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Original Article

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Abstract

Background: Handgrip strength is a crucial indicator of upper extremity muscular strength and is vital for monitoring disorders like cardiac diseases that restrict a patient's physical activity and result in muscle atrophy. The aim of our study was to evaluate whether muscle strength loss is present in patients with pulmonary hypertension and whether this test can be an alternative to 6-minute walk test. **Materials and methods:** The study included 39 healthy children who were admitted to the outpatient clinic and 16 children with a diagnosis of pulmonary hypertension who were being followed in our centre. We assessed the differences in upper extremity handgrip strength using the Jamar Hydraulic Hand Dynamometer device among both healthy children and those diagnosed with pulmonary hypertension. Moreover, we compared the handgrip strength of pulmonary hypertension patients with significant prognostic indicators such as NYHA class, 6-minute walk test, and pro-brain natriuretic peptide. **Results:** The mean dominant handgrip strength was 20.8 ± 12 kg in the patient group and 21.6 ± 12.4 kg in the control group ($p = 0.970$). Handgrip strength was shown to be negatively connected with pro-brain natriuretic peptide ($r = -0.565$, $p = 0.023$) and positively correlated with 6-minute walk test ($r = 0.586$, $p = 0.022$) during the patient group evaluation. **Conclusion:** Six-minute walk test needs a customised physical area (30 m of a straight hallway) and trained personnel for applying the test. The handgrip strength test, a different muscle strength indicator, can be used to more clearly and simply indicate the decline in patients' ability for effort. Additionally, it was found in our study that handgrip strength decreased as pro-brain natriuretic peptide levels rose, a crucial measure in the monitoring of pulmonary hypertension.

Pulmonary hypertension and associated pulmonary vascular disease are characterised by right ventricular dysfunction, left ventricular compression, filling abnormalities, and end-stage heart failure.¹ In children with pulmonary hypertension, there are certain tests that should be performed to determine the efficacy of treatment and prognosis. Echocardiographic findings and haemodynamic findings provide important information about prognosis and treatment efficacy. NYHA functional classification, 6-minute walk test, and pro-brain natriuretic peptide are factors that should definitely be used in the follow-up of children with pulmonary hypertension.² The results of these tests should be interpreted together with the clinical status and physical examination findings of the patient. The tests are affected by various factors, including the patient's height, weight, gender, age, medications, comorbidities, and compliance with treatment.

Handgrip strength is an important marker of upper extremity muscle strength.³ It is a valuable test in the follow-up of heart failure, which restricts the physical activity of the patient and consequently causes muscle atrophy. In patients with pulmonary hypertension, heart failure findings are also a clinical determinant. For this purpose, we evaluated the difference in upper extremity handgrip strength between healthy children and children diagnosed with pulmonary hypertension. In addition, handgrip strength in pulmonary hypertension patients was compared to such crucial prognostic markers as NYHA class, 6-minute walk test, and pro-brain natriuretic peptide.

The aim of this study was to examine whether muscle strength loss is more significant in patients with pulmonary hypertension than in healthy children to determine its relationship with prognostic factors and to determine whether this test could potentially used instead of the 6-minute walk test.

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Materials and methods

Study population

The study included 16 patients diagnosed with pulmonary hypertension who were being followed up in Gazi University Faculty of Medicine, Department of Pediatric Cardiology. As a control group, 39 healthy children were included in the study. Age, gender, weight, height, NYHA class, medications, complete blood count, pro-brain natriuretic peptide, troponin-T, biochemical parameters, catheterisation findings at the time of diagnosis, echocardiographic findings, presence of CHD, and shunt were recorded.

We included children and adolescents under the age of 18 years who had no known illness, no structural cardiac defects or rhythm abnormalities, and no family history of heart disease or sudden death. Children under the age of 5 years and children with mental impairment were omitted from both groups because they were unable to meet with the conditions of the testing. The study has been registered on ClinicalTrials.gov with the identification number NCT05447390. The parents of all children who were included in the study signed the informed consent form.

Implementation of the hand dynamometer test

In the study, handgrip strength test was performed with Jamar Hydraulic Hand Dynamometer (Jamar, USA) equipment. The participants were informed about the test before the handgrip strength test. The hand lengths of the patients were measured. To avoid the learning period from influencing the study's outcomes, the test was explained to the participants and conducted once in both hands, with no data recorded. The subjects sat upright, forearms bent 90 degrees, palms facing inwards, and repeated the test three times in each hand. All obtained findings were averaged and individually recorded for the dominant and non-dominant hand.

