Effects on serum protein levels from one bout of high intensity interval training in individuals with axial spondyloarthritis and controls

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Abstract

Background

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease primarily affecting the axial skeleton causing pain, inflammation, and stiffness. Individuals with axSpA are at greater risk of developing cardiovascular disease, which can be counteracted by physical activity. High-intensity interval training (HIIT) has been shown to improve cardiovascular health, but the effect on disease activity and the level of inflammation in axSpA has been less studied. With the aim of investigating how levels of inflammatory cytokines, myokines, and protein markers for bone metabolism are acutely affected by one bout of HIIT, we studied serum from individuals with axSpA and healthy controls (HC).

Methods

Ten participants with axSpA and 11 age- and sex-matched HC performed a single HIIT bout on a cycle ergometer: 4x4 minutes intervals with three minutes active rest in between. Blood samples were taken before and one hour after the HIIT bout. Serum proteins (IL-6, IL-17, IL-18, TNFa, CXCL-10, VEGF-A, BDNF, DKK-1, osteoprotegerin, osteocalcin, osteopontin, BMP-7, CRP) were analyzed with a Luminex system or ELISA. Descriptive data are presented as mean with standard deviation. A two-way ANOVA was used for comparisons.

Results

A main effect from baseline to one hour post HIIT showed that both groups had a significant increase in serum levels (pg/ml) of IL-6: axSpA 2.2 (3.0) to 3.2 (1.8) and HC 0.4 (0.4) to 1.9 (2.0), $p = 0.03$. VEGF-A (pg/ml) was significantly lower in the axSpA group: 159 (138) vs. HC 326 (184), $p = 0.03$, but was not affected by the HIIT bout. BMP-7 (ng/ml) increased in both groups after the HIIT: axSpA 61.6 (13.1) to 75.2 (20.0) and HC 64.6 (20.8 to 75.0 (17.8), $p < 0.001$. For the other proteins analyzed, there were no significant differences in serum concentrations between individuals with axSpA and HC, or within the two groups before and after one bout of HIIT.

Conclusions

One acute bout of HIIT significantly increases the serum concentrations of IL-6 and BMP-7 after 1 hour in both individuals with axSpA and HC.

Background

Spondyloarthritis is an umbrella term for a group of inflammatory rheumatic diseases, including axial spondyloarthritis (axSpA), which primarily affects the axial skeleton and the sacroilical joint (1). The

clinical manifestations encompass stiffness, aching, and pain around the spine and pelvis and the disease process can lead to fusing of the vertebrae, but also of the sacroiliac joints (i.e., ankylosis) (2–4). axSpA includes patients with X-ray changes in the sacroiliac joint or spine, in addition to patients without X-ray verified changes (non-radiographic axSpA) (1).

Studies have shown that individuals with axSpA have an increased risk of cardiovascular disease, which influences the treatment of the disease and overall health (5). The elevated cardiovascular risk is believed to be the result of a chronic systemic inflammation and insufficient level of physical activity, but other comorbidities might play a role as well (6, 7). Recommended treatment of axSpA is a combination of pharmacological and non-pharmacological treatment including exercise interventions (8, 9), but to date, the most suitable form of exercise for individuals with axSpA is not known (8, 10). Exercise guidelines for individuals with axSpA include domains of cardiovascular-, flexibility-, and resistance training. Moreover, guidelines need to be individually tailored and be based on shared decision making (8, 10).

