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Assessment of sarcopenia in young patients with inflammatory arthritis: a cross-sectional study

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Sarcopenia is a disease characterized by decreasing muscle mass and strength or performance. The prevalence of sarcopenia in rheumatic diseases has been evaluated in single diseases using various diagnostic approaches, generating conflicting data. The study aims to investigate sarcopenia prevalence in young adults with inflammatory arthritis (IA) and to detect factors associated with low muscle mass and strength. The single-center, cross-sectional study included 138 young adults with IA. Dynamometry with a Jamar hand dynamometer was used to determine handgrip strength. Thresholds for reduced muscle strength were < 27 kg for males and < 16 kg for females. To determine skeletal mass index (SMI), dual photon X-ray absorptiometry (DXA) was done with such cut-off points < 5.67 kg/m^2 in females and < 7.0 kg/m^2 in males. Patients with both reduced muscle mass and strength were considered as sarcopenic. Logistic regression analyses estimated between sarcopenia and associated factors. Statistical significance was defined as a p-value < 0.05. The prevalence of sarcopenia was about 47% in all IA and was significantly different between juvenile idiopathic arthritis (JIA), spondyloarthritis (SpA), and rheumatoid arthritis (RA) groups (p = 0.006). At multivariable analysis, body mass index (BMI) (OR 0.84; CI 95% 0.72–0.86, p = 0.02), bone mineral density (BMD) at femur neck (OR 0.01; CI 95% 0.001–0.268, p = 0.01), 25-hydroxyvitamin D (25(OH)D) (OR 0.96; CI 95% 0.93–0.98, p = 0.001), and disability by Health Assessment Questionnaire (HAQ) (OR 14.54; CI 95% 4.92–51.77, p < 0.001) were associated with a significantly increased risk of sarcopenia. The results of our study demonstrate a high prevalence of sarcopenia among young patients with IA. In these participants, lower BMI, lower BMD, 25(OH)D concentration, and higher HAQ were linked to sarcopenia.

Keywords Juvenile idiopathic arthritis, Muscle mass, Muscle strength, Rheumatoid arthritis, Sarcopenia, Spondyloarthritis

The concept of sarcopenia was initially introduced to characterize the age-associated decline in muscle mass observed in elderly people, commonly referred to as "primary sarcopenia". In due course, the scope of sarcopenia research has expanded to explore the condition in various diseases, often denoted as "secondary sarcopenia", wherein the primary pathogenic mechanism is recognized to be the heightened inflammatory disease activity[1]. Consensus in research and clinical practice is still lacking for sarcopenia, especially among young adults. Sarcopenia is defined by the European working group on sarcopenia in older people (EWGSOP2)[2] as a progressive and generalized skeletal muscle disorder associated with an increased risk of adverse outcomes, including falls, fractures, physical disability, and mortality. Complementing this definition, the global leadership initiative in sarcopenia (GLIS)[3] specifies sarcopenia as a condition characterized by reduced muscle mass accompanied by impaired muscle strength. It is important to note that new research in this area indicates that the relationship between "muscle quantity" (muscle mass) and "muscle function" (muscle strength or physical performance) is relatively weak. Thus, muscle mass was found to have a low predictive value for functional limitations, walking speed, and mortality in distinction from muscle function[4,5]. Diminished skeletal muscle strength and impaired muscle function have been empirically established as robust indicators of elevated mortality risk, heightened susceptibility to functional dependence, falls, subsequent fractures, and increased vulnerability to physical disability[6–11].

Despite the conventional rationale of sarcopenia as an age-associated condition has been challenged by emerging evidence suggesting a correlation between sarcopenia and a diverse array of diseases, including rheumatic disorders[12–14]. One of the most extensively studied associations is that between sarcopenia and

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rheumatoid arthritis[15,16]. This is explained by chronic inflammation and is associated with a significant increase in the level of pro-inflammatory cytokines: interleukins (IL)-IL-1, IL-6, C-reactive protein (CRP), and tumour necrosis factor-alpha (TNF-α). Cytokines stimulate the ubiquitin-proteasome pathway, leading to the proteolytic breakdown of myofibrils. Chronic low-grade inflammatory states have been demonstrated to induce anabolic resistance, whereby the skeletal muscle's capacity for protein synthesis in response to typical anabolic stimuli is significantly diminished[17–19]. In addition to the inflammatory component, the issue of reduced physical activity associated with the pathogenesis of arthritis also warrants careful consideration and evaluation. The influence of a sedentary lifestyle on reducing muscle mass and muscle strength is well-known. Skeletal muscle is an endocrine organ that produces hormone-like factors—myokines, which have auto-, para- and endocrine effects. Anti-inflammatory myokines that have a trophic effect on muscle tissue are produced only in an actively working muscle. Thus, IL-6, secreted by an actively contracting muscle, induces glucose absorption and β-oxidation of fatty acids in muscles and stimulates lipolysis and gluconeogenesis in the liver[20]. Conversely, the state of physical inactivity associated with the arthritic condition elicits the upregulation of myostatin, a potent negative regulator of muscle hypertrophy, thereby promoting the catabolism of muscle protein. Furthermore, elevated myostatin levels have been implicated in developing insulin resistance and obesity[21].

The role of vitamin D in musculoskeletal changes is already known. A recent study in military personnel with a mean age of 20 years found that lower 25-hydroxyvitamin D [25(OH)D] status was associated with a higher risk of stress fractures[22]. Another cross-sectional study that included 165 participants (83 men, 82 women, 18–30 years of age) and measured bone microarchitecture revealed 43.6% of participants had low 25(OH)D (< 50 nmol/mL), and lower 25(OH)D levels were associated with worse bone outcomes in the distal radius and tibia during peak bone mass, deserving additional consideration to vitamin D status in young adults[23]. Both skeletal muscle atrophy and poor muscle function are consequences of low vitamin D status[24]. Vitamin D deficiency has been associated with reduced oxygen consumption and mitochondrial dysfunction[25,26].

