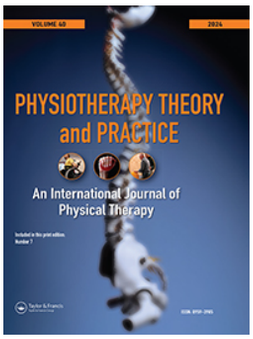

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RESEARCH REPORT

Comparison of respiratory functions, muscle strength, and physical activity among children with primary ciliary dyskinesia with and without Kartagener's syndrome and healthy controls

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ABSTRACT

Introduction: Kartagener's syndrome (KS), consisting of bronchiectasis, situs inversus totalis, and sinusitis, is a subtype of primary ciliary dyskinesia (PCD). The presence of KS may affect respiratory and physical functions.

Purpose: This study aimed to compare respiratory functions, exercise capacity, muscle strength, and physical activity levels among children with PCD with/without KS and healthy peers.

Methods: Fifteen patients with KS, 23 with PCD without KS, and 27 controls were compared. Pulmonary function, functional exercise capacity (6-minute walk test – 6MWT), maximal inspiratory, expiratory (MIP, MEP), and skeletal muscle strength, inspiratory muscle endurance (IME), and physical activity level were evaluated.

Results: The forced expiratory volume in one second (FEV_1) % ($p = .009$), forced expiratory flow from 25%-75% ($FEF_{25-75\%}$) % ($p = .001$), MIP ($p = .034$), MEP ($p = .003$), 6MWT distance ($p = .001$), and daily steps ($p = .034$) were significantly different among the groups. Quadriceps femoris (QF) muscle strength and IME were similar in groups ($p > .05$). FEV_1% ($p = .002$), $FEF_{25-75\%}$ % ($p = .001$), MIP ($p = .027$), MEP ($p = .001$), and 6MWT distance ($p = .003$) in patients with KS; 6MWT distance ($p = .003$) in patients with PCD without KS was significantly lower than controls.

Conclusion: The presence of KS affects pulmonary function, respiratory muscle strength, and physical activity more. Exercise capacity and physical activity levels are decreased, inspiratory muscle endurance and QF muscle strength are preserved in patients with KS and PCD without KS. Kartagener's syndrome further impairs pulmonary and extrapulmonary outcomes; the reasons should be investigated, and the necessity of rehabilitation approaches that will prevent deterioration come to the fore.

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Exercise tolerance; physical activity; primary ciliary dyskinesia

Introduction

Primary ciliary dyskinesia (PCD) is a rare genetic disorder of motile cilia and causes upper and lower respiratory infection, cough, sputum production, and impaired lung function. Nearly half of the patients have laterality defects, mostly situs inversus totalis. Kartagener's Syndrome (KS), a type of PCD, comprises the triad of bronchiectasis, situs inversus totalis, and sinusitis (Hogg, 2009; Werner, Onnebrink, and Omran, 2015). Several studies have evaluated respiratory and peripheral muscle function, exercise capacity, and physical activity levels of child/adolescent patients with PCD, and the results are controversial. The studies reported that children with PCD had decreased and/or preserved pulmonary function, respiratory muscle strength, exercise capacity, peripheral muscle strength, and total energy expenditure than healthy controls (Denizoglu Kulli et al., 2020; Firat et al., 2022; Madsen et al., 2013; Simsek et al., 2018; Sonbahar-Ulu et al., 2022).

Compared to PCD patients without KS, accompanying situs inversus totalis and bronchiectasis in KS may cause worse clinical outcomes. A study reported that children with KS had lower maximal exercise capacity and higher fatigue perception than children with PCD without KS. The authors thought these results might be due to chronotropic insufficiency (Ince et al., 2016). In a case study, it was reported that a patient with KS had lower pulmonary function parameters, exercise capacity, and physical activity level according to the expected values (Cakmak et al., 2019). Apart from this study, no study comparing pulmonary and extrapulmonary features in PCD children with and without KS has been found. The aim of the current study was, therefore, to compare respiratory functions, functional exercise

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capacity, peripheral muscle strength, and physical activity level among PCD children with KS, PCD children without KS, and healthy peers.

