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Handgrip strength, physical activity, and body composition in young adults with juvenile idiopathic arthritis

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Abstract. ***Background.*** Handgrip strength (HGS) and physical activity (PA) reflect an individual's overall health and can predict morbidity and mortality. ***The purpose*** of the study was to investigate the level of PA and HGS and associated factors in young adults with juvenile idiopathic arthritis (JIA) and determine the connection with body composition parameters. ***Materials and methods.*** We conducted a cross-sectional monocentric study of 40 young adults aged 18–30. We collected data on PA and anthropometric and clinical measurements, including disease activity and articular and extra-articular damages. All patients had the following evaluations performed: body composition (dual X-ray absorptiometry), PA level (International Physical Activity Questionnaire), and HGS measurement (using manual hand dynamometer). ***Results***. Sixteen (40 %) patients were considered sedentary, and 32 (80 %) JIA patients had low HGS. The reduced HGS was likely in women, patients with lower body mass index, higher disease activity, and articular damage. In contrast, bone mineral density (BMD) and lean mass were protective factors for reduced HGS ($p < 0.05$). The level of PA was positively correlated with BMD and lean mass and negatively correlated with fat mass, swollen joint count, and articular damage ($p < 0.05$). ***Conclusions***. JIA leads to changes in body composition parameters, particularly lean (muscle) mass and muscle strength, and therefore is a risk factor for the development of sarcopenia.

Keywords: juvenile idiopathic arthritis; handgrip strength; physical activity; body composition

Introduction

Juvenile idiopathic arthritis (JIA) is characterized by the development of pathological changes in the musculoskeletal system, such as osteoporosis and myopathy, which can aggravate the severity of functional disorders [1–3]. Disease activity persisted in 33–46 % of adult patients with JIA [4, 5]. Joint impairment, extra-articular damage, and functional disability are associated with low quality of life in young adults with JIA [1, 6, 7]. All of the mentioned proves JIA is not limited only to joint damages and children's age.

Loss of muscle strength and muscle mass leads to limited daily activities, deterioration of quality of life, and an increased risk of falls, fractures, and death [8]. Muscle strength is associated with many conditions and may predict the risk of adverse outcomes of diseases [9]. Moreover, reduced HGS, not lean mass, is associated with an increased risk of hospital-associated activities of daily living and disability [10]. A comparison between different values of HGS reflects an association with body composition parameters. Thus, BMD, lean, and fat mass were significant predictors of HGS value changes [11].

Among the mechanisms of reduced muscle strength are the following: chronic arthritis, the persistence of disease activity, systemic inflammation with increasing levels of inflammatory cytokines such as interleukin-6, tumor necrosis factor-α and interleukin-1β, reduced PA, articular and extra-articular damages [5]. The synergistic effect of these factors leads to the degradation of muscle tissue, manifested by atrophy, reduced muscle strength, and decreased ability to regenerate myocytes.

Hand dynamometry is the most accessible and affordable method of assessing muscle strength [12]. It is shown that HGS strongly correlates with the strength of the lower limb muscles and the cross-sectional area of the muscles detected by computer tomography [13]. The availability of the method makes it possible to recommend it for routine daily practice.

To date, proven that purposeful activities with various types of motor activity contribute to the preservation and strengthening of health, the prevention of several diseases, the increase of physical strength, and the formation of an active life position [14, 15]. Lack of PA negatively affects health in general [16]. There is evidence that PA, especially

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aerobic exercise and resistance training, increases muscle strength and improves the quality of children's and young adults' life with JIA [17–20].

Low BMD, increased risk of falls, reduced quality of life, functional capabilities, and increased mortality are reliably associated with losing skeletal muscles and their functions [9]. Thus, sarcopenia and osteoporosis are multifactorial cross-linked syndromes characterized by decreased bone and muscle mass, increased risk of falls and fractures, and early disability [19, 20]. Several questions remain open regarding changes in body composition and muscle strength in patients with rheumatic diseases, apparently in young adults with JIA. Published works devoted to this problem are limited, highlighting the relevance of further research in this area.