Studies in rheumatic diseases often focus primarily on muscle mass, giving less consideration to the equally important aspects of muscle strength and function[27–33]. Studies have included patients with a variety of rheumatic diseases and different diagnostic criteria and have used variable methods and cut-offs to define low muscle mass (dual-energy X-ray absorptiometry (DXA) or bioelectrical impedance analysis (BIA)) and muscle function (dynamometry or different tests of physical performance)[34–37], making their comparison difficult. In the present study, the assessment of sarcopenia and severe sarcopenia was based on the EWGSOP2 criteria[2]. Furthermore, a comparative analysis of these conditions was conducted for the first time within the context of three distinct rheumatic diseases: juvenile idiopathic arthritis (JIA), spondyloarthritis (SpA), and rheumatoid arthritis (RA) (primary endpoint). Polyarticular JIA, compared to RA, is well-founded due to shared immunopathological mechanisms, including the role of pro-inflammatory cytokines like TNF-α and IL-6 and autoantibodies in certain cases[38]. Similarly, oligoarticular and enthesitis-related JIA demonstrate clinical features closely paralleling SpA, including asymmetric arthritis, sacroiliitis, enthesitis, and a high prevalence of HLA-B27 positivity[39,40]. These similarities are consistent with evidence showing that enthesitis-related JIA and juvenile-onset SpA frequently evolve into adult SpA[41]. Excluding systemic JIA in our analysis, which follows a distinct autoinflammatory pathway, ensures the focus remains on JIA subtypes that share pathophysiological and clinical characteristics with RA and SpA patients. This approach is supported by research demonstrating significant category transitions from childhood to adulthood, with RF-positive JIA cases often reclassified as RA and enthesitis-related JIA aligning with SpA[42]. In addition to the primary analyses, the present study also aimed to evaluate the influence of clinical factors on the development of sarcopenia (secondary endpoint).

Results

Clinical characteristics of young adults with IA

A total of 138 patients who underwent DXA were included in this study. The median age was 28.5 years; 76 (55%) were female, and 62 (45%) were males. The present study included 70 patients (50.7%) with JIA, 51 patients with SpA (37%) and 17 (12.3%) with RA. Thirty-three patients (24%) were treated with GC at enrollment, and seventy-three patients (53%) were treated with GC before admission. Patients with JIA took GC significantly more often and for a longer time ($p < 0.05$). The majority of patients received disease-modifying antirheumatic drugs (DMARDs), with methotrexate being the most commonly used, taken by 79 individuals (57%). Other synthetic DMARDs were used significantly less frequently: sulfasalazine was administered to 11 patients (8%), hydroxychloroquine to 3 patients (2%), and leflunomide to 6 patients (4%). Among the patients receiving biological disease-modifying antirheumatic drugs (bDMARDs) ($n = 47$), monotherapy with bDMARDs was observed in 29 patients (21% of the total sample). Table 1 summarizes all patients' anthropometric, clinical, laboratory, and disease-related data.

Prevalence of probable sarcopenia, sarcopenia, and severe sarcopenia in young adults with IA

As illustrated in Fig. 1, the prevalence of probable sarcopenia, sarcopenia, and severe sarcopenia in the entire patient cohort was 55, 47, and 22%, respectively. When we examined specific disease groups separately, the prevalence of sarcopenia varied significantly (Chi^2 $p = 0.006$) and was 57% in patients with JIA, 29% in patients with SpA, and 59% in patients with RA. The prevalence of probable sarcopenia was found to be 63% among patients with JIA, 33% among SpA patients, and 88% among RA patients (Chi^2 $p = 0.001$). The prevalence of severe sarcopenia was found to be 33% among JIA patients, 10% among SpA patients, and 18% among RA patients (Chi^2 $p = 0.01$).

Variable		JIA (70)	SpA (51)	RA (17)	P-value
Age, years		20.5 [18.0–25.0]	36.0 [30.0–40.0]	33.0 [30.0–40.0]	0.001**
Sex	F	42 (60%)/	17 (33%)/	17 (100%)	–
	M	28 (40%)	34 (67%)	–	
Height, m		1.69 [1.65–1.74]	1.72 [1.68–1.78]	1.71 [1.66–1.72]	0.051
Weight, kg		60.0 [52.0–68.0]	72.0 [62.0–87.0]	60.0 [56.6–61.7]	0.001**
BMI, kg/m^2		20.8 [18.4–23.2]	23.4 [20.9–28.4]	20.5 [19.1–24.2]	0.001**
Onset of disease, years		11.0 [8.0–15.0]	25.0 [22.0–32.0]	29.0 [25.0–32.0]	0.001**
Time before diagnosis, months		6.0 [3.0–12.0]	13.0 [7.0–25.0]	6.0 [3.0–12.0]	0.001**
Duration of disease, years		11.0 [7.0–17.0]	7.0 [4–12]	4.0 [2.0–8.0]	0.001**
25(OH)D, nmol/l		42.5 [29.9–54.2]	54.2 [33.6–62.3]	56.6 [32.2–72.1]	0.036*
ESR, mm/h		12.0 [5.0–23.0]	12.0 [5.0–25.0]	16.0 [12.0–25.0]	0.524
CRP, mg/L		4.1 [2.0–16.0]	4.2 [2.0–8.9]	11.5 [5.5–13.0]	0.082
TJC28		2.0 [2.0–4.0]	3.0 [2.0–4.0]	5.0 [2.0–6.0]	0.044*
SJC28		1.0 [0–2.0]	2.0 [1.0–3.0]	3.0 [2.0–4.0]	0.003*
Patient's assessment of arthritis pain, mm		30.0 [20.0–50.0]	20.0 [10.0–40.0]	30.0 [20.0–40.0]	0.278
cJADAS27		7.5 [3.0–14.5]	–	–	–
ASDAS-CRP		–	1.9 [1.4–2.7]	–	–
BASDAI		–	2.1 [1.5–4.0]	–	–
DAS28-CRP		3.2 [2.5–4.0]	–	4.0 [3.4–4.4]	0.025*
Cumulative dose of GC, mg		720.0 [80–7200]	0.0 [0.0–440]	240.0 [0.0–1720]	0.001**
HAQ score		0.3 [0–1.0]	0.0 [0–0.4]	0.6 [0.2–1.2]	0.001**