Statistical analysis

Statistical evaluation of the data was performed with Statistical Package for Social Sciences (SPSS) version 23 (IBM Corp, Armonk, NY) software. Mean and standard deviation or median and minimum-maximum values were used to present data related to quantitative variables, and frequency and percentage values were used to present data related to qualitative variables. The Chi-Square (χ^2) test was used to assess qualitative variables, and the Fisher exact test was utilised to analyse qualitative variables when necessary. The compliance of the quantitative variables with normal distribution was analysed by Shapiro–Wilk test. For statistical comparison of patient and control groups for quantitative variables, independent samples Student's t-test was used for normally distributed data and Mann–Whitney U test was used for non-normally distributed data. Spearman's correlation analyses were performed to examine the relationships between variables. The significance level of $p < 0.05$ was used in all statistical analyses.

Results

The study included 16 patients with pulmonary hypertension and 39 healthy controls. There were 10 females and 6 males in the patient group and 24 males and 15 females in the control group. The mean age was 12.6 ± 4.4 years in the patient group and 11.5 ± 3.2 years in the control group. The mean body mass index

was 19.6 ± 5.2 kg/m² in the patient group and 18.9 ± 4.6 kg/m² in the control group (Table 1).

Among 16 patients with pulmonary hypertension, 8 (50%) were idiopathic pulmonary arterial hypertension, 6 (37.6%) were Eisenmenger, 1 (6.2%) was residual pulmonary arterial hypertension, and 1 (6.2%) was segmentary pulmonary arterial hypertension. When the distribution of the patient group according to treatment status was evaluated, eight patients (50%) received bosentan, three patients (18.8%) sildenafil and bosentan, two patients (12.6%) sildenafil, bosentan, and treprostinil, one patient (6.2%) was on bosentan and iloprost, one patient (6.2%) was on sildenafil, bosentan, and iloprost, and one patient (6.2%) was on sildenafil, macitentan, and treprostinil (Table 2).

All of the patients in our study were classified as NYHA functional class II. The handgrip strengths of the patient group and the control group were classified as dominant and non-dominant according to the hand used dominantly in daily life. The median (min-max) values of the handgrip strengths of the patient and control groups according to dominant and non-dominant hand are given in Table 3. The median value of the dominant handgrip strength was 19.2 (5.0–50.0) kg in the patient group and 19.3 (4.7–55.7) kg in the control group. When the non-dominant handgrip strength was evaluated, the median value was 18.4 (5.3–43.7) kg in the patients and 17.3 (4.3–52.3) kg in the control group. Both dominant and non-dominant handgrip strengths did not show statistically significant difference in the patient and control groups ($p > 0.05$).

The correlation between the dominant handgrip strength of 16 patients receiving pulmonary hypertension treatment and the tests used in the follow-up and 6-minute walk test was compared. Handgrip strength was positively correlated with 6-minute walk test ($r = 0.586$, $p = 0.022$) and negatively correlated with pro-brain natriuretic peptide ($r = -0.565$, $p = 0.023$). There was no statistically significant correlation between troponin-T, uric acid, or full blood count parameters (Table 4).

Eight patients (50%) were classified into idiopathic pulmonary arterial hypertension and eight patients (50%) were put into other groups when examined according to diagnostic categories, and handgrip strengths were compared in both groups. The median dominant handgrip strength of idiopathic pulmonary arterial hypertension patients was 14.5 (5–50) kg and the median non-dominant handgrip strength was 13.2 (5.3–43.7) kg ($p = 0.092$). In eight patients with other diagnoses, the median dominant handgrip strength was 22 (9.7–34.3) kg and the median non-dominant handgrip strength was 21.2 (8.7–37.7) kg ($p = 0.528$). When the dominant handgrip strengths ($p = 0.248$) and non-dominant handgrip strengths ($p = 0.248$) of the idiopathic pulmonary arterial hypertension and other patient groups were evaluated, no statistically significant difference was identified.

Patients with pulmonary hypertension were divided into treatment groups and examined. Of the total patients, eight (50%) were getting monotherapy, four (25%) were receiving dual therapy, and four (25%) were receiving triple therapy. The median dominant handgrip strength of the patient group receiving monotherapy was 22 kg (7.7–34.3 kg) and the median non-dominant handgrip strength was 21.2 kg (6.3–31.3 kg) ($p = 0.183$). In the patient group receiving dual treatment, the median dominant handgrip strength was 16.7 kg (5–34.3 kg) and the median non-dominant handgrip strength was 16 kg (5.3–37.7 kg) ($p = 0.465$). In the patient group receiving triple treatment, the median dominant handgrip strength was 18.9 kg (9.3–50 kg) and the median non-dominant handgrip strength was 17.4 kg

Table 1. Distribution of the patient and control groups according to gender groups and mean age.