Methods

Participants

A retrospective and cross-sectional study was conducted at Gazi University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation. The results of patients with PCD with and without KS who were referred from departments of pediatric chest diseases from all over Türkiye for pulmonary rehabilitation from October 2016 to July 2022 were evaluated, and those who met the inclusion criteria but did not meet the exclusion criteria were included. The data from age and gender-matched healthy controls were obtained from our research databases.

The inclusion criteria for the patients with PCD were being 6–18 years old and diagnosed with PCD. The diagnosis of PCD is defined by laboratory tests based on high-speed video microscopy or, transmission electron microscopy or genetic testing, and typical clinical symptoms according to American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines (Dalrymple and Kenia, 2019; Lucas et al., 2017; Shapiro et al., 2016, 2018). The inclusion criteria for the patients with KS were 6–18 years old and diagnosed with KS according to the triad of situs inversus, chronic sinusitis, and bronchiectasis (Dalrymple and Kenia, 2019). The exclusion criteria for the patients were being: uncooperative; having problems that would restrict functional capacity; having acute infections or pneumonia four weeks before the evaluation; and being a current or ex-smoker. The inclusion criteria for the healthy controls were willingness to participate and being 6–18 years. The exclusion criteria for the controls were being uncooperative, having any chronic or systemic disease, and having physical limitations. The study was approved by the Gazi University Ethics Committee (2022–740), and the study was registered (ClinicalTrials number: NCT05816889). Written informed consent was obtained from all pediatric patients and healthy children as well as their parents.

Assessments

Clinical characteristics were noted from the patient's medical files. The weight, height, and body mass index (BMI) were recorded and expressed according to Z scores. Malnutrition was defined as a BMI of ≤ −2 Z scores (World Health Organization, 2007).

Pulmonary function

Pulmonary function was evaluated using a spirometer (Cosmed, Class II/Internally Powered Equipment, Italy) according to the ATS/ERS criteria. Forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), FEV_1/FVC, peak expiratory flow (PEF), and forced expiratory flow from 25% to 75% ($FEF_{25-75\%}$) were measured (Miller et al, 2005).

Functional exercise capacity

Functional exercise capacity was assessed using the 6-minute walk test (6MWT) based on ATS/ERS guidelines. The test was repeated twice on the same day at 30-minute intervals in a 30-meter straight corridor, and the highest distance was recorded as a meter (Holland et al., 2014). Before and after the test, heart rate (Polar FT 100, China), dyspnea, and fatigue [modified Borg (M. Borg) scale] (Wilson and Jones, 1989) were recorded.

Respiratory muscle strength

Maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) values were assessed using an electronic mouth pressure device (MicroRPM, Micromedical, Kent, UK) according to ATS/ERS guideline, and the highest value was recorded as cmH_2O and analyzed (American Thoracic Society/European Respiratory Society, 2002). The minimum clinically important difference (MCID) is 13 cmH_2O for MIP (Gosselink et al., 2011).

Inspiratory muscle endurance

Inspiratory muscle endurance was measured using an inspiratory muscle training device (Power Breathe®, HaB International Ltd. Southam, UK) with the maximal incremental load test. The test started against a load of 20% of MIP, and resistance was elevated by 20% every 2 min. The test was completed when severe shortness of breath, severe fatigue, or inability to take three consecutive deep breaths. The inspiratory muscle endurance was calculated by multiplying the total duration of the test with the maximum pressure value that could be sustained for at least one minute (Basso-Vanelli et al., 2018; Laveneziana et al., 2019).

Peripheral muscle strength

Quadriceps femoris (QF) was measured using a hand dynamometer (JTECH Power Track Commander, Baltimore, USA). The measurements were repeated

three times on both sides, and the highest values were recorded as Newtons (N) (Beenakker, van der Hoeven JH, Fock, and Maurits, 2001).