Table 1. Demographic, clinical and disease-related data in young adults with IA. Values are shown as median (25–75th interquartile range) or n (%). *IA* inflammatory arthritis, *JIA* juvenile idiopathic arthritis, *SpA* spondyloarthritis, *RA* rheumatoid arthritis, *BMI* body mass index, *25(OH)D* 25-hydroxyvitamin D, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *TJC* tender joint count, *SJC* swollen joint count, *cJADAS-27* clinical juvenile arthritis disease activity score 27, *ASDAS* the ankylosing spondylitis disease activity score, *BASDAI* the bath ankylosing spondylitis disease activity index, *DAS28* disease activity score 28, *GC* glucocorticoids, *HAQ* health assessment questionnaire. *$p<0.05$; **$p<0.01$.

Sarcopenia components in young adults with IA

Significant differences were identified in handgrip strength, total lean mass, LMI, ALM, SMI, and ALM/weight and BMI ratios among the groups. Patients with SpA demonstrated the highest values across these parameters, outperforming JIA and RA in most comparisons, while RA patients exhibited the lowest values. In contrast, no significant differences were observed in gait speed and FMI, indicating comparable walking performance and fat mass distribution across the groups. Data is presented in (Table 2).

Comparison between sarcopenic and non-sarcopenic patients among the groups and all IA

Patients with sarcopenia and IA had lower BMI and levels of 25(OH)D, higher levels of ESR, CRP, lower BMD total, lumbar spine and femur neck, and higher levels of disability. Comparative characteristics between patients with and without sarcopenia are presented in (Table 3).

Factors associated with sarcopenia in young adults with IA

In a univariable analysis, sarcopenia was more frequent in females (OR 2.65; 95% CI 1.33–5.27, p = 0.006), patients with earlier onset of disease (OR 0.95; 95% CI 0.92–0.98, p = 0.005), with higher ESR (OR 1.04; 95% CI 1.01–1.07, p = 0.005), lower BMD total, at the lumbar spine, femur neck (OR 0.001; 95% CI 0.0001–0.41, p = 0.0001; OR 0.04; 95% CI 0.005–0.297, p = 0.002 and OR 0.003; 95% CI 0.001–0.04, p = 0.001, respectively) and in patients with higher disabilities (OR 9.63; 95% CI 4.27–22.57, p = 0.0001). Peripheral involvement of joints as tender joint count (TJC) and swollen joint count (SJC) > 3 was associated with a higher risk of sarcopenia (OR

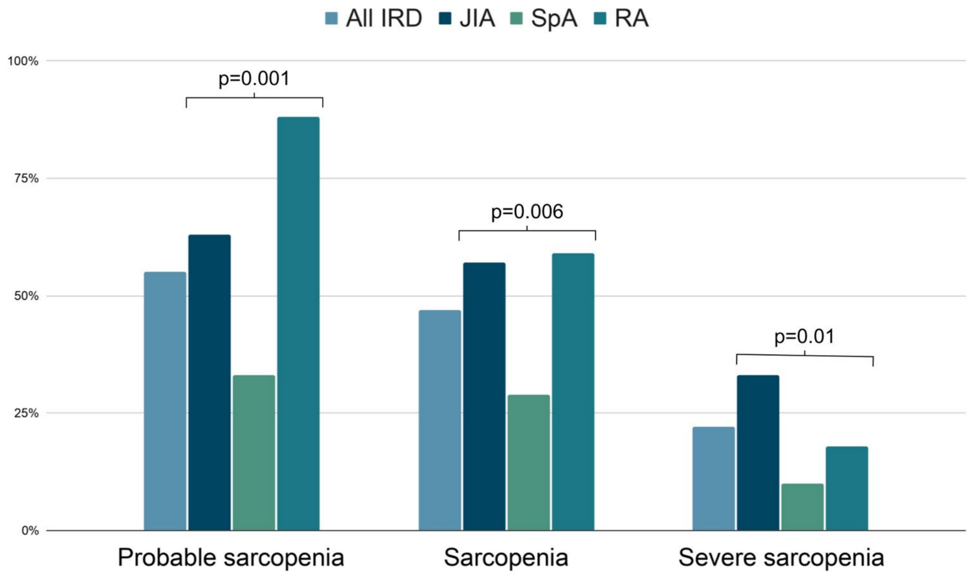

Fig. 1. Prevalence of probable sarcopenia, sarcopenia and severe sarcopenia in all 138 patients.