Traditionally, exercise interventions for individuals with axSpA involve moderate intensity exercise training, but lately some researchers have promoted the incorporation of high intensity interval training (HIIT) (11, 12). HIIT is described as high intensity exercise bouts separated by periods of active recovery phases. It has been demonstrated that regular HIIT bouts can lead to better cardiovascular health through increased VO_{2max} and improved muscle metabolism (13, 14). Moreover, studies in metabolic disorders show that HIIT has a positive effect on systemic inflammatory markers linked to the disease state (15, 16). The significance of HIIT for disease development in rheumatic disorders in general, including the response in levels of inflammatory markers, have not been widely studied. A three-month HIIT intervention improved disease symptoms and cardiovascular health, in addition to maintaining an unaltered C-reactive protein (CRP) level, in individuals with axSpA (11, 12). Levels of pro-inflammatory cytokines were not affected when measured 48 hours after the HIIT-bout (11). During extensive muscle activity, a large set of proteins, called myokines, are released which are suggested to influence many organ systems with impact on metabolism and inflammation among other functions (17, 18). One of the most studied myokines, IL-6, is immediately released in response to muscle activity (19). IL-6 is a pleiotropic cytokine with both pro-inflammatory and anti-inflammatory effects. The release of myokines, like IL-6, upon exercise is suggested to counteract inflammation and, thus, cardiovascular issues in rheumatic diseases, since systemic inflammation is an important factor in atherosclerosis (18, 20). Other examples of proteins produced by muscle and other tissues are brain derived neurotrophic factor (BDNF), a neurotrophin with effects on synapse activities in the brain (21), and vascular endothelial growth factor (VEGF) important for vascularization of skeletal muscle tissue in response to exercise training (22).

The ankylosis that features axSpA is part of bone metabolism, which extends from the formation of new bone (syndesmophytes) to osteoporosis and bone erosion (23). It is not yet fully understood whether bone metabolism with new bone formation is linked to the inflammatory process in axSpA. Moreover, changes in levels of proteins involved in bone metabolism in response to exercise training have not been studied in this disease.

To safely recommend HIIT training to individuals with axSpA, it is important to first study the acute effects after a single HIIT bout regarding disease symptoms and state of inflammation. Previous studies on the acute effect of a single bout of HIIT in healthy adults, overweight, and obese individuals have shown that changes in levels of serum inflammatory markers are dependent on exercise intensity and metabolic status (24), and that there is no severe inflammation due to muscle damage (25).

With an overall research aim to study the role for HIIT as an exercise intervention in individuals with axSpA regarding influence on systemic inflammation and bone metabolism, in addition to the effect on lowering of the risk for cardiovascular disease, we performed the herein presented study. This cross-sectional study was undertaken to provide a controlled evaluation of the acute effects of one HIIT bout on disease activity measured through serum levels of a set of inflammatory cytokines, myokines, and markers for bone metabolism in age- and sex-matched individuals with axSpA and HC.

Methods

Participants

The study included 21 individuals (10 females) between the ages of 18 and 50 (mean ± SD age 40 ± 7). Ten participants from two rheumatology clinics in southern Sweden were diagnosed with axSpA according to the Assessment in Spondylo-Arthritis international Society (ASAS) classification criteria (26) and eleven participants were age- and sex-matched HC. Exclusion criteria were cardiovascular disease, lung disease, or any other disease that reduced the physical capacity or the possibility of completing a HIIT bout. The individuals in the axSpA group, except for one participant, used anti-inflammatory drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) and biologics. Participants were asked to avoid food and drinks two hours before arrival, tobacco 30 minutes before, and to avoid exercising at high intensity the evening before the testing procedures (see below) and the HIIT bout. The study was approved by the national ethical review board (Dnr: 2019–04155 and Dnr: 2022-03114-02) and followed the ethical principles of the declaration of Helsinki.

Testing procedures

Before inclusion, electrocardiogram (ECG) and blood pressure were measured. In the event of deviating results regarding ECG and/or a blood pressure > 140/90, the person was excluded and referred to the health center for further investigation. Anthropometrics such as height was measured with a stadiometer and body composition with bioelectrical impedance analysis (InBody 770, Body Space South Korea) (Table 1). Thereafter, participants were fitted with a heart rate (HR) monitor (Polar, Finland) and the Åstrand's submaximal cycle ergometer (Monark, Vansbro, Sweden) test for prediction of maximal oxygen consumption (VO_{2max}) was performed (27).

