Sarcopenia: a new issue in juvenile idiopathic arthritis. A study Protocol

La sarcopénie: un nouveau concept dans l'arthrite juvénile idiopathique. Protocole de recherche

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Abstract

Background : The decrease in muscle function and mass is defined as sarcopenia. Known for a long time as an age-related disorder, sarcopenia is nowadays well recognized in childhood. Juvenile idiopathic arthritis (JIA), a chronic inflammatory joint disease may be associated with loss of skeletal mass.

Objective : This protocol aims to evaluate the prevalence rate of sarcopenia and its associated factors in JIA.

Methods : To evaluate the prevalence rate and factors associated with sarcopenia in juvenile idiopathic arthritis, we are enrolling 30 children with JIA and 30 healthy children aged between 4-and 16 years. Clinical data will report: age, sex, body mass index, disease duration, and therapeutic management. All participants will undergo the Whole-body Dual-energy X-ray absorptiometry to assess the skeletal muscle mass. The muscle strength will be measured using the handgrip dynamometer and adjusted to the body mass index. Data will be analyzed and compared to age and sex reference curves.

Results : This study aims to detect sarcopenia in JIA children and identify subsequently the main associated factors. By collecting anthropometric data and extracting the main features of the disease, specific metrics will be extracted. Body composition will be obtained using the DXA scans, including appendicular lean mass and skeletal muscle mass. Muscle strength will also be assessed.

Conclusion : This study aims to assess sarcopenia in JIA patients, using the sarcopenia update definition. If we will provide conclusive results, it will be possible to better identify the associated factors of sarcopenia and to prevent children from this complication.

Clinical trials registration NCT05291416

Keywords: Sarcopenia, Juvenile Idiopathic Arthritis, Dual-energy X-ray absorptiometry

Résumé

Introduction : La diminution de la force et de la masse musculaire définit la sarcopénie. Longtemps connue comme un trouble lié à l'âge, la sarcopénie est aujourd'hui bien identifiée chez l'enfant. Au cours de l'arthrite juvénile idiopathique (AJI), une perte de la masse musculaire squelettique peut être observée.

But : Ce protocole de recherche vise à évaluer la prévalence de la sarcopénie et ses facteurs associés dans l'AJI.

Méthodes : Nous allons recruter 30 enfants atteints d'une AJI et 30 enfants sains âgés de 4 à 16 ans. Les données suivantes seront rapportées: l'âge, le sexe, l'indice de masse corporelle (IMC), la durée de la maladie et les traitements utilisés. Tous les participants effectueront une absorptiométrie biphotonique à rayons X (DEXA) du corps entier afin d'évaluer la masse musculaire squelettique. La force musculaire sera mesurée à l'aide d'un dynamomètre à poignée et sera ajustée à l'IMC. Les données seront analysées et comparées aux courbes de référence selon l'âge et le sexe.

Résultats : En collectant les données anthropométriques et les principales caractéristiques de la maladie, des mesures spécifiques seront élaborées, dont la mesure de la composition corporelle qui sera obtenue à l'aide de la DEXA, incluant la masse maigre appendiculaire et la masse musculaire squelettique. La force musculaire sera également évaluée.

Conclusion : Si les résultats de l'étude seront concluants, il sera possible de connaitre les facteurs incriminés dans la sarcopénie et d'en prévenir les complications.

Clinical trials registration: NCT05291416

Mots-clés : Sarcopénie, arthrite juvénile idiopathique, absorptiométrie biphotonique à rayons X.

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BACKGROUND

Sarcopenia was firstly described as a skeletal muscle disorder associated with falls, fractures, physical disability, and mortality. In 2019, the European Working Group on Sarcopenia in Older People (EWGSOP) has updated this definition highlighting muscle failure as a prevalent determinant in this condition (1). Sarcopenia is typically associated with chronic affections, and aging, but currently, this concept is recognized in childhood. The muscle disease may have negative effects on the growth, puberty, and psychological development of the child. Detection of childhood sarcopenia is crucial to avoid the extent of this disability in adulthood. However, the lack of diagnostic criteria and the validated measurement in children limited the identification of sarcopenia in daily practice (2).

Juvenile idiopathic arthritis (JIA) is a frequent inflammatory disease in children, characterized by pain, arthritis, and deformities. Chronic inflammation leads to physical inactivity and can be associated with muscle weakness around affected joints, low bone strength, and mass(3). To our knowledge, no study has focused on the prevalence of sarcopenia in JIA and the data on the muscle disorder are lacking. The purpose of the present study is to detect sarcopenia and identify associated factors in children with JIA.

METHODS

Study design

This is a monocentric case-control study, being conducted in the Rheumatology department of Kassab Institute.

Patients and public involvement

We will recruit 30 healthy children aged between 4 and 16 years, 30 suffering from JIA, and fulfilling the ILAR criteria(4). The sample size is acceptable after calculating the minimal number of necessary samples to meet the desired statistical constraints. Randomization and blinding are not appropriate in our study.

For all patients, we will collect the anthropometric data including weight, height; and express it as Z-scores for age and sex. Body mass index (BMI) will be calculated as weight (kg)/height (m2). The disease duration, JIA subtype, disease activity, and treatment are being recorded.

Non-inclusion criteria:

- Patients who cannot undergo a DXA scan (patients with orthopedic hardware, positioning difficulties, abnormal skeletal morphometry, severe scoliosis).
- Patients who cannot use a dynamometer (patients who have a hand arthritis or deformities)

Exclusion criteria:

- Patients who have nutritional problems, vitamin D disorder, inflammatory bowel disease, coeliac disease, temporomandibular involvement, or another chronic disease

Measurement

Muscle quantity

Body composition is obtained using the Whole-body Dual-energy X-ray absorptiometry (DXA) scans (General Electric LUNAR). DXA is the current reference standard for fat evaluation, due to its wide availability, and being inexpensive, easy to use and low radiation dose (1–6 µSv).