The purpose of the study was to determine HGS, PA level, and body composition in young adults with JIA and to indicate factors associated with HGS and PA.

Materials and methods

This cross-sectional study in a single center included forty patients who applied to the Rheumatology department of the Communal non-commercial institution "Oleksandrivska Clinical Hospital" (Kyiv, Ukraine). Written and informed consent were obtained from all patients for participating in the study. The Commission on Bioethical Expertise and Research Ethics of the Bogomolets National Medical University approved the study (Registration number 138 dated 10.11.2020).

Inclusion criteria were as follows: patients with JIA, 18–44 years old. Exclusion criteria: patients with congestive heart failure, end-stage renal disease, acute kidney disease, hematologic or oncologic malignancy, patients with arm or leg amputation, patients with hip or knee replacement, diabetes mellitus, and obesity. The evaluation of the level of erythrocyte sedimentation rate (ESR), the C-reactive protein (CRP), disease activity score (DAS28) and juvenile arthritis disease activity score (JADAS27), Juvenile arthritis damage index (JADI), which consists of two parts measuring articular (JADI-A) and extra-articular (JADI-E) damage, were done [21, 22].

Muscle strength was determined using a handgrip dynamometer (JAMAR). Measurements were taken three times for both hands with the time of rest [19]. The result was taken as the average value of three consecutive measurements. We used such thresholds for reduced HGS: < 27 kg for males; < 16 kg for females. To determine body composition, we used dual X-ray absorptiometry (DXA), measuring appendicular lean mass (ALM), total lean mass, and total fat, with a calculation of skeletal mass index (SMI = appendicular lean mass, kg/height^2), fat mass index (FMI = fat mass, kg/height^2).

Patients responded to the International Physical Activity Questionnaire-Short form (IPAQ-SF) [23, 24]. The metabolic equivalent (MET), an indicator that characterizes the energy consumption for PA, was calculated [25]. To determine the level of PA, the following categories were used: category 1 — low PA (patients who do not meet the criteria for the following two categories are considered inactive); category 2 — moderate PA (includes subjects who meet any of the following 3 criteria: vigorous activity 3 or more days per week for at least 20 minutes a day; activity of moderate intensity 5 or more days per week or walking for at least 30 minutes per day; any combination of intensity 5 or more days per week to achieve at least 600 MET-minutes per week); category 3 — vigorous PA (includes people who meet any of the following 2 criteria: vigorous activity for at least 3 days per week, achieving at least 1500 MET-minutes per week; any combination of intensity 7 days per week with the achievement of no less than 3000 MET-minutes per week).

Statistical analysis

Statistical analysis was performed using the IBM® SPSS Statistics software (version 28.0.1.1.14). Continuous data were analyzed using the Shapiro-Wilk normality test to detect distribution. Depending on the result, the data are presented as mean (M) ± standard deviation (SD) or median and interquartile range (IQR) (Me [25th — 75th percentile]). To identify factors associated with HGS, univariate logistic regression analysis was used to calculate the odds ratio and identify the numerical indicator of the area under the curve (AUC). Spearman's rank correlation coefficient was used to identify factors associated with PA. The level of significance was set at $p \leq 0.05$.

Results

The study involved 23 female and 17 male patients. The median age of the patients was 20 [IQR 18–25] years; the median age at the onset of the disease was 10 [IQR 5–14] years. The types of JIA were as follows: systemic JIA, 6 (15 %); enthesitis-related arthritis, 2 (5 %); oligoarticular JIA, 18 (46 %); rheumatoid factor (RF)-positive polyarticular JIA, 7 (18 %); RF-negative polyarticular JIA, 6 (15 %), juvenile psoriatic arthritis, 1 (2.5 %). The median body mass index (BMI) was 20 [IQR 19–23] kg/m^2. The median ESR was 15 [IQR 6–33] mm/h; the median CRP — 5 [IQR 4–24] mg/l. The median DAS28-ESR was 4 [IQR 2–4]; JADAS27 — 10 [IQR 7–19]. Sixteen patients (40 %) took glucocorticoids (GC) for more than 3 months. The median duration of GC treatment was 24 [IQR 1–48] months; the median daily dose of GC at the moment of enrollment to the study — was 5 [IQR 1–10] mg. Eighteen patients (45 %) took conventional disease-modifying antirheumatic drugs (cDMARDs), 3 of them with a combination of biological disease-modifying antirheumatic drugs (bDMARDs), one of them — monotherapy with tocilizumab.