Physical activity level

Physical activity level including total and active energy expenditure (joule/day), physical activity duration (min/day) [>3 metabolic equivalents (METs)], average METs (METs/day), number of steps (NOS) (steps/day), lying time (min/day), and sleep duration (min/day) were recorded for two consecutive weekdays using a metabolic holter device (SenseWear® Armband Model MF-SW, BodyMedia®, Inc. Pittsburgh PA 15,222, USA). Physical activity levels were classified according to NOS and METs (Ridgers et al., 2016; Tudor-Locke et al., 2011). The MCID for daily NOS is 427 steps/day in patients with chronic obstructive pulmonary disease (Polgar et al., 2021).

Statistical analysis

Statistical analysis was performed using SPSS 15.0 (SPSS, Chicago, Illinois). The sample size was calculated using 6MWT distance pilot study data for the effect size of 0.66, an α value of 0.05, and 95% power of at least 13 participants for each group. Visual (histogram and plots) and analytical (Shapiro-Wilk test) tests were used to evaluate normality. Descriptive analyses were performed using mean difference [95% confidence interval (CI)], standard deviation (SD), percent (%) value for normally distributed, and median, interquartile range (IQR) values for non-normally distributed variables. Categorical variables were compared using the chi-square test. Student's t-test and One-way ANOVA (post-hoc Tukey and Tamhane's T2 test) were used to compare normally distributed variables, and Kruskal-Wallis (Bonferroni correction) test was used for non-distributed variables. Power analysis was conducted using the 6MWT distance values. The probability of error was determined as $p \leq .05$.

Results

Fifteen patients with KS, 23 with PCD without KS, and 27 healthy controls were compared. Ten patients with PCD were excluded; one had hearing loss, one had pulmonary exacerbations, and eight were not volunteer

Table 1. Comparisons of demographic characteristic in children with KS, PCD without KS, and healthy controls.

	KS Patients ($n = 15$) (1)	PCD Patients without KS ($n = 23$) (2)	Healthy Control ($n = 27$) (3)	
Characteristics	Mean ± SD/ Median (IQR)	Mean ± SD/ Median (IQR)	Mean ± SD/ Median (IQR)	p Among group comparisons
Age (years)	12.87 ± 3.16	14.22 ± 3.80	12.22 ± 3.62	0.150
Male; Female (n/%)	5/33.33%; 10/66.7%	12/52.2%; 11/47.8%	13/48.1%; 14/51.9%	0.504
Height Z scores (SD)	−.13 ± 1.58	−.52 ± 1.02	.45±.94	**0.014$^{\alpha}$** **2–3: 0.003***
Weight Z scores (SD)	−.13 (−1.26–0.12)	−.40 (−1.15–.33)	.25 (−.27–.93)	**0.046$^{\beta}$**
BMI Z scores (SD)	.02 (−1.76–.69)	−.64 (−1.39–.77)	.26 (−.49–.82)	0.236
Malnutrition (n/%)	3/20%	1/4.3%	-	0.153
Age at diagnosis (month)	82.71 ± 41.98	112.43 ± 42.59		**0.047*****
Bronchiectasis (n/%)	15/100%	7/3.4%		**<0.001^^**
FVC (%)	89.64 ± 12.77	94.17 ± 19.73	95.15 ± 13.18	0.560
FEV_1 (%)	79 (69–87)	87 (71–100)	93 (84–104)	**0.009$^{\beta}$** **1–3: 0.002****
FEV_1/FVC	79.50 (68–89)	85 (79–91)	108 (101–110)	**<0.001$^{\beta}$** **1–3: <0.001**** **2–3: <0.001****
PEF (%)	74.36 ± 21.48	83.91 ± 21.00	91.19 ± 21.57	0.062
$FEF_{25-75\%}$ (%)	58.50 (42–62)	76.50 (57–94)	93.70 (77.75–101.75)	**0.001$^{\beta}$** **1–3: 0.001****

Descriptive analyses were presented using (X±SD) and median (IQR) for normally and non-normally distributed variables, respectively. 1–3: KS group versus control. 2–3: PCD group versus and control. $^{\alpha}p$ <.05 One-way ANOVA. *p <.05 Tamhane. $^{\beta}p$ <.05 Kruskal-Wallis. ^p < .05 Pearson. ***p <.05 Independent sample T-test. ^^p <.05 Chi-Square test. **p < .017 MWU. Abbreviations: BMI: body mass index, FEV_1: forced expiratory volume in 1 s, FVC: forced vital capacity, PEF: peak expiratory flow, FEF_{25-75}%: forced expiratory flow 25–75%.