Variable	JIA (70)	SpA (51)	RA (17)	P-value	P1-2	P1-3	P2-3
	Me [Q25-Q75]						
Handgrip strength, kg	18.0 [14.0–25.0]	28.0 [18.0–32.0]	13.0 [13.0–15.0]	0.001**	< 0.001***	0.007**	< 0.001***
Gait speed, m/s	1.1 [0.8–1.2]	1.1 [1.0–1.2]	1.1 [0.9–1.2]	0.455	–	–	–
Total lean mass, kg	38.506 [34.114–49.590]	49.900 [36.729–56.825]	36.426 [34.511–43.231]	0.002**	0.003**	1.00	0.013
Lean mass index, kg/m^2	13.8 [12.1–16.3]	16.3 [13.3–18.5]	13.3 [12.2–14.7]	0.001***	0.005**	0.54	0.005**
Appendicular lean mass, kg	16.7 [13.6–21.8]	22.6 [16.8–26.2]	14.9 [13.5–18.3]	0.001***	< 0.001***	0.59	< 0.001***
SMI, kg/height^2	6.1 [5.0–7.2]	7.4 [6.1–8.6]	5.5 [4.7–5.9]	0.001***	< 0.001***	0.28	< 0.001***
Appendicular lean mass/weight	0.28 [0.23–0.32]	0.31 [0.26–0.33]	0.25 [0.23–0.28]	0.003**	0.14	0.19	< 0.001***
Appendicular lean mass/BMI	0.81 [0.65–0.96]	0.95 [0.77–1.09]	0.75 [0.63–0.81]	0.004**	0.05	0.64	0.004**
Fat mass index, kg/m^2	5.9 [4.2–8.6]	6.3 [4.8–8.4]	6.5 [5.1–7.4]	0.944	–	–	–

Table 2. Sarcopenia components in young adults with IA. Values are shown as median (25–75th interquartile range). *IA* inflammatory arthritis, *JIA* juvenile idiopathic arthritis, *SpA* spondyloarthritis, *RA* rheumatoid arthritis, *SMI* skeletal muscle mass index, *BMI* body mass index. *p < 0.05; **p < 0.01; *** < 0.001. P1-2 comparison between JIA and RA; P1-3 comparison between JIA and RA; P2-3 comparison between SpA and RA.

3.83; 95% CI 1.71–8.64, p = 0.001 and OR 26.42; 95% CI 3.4–205.3, p = 0.002, correspondingly). The CRP and cumulative dose of GC were not linked to an augmented probability of sarcopenia.

The analysis of sarcopenia prevalence among patients receiving different DMARDs revealed significant variations. The highest prevalence was observed in the leflunomide group, where 83% of patients were diagnosed with sarcopenia. Among methotrexate users, 58% were diagnosed with sarcopenia, compared to 42% who were not. For sulfasalazine users, 18% had sarcopenia, while 82% did not. Statistical analysis confirmed a significant association between treatment type and sarcopenia ($\chi^2 = 17.62$, df = 4, p = 0.001; Fisher's exact test, p < 0.001). Logistic regression analysis revealed that methotrexate significantly increased the risk of sarcopenia (OR 2.93, 95% CI 1.46–6.03, p = 0.002). Sulfasalazine was associated with a reduced risk (OR 0.23, 95% CI 0.03–0.92, p = 0.06), though this finding was not statistically significant. The use of bDMARD monotherapy at enrollment was associated with a reduced risk of sarcopenia (OR 0.28, 95% CI 0.10–0.68, p = 0.007). All factors that are related to sarcopenia are presented in (Table 4).

In a multivariable analysis, BMI, BMD at femur neck, 25(OH)D, and disability were associated with an increased risk of sarcopenia (p < 0.05). The prognostic formula for assessing the risk of sarcopenia in patients with IA is as follows: log-odds = 9.009 − 0.191 × BMI − 0.039 × 25(OH)D − 4.76 × BMD at femur neck + 2.736 × HAQ.

The following equation is used to estimate the probability: $p = \frac{e^{log-odds}}{1+e^{log-odds}}$

Two clinical cases are presented to demonstrate the application of this formula. In the first case, a patient with a BMI of 22 kg/m^2, a 25(OH)D level of 50 nmol/L, a BMD at the femur neck of 0.851 g/cm^2, and an HAQ score of 0.1 was found to have a sarcopenia risk of 28.6%. In the second case, a patient with a BMI of 24 kg/m^2, a 25(OH)D level of 35 nmol/L, a BMD at the femur neck of 0.811 g/cm^2, and a HAQ score of 0.8 demonstrated