Thirty-two patients had reduced muscle strength (80 %). In a univariate analysis, it turned out that HGS was associated with BMI (odds ratio (OR) = 0.78; 95% confidence interval (CI): 0.61–0.99; p = 0.04), with JIA duration (OR = 4.15; 95% CI: 1.03–1.37; p = 0.02), with a disease activity by JADAS27 (OR = 1.18; 95% CI: 1.02–1.35; p = 0.02), as well as articular damage index JADI-A (OR = 2.2; 95% CI: 1.02–4.75; p < 0.04). Protective factors for reduced HGS were as follows: male sex (OR = 0.12; 95% CI: 0.02–0.56; p < 0.0001), total BMD (OR = 0.001; 95% CI 0.000–0.12; p < 0.001), lean mass (lean arm mass

OR = 0.32; 95% CI: 0.16–0.63; p < 0.001; lean leg mass OR = 0.48; 95% CI: 0.31–0.74; p < 0.001; ALM OR = 0.61; 95% CI: 0.46–0.81; p < 0.001; total lean mass OR = 0.99; 95% CI: 0.9996–0.9999; p < 0.001; SMI OR = 0.97; 95% CI: 0.86–0.99; p < 0.001); and PA (OR = 0.33; 95% CI: 0.17–0.64; p < 0.0001). Fat limb percentage increases the risk of reduced HGS (fat percentage arms OR = 1.09; 95% CI: 1.02–1.16; p = 0.01; fat percentage legs OR = 1.09; 95% CI: 1.10–1.17; p = 0.007). We didn't find a relationship between HGS and ESR, CRP, DAS28-ESR, GC use, and extra-articular damage index JADI-E. Factors associated with HGS are presented in Table 2.

IPAQ results were distributed as follows: 40 % of patients were in the "low PA" category, 25 % were in the "moderate PA" while 35 % of the patients were in the "high PA". The median of vigorous PA was 120 [IQR 0–960] MET-min/week; the median moderate PA was 320 [IQR 152–1520] MET-min/week; the median walking time was 248 [IQR 99–1073] min/day; the median sitting time was 330 [IQR 260–440] min/day; the median sum of PA — 728 [IQR 359–3846] MET-min/week. The sum level of PA was positively correlated with total BMD (rS = 0.392, p = 0.02), femoral neck BMD (rS = 0.429, p = 0.02), ultra-distal radius BMD (rS = 0.534, p = 0.05), total lean mass (rS = 0.707, p < 0.001), ALM (rS = 0.758, p < 0.001), SMI (rS = 0.771, p < 0.001), HGS (rS = 0.617, p < 0.001); and negatively correlated with total fat (g) (rS = –0.340, p = 0.03), fat mass index (rS = –0.38, p = 0.01), swollen joint count (rS = –0.31, p = 0.05) and articular damage index JADI-A (rS = –0.31, p = 0.05). Interestingly, disease activity by DAS28 and JADAS27 and cumulative dose of GC was not correlated with the sum level of PA in young patients with JIA (p > 0.05). Factors correlated with PA are presented in Table 3.

