Rheumatology International (2019) 39:1037–1043
https://doi.org/10.1007/s00296-019-04301-z

Rheumatology
INTERNATIONAL

OBSERVATIONAL RESEARCH

Serum visfatin levels in patients with axial spondyloarthritis and their relationship to disease activity and spinal radiographic damage: a cross-sectional study

Hana Hulejová[1] · Tereza Kropáčková[1,2] · Kristýna Bubová[1,2] · Olga Kryštůfková[1,2] · Mária Filková[1,2] · Heřman Mann[1,2] · Šárka Forejtová[1,2] · Michal Tomčík[1,2] · Jiří Vencovský[1,2] · Karel Pavelka[1,2] · Ladislav Šenolt[1,2]

Received: 4 February 2019 / Accepted: 9 April 2019 / Published online: 25 April 2019

Abstract

The purpose of this cross-sectional study was to assess the visfatin levels in patients with axial spondyloarthritis (axSpA) and to investigate the association between visfatin, disease activity and radiographic spinal damage. Serum visfatin levels were determined by enzyme-linked immunosorbent assay in 64 patients with axSpA (46 with radiographic axSpA (r-axSpA) and 18 with non-radiographic axSpA (nr-axSpA)) and 61 age-/sex-matched healthy individuals. Patients with r-axSpA were further divided into two subsets based on radiographic spinal damage using modified Stoke Ankylosing Spondylitis Spine Score (mSASSS = 0 and mSASSS ≥ 1). The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to assess disease activity. C-reactive protein (CRP) levels and human leukocyte antigen (HLA)-B27 were determined. Visfatin levels were significantly higher in patients with axSpA and in the subgroup of patients with r-axSpA than in healthy individuals ($p = 0.010$ and $p = 0.005$, respectively), with no difference between patients with r-axSpA and with nr-axSpA. In general, disease activity was high (mean BASDAI 5.01) and was moderately correlated with visfatin levels ($r = 0.585$; $p = 0.011$) in patients with nr-axSpA. Visfatin levels correlated with mSASSS ($r = 0.281$; $p = 0.026$) and were significantly higher in axSpA patients with mSASSS ≥ 1 than in those with mSASSS = 0 ($p = 0.025$). Our study showed that circulating visfatin levels are elevated in axSpA patients, may be associated with disease activity in early phase of the disease and with the degree of radiographic spinal involvement.

Keywords Axial spondyloarthritis · Visfatin · Disease activity · Radiographic damage

Abbreviations

ASDAS	Ankylosing Spondylitis Disease Activity Score
axSpA	Axial spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BMI	Body mass index
csDMARDs	Conventional synthetic disease-modifying anti-rheumatic drugs
bDMARDs	Biological disease-modifying anti-rheumatic drugs
CRP	C-reactive protein
ELISA	Enzyme-linked immunosorbent assay
HLA	Human leukocyte antigen
IQR	Interquartile range
MRI	Magnetic resonance imaging
mSASSS	Modified Stoke Ankylosing Spondylitis Spine Score
NAMPT	Nicotinamide phosphoribosyltransferase
nr-axSpA	Non-radiographic axial spondyloarthritis
NSAIDs	Non-steroidal anti-inflammatory drugs
PBEF	Pre-B cell colony-enhancing factor
r-axSpA	Radiographic axial spondyloarthritis
SIJ	Sacroiliac joints

Hana Hulejová and Tereza Kropáčková contributed equally to this manuscript.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00296-019-04301-z) contains supplementary material, which is available to authorized users.

✉ Hana Hulejová
hulejova@revma.cz

Extended author information available on the last page of the article

Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory disease predominantly affecting the axial skeleton (sacroiliac joints (SIJ) and spine). Peripheral and extra-articular manifestations, such as dactylitis, enthesitis, uveitis, inflammatory bowel disease and psoriasis, can also be associated with axSpA. Depending on the presence of radiographic sacroiliitis, patients with axSpA are further classified as having non-radiographic axSpA (nr-axSpA) or radiographic axSpA (r-axSpA) [1].