Variable	JIA (70)			SpA (51)			RA (17)			All IA (138)		
	Sarcopenic	Non-sarcopenic	P-value	Sarcopenic	Non-sarcopenic	P-value	Sarcopenic	Non-sarcopenic	P-value	Sarcopenic	Non-sarcopenic	P-value
Age, years	21.5 [18.0–24.3]	20.0 [18.3–28.5]	0.85	36.0 [29.0–41.0]	35.0 [30.0–40.0]	0.93	31.0 [30.0–36.0]	36.0 [33.0–42.0]	0.17	24.0 [20.0–33.0]	31.0 [23.0–37.0]	0.04*
BMI, kg/m^2	19.5 [17.4–21.5]	23.1 [21.0–26.8]	< 0.01**	22.0 [19.4–23.2]	25.2 [22.0–29.0]	0.02*	19.5 [17.8–20.7]	24.2 [20.3–24.8]	0.07	20.0 [17.6–22.3]	23.9 [21.1–28.0]	< 0.01**
Onset of disease, years	10.0 [5.8–13.3]	12.0 [10.5–15.0]	0.11	25.0 [22.0–30.0]	25.0 [21.0–33.0]	0.74	28.0 [24.2–31.0]	33.0 [28.8–37.0]	0.09	15.0 [8.8–24.3]	20.0 [13.3–31.0]	< 0.01**
Time before diagnosis, months	8.0 [4.5–12.0]	6.0 [3.0–9.0]	0.18	13.0 [6.0–24.0]	12.0 [11.0–36.0]	0.79	9.0 [4.0–12.0]	4.0 [3.0–9.0]	0.32	12.0 [6.0–12.0]	9.0 [3.0–24.0]	0.87
Duration of disease, years	13.0 [7.8–18.0]	10.0 [7.0–16.1]	0.27	8.0 [2.0–13.0]	6.0 [4.0–10.0]	0.59	4.5 [4.0–8.0]	2.0 [1.8–3.5]	0.15	9.5 [5.8–15.3]	7.0 [4.0–12.0]	0.07
25(OH)D, nmol/l	34.3 [26.9–43.1]	52.5 [44.7–66.3]	< 0.01**	32.2 [25.2–49.8]	58.2 [48.3–65.5]	< 0.01**	58.6 [38.1–72.5]	55.6 [28.9–61.0]	0.41	34.3 [27.4–49.4]	55.5 [45.4–66.1]	< 0.01**
ESR, mm/h	14.0 [6.0–25.3]	6.5 [3.3–15.8]	0.03*	22.0 [12.0–32.0]	11.0 [4.8–16.2]	0.03*	22.0 [12.0–26.0]	12.0 [5.0–19.0]	0.22	19.0 [7.0–26.5]	10.0 [4.0–16.0]	< 0.01**
CRP, mg/L	5.0 [3.0–22.5]	4.0 [2.0–5.9]	0.29	12.0 [5.5–16.0]	4.0 [1.9–6.0]	< 0.01**	11.5 [9.0–12.0]	5.0 [3.0–14.0]	0.52	8.4 [3.9–16.3]	4.0 [2.0–6.0]	< 0.01**
cJADAS27	11.0 [7.0–19.0]	4.0 [1.3–7.8]	< 0.01**	–	–	–	–	–	–	–	–	–
ASDAS-CRP	–	–	–	2.9 [2.7–3.6]	1.70 [1.3–1.9]	< 0.01**	–	–	–	–	–	–
BASDAI	–	–	–	4.1 [4.0–4.7]	1.7 [1.4–2.1]	< 0.01**	–	–	–	–	–	–
DAS28-CRP	–	–	–	–	–	–	4.1 [4.0–4.5]	2.8 [2.6–3.9]	0.06	–	–	–
BMD at lumbar spine, g/cm^2	0.904 [0.812–1.152]	1.074 [0.916–1.196]	0.04*	0.871 [0.787–0.985]	1.019 [0.919–1.137]	< 0.01**	0.942 [0.924–0.983]	1.050 [0.971–1.103]	0.03*	0.912 [0.812–1.069]	1.048 [0.932–1.173]	< 0.01**
BMD at femur neck, g/cm^2	0.802 [0.702–0.888]	0.927 [0.788–1.053]	0.01**	0.751 [0.725–0.769]	0.853 [0.765–0.989]	< 0.01**	0.737 [0.702–0.766]	0.815 [0.760–1.026]	0.07	0.766 [0.704–0.822]	0.898 [0.782–1.016]	< 0.01**
BMD total, g/cm^2	1.001 [0.966–1.086]	1.099 [1.035–1.166]	0.01**	1.055 [0.985–1.135]	1.120 [1.07–1.19]	0.11	1.083 [1.010–1.112]	1.072 [1.043–1.171]	0.53	1.031 [0.967–1.109]	1.112 [1.035–1.171]	< 0.01**
Cumulative dose of GC, mg	2880.0[80.0–7360.0]	1590.0[159.0–6700.0]	0.53	0.0 [0.0–440.0]	0.0 [0.0–720.0]	0.91	480.0 [0.0–1720.0]	0.0 [0.0–2160.0]	0.72	480.0 [0.0–720.0]	228.0 [0.0–3000.0]	0.06
HAQ score	0.8 [0.2–1.2]	0.0 [0.0–0.2]	< 0.01**	0.8 [0.3–1.2]	0.0 [0.0–0.0]	< 0.01**	0.9 [0.6–1.2]	0.2 [0.0–0.3]	0.02*	0.8 [0.2–1.2]	0.0 [0.0–0.0]	< 0.01**

Table 3. Comparison of sarcopenic and non-sarcopenic patients among the groups and in all IA patients. Values are shown as median (25–75th interquartile range). *IA* inflammatory arthritis, *JIA* juvenile idiopathic arthritis, *SpA* spondyloarthritis, *RA* rheumatoid arthritis, *BMI* body mass index, *25(OH)D* 25-hydroxyvitamin D, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *cJADAS-27* clinical juvenile arthritis disease activity score 27, *ASDAS* the ankylosing spondylitis disease activity score, *BASDAI* the bath ankylosing spondylitis disease activity index, *DAS28* disease activity score 28, *GC* glucocorticoids, *BMD* bone mineral density, *HAQ* health assessment questionnaire. *$p < 0.05$; **$p < 0.01$.

Variable	Univariable analysis			Multivariable analysis		
	Odds ratio, OR	95% CI	P-value	Odds ratio, OR	95% CI	P-value
Type of IA	0.73	0.45–1.21	0.21	–	–	–
Female sex	2.65	1.33–5.27	0.006	–	–	–
Age onset of disease, years	0.95	0.92–0.98	0.005	–	–	–
BMI, kg/m^2	0.75	0.67–0.84	< 0.001	0.84	0.72–0.96	0.02
Spinal involvement	0.46	0.24–0.91	0.02	–	–	–
Peripheral involvement	3.01	1.18–7.67	0.02	–	–	–
TJC > 3	3.83	1.71–8.64	0.001	–	–	–
SJC > 3	26.42	3.4–205.3	0.002	–	–	–
D25OH, nmol/l	0.95	0.94–0.98	< 0.001	0.96	0.93–0.98	0.001
ESR, mm/h	1.04	1.01–1.07	0.005	–	–	–
CRP, mg/L	1.005	0.91–1.02	0.47	–	–	–
cJADAS27	1.10	1.04–1.17	0.002	–	–	–
ASDAS-CRP	3.61	2.44–5.32	< 0.001	–	–	–
BASDAI	5.99	2.48–14.48	< 0.001	–	–	–
DAS28-CRP	2.43	1.36–4.36	0.005	–	–	–
BMD at lumbar spine, g/cm^2	0.04	0.005–0.29	0.002	–	–	–
BMD at femur neck, g/cm^2	0.003	0.001–0.04	< 0.001	0.01	0.001–0.268	0.01
BMD total, g/cm^2	0.001	0.0001–0.04	< 0.001	–	–	–
Cumulative dose of GC	1.0	1.0–1.0	0.04	–	–	–
Methotrexate use at the time of enrollment	2.93	1.46–6.03	0.002	–	–	–
Sulfasalazine use at the time of enrollment	0.23	0.03–0.92	0.06	–	–	–
bDMARDs monotherapy at the time of enrollment	0.28	0.10–0.68	0.007	–	–	–
HAQ	9.63	4.27–22.57	< 0.001	14.54	4.92–51.77	< 0.001