Table 2. Comparisons of respiratory muscle strength and endurance in children with KS, PCD without KS, and healthy controls.

	KS Patients ($n = 15$) (1)	PCD Patients without KS ($n = 23$) (2)	Healthy Control ($n = 27$) (3)	
	Mean ± SD/ Median (IQR)	Mean ± SD/ Median (IQR)	Mean ± SD/ Median (IQR)	p Among group comparisons
MIP (cmH_2O)	86 ± 29.49	97.74 ± 24.57	108.19 ± 25.15	**0.034[α]** **1–3: 0.027+**
MEP (cmH_2O)	95 (84–111)	113 (97–144)	119 (100–131)	**0.003[β]** **1–2: 0.005**** **1–3: 0.001****
Inspiratory muscle endurance (cmH_2O) x Time (sec)	3738.80 (2580 –15,980)	3751.80 (1924–9384)	8262.80 (2448–9984)	0.636
Quadriceps femoris muscle strength (N)	259 (195–312)	253 (187–325)	244 (167–330)	0.825

Descriptive analyses were presented using (X ± SD) and median (IQR) for normally and non-normally distributed variables, respectively. 1–2: KS group versus PCD. 1–3: KS group versus control. 2–3: PCD group versus and control. [α]p <.05 One-way ANOVA. [+]p <.05 Tukey. [β]p <.05 Kruskal-Wallis. **p < .017 MWU. Abbreviations: %: percentage; MIP: maximum inspiratory pressure; MEP: maximum expiratory pressure; N: newton.

Table 3. Comparisons of functional exercise capacity and physical activity levels in children with KS, PCD without KS, and healthy controls.

	KS Patients ($n = 15$) (1)	PCD Patients ($n = 23$) (2)	Healthy Control ($n = 27$) (3)	
	Mean ± SD/ Median (IQR)	Mean ± SD/ Median (IQR)	Mean ± SD/ Median (IQR)	p Among group comparisons
6MWT (m)	574.19 ± 78.94	582.83 ± 52.47	644.87 ± 63.37	**0.001[α]** **1–3: 0.003+** **2–3: .003+**
ΔHR (beat/min)	49.67 ± 2.99	49.48 ± 16.81	66.07 ± 18.15	**0.003[α]** **1–3: 0.020+** **2–3: .006+**
ΔDyspnea (MBS) (0–10)	2 (.50–3)	.50 (0–1)	0 (0–1)	**0.024[β]** **1–3: 0.008****
ΔFatigue (MBS) (0–10)	1 (0–3.50)	.50 (0–1)	0 (0–.50)	**0.007[β]** **1–3: 0.003****
Total energy expenditure (joule/day)	7252.17 ± 1386.24	8154.90 ± 3351.88	8318.74 ± 2903.24	0.551
Physical activity duration (>3 METs) minutes/day	111.50 (74.50–137)	130 (80–273)	187 (69–288)	0.193
Average METs (METs/day)	1.60 (1.45–1.75)	1.70 (1.50–2.00)	1.80 (1.60–2.10)	0.214
Lying down (hours/day)	515.25 ± 148.37	537.67 ± 103.31	487.11 ± 103.19	0.312
Active energy expenditure (>3 METs) (joules/day)	1367 (888.50–1944.50)	1640 (1111–4461)	2015 (977–4399)	0.316
Number of steps (steps/day)	8033.50 (6547.50 –10,916.50)	9358 (6556 –11,972)	12143 (8202 –14,509)	**0.034[β]**
According to the number of steps				0.536
Inactive (n/%)	6/50%	9/42.9%	5/18.5%	
Low active (n/%)	4/33.3%	5/23.8%	6/22.2%	
Active (n/%)	1/8.3%	3/14.3%	4/14.8%	
Somewhat active (n/%)	0/0%	4/19%	7/25.9%	
Highly active (n/%)	1/8.3%	0/0%	5/18.5%	
According to average METs				
Inactive (n/%)	3/25%	3/14.3%	3/11.1%	0.148
Low active (n/%)	9/75%	18/85.7%	24/88.9%	
Sleep duration (minutes/day)	418.25 ± 75.75	422.43 ± 93.17	4.41 ± 9.68	0.670