However, the diagnosis of the early phases of axSpA remains challenging. In recent years, great effort has been made to find a reliable biomarker of the disease [2–4]. A biomarker is defined as "a characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention" [5]. In patients with axSpA, such a biomarker could be used not only for the early detection of the disease but also for the evaluation of disease activity, disease progression and treatment response [3]. Currently, human leukocyte antigen (HLA)-B27 is considered to be the marker with the highest diagnostic value, while C-reactive protein (CRP) is useful for assessing disease activity and predicting disease progression or treatment response [4].

Adipokines are biologically active substances that are produced and released predominantly by adipose tissue. They have many regulatory functions in energy metabolism, as well as in inflammation and joint tissue metabolism [6, 7]. Several studies have already reported associations between some adipokines and r-axSpA [8, 9]. However, their exact role in the pathogenesis of the disease and their potential to serve as a disease biomarker is still unclear.

Visfatin, which is also known as pre-B-cell colony-enhancing factor (PBEF) or nicotinamide phosphoribosyltransferase (NAMPT), is a 52-kDa adipokine that is expressed in a wide range of tissues, including the bone marrow, liver and muscle [10]. Visfatin has proinflammatory properties [11], and its expression is enhanced in a variety of metabolic and inflammatory diseases [12]. In previous studies, visfatin was shown to play a role in bone homeostasis by stimulating osteoblast proliferation [13] and inhibiting osteoclastogenesis [14, 15].

Recently, serum visfatin levels were found to be increased in patients with r-axSpA compared with healthy controls, and higher baseline visfatin levels were associated with subsequent progression of radiographic damage in r-axSpA [8]. Although several other studies have analysed visfatin in r-axSpA [16, 17], the data regarding patients with non-radiographic axSpA are lacking. Therefore, the aim of our study was to assess the serum visfatin levels in patients with r-axSpA and nr-axSpA and to investigate the association between visfatin, disease activity and radiographic damage.

Materials and methods

Patients

Sixty-four patients who fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA were included in this study [18]. Based on imaging, patients were further classified as r-axSpA ($n=46$) and nr-axSpA ($n=18$). Patients with r-axSpA were divided into two subsets based on radiographic findings using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS: mSASSS = 0 (22 patients with SIJ involvement only) and mSASSS ≥ 1 (24 patients with involvement of both the SIJ and the spine).

The following information was collected: clinical and laboratory disease activity measures; demographic status; disease-related factors, such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and CRP levels; current medications (non-steroidal anti-inflammatory drugs (NSAIDs), conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), glucocorticoids, biological treatments (bDMARDs)); age, gender; body mass index (BMI); initial symptoms (e.g., back pain, peripheral arthritis, extra-articular manifestations); age at diagnosis; occurrence of peripheral arthritis and extra-articular manifestations; and the presence of HLA-B27 antigen. Sixty-one age- and sex-matched healthy subjects were enrolled in the study. The local ethics committee of the Institute of Rheumatology in Prague approved this study. Written informed consent was obtained from all individuals prior to initiation of the study.

Imaging

Radiographs of the SIJ, lumbar and cervical spine were obtained from majority of patients (except for one patient) prior to blood collection. A trained rheumatologist and a central radiologist scored the radiographs for the initial disease classification, and both were blinded to all the clinical data. Cervical and lumbar spine radiographs were scored according to the mSASSS [18].

Patients were classified as r-axSpA according to the New York classification criteria [19] and as nr-axSpA if the radiographic findings of the SIJ were negative (grade I bilaterally or grade II unilaterally) and the magnetic resonance imaging (MRI) was positive (i.e., characteristic bone marrow oedema) with at least one feature of SpA, according to the ASAS classification criteria for axial spondyloarthritis [18].

MRI images were obtained prior to recruitment and scored by a trained rheumatologist who was blinded to all the clinical data.

Laboratory analysis

Fasting blood samples were collected from all the individuals and immediately centrifuged. The serum samples were stored at − 80 °C until analysis. Serum visfatin levels were analysed by a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Biovision, Milpitas, CA, USA) according to the manufacturer's protocol. The absorbance was measured using a Sunrise ELISA reader (Tecan, Salzburg, Austria) with 450 nm as the primary wavelength. The assay sensitivity was 30 pg/mL, and the detection limit (cut-off) was 0.125 ng/mL. The intra- and inter-assay coefficient of variation was 3.5% and 5.3%, respectively.