Table 4. Univariable and multivariable logistic regression analyses: factors associated with sarcopenia in young adults with IA. *IA* inflammatory arthritis, *BMI* body mass index, *TJC* tender joint count, *SJC* swollen joint count, *25(OH)D* 25-hydroxyvitamin D, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein, *cJADAS-27* clinical juvenile arthritis disease activity score 27, *ASDAS* the ankylosing spondylitis disease activity score, *BASDAI* the bath ankylosing spondylitis disease activity index, *DAS28* disease activity score 28, *BMD* bone mineral density, *GC* glucocorticoids, *bDMARDs* biologic disease-modifying anti-rheumatic drugs, *HAQ* health assessment questionnaire.

a sarcopenia risk of 80.9%. The predictive model demonstrated a sensitivity of 84.6%, a specificity of 85.5%, area under the ROC curve of 0.851 (0.782–0.919). Figure 2 illustrates the operative characteristics of the ROC curve.

Discussion

To our knowledge, this is the first study to analyze the prevalence of probable sarcopenia, sarcopenia, and severe sarcopenia among young adults with three different IA and to identify factors associated with sarcopenia. The younger adult population was intentionally selected to exclude older individuals, thereby minimizing the confounding effects of primary sarcopenia—a well-documented phenomenon associated with ageing. By focusing on a younger demographic, this study aimed to assess the prevalence of changes in muscle mass and strength during early adulthood and isolate the disease's direct impact, independent of age-related factors. This methodological approach provides a clearer understanding of the disease's role as a primary contributor to alterations in muscle health. Furthermore, the lack of standardized diagnostic criteria and the use of diverse methodological approaches across studies pose additional challenges to making meaningful comparisons.

The prevalence of sarcopenia in patients with IA has been explored in various studies; however, data on younger populations remains limited. Barone et al.[14] reported a sarcopenia prevalence of 21% in 168 middle-aged patients with RA, PsA, and AS. This was the first study to employ a combined approach for identifying sarcopenia, assessing both low muscle mass (via BIA) and low muscle strength. Age and disability were the only independent predictors of sarcopenia, findings that were consistent across RA, AS, and PsA. Notably, disease activity indices such as DAS28, CDAI, SDAI, DAPSA, ASDAS-CRP, and ASDAS-ESR showed no association with sarcopenia, except for BASDAI[14]. By utilizing DXA for precise muscle mass assessment and excluding age-related sarcopenia, our study identified BMI, BMD, vitamin D levels, and disability as independent risk factors for sarcopenia. These findings offer novel insights into the early onset and distinct patterns of sarcopenia in young IA patients. Hanaoka et al.[13] highlighted the role of high-dose GC therapy in accelerating sarcopenia progression among hospitalized rheumatic patients, attributing early weight loss to muscle mass reduction. However, their study primarily focused on hospitalized patients undergoing remission induction. In contrast, our research investigates non-hospitalized young adults with IA (18–40 years) and reveals a significant prevalence of sarcopenia across three IA subtypes. Notably, we found no significant influence of GC therapy on sarcopenia in our cohort.

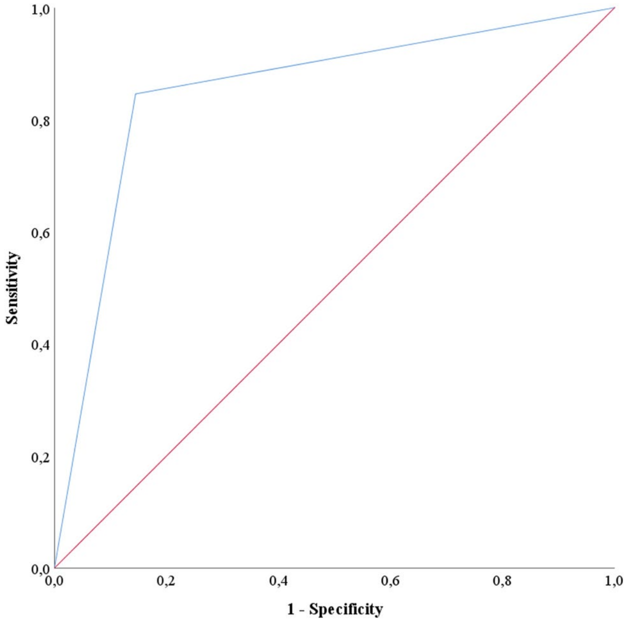

Fig. 2. ROC curve for predicting the risk of sarcopenia in young adults with IA.