Descriptive analyses were presented using (X ± SD) and median (IQR) for normally and non-normally distributed variables, respectively. 1–2: KS group versus PCD. 1–3: KS group versus control. 2–3: PCD group versus and control. [α]p <.05 One-way ANOVA. [+]p <.05 Tukey. [β]p <.05 Kruskal-Wallis. **p < .017 MWU. Abbreviations: 6MWT: six-minute walk test; %: percentage; Δ: difference between post and pretest; HR: heart rate, SpO_2: oxygen saturation; MBS: modified Borg scale, METS: metabolic equivalents task units.

to participate in the study. Thirteen (86.7%) of patients with KS' and 19 (82.6%) of PCD diagnosis was based on high-speed video microscopy analysis. The diagnosis of two of the patients with PCD was based on genetic analysis, and the diagnosis of two patients in each group was based on high-speed video microscopy and genetic analysis. The age, gender, and Z scores for BMI were similar in groups ($p > .05$). There were statistically significant differences among groups in Z scores for weight and height ($p < .05$). There were statistically significant differences among the groups in FEV_1 (%) and $FEF_{25-75\%}$ (%). FEV_1 (%) and $FEF_{25-75\%}$ (%) in patients with KS were significantly lower compared to healthy controls ($p < .05$) (Table 1).

MIP and MEP values were significantly different between the groups ($p < .05$) (Table 2). MIP was clinically lower in patients with KS than PCD patients without KS and significantly lower than healthy controls. In particular, MEP in patients with KS was significantly lower than in patients with PCD without KS and healthy controls ($p < .05$). The inspiratory muscle endurance and QF muscle strength were similar ($p > .05$) (Table 2). The 6MWT distance was significantly shorter in patients with KS and PCD without KS than healthy controls ($p < .05$, 1-β: 0.95) (Table 3). Significant differences existed in Δ heart rate, Δ dyspnea, and Δ fatigue among the groups. The patients with KS had significantly lower Δ heart rate, higher Δ dyspnea and Δ fatigue; patients with PCD without KS had significantly lower Δ heart rate than the healthy controls ($p < .05$) (Table 3).

Three patients with KS and two PCD patients without KS did not want to wear the metabolic holter; therefore, missing data could not be presented. Total energy expenditure, physical activity duration, lying down, active energy expenditure, sleeping duration, and average METs were similar among groups ($p > .05$). There were statistically significant differences among the groups regarding NOS (KS versus controls: 4530.44 steps; PCD without KS versus controls: 3839.76 steps; KS versus PCD without KS: 690.76 steps, $p < .05$). According to NOS, 50% of the patients with KS, 42.9% of patients with PCD without KS, and 18.5% of the healthy controls were inactive ($p > .05$). According to the average METs, 25% of the patients with KS, 14.3% of patients with PCD without KS, and 11.1% of the healthy controls were inactive ($p > .05$) (Table 3).

Discussion

This is the first study that compared respiratory functions, functional exercise capacity, peripheral muscle strength, and physical activity level among PCD patients with and without KS and healthy peers. The main findings of the current study were that patients with KS had impaired respiratory functions including FEV_1 (%) and $FEF_{25-75\%}$ (%), MIP, MEP, exercise capacity and daily NOS compared to healthy peers; PCD patients without KS had reduced exercise capacity and daily NOS compared to healthy peers; patients with KS had impaired inspiratory (clinically), expiratory muscle strength and daily NOS (clinically) compared to PCD patients without KS; most of the patients with PCD with and without KS were physically inactive/low active. Inspiratory muscle endurance and QF muscle strength are preserved in patients with KS and PCD without KS.

