study, we think that this is the reason that there is no difference between two groups in stance, swing and single/double support phase. Therefore, more comprehensive studies are needed to examine the validity and reliability of the G-Walk accelerometer with more subjects in healthy and CF children. Stride length was lower in patients with CF compared to healthy controls in our study. Hausdorff et al. [28] found that whenever the systems regulating gait are dysfunctional, movement control may be impaired leading to reduced stride lengths.

Although there are some studies on gait parameters during walking in healthy subjects [11], neurological patients [12], and type-2 diabetes [13], to the best of our knowledge, there is no study evaluating gait parameters with a three-axis accelerometer in CF patients. Our study is the first study to evaluate and compare gait parameters such as gait speed, step length, cadence, stance, swing and single/double support phase using G-Walk accelerometer in CF patients and healthy subjects.

Awotidebe et al. [13] found that gait speed demonstrated significant correlation with exercise capacity in both patients with type-2 diabetes and healthy controls. Gait speed was found to be an easy-to-use and clinically relevant screening tool for exercise capacity in routine COPD assessment. The associations between gait speed and important clinical outcomes in COPD such as exercise capacity, physical activity level, cognitive function, depression and quality of life, provide a basis for the use of gait speed as a powerful and informative tool to improve clinical care in this population [29]. Lahousse et al. [30] reported that in subjects with COPD, gait alterations are related to a slower walking speed. A possible explanation for taking slower steps may be to decrease the oxygen needs of the leg muscles and thus allow for long-distance walking in people with impaired lung function. Walking speed is a convenient variable to measure overall gait and functional mobility. Slow walking speed is related to some factors, such as decreased muscle strength and power, loss of independence, morbidity, and mortality in patients with chronic diseases. The associations between gait speed and modified Shwachman score and FEV1 in CF patients shows that gait speed is a good parameter that can also represent CF conditions [7]. As a result of the correlation analysis in our study, a high positive correlation was found between gait speed and functional exercise capacity. Iwakura et al. [6] found significant associations between quadriceps muscle strength and gait parameters and stride length in patients with COPD. In our study, quadriceps muscle strength was correlated with cadence, stride length, stance, swing and double support phase. Iwakura et al. [6] also found a significant correlation between cadence and 6MWD. In our study, cadence was correlated with 6MWD, quadriceps muscle strength and FFM. In contrast to the study in COPD [6], in our study, FEV_1 was correlated with stride length, stance, swing and double support phase. Therefore, a three-axis accelerometer may be used to evaluate increased ventilatory responses while walking short distances.

Our study has some limitations. Only mild CF patients were compared with their healthy peers. Future studies should evaluate the effect of clinical outcomes on gait parameters in CF patients with different disease severity. Although the number of participants determined by power analysis was evaluated, more participants could be evaluated. Therefore, future studies should be conducted with more subjects to examine the effect of clinical outcomes on gait parameters in children with CF.

5. Conclusions

This is the first study to evaluate and compare gait parameters such as gait speed, step length, cadence, stance, swing, and single/double support phase using the G-Walk accelerometer in CF patients and healthy subjects. A three-axis accelerometer can be used to evaluate functional exercise capacity and gait parameters in CF at the clinics.

As a result, functional exercise capacity and gait parameters were found to be affected in mild CF patients. Gait parameters demonstrated a significant correlation with clinical outcomes in CF. Clinical outcomes in CF have an important role in determining gait parameters. We believe that our study will provide information on evaluating gait parameters in terms of easy application of the three-axis accelerometer and guide for the outcome measures to be used in assessing the efficacy of physiotherapy and rehabilitation programs for CF patients.

Status of ethical clearance

This study was approved by the noninvasive research ethics board of the Faculty of Medical Sciences of Dokuz Eylul University under decision number 2017/18-27.

Funding

This project was supported by the Department of Scientific Research Projects, Dokuz Eylül University under project number 2018.KB.SAG.020. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Declarations of Competing Interest

None.

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