Serum CRP levels were determined by an immuno-turbidimetric technique using an Olympus AU 680 biochemical analyser (Olympus Optical, Tokyo, Japan), reference range of CRP was 0–5 mg/L, the intra-assay variability was 5.73–0.8%, and the inter-assay variability was 6.5–2.3%.

HLA-B27 was detected by flow cytometry using an IOTest HLA-B27-FITC/HLA-B7-PE (Beckman Coulter-Immunotech SAS, Marseille, France) and a BDTM HLA-B27 Kit (BD Bioscience, San Jose, CA, USA).

Statistical analysis

Statistical analyses were performed with GraphPad Prism 5.1 (GraphPad Software, San Diego, CA, USA). The Kolmogorov–Smirnov test of normality was used for all the variables. Based on distribution, the data are presented as the median [interquartile range (IQR)] or mean ± SD. Because of non-normality of data, the non-parametric tests were used for group comparison and correlational analyses. Spearman's correlation coefficients were calculated to determine the association between visfatin levels and the other variables. For comparison between the groups, the Mann–Whitney *U* test was used. Fisher's exact test was performed for the analysis of categorical variables. *P* values less than 0.05 were considered statistically significant.

Results

Characteristics of patients

The patients' demographic and clinical characteristics are summarized in Table 1. Sixty-four patients with axSpA were enrolled in this study [47 males and 17 females, median (IQR) age 35.1 (29.3–40.1) years, 92% HLA-B27 positive]. The proportion of male patients with r-axSpA was higher

Table 1 Characteristics of patients with axial spondyloarthritis and healthy controls

Characteristic	nr-axSpA	r-axSpA	axSpA	HC
Patients (*n*)	18	46	64	61
Gender (male/female)	8/10	39/7	47/17	44/17
Age (years)	36.3 (29.1–42.8)	34.8 (29.2–39.4)	35.1 (29.3–40.1)	36.0 (31.0–48.0)
BMI (kg/m^2)	24.67 ± 4.06	26.61 ± 3.83	24.08 ± 3.95	27.05 ± 3.98
CRP (mg/L)	4.01 (1.26–12.74)	11.08 (5.04–19.60)	9.67 (3.48–16.43)	0.94 (0.13–7.00)
Visfatin (ng/mL)	2.25 (0.89–3.13)	2.77 (1.25–4.43)	2.69 (1.09–4.27)	1.62 (0.93–2.66)
Disease duration (years)	0.2 (0.0–4.0)	5.0 (2.0–9.0)	4.0 (0.5–8.0)	–
HLA-B27 positivity (*n*, %)	17 (94%)	42 (91%)	59 (92%)	–
BASDAI	4.78 (1.53–6.25)	5.38 (3.15–7.57)	5.01 (2.68–7.29)	–
csDMARDs (*n*, %)	6 (33%)	5 (11%)	11 (17%)	–
bDMARDs (*n*, %)	1 (6%)	14 (30%)	15 (23%)	–
mSASSS ≥ 1/mSASSS = 0 (*n*)	0/18	22/24	22/42	–
Extra-articular features (*n*, %)	15 (83%)	25 (54%)	40 (62%)	–
Enthesitis/tendinitis (*n*, %)	11 (61%)	12 (26%)	23 (36%)	–
Peripheral arthritis (*n*, %)	14 (77%)	19 (41%)	33 (52%)	–
Uveitis (*n*, %)	7 (38%)	15 (32%)	22 (34%)	–
Psoriasis (*n*, %)	0 (0%)	2 (4%)	2 (3%)	–
Dactylitis (*n*, %)	2 (11%)	3 (7%)	5 (8%)	–

Data are presented as the median (interquartile range) or mean ± SD

axSpA axial spondyloarthritis; *nr-axSpA* non-radiographic axial spondyloarthritis; *r-axSpA* radiographic axial spondyloarthritis; *HC* healthy controls; *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index; *CRP* C-reactive protein; *csDMARDs* conventional synthetic disease-modifying antirheumatic drugs sulfasalazine (*n* = 8), methotrexate (*n* = 2), azathioprine (*n* = 1); *bDMARDs* biological disease-modifying antirheumatic drugs [adalimumab (*n* = 1), golimumab (*n* = 2), etanercept (*n* = 9), infliximab (*n* = 3)]

than the proportion of those with nr-axSpA ($p = 0.003$). Patients with r-axSpA had a significantly longer disease duration ($p < 0.001$) and higher CRP levels ($p = 0.013$) than those with nr-axSpA. Peripheral arthritis, extra-articular manifestations, enthesitis and/or tendinitis were significantly more frequent in patients with nr-axSpA compared with patients with r-axSpA ($p = 0.012$, $p = 0.044$ and $p = 0.019$, respectively). Age, BMI, BASDAI and HLA-B27 positivity were comparable between the two subgroups of patients. Out of all, one patient suffered from diabetes mellitus type 2 and another patient had insulin resistance. Both patients were from nr-axSpA group.