Table 1. Characteristics of JIA patients included in the study

Data	Value
Age, years, median [IQR]	20 [18–25]
BMI, kg/m^2, median [IQR]	20 [19–23]
JIA duration, years, median [IQR]	13 [9–18]
ESR, mm/h, median [IQR]	15 [6–33]
CRP, mg/l, median [IQR]	5 [4–24]
DAS28 scores, median [IQR]	4 [2–4]
JADAS27 scores, median [IQR]	10 [7–19]
GC treatment > 3 months, n (%)	16 (40)
Duration of GC treatment, months, median [IQR]	24 [1–48]
Daily dose of GC for the year preceding the survey, mg, median [IQR]	5 [1–10]
cDMARD, n (%)	18 (45)
bDMARD, n (%)	4 (10)

Table 2. Factors associated with reduced HGS in young patients with JIA (univariate logistic regression analyses)

Variable		Coefficient, b ± m	P	OR (95% CI)	AUC (95% CI)
Age, years		0.07 ± 0.07	0.26	–	–
Sex	females				0.75 (0.58–0.87)
	males	–2.15 ± 0.80	0.001	0.12 (0.02–0.56)	
BMI, kg/m^2		–0.25 ± 0.12	0.04	0.78 (0.61–0.99)	0.74 (0.57–0.86)
Disease duration, years		0.17 ± 0.07	0.02	1.18 (1.03–1.37)	0.76 (0.60–0.89)
ESR, mm/hour		0.06 ± 0.03	0.055	–	–
CRP, mg/l		0.007 ± 0.010	0.52	–	–
DAS28		0.49 ± 0.27	0.07	–	–
JADAS27		0.16 ± 0.07	0.02	1.18 (1.02–1.35)	0.77 (0.60–0.89)
Articular damage index JADI-A		0.79 ± 0.39	0.045	2.20 (1.02–4.75)	0.78 (0.62–0.90)
Extra-articular damage index JADI-E		0.91 ± 0.48	0.059	–	–
BMD total, g/cm^2		–9.29 ± 3.64	0.01	0.001 (0.000–0.12)	0.77 (0.60–0.89)
Current medication of GC		1.39 ± 0.87	0.11	–	–
Cumulative dose of GC, mg		0.00026 ± 0.00015	0.08	–	–
Fat arms, %		0.086 ± 0.043	0.01	1.09 (1.02–1.16)	0.78 (0.62–0.90)
Lean mass arms, g		–1.14 ± 0.34	0.001	0.32 (0.16–0.63)	0.94 (0.81–0.99)
Fat legs, %		0.093 ± 0.035	0.007	1.10 (1.03–1.17)	0.77 (0.60–0.89)
Lean mass legs, g		–0.73 ± 0.22	0.001	0.48 (0.31–0.74)	0.96 (0.84–0.99)
ALM, g		–0.49 ± 0.14	0.001	0.61 (0.46–0.81)	0.96 (0.84–0.99)
Lean mass total, g		–0.00025 ± 0.00008	0.001	0.9997 (0.9996–0.9999)	0.94 (0.82–0.99)
SMI, kg/m^2		–2.29 ± 0.73	0.002	0.10 (0.02–0.42)	0.97 (0.86–0.99)
The sum level of PA, MET-min/week		–1.16 ± 0.35	0.001	0.33 (0.17–0.64)	0.95 (0.82–0.99)

Note: p-values ≤ 0.05 were considered significant.

The mean of body composition parameters of patients with JIA was as follows: total BMD — 1.060 ± 0.150 g/cm^2; total lean mass — 41,394.0 ± 9,985.6 g; mean ALM — 17.76 ± 5.80 kg; total fat mass — 21,695.58 ± 18,590.61 g; total BMC — 2.398.5 ± 662.2 g. The ALM positively correlated with HGS (rS = 0.8, p < 0.05), but the correlation between ALM and FMI was not statistically significant (rS = –0.1, p > 0.05). Interestingly to note, ALM negatively correlated with the duration of the disease (rS = –0.6, p < 0.05), with ESR (rS = –0.4, p < 0.05), with the disease activity by JADAS27 (rS = –0.4, p < 0.05), but not statistically significant with the CRP (rS = –0.07, p > 0.05).

Discussion

In the last decade, special attention has been attracted to the connection between muscle mass, strength, and rheumatic diseases [26]. There is insufficient data about the relationship between PA, HGS, body composition, and outcomes among young adults with JIA, which is important for implementing a non-pharmacological treatment plan to prevent long-term physical and psychological consequences.