The rate of sarcopenia in SpA patients has been reported to range from 5.1 to 85.6%[29,34,43–45]. Similarly, the frequency of sarcopenia in patients with RA also varies significantly; for example, the studies of M. Barone et al.[14] and A. Ngueuleu et al.[32] noted an almost two-fold difference in the frequency of sarcopenia (21 and 39.8%, respectively). Another research endeavor utilized BIA along with the methodological and threshold parameters advocated by the Asian working group for sarcopenia (AWGS) to demonstrate the substantial prevalence of sarcopenia within the RA patient population. This study reported a 37.1% prevalence of sarcopenia in the RA population[36]. In the recent review, the prevalence of sarcopenia in diverse autoimmune diseases, including RA, SpA, systemic sclerosis, inflammatory bowel disease, and autoimmune diabetes, was studied using various definitions of sarcopenia[12]. They reviewed the prevalence of sarcopenia in RA patients ranged from 10.1 to 45.1%[27,28,30,32,33,36,46–50], the prevalence of sarcopenia in SpA patients 22.7–34.3%[14,34], and 20–43.1% in PsA patients[14,35]. The prevalence of sarcopenia, where BIA was utilized to assess muscle mass, was reported as 36.3% among patients with AS. In contrast, the study that employed the same methodological algorithm and the criteria set forth by EWGSOP observed a higher prevalence of 50.4%[34].

The association between low bone mass and sarcopenia warrants particular attention, as muscle-bone crosstalk involves shared underlying mechanisms, including vitamin D deficiency, chronic inflammation, and reduced physical activity[51,52]. Our results highlight the intricate interplay between bone and muscle, demonstrating that low femoral neck BMD is a strong independent predictor of sarcopenia. These findings align with existing literature, such as the study by Verschueren et al.[53], which identified a significant correlation between sarcopenia, reduced BMD, and osteoporosis (OR 3.0; 95% CI 1.6–5.8). Moreover, our study's observed association between higher HAQ scores and sarcopenia highlights this condition's functional burden. Notably, low bone mass may significantly amplify fracture risk in sarcopenic patients due to the concurrent weakening of muscle and skeletal systems[54,55]. Although our study did not include data on fractures, these represent an important consequence of sarcopenia and low bone mass. Future research should explore the prevalence and impact of fractures in young adults with IA to better elucidate the clinical implications of sarcopenia on fracture risk.

In earlier studies, many different factors have been associated with sarcopenia among patients with RA, including age[36,49], BMI[32,48,49], body fat mass[48,50], disease duration[36,56], low BMD[36], joint damage[27,36,47], functional status[27,28,47,57,58], CRP[27,49,57,59], ESR levels [57,59], RF positivity [27,28], GC-use [50,57,60,61]. At the same time, the association between the decrease in muscle mass and the activity of the disease, assessed by DAS28, was not revealed in RA[27,30]. Sarcopenia in SpA patients is influenced by various factors, including disease activity, measured by BASDAI[29,34], and functional limitation, assessed by the Bath Ankylosing spondylitis functional index (BASFI)[29]. Recent research has further elucidated the determinants of sarcopenia in SpA. One study, using EWGSOP2 criteria, linked sarcopenia to elevated CRP, higher disease activity (BASDAI), reduced gait speed, and poorer quality of life[44]. Another study employing AWGS criteria highlighted older age, low BMI, and greater functional impairment (BASFI) as independent risk factors[45].

In our study, methotrexate was associated with a significantly higher risk of sarcopenia. However, this association likely reflects the clinical profiles of patients receiving these treatments rather than the direct pharmacological effects, as patients with polyarticular involvement are more likely to require methotrexate. In contrast, treatment with bDMARDs appeared to reduce the risk of sarcopenia. This aligns with findings from a systematic review and meta-analysis[62], which showed that while bDMARDs improved muscle mass parameters (e.g., total lean mass, SMI) in nearly half of the included patients, the overall meta-analysis failed to demonstrate a statistically significant effect on total lean mass. The authors attributed this discrepancy to heterogeneity in study designs, differences in assessment methods (DXA vs. BIA), and variability in treatment duration, highlighting the complex interplay between inflammation, treatment, and muscle health. Furthermore, as our study is cross-sectional, it inherently limits the ability to establish causality. Randomized controlled trials or longitudinal studies are needed to disentangle the independent effects of DMARDs from confounding factors such as disease severity. Until then, these findings should be interpreted with caution.

Sarcopenia in young adults with IA carries significant clinical implications. Our study demonstrates that higher disease activity, as measured by cJADAS, DAS28-CRP, ASDAS-CRP, and BASDAI indices, serves as a significant risk factor for sarcopenia in this population. Moreover, the observed association between sarcopenia and disability highlights its adverse impact on functional capacity and independence. Early identification of sarcopenia is essential to enable timely interventions aimed at mitigating its effects, such as optimizing vitamin D levels and addressing associated risk factors like low BMD. While a definitive cure for sarcopenia remains unavailable, effective management of inflammatory arthritis and its related sequelae—particularly through the reduction of systemic inflammation—offers the potential to slow sarcopenia progression and enhance overall patient outcomes. These conclusions are supported by existing literature and this study's findings.

Limitations
We acknowledge some limitations of our study as follows: the study did not control for all potential confounding factors, including physical activity and nutrition, patients were examined in a single clinical center, a small number of patients to examine differences within groups, absence of a control population that would match the patients in terms of sex and age; however, this particular aspect was not within the scope of the current study. In addition, the absence of data on cumulative disease-related damage could have further clarified the interplay between long-term IA complications and sarcopenia. Nevertheless, this study is the first to comprehensively assess all components of sarcopenia and investigate its prevalence among young adults with IA. The significant prevalence of sarcopenia observed in our study population emphasizes the necessity for further research to elucidate its occurrence with the nature and activity of specific rheumatological conditions.

Conclusion
Our study underscores the multifactorial nature of sarcopenia in young patients with JIA, RA, and SpA. Sarcopenia was more common in females, those with earlier disease onset, higher ESR, and reduced BMD. Multivariable analysis identified BMI, femur neck BMD, vitamin D levels, and disability as independent predictors with a reliable predictive model. These findings underline the importance of early identification of risk factors and targeted interventions to prevent sarcopenia in this vulnerable population. Future research should focus on developing strategies to improve muscle health and overall quality of life in young individuals with chronic inflammatory diseases.

Methods
Patients' characteristics
Patients with inflammatory arthritis (IA) were randomly included in this study and underwent a clinical examination by the Rheumatology Department group from November 2020 to December 2022. The study was conducted in accordance with the Declaration of Helsinki; all patients provided informed consent, and all procedures were approved by the local ethics committee (protocol No. 219 of November 4, 2020).

The study population included patients diagnosed with polyarticular and oligoarticular JIA, enthesitis-related JIA, RA, and SpA, according to the diagnostic criteria of the International League of Associations for Rheumatology[63], the American College of Rheumatology/European League Against Rheumatism[64], and the Assessment of SpondyloArthritis International Society[65], respectively. The inclusion criteria were: established diagnosis of IA, duration of disease > 1 year, age from 18 to 44, and consent to participate in the study. The exclusion criteria included systemic type of JIA, secondary rheumatic diseases, history of joint endoprosthesis, diabetes, mental disorders, and patient refusal to participate in the study.

For a prevalence of 5% at a 95% confidence level, the calculated required sample size is 73 participants, assuming a 5% margin of error is acceptable. This determination is based on a standard Z-value of 1.96 corresponding to the specified confidence level, with both prevalence and margin of error expressed as proportions (0.05). This result represents the minimum sample size necessary to ensure statistically reliable estimates within the given parameters[44].

Sarcopenia assessment
In this study, we identified three stages of sarcopenia based on the EWGSOP2 definition: probable sarcopenia, sarcopenia, and severe sarcopenia. Probable sarcopenia was indicated by low muscle strength, while sarcopenia was diagnosed when both reduced muscle mass and muscle strength were present. Severe sarcopenia was characterized by the presence of reduced muscle mass, low muscle strength, and impaired physical performance[2]. The estimation of appendicular lean mass (ALM) and skeletal mass index (SMI) was grounded on the determination of body composition assessed by DXA (Hologic®, USA). SMI was obtained as the ratio of appendicular lean mass to height^2. The reference values used for diagnosing muscle mass and muscle strength reduction were established as the following: SMI < 5.67 kg/m^2 in women and < 7.0 kg/m^2 in men, and handgrip strength < 27 kg in women and < 16 kg in men, respectively[1]. A handgrip dynamometer (Jamar®) ascertained muscle strength. The test was performed in triplicate for each side, and the mean value was utilized for subsequent analysis[2,66–70]. Muscle function was measured by testing gait speed using the six-meter walk test with a cut-off value of < 0.8 m/sec for both men and women[71].

Except for SMI, other muscle and fat-related indices were evaluated, such as ALM divided into BMI and ALM/weight indices[72,73]. Lean mass index (LMI) and fat mass index (FMI) were calculated, where LMI is lean mass, kg divided by height, m^2, and FMI is fat mass, divided by height, m^2[74]. Bone mineral density (BMD) at the lumbar spine, femur neck, and BMD total were measured on the same day.

Disease activity assessment
Disease activity was evaluated using standardized scoring systems. In JIA patients, the clinical juvenile arthritis disease activity score (cJADAS27) was employed[75–77]. Concerning patients with SpA, disease activity was quantified using the ankylosing spondylitis disease activity score-C reactive protein (ASDAS-CRP), bath ankylosing spondylitis disease activity index (BASDAI)[78–80]. The disease activity score 28 (DAS28) was also employed to evaluate disease activity in RA and polyarticular JIA patients[81].

Disability assessment
For disability assessment, the "health assessment questionnaire" (HAQ) was utilized[82,83]. HAQ scores span from 0 to 3, with elevated scores denoting greater disability.

Statistical analysis
Quantitative indicators were assessed for normality using the Kolmogorov–Smirnov criterion. Due to non-normal distribution, these indicators were presented as medians with 25 and 75th percentiles, while categorical variables were expressed as numbers (percentages). Nominal data were analyzed using the Chi-squared test. Quantitative indicators were compared between two groups with the Mann–Whitney U test, and comparisons across three groups used the Kruskal–Wallis test. Post-hoc pairwise comparisons following the Kruskal–Wallis test employed Bonferroni correction to adjust for multiple testing. Logistic regression analysis (both univariable and multivariable) was performed to evaluate associations with sarcopenia, reporting 95% confidence intervals (95% CI). A stepwise method was applied to include variables with $p < 0.05$ and exclude those with $p > 0.1$, ensuring the multivariable model retained the most significant predictors. The model's predictive accuracy was assessed using the receiver operating characteristic (ROC) curve. The area under the curve (AUC) was calculated to measure the model's discriminatory ability. The statistical analyses were performed using SPSS software, Version 26, for Windows (SPSS Inc., Chicago, IL). A p-value of 0.05 or less was deemed statistically significant.

Data availability
The data supporting this study findings are available from the corresponding author, M.K., upon reasonable request.

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Author contributions
M.K. was responsible for collecting and analyzing patient data, conducting statistical analysis, and writing the-manuscript. M.D. contributed to developing the research concept and design and reviewed the manuscript. Bothauthors have reviewed and approved the final version of the manuscript.

Declarations

Competing interests
The authors declare no competing interests.

Ethical standards
The study complied with the ethical principles of the Declaration of Helsinki. Written informed consent was obtained from all study participants. Ethical permission for the present investigation was obtained from the Regional Ethics Board in Kyiv, Ukraine (approval №219, dated 04.11.2020).

Additional information

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