Serum visfatin levels are elevated in patients with axSpA

Serum visfatin levels were significantly higher in patients with axSpA than in healthy individuals [2.69 (1.09–4.27) vs. 1.62 (0.93–2.70) ng/mL; $p = 0.009$] (Fig. 1a). After dividing the patients into r-axSpA and nr-axSpA subgroups, the difference remained statistically significant only for patients with r-axSpA [2.77 (1.25–4.43) vs. 1.62 (0.93–2.70) ng/mL; $p = 0.005$], but not for those with nr-axSpA [2.25 (0.89–3.13) vs. 1.62 (0.93–2.70) ng/mL; $p = 0.390$]. The concentrations of visfatin were comparable between patients with nr-axSpA and r-axSpA ($p = 0.235$) (Fig. 1b). There was no difference in the visfatin levels between patients receiving biological therapy compared to patients not receiving biological therapy [2.45 (1.45–4.28) vs. 2.75 (1.00–4.28) ng/mL; $p = 0.918$]. In addition, excluding the two patients with diabetes mellitus and insulin resistance from nr-axSpA group did not affect statistical visfatin level differences among groups (Supplementary Figure 1).

Visfatin levels in relationship to radiographic damage and disease activity

In patients with axSpA, serum visfatin levels were significantly higher in individuals with mSASSS ≥ 1 than in those with mSASSS = 0 [4.12 (1.65–5.41) vs. 2.33 (0.87–3.49) ng/mL; $p = 0.025$] (Fig. 2a). Furthermore, a positive correlation between visfatin levels and mSASSS was confirmed ($r = 0.281$; $p = 0.026$) (Fig. 2b). In the r-axSpA subgroup, patients with mSASSS ≥ 1 showed non-significantly higher levels of visfatin than those with mSASSS = 0 [3.05 (1.92–5.53) vs. 2.26 (0.85–3.34) ng/mL; $p = 0.053$]. Visfatin levels remained unchanged even after excluding the

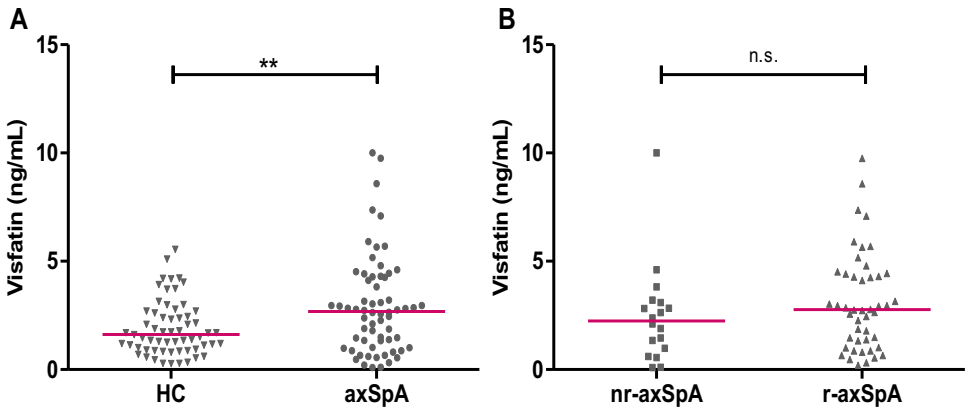

Fig. 1 Serum visfatin levels were significantly higher in patients with axial spondyloarthritis (axSpA) than in healthy controls (HC) (**a**), and they were comparable between patients with non-radiographic axial spondyloarthritis (nr-axSpA) and those with radiographic axSpA (r-axSpA) (**b**). The horizontal line represents the median. $^{**}p < 0.01$. *ns* non-significant