Thus, among young adults with JIA, 70 % noted moderate-to-severe disability by Health Assessment Questionnaire-Disability Index and performed a low physical capacity [27]. Furthermore, pain causes a fear of movement, as shown in a study that compared PA in patients with JIA and healthy peers [28]. Gait speed was 11–15 % slower, chair-rise repetitions were 28 % less, and stair-up and down times were 26–31 % slower in patients with JIA. The Tampa Scale of Kinesiophobia (TSK-11) assesses patient fear of movement, whereas pain was higher in patients with JIA compared to the control group. This again emphasizes the variety of cause-and-effect relationships between JIA and reduced PA and muscle strength.

The most frequently nominated domains affecting the quality of life in young subjects with JIA appeared PA, work or school, fatigue, and self-esteem [29]. Lack of PA due to pain and joint damage lead to decreased bone, muscle mass, and strength [30]. The studies [31–33] present that exercising reduces pain, improves the quality of life and increases the range of motion and muscle strength in children and adolescents with JIA. In a recent study [17] of 59 young adult JIA patients compared with 60 healthy peers, PA and body composition were studied using IPAQ and bioimpedance analysis (BIA), respectively, and paralleled with quality of life. Noteworthy, 66 % of patients with JIA had a sedentary lifestyle compared with 22 % from the control group, even though this study excluded patients with active JIA. Notably, no significant differences were found in body composition components by BIA. It was found that patients with higher PA had a better quality of life.

Reducing such pro-inflammatory cytokines as tumor necrosis factor-α and interleukin-6, and CRP positively affects muscle and bone tissue [17]. Thus, a large observational study showed that sarcopenia occurred significantly more often in patients with a higher level of CRP [34]. The con-

Table 3. Correlation between the mean scores of the IPAQ with the clinical, disease indexes, and body composition parameters of patients with JIA

Variable	Vigorous PA, MET-min/week	Moderate PA, MET-min/week	Walking time, min/day	Sum PA, MET-min/week
Duration of JIA, years	–0.282	–0.239	–0.276	–0.252
TJC	–0.171	–0.095	–0.082	–0.088
SJC	–0.484**	–0.333*	–0.172	–0.312*
HGS, kg	0.620**	0.636**	0.605**	0.617**
ESR, mm/h	–0.376*	–0.233	–0.172	–0.243
CRP, mg/dL	–0.242	–0.165	–0.102	–0.203
DAS28 score	–0.409**	–0.256	–0.287	–0.264
JADAS27 score	–0.376*	–0.265	–0.223	–0.241
Articular damage index JADI-A	–0.414**	–0.322*	–0.308*	–0.311*
Extra-articular damage index JADI-E	–0.342*	–0.273	–0.269	–0.245
Cumulative dose of GC, mg	–0.334	–0.206	–0.064	–0.163
ALM, g	0.798**	0.754**	0.718**	0.758**
SMI, kg/m^2	0.775**	0.745**	0.765**	0.771**
L1_L4 BMD, g/cm^2	0.213	0.205	0.288	0.243
Femoral neck BMD, g/cm^2	0.440*	0.357	0.543**	0.429*
Total BMD, g/cm^2	0.503**	0.399*	0.368*	0.392*
Ultradistal radius BMD, g/cm^2	0.506	0.599*	0.274	0.534
Total fat, g	–0.333	–0.334	–0.257	–0.340*
FMI, kg/m^2	–0.346*	–0.343*	–0.279	–0.381*
Total lean, g	0.748**	0.716**	0.682**	0.707**

Notes: TJC — tender joint count; SJC — swollen joint count; * — p-values ≤ 0.05; ** — p-values ≤ 0.001.

nection between an increasing concentration of CRP and reduced muscle strength was also noted in other investigations [35]. Results of our study demonstrate the correlation between disease activity by JADAS27 and reduced muscle strength, but not with CRP and ESR alone.