Evaluation of respiratory muscle function is essential in terms of symptom burden, prognosis, and treatment response and provides valuable information in clinical practice (Laveneziana et al., 2019). In our study, the inspiratory muscle strength of the patients with KS was lower than that of the healthy controls, and the expiratory muscle strength was lower than that of patients with PCD without KS and healthy peers. In the literature, studies comparing respiratory muscle strength in PCD patients with healthy controls are limited, and the results are controversial (Denizoglu Kulli et al., 2020; Firat et al., 2022; Sonbahar-Ulu et al., 2022). Likewise, findings about the respiratory muscle function of patients with cystic fibrosis are also under discussion (Heinzmann-Filho, Marostica, and Donadio, 2012). Previously, we reported reduced inspiratory muscle strength (33.3% of patients had KS) (Firat et al., 2022). Denizoglu Kulli et al. (2020) reported decreased expiratory muscle strength, and Sonbahar-Ulu et al. (2022) reported diminished respiratory muscle strength in PCD patients compared to healthy controls.

On the other hand, Denizoglu Kulli et al. (2020) and Sonbahar-Ulu et al. (2022) needed to provide details on whether their study population included patients with KS. In our study, it was observed that the respiratory muscles strength in patients with KS was impaired compared to healthy controls. These results may be due to the severity of airway obstruction. While FEV_1 is more sensitive to proximal, $FEF_{25-75\%}$ is to distal airway changes (Irving et al., 2013). In the present study, while patients with KS had worse pulmonary function, including FEV_1 (%) and $FEF_{25-75\%}$ (%) compared to healthy peers, PCD patients without KS' and healthy peers' results mentioned above were similar. The presence of bronchiectasis with increased airway obstruction in patients with KS may have resulted in decreased respiratory muscle strength. Genetic analysis was not performed on all patients in our study. Different mutations may cause varied ciliary characteristics and

respiratory function (Barbato et al., 2009). The effect of mutations on respiratory functions in patients with PCD with and without KS should be investigated in future studies.

Apart from pulmonary features, extrapulmonary features possibly affect respiratory muscle strength, including age, gender, nutritional status, and physical activity level. Physical activity and exercise could improve the movement of respiratory muscles and increase respiratory muscle strength (Dassios and Dimitriou, 2019). In our study, low exercise capacity and physical activity level may have caused decreased respiratory muscle strength in patients with KS.

In the current study, the results of the groups were similar in terms of inspiratory muscle endurance. Previously, we reported impaired inspiratory muscle endurance in PCD patients compared to healthy peers (Firat et al., 2022). The airway obstruction may improve inspiratory muscle endurance (Vendrusculo et al., 2016). On the other hand, it was stated that inspiratory muscle endurance is related to pulmonary function and nutrition status (body mass index classified according to Z-score) in obese and overweight adolescent patients with asthma (Heinzmann-Filho et al., 2016). In our study, the nutritional status of the groups was similar. As mentioned earlier by us, it is crucial to investigate the mechanisms affecting inspiratory muscle endurance in PCD patients.

There are inconsistent findings about the functional exercise capacity in patients with PCD. Some studies reported preserved exercise capacity (Denizoglu Kulli et al., 2020; Wells et al., 2011) while other studies, including ours, have emphasized that children with PCD have impaired exercise capacity compared to healthy peers (Firat et al., 2022; Fırat et al., 2023; Madsen et al., 2013; Simsek et al., 2018; Sonbahar-Ulu et al., 2022). Consistent with these results, the exercise capacity of both patients with KS and PCD without KS were similarly worse than the healthy ones in the present study. In addition, post hoc power was found to be high [$(1\text{-}\beta) = 95\%$] according to 6MWT distance. In a research abstract, it was reported that children with KS have a shorter modified shuttle walk test distance, heart rate change, chronotropic index, and higher fatigue perception than children with PCD (Ince et al., 2016). Contrary to these results, patients with KS and PCD without KS had similar walking distance, heart rate change, and sensation of fatigue in our study. The use of the 6MWT in our study, which is a submaximal test, may have resulted in a longer duration of the test, greater distances walked, and less perception of fatigue compared to using the aforementioned maximal test (Ince et al., 2016). While exercising, an increase in heart rate is vital for exercise performance. Low chronotropic response limits exercise capacity (Brubaker and Kitzman, 2011). In line with the literature, both patients with KS and PCD without KS had lower heart rate response during the test and exercise capacity compared to healthy peers in our study. On the other hand, the lower respiratory muscle strength and physical activity level of patients with KS may lead to a higher perception of shortness of breath and fatigue.