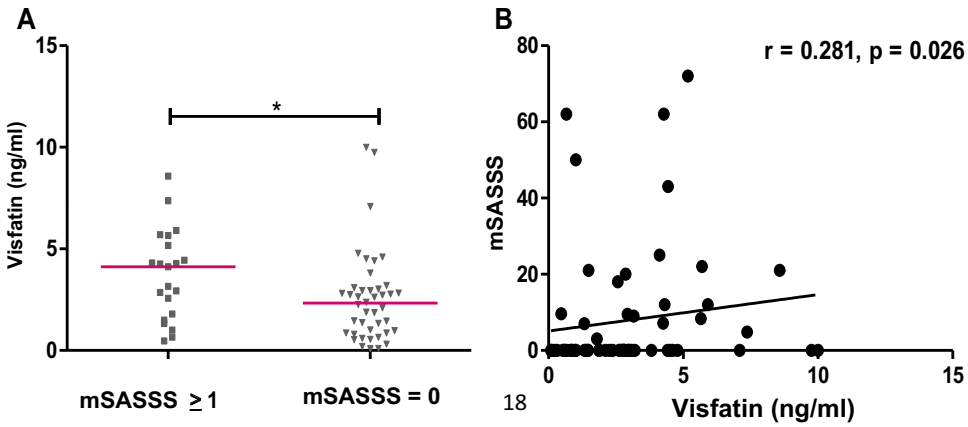

Fig. 2 Serum visfatin levels were significantly higher in axSpA patients with mSASSS ≥ 1 than in those with mSASSS = 0 (**a**) and were positively correlated with mSASSS (**b**). The horizontal line represents the median. $^{*}p < 0.05$. *mSASSS* modified Stoke Ankylosing Spondylitis Spine Score. *P* values are results of Mann–Whitney and Spearman correlation tests

two patients with diabetes mellitus and insulin resistance from nr-axSpA group.

The levels of visfatin did not differ between males and females or between patients with and without the presence of extra-articular manifestations, peripheral joint involvement or HLA-B27 antigen in any of the study groups. Similarly, there was no association of visfatin levels with age, disease duration, BMI or CRP levels. In patients with nr-axSpA, but not in patients with r-axSpA, visfatin levels were positively correlated with the BASDAI ($r=0.585$; $p=0.011$) (Fig. 3). After excluding the two patients with diabetes mellitus and insulin resistance, the correlation even improved ($r=0.732$, $p=0.001$). In the total group of axSpA patients, there was no difference in the visfatin levels between patients with BASDAI ≥ 4 compared to those with BASDAI < 4 [2.78 (1.33–4.28) vs. 2.11 (0.82–4.28) ng/mL; $p=0.395$].

Discussion

In the present study, we showed that higher serum visfatin levels are found in patients with axSpA than in healthy individuals and that there is an association between visfatin levels and radiographic spinal damage.

A number of studies have reported that visfatin regulates joint tissue metabolism and exerts proinflammatory effects [11, 13–15, 20]. However, the data regarding a possible link between visfatin, r-axSpA and nr-axSpA are limited. In the present study, we found higher levels of visfatin in patients with axSpA, and particularly in the subgroup of patients with r-axSpA, than in healthy controls. In line with our findings, higher serum visfatin levels were demonstrated in patients with r-axSpA than in healthy subjects in a previous study by Syrbe et al. [8]. As far as we know, visfatin levels in patients with nr-axSpA have not been studied to date. We showed that visfatin levels in patients with nr-axSpA are comparable to those in patients with r-axSpA but are not significantly higher than those in healthy controls. Interestingly, after dividing the patients into r-axSpA and nr-axSpA subsets, we observed significantly positive correlation between visfatin levels and the BASDAI in patients with nr-axSpA. However, this relationship was not found neither in patients with r-axSpA nor in the entire cohort of patients with axSpA. This discrepancy could be explained by lower number of patients with nr-axSpA and their slightly lower disease activity compared to those with r-axSpA. Since limited data on biomarkers in nr-axSpA exists, there is evidence that serum CRP levels are lower in patients with nr-axSpA compared to those with r-axSpA [21]. On the other side, Huang et al. [22] found that serum calprotectin levels were comparable between both subsets, correlated with inflammatory measures of axSpA, and were higher in both subsets compared to healthy subjects. In line with our study, calprotectin, however, did not contribute to discriminate between non-radiographic and radiographic form of the disease.