Table 1
Baseline data for participants with axial spondyloarthritis (axSpA) and age- and sex matched healthy controls (HC).

	axSpA (n = 10)	HC (n = 11)	p-value[a]
Age	41 (7)	40 (7)	0.705
Sex (men/women)	5/5	5/6	NA
Skeletal muscle mass (kg)	32.8 ± 5.8	33.5 ± 8.5	0.705
Body fat (%)	22.0 ± 5.8	19.8 ± 7.8	0.468
Systolic blood pressure (mm Hg)	127 (11)	128 (9)	0.710
Diastolic blood pressure (mm Hg)	81 (6)	80 (5)	0.824
VO_2max (ml O2/kg/min)	39.9 ± 8.4	42.6 ± 10.7)	0.973
Smoker or using tobacco in other forms	3	2	NA
EQ-5D, 0-1[b] health status	0.87 (0.11)	0.93 (0.10)	0.251
BASDAI, 0-10[c] disease activity	1.6 (0.8)	NA	NA
BASFI, 0-10[c] physical function	0.7 (0.8)	NA	NA
BASG 0-10[c] wellbeing	1.5 (1.0)	NA	NA
Anti-inflammatory drugs[d]	9/10	2/11	NA
Drugs other than anti-inflammatory[e]	0/10	1/11	NA

Results presented as mean (± SD). [a]Difference between axSpA and HC analyzed with Mann-Whitney U-test. [b]Worst to best. [c]Best to worst. [d]Non-steroidal anti-inflammatory drugs (NSAID), TNFa-inhibitors, Corticosteroids (allergy/asthma). [e]Synthetic thyroid hormone. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASG, Bath Ankylosing Spondylitis Global.

After a brief rest, participants began the HIIT-bout while wearing a HR monitor. HIIT was performed on a rpm-independent ergometer bike (LC-6 or 928E, Monark, Vansbro. Sweden) and included four high intensity intervals, each 4 minutes in duration, with 3 minutes active rest (about 70% of maximum HR) between intervals. During the high intensity intervals, the participants should reach > 17 on the rating of the perceived exertion (RPE) scale (28) and reach 90% of estimated maximum HR (HR_{max}) any time during the interval (29). After the HIIT-bout, the participants filled out the disease-specific questionnaire Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) on disease activity scoring 0–10 (best-worst) (30). For descriptive data, health status was measured with the generic questionnaire EuroQol-5

domain (EQ-5D) consisting of five questions covering mobility, self-care, usual activity, pain/discomfort, and anxiety/depression scoring 0–1 (no health to full health) (31).

Blood samples were collected before (baseline) and one hour after the HIIT-bout ended. Blood samples rested for 30 minutes followed by centrifugation for 10 minutes. The serum supernatant was aliquoted and stored at -80ºC in biobank number 85 at FoU Spenshult, Halmstad. Baseline plasma levels of lipids (P-cholesterol, P-triglycerides, P-LDL, P-HDL) and glucose were analyzed at clinical chemistry departments at the nearest hospitals.