This study showed that patients with KS, PCD patients without KS, and healthy peers had similar lower extremity muscle strength. However, previous studies, including our study, reported that PCD patients had decreased muscle strength compared to healthy controls (Denizoglu Kulli et al., 2020; Firat et al., 2022; Simsek et al., 2018; Wells et al., 2011). Peripheral muscle weakness is a critical extrapulmonary manifestation of chronic lung disease, and hypoxia, malnutrition, systemic inflammation, gas exchange dysfunction, airway obstruction, drug use, anabolic deficiency, lower functional capacity, and physical activity level may affect peripheral muscle function (Arikan et al., 2015; Gea, Agustí, and Roca, 2013; Villa et al., 2011). The fact that our patients with KS and PCD without KS had better pulmonary function and respiratory muscle strength compared to the patients in the study by Denizoglu Kulli et al. (2020) may have caused preserved peripheral muscle strength. The factors associated with muscle strength in patients with PCD with and without KS should be investigated.

In the present study, patients with KS (8034 steps/day) had numerically lowest NOS compared to both PCD patients without KS (9358 steps/day) and healthy peers. While post hoc analysis did not show any significant difference within groups, patients with KS had clinically lower NOS than both PCD patients without KS and healthy controls. Similarly, PCD patients without KS had lower NOS than healthy controls according to MCID for daily NOS. In addition, almost 50% of the patients with KS and PCD without KS were inactive according to the daily average step count. A limited number of studies have evaluated the physical activities of PCD patients (Firat et al., 2022; Lam et al., 2022; Simsek et al., 2018; Valerio et al., 2012). The studies reported that children with PCD and healthy peers had similar physical activity levels (Simsek et al., 2018; Valerio et al., 2012). Previously, we reported that PCD patients had lower daily total energy expenditure than healthy controls, and 66.7% of the PCD patients had below-optimal daily NOS. In addition, other measured physical activity parameters were similar in the

groups (Firat et al., 2022). The fact that patients with KS had lower physical activity than PCD patients without KS in our study may be due to deterioration in respiratory functions. One study concluded that adults with PCD have lower total physical activity levels per week than children with PCD (Lam et al., 2022). Physical activity levels of both patients with KS and PCD patients without KS may decrease as aging.

The main limitation of this study is that the assessment of some PCD patients with and without KS coincided with the COVID-19 pandemic, which may have affected their physical activity levels. It has been shown that physical activity decreased in pediatric patients with chronic respiratory diseases during the pandemic period (Cahal et al., 2021). Therefore, this pandemic effect on physical activity in patients should be elucidated in further studies.

Even though the power of this study is very high (95%), the sample size may need to be revised for some outcome measures. Since PCD/KS is a rare disease, it was not possible to include more patients in the study during six years. Another limitation is that static lung volumes and DLCO were not measured in this study, which could provide additional information to explain pulmonary function abnormalities. In addition, there is no specific MCID value for the daily number of steps, which is specified for COPD and used for clinical comparison.

Conclusions

This is a first and high-power study comparing respiratory functions, functional exercise capacity, peripheral muscle strength, and physical activity level among PCD patients with and without KS and healthy peers. The main findings of this study were that patients with KS had impaired respiratory functions, exercise capacity, and daily NOS; PCD patients without KS had reduced exercise capacity and daily NOS compared to healthy peers. The presence of KS seems to affect pulmonary function, respiratory muscle strength, and physical activity more. In addition, expiratory muscle strength and daily NOS were worse in patients with KS than PCD patients without KS. The majority of the patients with PCD with and without KS were physically inactive/low active. Therefore, comprehensive evaluation, including exercise capacity, respiratory muscle strength, pulmonary function, and physical activity, should be performed in patients with PCD with and without KS, and a pulmonary rehabilitation program should be planned according to the needs of the patients.

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