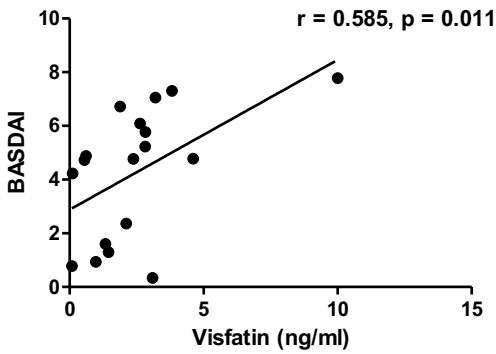

Fig. 3 Serum levels of visfatin were positively correlated with the BASDAI in patients with non-radiographic axial spondyloarthritis (nr-axSpA). *BASDAI* Bath Ankylosing Spondylitis Disease Activity Index

In addition, we demonstrated comparable levels of visfatin between patients with axSpA with and without the presence of extra-articular manifestations, peripheral arthritis or the presence of HLA-B27 antigen. Furthermore, we did not observe any difference in visfatin levels due to sex, and there were no associations between visfatin levels and age, disease duration, BMI or CRP levels. These findings are consistent with those reported in other studies that evaluated patients with r-axSpA [8, 16, 17].

According to recent findings, MRI defined fatty lesions at anterior vertebral corners on spine are predictive of new bone formations [23]. Fatty lesions are thought to replace the active inflammatory lesions of bone marrow edema and from preliminary reports on biopsies performed from these sites, fatty lesions correspond to fat deposition in the bone marrow of patients with advanced r-axSpA. Since vertebral bone marrow is harbouring hematopoiesis, r-axSpA seems to lead to local disruption of hematopoiesis in the bone marrow microenvironment, which is followed by fat replacement [24]. Therefore, it can be speculated that adipokines might have some effects on the disease progression. Although increased visfatin is known to play a role in diabetes mellitus [25], excluding the two diabetic and prediabetic patients did not affect our results. As far as we know, there is no association between diabetes mellitus and radiographic progression of axSpA, which is worth to explore in future studies.

It has recently been demonstrated that visfatin induces osteoblast proliferation and type I collagen production in vitro [13]. Moreover, visfatin has been shown to inhibit osteoclast formation and differentiation [14, 15]. Therefore, we hypothesized that visfatin concentrations could be affected by bone changes and thus reflect syndesmophyte formation. In line with this, we found a positive correlation between visfatin levels and radiographic damage as

assessed by the mSASSS in patients with axSpA and significantly higher visfatin concentrations in patients with spinal involvement than in those without spinal radiographic changes. On the other hand, we did not find any relationship between visfatin levels and mSASSS in a subgroup of patients with r-axSpA. Previous studies examining the association between visfatin levels and radiographic changes in axSpA included only patients with radiographic form of the disease. Consistent with our findings, Syrbe et al. [8] also reported no significant association between visfatin levels and structural damage based on the mSASSS in patients with r-axSpA. Nevertheless, elevated baseline visfatin levels were found to be predictive of subsequent radiographic progression and new syndesmophyte formation after 2 years [8]. However, ENRADAS study did not reveal correlation between visfatin levels and radiographic spinal progression or new syndesmophyte formation [9]. Thus, the association between visfatin levels and radiographic spinal damage or progression in patients with r-axSpA is not consistent across all studies and needs to be further determined.

Our study has several limitations. First, design of the study was cross-sectional. Therefore, a longitudinal association between visfatin levels and disease activity/improvement could not be assessed. Long-term prospective study is needed to further investigate the role of visfatin in patients with axSpA. Second, the Ankylosing Spondylitis Disease Activity Score (ASDAS) was not calculated in majority of the patients, therefore, only the BASDAI was used for the evaluation of disease activity in this study. Third, low number of patients with nr-axSpA was included in our cohort.

Conclusion

In conclusion, we demonstrated elevated visfatin levels in patients with axSpA, particularly in those with r-axSpA. Furthermore, we found higher visfatin levels in patients with radiographic spinal involvement and a positive correlation between visfatin levels and radiographic spinal damage. These findings further support a possible role of visfatin in bone remodelling, the exact link between visfatin, new bone formation and a putative role of visfatin in early phases of axSpA pathogenesis need to be confirmed in a larger cohort of patients.