There is a paucity of data regarding muscle strength in young adults with JIA. Simultaneously, the results of studies on children with JIA are controversial. One study compared the HGS of 23 children and adolescents with JIA patients with 46 healthy peers and found a negative correlation between grip strength and disease activity by JADAS27, juvenile arthritis functionality scale (JAFS), and a positive correlation with the pediatric quality of life inventory (PedsQL) [36] and determined HGS as a predictor of disease activity, functional state and quality of life which coincides with the results of our study. Another research showed decreased muscle strength compared to healthy peers [37], in contrast with a recent study that found no such difference [38], explaining this milder course of the disease and early diagnosis in their study population. Thus, the study showed that JIA patients have lower total BMD and muscle strength than the control group, although no connection was found with disease activity [37]. The authors explain this by the low disease activity among participants, emphasizing that 42 % of patients took bDMARDS. Appear plausible to explain the results of the studies mentioned above and our research, which demonstrate a correlation between BMD, muscle mass, and strength, by "mechanostat theory" [39] and the interplay between the bone-muscle axis.

Study limitations. We performed a monocentric study with a small sample size and could not analyze different JIA subtypes. Also, we realize that the estimation of PA by the questionnaire is subjective. However, this study has important clinical connotations. Many of our young adults with JIA have decreased HGS and low PA. Our study demonstrates that it is connected with disease activity and body composition, which can explain increased cardiovascular, osteoporosis, sarcopenia, falls and fracture risk, and other comorbidities. This is the first study that has searched for the connections between grip strength, PA, and body composition in young adults with JIA. The results establish the need for further investigations.

Conclusions

The results of our study demonstrate a high prevalence of low HGS, up to 80 % among young patients with JIA. In this study, lower BMI, lower total BMD and arms, legs, total lean mass, and SMI, longer disease duration, and higher disease activity by JADAS27 and articular index damage JADI-A, higher percentage fat were predictors of reduced HGS. Young patients with JIA demonstrate different levels of PA. PA was associated with lean and bone mass, HGS, and articular damage. Encouraging patients to lead an active lifestyle can significantly contribute to bone, muscle, and overall health.

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Сила стискання, фізична активність та композиційний склад тіла в молодих дорослих із ювенільним ідіопатичним артритом

Резюме. ***Актуальність.*** Сила стискання кисті (ССК) і рівень фізичної активності (ФА) відображають стан здоров'я людини в цілому й на сьогодні розглядаються як предиктори підвищеної захворюваності та смертності. ***Мета:*** визначити рівень ФА, ССК та композиційний склад тіла, а також фактори, пов'язані з цими показниками, в молодих осіб з ювенільним ідіопатичним артритом (ЮІА). ***Матеріали та методи.*** В одноцентровому дослідженні за участю 40 молодих дорослих осіб з ЮІА віком 18–30 років зібрані дані про ФА, активність захворювання, суглобові та позасуглобові ураження й оцінено деякі клінічні та антропометричні параметри. Усім обстеженим визначали композиційний склад тіла за допомогою двофотонної рентгенівської абсорбціометрії, рівень ФА — короткої версії міжнародного опитувальника ФА (International Physical Activity Questionnaire), силу стискання — за допомогою ручного динамометра. ***Результати.*** У 16 (40 %) пацієнтів з ЮІА відмічено малорухомий спосіб життя, у 32 (80 %) — знижену ССК. Остання була пов'язана з жіночою статтю, нижчим індексом маси тіла, вищою активністю захворювання та індексом суглобових уражень, тоді як мінеральна щільність кісткової тканини (МЩКТ) і знежирена маса тіла виявилися факторами, що запобігають зниженню м'язової сили ($p < 0,05$). Рівень ФА позитивно корелював із показниками МЩКТ та знежиреної маси тіла і негативно — із жировою масою, кількістю набряклих суглобів й індексом суглобових уражень ($p < 0,05$). ***Висновки.*** ЮІА призводить до змін композиційного складу тіла, зокрема м'язової маси, та м'язової сили, а тому є окремим фактором ризику розвитку саркопенії.

Ключові слова: ювенільний ідіопатичний артрит; сила стискання; фізична активність; композиційний склад тіла