Serum analyses of cytokines, myokines and bone-associated proteins

Serum was analyzed with the Luminex MAGPIX® (Luminex corporation, Austin, US) and ELISA (Spectramax Plus 384, Molecular Devices, San Jose, US). Selected markers from the Human Cytokine/Chemokine/Growth Factor Panel A (HCYTA-60K), Human Myokine Panel (HMYOMAG-56K), and Human Bone Panel (HBNMAG-51K) (Merck KGaA, Darmstadt, Germany) were used for the analysis of IL-6, IL-17, IL-18, TNFa, CXCL-10, VEGF-A, BDNF, DKK-1, osteoprotegerin, osteocalcin, and osteopontin. The Belysa™ Immunoassay Curve Fitting Software (Merck KGaA, Darmstadt, Germany) was used for analysis of Luminex MAGPIX data. CRP and BMP-7 were analyzed with Human C-reactive protein and BMP-7 Quantikine ELISA (R&D systems INC Minneapolis, US), respectively, according to the manufacturers protocol. For ELISA data, the "Quest Graph™ Four Parameter Logistic (4PL) Curve Calculator." *AAT Bioquest, Inc.* https://www.aatbio.com/tools/four-parameter-logistic-4pl-curve-regression-online-calculator was used for the standard curve fitting. The lowest limit of detection for the different serum proteins was: IL-6 (0.18 pg/ml), IL-17 (0.89 pg/ml), IL-18 (0.42 pg/ml), CXCL-10 (2.47 pg/ml), TNFa (4.4 pg/ml), VEGF-A (0.91 pg/ml), BDNF (3 pg/ml), DKK-1 (1.2 pg/ml), osteoprotegerin (1.8 pg/ml), osteocalcin (37.5 pg/ml), osteopontin (15.6 pg/ml), BMP-7 (2.44 pg/ml), CRP (0.010 ng/ml). For a few samples some protein levels were below detection as indicated in Table 2.

Table 2

Serum protein levels in individuals with axial spondyloarthritis (axSpA) and age- and sex matched healthy controls (HC) at baseline and one hour after a 4 minutes x 4 times high intensity interval training (HIIT) session. All values are means ± standard deviations.

Serum analyte	axSpA baseline (n = 10)	HC baseline (n = 11)	axSpA post-HIIT (n = 10)	HC post-HIIT (n = 11)	2*2 ANOVA p-value	Post-Hoc p-value
IL-6 (pg/ml)	2.2 ± 3.0 n = 8[a]	0.4 ± 0.4 n = 10	3.2 ± 1.8 n = 8	1.9 ± 2.0 n = 10	MEpre-post 0.03	AxSpA 0.23 HC 0.04
IL-17 (pg/ml)	3.5 ± 5.1 n = 5	4.9 ± 3.1 n = 8	3.7 ± 4.5 n = 5	4.8 ± 3.2 n = 8	> 0.05	NA
IL-18 (pg/ml)	14.9 ± 7.1 n = 9	24.4 ± 14.4 n = 10	16.2 ± 6.8 n = 9	24.7 ± 14.6 n = 10	> 0.05	NA
TNFa (pg/ml)	51.6 ± 94.0	29.0 ± 47.9	48.2 ± 75.1	41.2 ± 88.2	> 0.05	NA
CXCL-10 (pg/ml)	82.7 ± 65.1	68.9 ± 35.4	75.7 ± 54.5	66.3 ± 31.4	> 0.05	NA
VEGF-A (pg/ml)	159 ± 138	326 ± 184	172 ± 122	325 ± 170	MEgroup 0.03	Baseline 0.031 Post 0.030
BDNF (ng/ml)	15.6 ± 5.2	15.8 ± 3.9	16.1 ± 3.9	16.3 ± 3.3	> 0.05	NA
DKK-1 (pg/ml)	1744 ± 379	1527 ± 212	1767 ± 364	1549 ± 207	> 0.05	NA
OPG (pg/ml)	280 ± 68	261 ± 39	278 ± 57	267 ± 47	> 0.05	NA
OC (ng/ml)	16.2 ± 9.1	14.5 ± 5.3 n = 10	16.1 ± 8.4	15.1 ± 6.0 n = 10	> 0.05	NA
OPN (ng/ml)	18.4 ± 14.3	17.8 ± 6.8	14.8 ± 11.1	16.7 ± 9.1	> 0.05	NA

[a]number of values included in the calculation if different from the total number; ME, main effect; IL-6,-17,-18, Interleukin-6,-17,-18; TNFa, Tumor Necrosis Factor alpha; CXCL-10, C-X-C motif chemokine ligand 10; VEGF-A, Vascular Endothelial Growth Factor-A; BDNF, Brain Derived Neurotrophic Factor; DKK-1, Dickkopf WNT signaling pathway inhibitor 1, OPG, Osteoprotegerin; OC, Osteocalcin; OPN, Osteopontin; BMP-7, Bone Morphogenetic Protein-7; CRP, C-reactive protein.

Serum analyte	axSpA baseline (n = 10)	HC baseline (n = 11)	axSpA post-HIIT (n = 10)	HC post-HIIT (n = 11)	2*2 ANOVA p-value	Post-Hoc p-value
BMP-7 (pg/ml)	61.6 ± 13.1	64.6 ± 20.8	75.2 ± 20.0	75.0 ± 17.8	MEpre-post < 0.001	AxSpA 0.004 HC 0.018
CRP (µg/ml)	1.12 ± 1.06	0.77 ± 0.85	1.11 ± 1.12	0.71 ± 0.75	> 0.05	NA

[a]number of values included in the calculation if different from the total number; ME, main effect; IL-6,-17,-18, Interleukin-6,-17,-18; TNFa, Tumor Necrosis Factor alpha; CXCL-10, C-X-C motif chemokine ligand 10; VEGF-A, Vascular Endothelial Growth Factor-A; BDNF, Brain Derived Neurotrophic Factor; DKK-1, Dickkopf WNT signaling pathway inhibitor 1, OPG, Osteoprotegerin; OC, Osteocalcin; OPN, Osteopontin; BMP-7, Bone Morphogenetic Protein-7; CRP, C-reactive protein.

Statistics

Statistical analyses were performed with SPSS (version 28.0, IBM SPSS Statistics, IBM corp. USA). Differences in baseline descriptive data was calculated with Mann-Whitney U test. A repeated measures analysis of variance (ANOVA) was used to detect differences between groups and before and after a single HIIT bout in a 2 (group) * 2 (pre-post) design. For main effects or interactions significant at $p \leq 0.05$, Least Significant Difference (LSD) post-hoc analyses were performed. Data is reported as mean ± standard deviation (SD) and statistical significance was set to $p \leq 0.05$.

Results

Twenty-two participants were recruited, of which one was excluded due to abnormal ECG in the clinical screening. Ten individuals diagnosed with axSpA (age 41 ± 7 years), and 11 HC (mean age 40 ± 7 years) completed the HIIT-bout. Physiological measurements, values of self-reported disease activity and health status, are shown in Table 1. Except for the self-reported disease parameters not applicable for HC, the participants in the two groups were well matched for body composition (skeletal muscle mass: axSpA 32.8 ± 5.8, HC 33.5 ± 8.5 kg; body fat: axSpA 22.0 ± 5.8, HC 19.8 ± 7.8%), resting blood pressure (axSpA 127/81 ± 11/6, HC 128/80 ± 9/5 mmHg) and maximal oxygen consumption (VO_{2max}) (axSpA 40 ± 8, HC 43 ± 10 mlO_2/kg/min) (Table 1). Furthermore, no significant differences were observed for CRP (Table 2), plasma lipoproteins, triglycerides, and glucose (data not shown). All participants with axSpA, except one, were treated with anti-inflammatory drugs (Table 1).

Baseline and post-HIIT levels of cytokines, myokines and bone-associated proteins

Sera from the two participating groups were analyzed for proteins involved in inflammation and bone metabolism, in addition to myokines (Table 2). A significant ANOVA pre-post main effect ($p = 0.03$) was seen for IL-6 (pg/ml): axSpA 2.2 (3.0) to 3.2 (1.8) and HC 0.4 (0.4) to 1.9 (2.0). Post-hoc analyses showed increased levels of IL-6 in HC from baseline to post-HIIT ($p = 0.04$) but not in axSpA ($p = 0.23$). There was no difference in the level of IL-6 (pg/ml) between the axSpA and HC groups at baseline: axSpA 2.2 (3.0) and HC 0.4 (0.4) ($p = 0.07$) or post-HIIT: axSpA 3.2 (1.8) and HC 1.9 (2.0) ($p = 0.20$) (Table 2). We found a significant group main effect ($p = 0.03$) for the level of serum VEGF-A (pg/ml), with lower levels in the axSpA group at both baseline: axSpA 159 (138) and HC 326 (184) ($p = 0.03$), and post-HIIT: axSpA 172 (122) and HC 325 (170) ($p = 0.03$) (Table 2). No differences in serum levels (ANOVA $p > 0.05$) for any of the remaining myokines and cytokines analyzed were observed between or within the axSpA and HC groups at baseline and post-HIIT (Table 2). For the bone associated proteins a significant pre-post main effect ($p < 0.001$) was found for BMP-7. The serum-concentration of BMP-7 (pg/ml) increased significantly from baseline: axSpA 61.6 (13.1) and HC 64.6 (20.8), to post-HIIT: axSpA 75.2 (20) ($p = 0.004$) and HC 75.0 (17.8) ($p = 0.02$) (Table 2).

Discussion

HIIT is an exercise form that has become popular in recent years, not only in healthy populations but also in individuals with different chronic diseases. Briefly, the health benefits associated with HIIT are: increased cardiovascular capacity, lower blood pressure and improved arterial function (32–34); increased metabolic health with weight control and improved insulin sensitivity (35); increased muscle strength; and influence on mental health with reports on reduced depression and anxiety (36). HIIT has, however, not been extensively studied as an exercise intervention in individuals with various rheumatic disorders, and therefore it is important to understand the acute effects of a HIIT-bout on disease symptoms and the state of inflammation before starting a HIIT-intervention. In the present study, we investigated a set of serum markers and physiological measurements in age- and sex-matched individuals with axSpA and HC before and after one bout of HIIT with the aim of determining levels of specific serum markers in axSpA and how these are affected by one acute bout of HIIT. One goal with the present and other ongoing studies in our group, is to establish biomarkers that could be used for the evaluation of disease progression and the effect of regular HIIT bouts on the disease process to optimize and individualize HIIT-based interventions. Furthermore, due to the systemic inflammation, individuals with axSpA are at higher risk for developing cardiovascular disease and HIIT has been shown to be a possible intervention to manage the disease and comorbidities when appropriate (12).

In this study, we analyzed serum markers including pro-inflammatory cytokines, myokines, and proteins involved in bone metabolism, in addition to CRP (Table 2). Except for IL-6, no significant differences in cytokine levels were observed between the two groups at baseline or post-HIIT. The acute increase in IL-6 levels, where the levels from baseline to post-HIIT increased more in the HC than in axSpA, is consistent with previous studies on the effect of one acute bout of HIIT on serum IL-6 (37–39). We choose to measure the serum analytes one hour after the HIIT bout, since this time point may detect proteins released already during the HIIT bout, but also proteins that emerge in serum at different times after the

HIIT bout. In a preliminary study on 12 healthy young individuals (age 18–29), we showed that already at five minutes post-HIIT, the levels of IL-6 increased 2.4 times compared to the baseline level. After one hour this increase was only 1.6 times the baseline level (see Additional file 1). This is in line with previous studies (38, 39) and indicates that measuring the IL-6 serum concentration already at five minutes post HIIT may show a more exact increase in the individual production of IL-6.

The pathogenesis of axSpA is strongly dependent on the genetic linkage to HLA-B-27, but other associated genes have also been identified (1). Non-genetic factors suggested to be involved in the triggering of the disease are gut dysbiosis and mechanical stress contributing to enthesitis and pathology in the subchondral bone (2). It is believed that inflammation is primarily driving bone destruction, but there might also be an interaction between inflammation-driven factors and new bone formation ongoing in the inflamed tissue. We did not find any differences in the levels of analyzed proteins involved in bone metabolism (DKK-1, OPG, OC, OPN), except for BMP-7 where an increase in serum concentration after HIIT was found in both groups (Table 2). The bone morphogenetic proteins (BMPs) belong to the transforming growth factor (TGF)-ß family and have important roles in osteogenesis and bone formation (40). It has been suggested that new bone formation in axSpA is partly driven by BMPs (41). BMP-7 is a growth factor involved in many cellular processes, including those having anti-inflammatory effects (40, 42), but is considered most important for bone formation (43). Studies have shown an increase in levels of BMP-7 in axSpA patients (44) with a correlation to radiographic damage, which is linked to new bone formation (45, 46). To our knowledge, BMP-7 has not been studied in the context of HIIT, but it has been shown that BMP-7 levels decrease with increasing age and that exercise and subsequent release of myokines, including BMP-7, is important for bone health in the elderly (43). The fact that we observe an increase in serum concentrations of BMP-7 post HIIT, may indicate that HIIT can contribute to improvement of bone metabolism as well as inflammation through BMP-7. More research is however needed to understand the role for BMP-7 in axSpA with regards to pathological bone formation versus anti-inflammatory features.

VEGF-A is a main signaling factor in angiogenesis by regulating proliferation of endothelial cells and vascular permeability. It is released by many different cell types and can activate inflammatory cells and the production of pro-inflammatory mediators. The level of VEGF in healthy adults has been shown not to be influenced by HIIT in the short term, which is in line with the present results (47, 48). In individuals with axSpA VEGF-levels are elevated, but the levels are significantly decreased by anti-inflammatory treatment such as TNFa inhibitors (49, 50). The participants with axSpA in the present study had lower levels of VEGF-A compared to the HCs, which could be explained by the fact that all, but one, were on treatment with anti-inflammatory drugs. Similarly, there was no difference in the baseline levels of CRP between the two groups. Reports from studies on the effect of HIIT on CRP levels have shown conflicting results probably due to a variation in disease status and group size (36, 51). In the present study there was no significant difference in CRP levels between the axSpA and HC groups and we did not observe any changes in CRP levels from baseline to post-HIIT, which suggests that one bout of HIIT does not influence the general inflammatory status and can be safely performed.

The present study was performed to address the impact of one single bout of HIIT on serum levels of inflammatory cytokines, myokines, and markers for bone metabolism in individuals with axSpA and HC. One limitation of the study is the small group sizes, which however were well matched regarding sex, age, and physiological measures. Due to the small groups, there was not sufficient power in the calculations to analyze sex differences for the different serum markers. In addition, all participants with axSpA, except one, were treated with anti-inflammatory drugs, which had a considerable impact on certain serum markers.

Conclusion

In this study we investigated how one bout of HIIT acutely affect serum levels of specific pro- and anti-inflammatory cytokines, myokines, and proteins involved in bone metabolism in age- and sex-matched individuals with axSpA compared to HC. From the herein presented results we conclude that one bout of HIIT significantly increases the serum concentrations of IL-6 and the bone associated protein BMP-7 in both groups, but that the concentrations of none of the other proteins investigated, including CRP and VEGF-A, were significantly changed.

Abbreviations

axSpA	Axial spondyloarthritis
BDNF	Brain derived neurotrophic factor
BMP-7	Bone morphogenetic protein-7
CRP	C-reactive protein
DKK-1	Dickkopf-related protein 1
HC	Healthy controls
HIIT	High-intensity interval training
IL-6, -17, -18	Interleukin-6, -17, -18
NSAID	Non-steroidal anti-inflammatory drugs
OC	Osteocalcin
OPG	Osteoprotegerin
OPN	Osteopontin
TNFa	Tumor Necrosis factor alpha

VEGF Vascular endothelial growth factor

Declarations

Ethics approval and consent to participation

The study was approved by the Swedish Ethics Review Authority (Dnr: 2019-04155 and Dnr: 2022-03114-02) and performed in accordance with the Declaration of Helsinki. Each participant signed an informed consent for participation in the study.

Consent for publication

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors contributions

ÅA, EH, MCO conceived and designed the study. All authors participated in the acquisition of data. ÅA performed the serum analyses and ÅA, MCO and EH drafted the manuscript. MCO and EH performed the statistical analyses. All authors contributed to the interpretation of the results. All authors read and and approved the final manuscript.

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