Acknowledgements This work was supported by the Ministry of Health of the Czech Republic project 17-33127A.

Author contributions LŠ and JV were responsible for the study concept and design. HH performed ELISA tests. KB, MF, HM, ŠF, JV and LŠ were involved in enrolling the patients and made clinical assessments. HH, TL and OK carried out the statistical analysis. HH, TL and LŠ were responsible for data interpretation and manuscript preparation. MT, JV, KP and LŠ revised the manuscript critically for important intellectual content. All authors read and approved the final version of the manuscript.

Compliance with ethical standards

Ethical approval All procedures performed in this study involving human participants were in accordance with the ethical standard of the local ethics committee of the Institute of Rheumatology in Prague, Czech Republic.

Informed consent Written informed consent was obtained from all participants.

Conflict of interest Hana Hulejová declares that she does not have competing interests. Tereza Kropáčková declares that she does not have competing interests. Kristýna Bubová declares that she does not have competing interests. Olga Kryštůfková declares that she does not have competing interests. Mária Filková declares that she does not have competing interests. Šárka Forejtová declares that she does not have competing interests. Heřman Mann declares that he does not have competing interests. Michal Tomčík declares that he does not have competing interests. Jiří Vencovský declares that he does not have competing interests. Karel Pavelka declares that he does not have competing interests. Ladislav Šenolt declares that he does not have competing interests.

References

1. Sieper J, Poddubnyy D (2017) Axial spondyloarthritis. Lancet 390(10089):73–84
2. Turina MC, Yeremenko N, van Gaalen F et al (2017) Serum inflammatory biomarkers fail to identify early axial spondyloarthritis: results from the SpondyloArthritis Caught Early (SPACE) cohort. RMD Open 3(1):e000319
3. Poddubnyy D, Conrad K, Haibel H et al (2014) Elevated serum level of the vascular endothelial growth factor predicts radiographic spinal progression in patients with axial spondyloarthritis. Ann Rheum Dis 73(12):2137–2143
4. Prajzlerova K, Grobelna K, Pavelka K, Senolt L, Filkova M (2016) An update on biomarkers in axial spondyloarthritis. Autoimmun Rev 15(6):501–509
5. Biomarkers Definitions Working Group (2001) Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clin Pharmacol Ther 69(3):89–95
6. Ouchi N, Parker JL, Lugus JJ, Walsh K (2011) Adipokines in inflammation and metabolic disease. Nat Rev Immunol 11(2):85–97. http://www.nature.com/articles/nri2921. Accessed 21 Jan 2011
7. Neumann E, Junker S, Schett G, Frommer K, Muller-Ladner U (2016) Adipokines in bone disease. Nat Rev Rheumatol 12(5):296–302. <Go to ISI>://WOS:000375276700006
8. Syrbe U, Callhoff J, Conrad K et al (2015) Serum adipokine levels in patients with ankylosing spondylitis and their relationship to clinical parameters and radiographic spinal progression. Arthritis Rheumatol 67(3):678–685
9. Hartl A, Sieper J, Syrbe U et al (2017) Serum levels of leptin and high molecular weight adiponectin are inversely associated with radiographic spinal progression in patients with ankylosing spondylitis: results from the ENRADAS trial. Arthritis Res Ther 19(1):140. https://doi.org/10.1186/s13075-017-1350-9 **(Published online first 2017/06/18)**