		Patient (n = 16)		Control (n = 39)		p
		n	(%)	n	(%)	
Gender	Male	6	(20.0)	24	(80.0)	0.104
	Female	10	(40.0)	15	(60.0)	
Age (year) ($\bar{x} \pm SD$)		12.6 \pm 4.4		11.5 \pm 3.2		0.331
BMI (kg/m ²) ($\bar{x} \pm SD$)		19.6 \pm 5.2		18.9 \pm 4.6		0.580

BMI = body mass index; SD = standard deviation.

Table 2. Distribution of the patient group according to diagnosis and treatment (n=16).

		n	%
Diagnosis	IPAH	8	50.0
	Eisenmenger	6	37.6
	Residual PAH	1	6.2
	Segmentary PAH	1	6.2
Treatment	Bosentan	8	50.0
	Sildenafil, Bosentan	3	18.8
	Bosentan, Iloprost	1	6.2
	Sildenafil, Bosentan, Treprostinil	2	12.6
	Sildenafil, Bosentan, Iloprost	1	6.2
	Sildenafil, Macitentan, Treprostinil	1	6.2

PAH = pulmonary arterial hypertension; IPAH = idiopathic pulmonary arterial hypertension; PH = pulmonary hypertension.

Table 3. Handgrip strengths of patients and control group.

	Patient	Control	p
	Median (min-max)	Median (min-max)	
Dominant hand (Kg)	19.2 (5.0-50.0)	19.3 (4.7-55.7)	0.970
Non-dominant hand (Kg)	18.4 (5.3-43.7)	17.3 (4.3-52.3)	0.978
p	0.720	0.310	

(7-43.7 kg) (p = 0.144). No statistically significant difference was found when the dominant handgrip strengths (p = 0,860) and non-dominant handgrip strengths (p = 0,928) of three different treatment groups were compared.

Discussion

Patients with chronic diseases experience a decline in muscle mass as a result of reduced physical activity over time. In patients with cardiac diseases, the reduction in muscle mass and strength that occurs during the progression of the disease results in a decline in their ability to engage in physical activities and negatively impacts their overall quality of life. Consequently, this is associated with a

Table 4. Correlations with dominant handgrip strength in the treatment group.

	Rho	p
Hb (g/dl)	0.355	0.177
Htc (%)	0.409	0.116
MCV (fL)	-0.069	0.799
RDW (%)	0.007	0.978
Pro-BNP (pg/mL)	-0.565	0.023
Uric Acid (mg/dL)	0.150	0.580
6MWT (mt)	0.586	0.022
Troponin-T (ng/L)	0.131	0.629

Hb = hemoglobin; Htc = hematocrit; MCV = mean corpuscular volume; RDW = Red cell distribution width; pro-BNP = pro-brain natriuretic peptide; 6MWT = 6 minute walk test. Rho: Spearman's correlation coefficient.

The p values in bold are statistically significant (p < 0.05).

less promising prognosis and an elevated risk of mortality.⁴ Exercise intolerance is a common sign of pulmonary hypertension and appears early in the course of the disease.⁵ Due to symptoms such as dyspnea, bendopnea, syncope, and fatigue, sedentary time increases and the level of physical activity decreases over time.⁶

Handgrip strength has been used as a marker of physical activity for many years. In several studies, normal handgrip strength values in healthy children were analysed according to age and gender. In the study by Mathiowetz et al., it was reported that handgrip strength increased with age and male gender, and this increase was higher in males aged 14-19 years. In addition, it was concluded that the dominant hand did not have more handgrip strength than the non-dominant hand.⁷ In our study, despite the fact that the dominant handgrip strength was greater than the non-dominant handgrip strength in both the patient group and the healthy group, there was not a significant difference between the two groups when the data were analysed separately (healthy group, p = 0.310; patient group, p = 0.720). Patients in NYHA stage II are considered to be comfortable at rest with slightly restricted physical activity.⁸ It is comprehensible that there was no statistically significant difference between the handgrip strengths of the two groups in the handgrip strength test, which is performed out while sitting and is more related to upper extremity muscle strength, given that all patients in the study group were in NYHA functional class II.

In a study conducted by Ross and Rösblad in 2002 involving 530 healthy children aged 4-16 years, it was observed that handgrip strength increased in parallel in girls and boys until the age of 10 years, but after the age of 10 years, boys' handgrip

strength increased faster. It was reported that height, weight, and especially hand length were effective on handgrip strength.⁹ Due to the low prevalence of paediatric pulmonary hypertension, our study's sample size was insufficient to assess handgrip strength in relation to age and gender.

To identify high-risk patients, it is essential to have an efficient and user-friendly test in addition to the physician's awareness. A review of the medical literature indicates that the handgrip strength test conducted using a dynamometer in patients with cardiac issues yields valuable information regarding the patient's clinical condition and future prognosis.

In the study by Neidenbach et al., it was observed that the handgrip strength of the healthy control group was higher than that of the patient group with CHD. The results of the study confirm that there is a decrease in muscle mass and loss of muscle strength in patients with CHD.⁴ In another study in which 56 children with heart disease were compared with healthy controls, both 6-minute walk test and handgrip strength results were found to be lower in the group with heart disease ($p < 0.001$). According to the findings, there was a significant correlation between handgrip strength and the 6-minute walk test ($r = 0.7$, $p = 0.01$).¹⁰ In our study, although the control group's handgrip strength in the dominant hand was found to be higher than that of the patient group, there was no statistically significant difference ($p = 0.970$). However, a positive correlation was observed between the patient group's dominant handgrip strength and 6-minute walk test, indicating a significant relationship between them ($r = 0.586$, $p = 0.022$).

The only study in the literature on the relationship between handgrip strength and pro-brain natriuretic peptide in children with pulmonary hypertension was conducted in the Netherlands in 2023. A study evaluating handgrip strength, 6-minute walk test, functional class, NT-pro-brain natriuretic peptide, and time since diagnosis in 16 children with pulmonary arterial hypertension revealed no correlation between NT-pro-brain natriuretic peptide levels and muscle strength.¹¹ It is well established that higher plasma pro-brain natriuretic peptide levels are associated with worse haemodynamics, low survival rates, and shorter 6-minute walk test. In 88 children with pulmonary arterial hypertension, Takatsuki et al. demonstrated a substantial correlation between pro-brain natriuretic peptide levels, morbidity, and mortality.^{12,13} In our study, pro-brain natriuretic peptide levels were negatively correlated with dominant handgrip strength in 16 patients receiving pulmonary hypertension treatment ($r = -0.565$, $p = 0.023$). The results of a lower handgrip strength in patients with higher pro-brain natriuretic peptide levels, when considered together with other indicators used in the follow-up of pulmonary hypertension, are remarkably consistent and suggest that handgrip strength is also an appropriate method to be used in the monitoring of pulmonary hypertension.

Hand dynamometer measurements of handgrip strength may be helpful for a variety of purposes, including comparing the patient group with the healthy group or assessing the effectiveness of medical therapy. They may also be utilised to demonstrate improved muscular strength in patients undertaking cardiac rehabilitation programmes. In a study in which 15 patients with CHD were included in a cardiopulmonary rehabilitation programme, the muscle strength of the patients was evaluated by hand dynamometer and a significant increase was found compared to the pre-programme muscle strength ($p < 0.001$).¹⁴

Limitations

Our study has a limitation in terms of a relatively small sample size. Despite the rarity of paediatric pulmonary hypertension, conducting multicentre studies with a more extensive participant pool is imperative. This approach is crucial for comprehensively assessing whether handgrip strength mirrors the patient's clinical condition and its correlation with other diagnostic tests.

Conclusion

Exertional capacity in patients with pulmonary hypertension decreases with the severity of the disease. Currently, 6-minute walk test is accepted as the best indicator of this condition. Unfortunately, specially structured physical space and trained personnel are required for 6-minute walk test. Another muscle strength indicator, the handgrip strength test, can be used to more easily demonstrate the decline in patients' exertional capacity. The data of our study are also important in terms of showing that handgrip strength can provide a good alternative to 6-minute walk test in the evaluation of muscle strength, especially in pulmonary hypertension patients with advanced functional class and wheelchair-dependent life.

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Competing interests. All authors declare that: (1) they did not receive any support from any organisation that has financial or other interest in the submitted work; (2) there are no other relationships or activities that may affect the submitted work. All the authors do not have any conflicts of interest.

Ethical approval. This study was in compliance with the "Declaration of Helsinki" and was approved by the Ethics Committee of Gazi University.

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Clinical registration. This study was registered at the US National Library of Medicine Clinical Trials (code:NCT05447390).

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