The appendicular lean mass (ALM) is the sum of the lean mass in arms and legs and it is adjusted to the body mass index (ALM/BMI). The skeletal muscle mass (SMM) is derived from the appendicular lean mass and will be adjusted following the Kim equation (5).

SMM (kg)= 1.115 x ALM (kg)) – 1.135 for children aged 15 or below and SMM (kg)= 1.19 x ALM (kg)) – 1.65 for children aged 16 and beyond (6). SMM-z will be calculated using age- and gender-dependent values of SMM in healthy children (5).

Muscle quality

Muscle strength will be assessed using the Handgrip dynamometer and will be adjusted to the BMI. We will use the handgrip dynamometer (KERIN), with maximum power at 80 kg.

For all patients, we are choosing the higher measurement found after three trials for the right and left hand. For each trial, the patient is requested to positioner its humerus at the side of the body with the elbow flexion at 90°, and press the dynamometer with the maximal effort for three minutes.

Sarcopenia diagnosis

While the adult definition of sarcopenia is not adapted to the pediatric population, we followed the definition used by Weber et al. (5) The diagnosis of sarcopenia will be considered in case of a decrease in muscle quality and quantity. Sarcopenia will be defined as an SMM-z score < – 2 standard deviation (SD) (5).

Ethical statement and dissemination: Parental or legal guardian consent is required before patient inclusion. Written consent will be mandatory before including patients.

The institute's ethics committee approves the study.

Due to the nature of this research, participants of this study are not agreeing for their data to be shared publicly, so supporting data is not available.

Statistical analysis

The study data will be collected, recorded and analyzed by the Statistical Package for the Social Sciences (SPSS) statistical software (version 23.0). Quantitative variables will be expressed by their means with the estimation of the SD. Differences between groups will be analyzed using the chi-square test (or Fisher's exact test when appropriate) for qualitative variables and Student's test for quantitative variables. P values less than 0.05 will be considered as significant.

DISCUSSION

This study aims to detect sarcopenia in JIA children and identify subsequently the main associated factors of the disease. Sixty subjects will be included in this study and will be divided into two groups: thirty JIA children compared with thirty healthy ones. By collecting anthropometric data and extracting the main features of the disease, specific metrics will be extracted. Body composition will be obtained using the DXA scans. The ALM will be calculated by summing the lean mass in arms and legs and will be adjusted to the BMI (ALM/BMI). SMM will be derived from the appendicular lean mass and will be adjusted following the Kim equation (6). Muscle quality will also be assessed using the handgrip dynamometer and will be adjusted to the BMI. Sarcopenia diagnosis will therefore be established definitively, based on all the data collected. It will be defined as an SMM-z score < -2 SD (5).

Sarcopenia is common in inflammatory rheumatic diseases and has been linked with functional disability (7,8) but it is also related to somatic issues, including heart and respiratory conditions (9,10). It is a progressive generalized loss of skeletal muscle involving muscle function and interfering with its strength. Recently, this concept has been supported in the 2019 sarcopenia consensus update (EWGSOP2), which also emphasized the detection of low muscle quantity and quality (1).

To our knowledge, the available data about sarcopenia in children with JIA remains poor. Dzhus et al. have confirmed recently the presence of severe sarcopenia in forty young adults with JIA, despite their young age(8). They used DXA to assess low muscle mass, dynamometry to determine gait speed and short physical performance battery to assess physical function. The authors concluded that sarcopenia was associated with a higher level of disease activity, articular and extraarticular damage, reduced bone mineral density, and longer disease duration. However, the number of patients included is small and was not compared to healthy subjects. In addition, the lack of data concerning the factors influencing sarcopenia in children and especially in JIA patients, calls for further studies on this topic. It is well known that sarcopenia is associated with rheumatic diseases, mainly due to persistent chronic inflammation which is considered a primary risk factor.

Several reviews have well addressed the relationship between rheumatoid arthritis (RA) and sarcopenia and less so with spondyloarthritis (SpA) and other autoimmune disorders (7). It is established that in RA patients, pro-inflammatory cytokines are associated with sarcopenia (11). Longer disease duration, bone erosion, low bone mineral density, malnutrition, joint damage, and rheumatoid factor (RF) were also predictive of muscle loss. Anthropometric factors such as BMI and high body fat mass were also associated with sarcopenia in RA patients according to several studies (12–14). The muscle loss was occasionally accompanied by "sarcopenic obesity" which is an increase in fat mass, subsequently accompanied by overall body composition loss, including muscle and fat, which is a severe consequence called 'rheumatoid cachexia' (15). Furthermore, recent studies have reported that aging in RA was associated with sarcopenia (12,13). However, being not applicable in JIA, this feature will probably be replaced by other specific factors. As for SpA, sarcopenia was evaluated only in ankylosing spondylitis (AS) and Psoriatic Arthritis (PsA). It was mainly correlated with Bath Ankylosing Spondylitis Functional Index (BASFI) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)(16).

The main strength of our study will be to be part of the few study protocols that will aim to assess sarcopenia in JIA patients. It will allow us to identify sarcopenia prevalence in JIA patients compared with healthy infants. We will also evaluate the associated factors among JIA, comparatively with the other rheumatic diseases in the forthcoming studies.

From this point of view, sarcopenia prevalence in JIA and

specific risk factors need to be confirmed in more studies, mainly focusing on treatment strategies.

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