10. Samal B, Sun Y, Stearns G, Xie C, Suggs S, McNiece I (1994) Cloning and characterization of the cDNA encoding a novel human pre-B-cell colony-enhancing factor. Mol Cell Biol 14(2):1431–1437
11. Moschen AR, Kaser A, Enrich B et al (2007) Visfatin, an adipocytokine with proinflammatory and immunomodulating properties. J Immunol 178(3):1748–1758
12. Luk T, Malam Z, Marshall JC (2008) Pre-B cell colony-enhancing factor (PBEF)/visfatin: a novel mediator of innate immunity. J Leukoc Biol 83(4):804–816
13. Xie H, Tang SY, Luo XH et al (2007) Insulin-like effects of visfatin on human osteoblasts. Calcif Tissue Int 80(3):201–210
14. Moschen AR, Geiger S, Gerner R, Tilg H (2010) Pre-B cell colony enhancing factor/NAMPT/visfatin and its role in inflammation-related bone disease. Mutat Res 690(1–2):95–101
15. Baek JM, Ahn SJ, Cheon YH, Lee MS, Oh J, Kim JY (2017) Nicotinamide phosphoribosyltransferase inhibits receptor activator of nuclear factor-kappaB ligand-induced osteoclast differentiation in vitro. Mol Med Rep 15(2):784–792
16. Hulejova H, Levitova A, Kuklova M et al (2012) No effect of physiotherapy on the serum levels of adipocytokines in patients with ankylosing spondylitis. Clin Rheumatol 31(1):67–71. https://doi.org/10.1007/s10067-011-1773-7. <Go to ISI>://WOS:000299768200009
17. Miranda-Filloy JA, Lopez-Mejias R, Genre F et al (2013) Leptin and visfatin serum levels in non-diabetic ankylosing spondylitis patients undergoing TNF-alpha antagonist therapy. Clin Exp Rheumatol 31(4):538–545
18. Rudwaleit M, van der Heijde D, Landewe R et al (2009) The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis 68(6):777–783
19. van der Linden S, Valkenburg HA, Cats A (1984) Evaluation of diagnostic-criteria for ankylosing-spondylitis—a proposal for modification of the New-York criteria. Arthritis Rheum 27(4):361–368. <Go to ISI>://WOS:A1984SN19400001
20. Brentano F, Schorr O, Ospelt C et al (2007) Pre-B cell colony-enhancing factor/visfatin, a new marker of inflammation in rheumatoid arthritis with proinflammatory and matrix-degrading activities. Arthritis Rheum 56(9):2829–2839
21. Baraliakos X, Braun J (2015) Non-radiographic axial spondyloarthritis and ankylosing spondylitis: what are the similarities and differences? RMD Open. https://doi.org/10.1136/rmdopen-2015-000053
22. Huang J, Yin Z, Song G et al (2017) Discriminating value of calprotectin in disease activity and progression of nonradiographic axial spondyloarthritis and ankylosing spondylitis. Dis Markers 2017:7574147. https://doi.org/10.1155/2017/7574147 **(Published online first 2017/06/21)**
23. Baraliakos X (2014) The contribution of imaging in the diagnosis and treatment of axial spondyloarthritis. Eur J Clin Investig 45(1):81–86. https://doi.org/10.1111/eci.12369 **(Published online first 2014/11/08)**
24. Baraliakos X, Boehm H, Samir Barakat A et al (2018) OP0242 Fatty lesions detected on MRI scans in patients with ankylosing spondylitis are based on the deposition of fat in the vertebral bone marrow. Ann Rheum Dis 77(Suppl 2):170. https://doi.org/10.1136/annrheumdis-2018-eular.7158
25. Esteghamati A, Alamdari A, Zandieh A et al (2011) Serum visfatin is associated with type 2 diabetes mellitus independent of insulin resistance and obesity. Diabetes Res Clin Pract 91(2):154–158. https://doi.org/10.1016/j.diabres.2010.11.003 **(Epub 2010 Nov 30)**

Affiliations

Hana Hulejová[1] · Tereza Kropáčková[1,2] · Kristýna Bubová[1,2] · Olga Kryštůfková[1,2] · Mária Filková[1,2] · Heřman Mann[1,2] · Šárka Forejtová[1,2] · Michal Tomčík[1,2] · Jiří Vencovský[1,2] · Karel Pavelka[1,2] · Ladislav Šenolt[1,2]

Tereza Kropáčková
kropackova@revma.cz

Kristýna Bubová
bubova@revma.cz

Olga Kryštůfková
krystufkova@revma.cz

Mária Filková
filkova@revma.cz

Heřman Mann
mann@revma.cz

Šárka Forejtová
forejtova@revma.cz

Michal Tomčík
tomcik@revma.cz

Jiří Vencovský
vencovsky@revma.cz

Karel Pavelka
pavelka@revma.cz

Ladislav Šenolt
senolt@revma.cz

[1] Institute of Rheumatology, Na Slupi 4, 12850 Prague 2, Czech Republic

[2] Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic