Plasma Phospholipid Fatty Acid Content Is Related to Disease Activity in Ankylosing Spondylitis

BJÖRN SUNDSTRÖM, GUNNAR JOHANSSON, HEIDI KOKKONEN, TOMMY CEDERHOLM, and SOLVEIG WÅLLBERG-JONSSON

ABSTRACT. ***Objective.*** To investigate fatty acid composition in the diet, plasma phospholipids, and adipose tissue in a cohort of patients with ankylosing spondylitis (AS), and to determine their correlations to disease activity and blood lipids in a cross-sectional study.

Methods. Diet was assessed using a food frequency questionnaire in 66 patients with AS. Polyunsaturated fatty acids in plasma phospholipids and gluteal adipose tissue were measured using gas chromatography. Disease status was quantified using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), erythrocyte sedimentation rate (ESR), high sensitivity C-reactive protein, and proinflammatory cytokines.

Results. Diet did not correlate with disease activity assessed by the BASDAI, but there were negative correlations between the dietary intake of long-chain omega-3 fatty acids and ESR ($r_s = –0.27$, $p < 0.05$). The plasma phospholipid content of arachidonic acid correlated significantly with the BASDAI score ($r_s = 0.39$, $p < 0.01$). There were correlations between the intake of long-chain omega-3 fatty acids and high-density lipoproteins and serum triglycerides ($r_s = 0.26$ and $r_s = –0.25$, respectively, $p < 0.05$).

Conclusion. There was a positive correlation between levels of arachidonic acid in plasma phospholipids and disease activity assessed by BASDAI in patients with AS. A Western diet does not appear to influence this correlation, but seems to affect blood lipids involved in atherogenic processes. (First Release Dec 15 2011; J Rheumatol 2012;39:327–33; doi:10.3899/jrheum.110575)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS DISEASE ACTIVITY FATTY ACIDS DIET

Ankylosing spondylitis (AS) is considered the prototype disease in the group of seronegative spondyloarthropathies (SpA)[1]. The disease affects mainly the axial skeleton and may, because of enthesitis, lead to total bone ankylosis of the spine. It also affects the larger peripheral joints, and often exhibits extraarticular symptoms such as uveitis and aortitis. This group of diseases has been reported to be associated with an increased prevalence of cardiovascular diseases[2,3]. Nonsteroidal antiinflammatory drugs (NSAID) constitute the basic treatment for pain and stiffness for patients with AS[4]. A major hallmark of both AS and SpA is the good symptom relief achieved with NSAID medication[5]. The positive response to NSAID therapy is sufficiently distinguished for it to be used as a diagnostic criterion in patients with SpA[6].

NSAID act by blocking the synthesis of eicosanoids that are derived from 20-carbon long-chain polyunsaturated fatty acids (LCPUFA), i.e., arachidonic acid (AA; 20:4n6), dihomo-gamma-linolenic acid (DGLA; 20:3n6) and eicosapentaenoic acid (EPA; 20:5n3). These fatty acids are obtained from the diet or from endogenous elongation of shorter dietary polyunsaturated fatty acids (PUFA) like linoleic acid (LA; 18:2n6) and alpha-linolenic acid (ALA; 18:3n3)[7]. The endogenous production of LCPUFA is almost exclusively performed through elongation of ALA into EPA and LA into AA by a series of enzymatic steps of desaturation and elongation. The biotransformation of ALA into EPA is a slow process, and therefore EPA is provided mainly by the diet, e.g., by oily fish. The conversion of LA to AA is a swifter process, but the diet usually contains a fairly large amount of AA mainly derived from animal sources. The 20-carbon LCPUFA, cleaved from the cellular membrane by PLA_2-activation, act as sources for production of various eicosanoids[8]. AA is a source of more proinflammatory eicosanoids, such as prostaglandin E_2 (PGE_2). Other LCPUFA, for example EPA and DGLA, are sources for less potent proinflammatory and antiinflammatory eicosanoids, such as PGE_3 and PGE_1, respectively.

From the Division of Rheumatology, Department of Public Health and Clinical Medicine, Umeå University, Umeå; Umeå School of Social and Health Sciences, Halmstad University, Halmstad; and the Division of Clinical Nutrition and Metabolism, Department of Public Health and Caring Science, Uppsala University, Uppsala, Sweden.

Supported by grants from the Northern County Councils Visare Norr, the Borgerskapet Fund in Umeå, and the Department of Research, Norrbotten County Council.

B. Sundström, RPT, BSc, MSc, Department of Public Health and Clinical Medicine, Rheumatology, Umeå University; G. Johansson, Professor of Food and Nutrition, School of Social and Health Sciences, Halmstad University; H. Kokkonen, MS, Department of Public Health and Clinical Medicine, Rheumatology, Umeå University; T. Cederholm, MD, Professor of Clinical Nutrition, Division of Clinical Nutrition and Metabolism, Department of Public Health and Caring Science, Uppsala University; S. Wållberg-Jonsson, MD, Department of Public Health and Clinical Medicine, Rheumatology, Umeå University.

Address correspondence to B. Sundström, Department of Public Health and Clinical Medicine, Rheumatology, University Hospital, SE-90185, Umeå, Sweden. E-mail: bjorn.sundstrom@medicin.umu.se

Accepted for publication September 6, 2011.

The responsiveness to NSAID among patients with AS indicates that they may have alterations in LCPUFA metabolism, especially regarding AA. As far as we know there have been no previous studies on fatty acid composition and metabolism and disease activity in patients with either AS or SpA. The aim of this cross-sectional study was therefore to investigate the fatty acid composition in the diet, plasma phospholipids, and adipose tissue of patients with AS, and to evaluate their correlations with clinical and laboratory measures of disease activity. Further, we investigated whether diet affects blood lipids involved in atherogenic processes.

MATERIALS AND METHODS

Subjects. Sixty-six patients diagnosed with AS and fulfilling the modified New York criteria[9] (51 men, 15 women, mean age 48 ± 10 yrs) were recruited into the study from the Department of Rheumatology, University Hospital of Umeå. Inclusion criteria included age 18–70 years, and exclusion criteria were pregnancy, lactation, use of lipid-lowering medication, or treatment with dalteparin sodium, warfarin, or biological products, such as inhibitors of tumor necrosis factor (TNF), during the 3 months prior to enrollment. The study was approved by the local ethics committee at the medical faculty of Umeå University (Dnr 07-173) and was performed consistent with the Helsinki Declaration.

Age, sex, education level, social status, smoking history, and dietary habits were established from the responses to questionnaires used in population studies[10]. The patients were classified as smokers when reporting consumption of 1 or more cigarettes per day. Patients' use of medication(s) was investigated by an open question in which they were asked to specify the type of medication and the frequency it was used to control the symptoms of AS disease.

A validated, 84-question semiquantitative food frequency questionnaire (FFQ)[11,12] was used to assess dietary habits. This consisted of questions regarding the frequency of intake of different foodstuffs with an option to provide answers ranging from never to 4 times or more per day. The questionnaire also contained diagrammatic examples of portion sizes on 4 different plates regarding vegetables, meat, and staple food. Food frequencies reported by patients were recalculated to a monthly basis and pooled into groups to describe food patterns. Data from the FFQ were also used to calculate the nutritional and energy intake based on data in the national food database[13]. For food not illustrated in the plate diagrams in the FFQ, the standard portion sizes in the database were used. Nutrient data were analyzed in terms of the total energy intake in order to make data comparable for patients of different sex, weight, and physical activity, and to lessen the influence of over- and under-reporters in the FFQ.

The distribution of fatty acids was calculated as the ratio between the mass of each separate or group of fatty acids and the corresponding mass of total fatty acid intake. Subgroups of fatty acids analyzed were the saturated fatty acids (SFA), PUFA [calculated as the sum of LA, ALA, AA, EPA, docosapentaenoic acid (DPA), and docosahexaenoic acid (DHA)], and long-chain omega-3 fatty acids (calculated as the sum of EPA, DPA, and DHA).

Patients completed the Swedish version of the self-administered Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questionnaire[14]. To assess functional capacity, patients completed the Swedish version of the Bath Ankylosing Spondylitis Functional Index (BASFI)[15]. On BASDAI and BASFI, higher values indicate higher disease activity/worse function. Weight was measured while wearing light clothing but without shoes using a digital calibrated scale (Seca Delta model 707). Height was measured, without shoes, using a wall-mounted tape measure. Physical activity was assessed by 2 questions, for activity at work and during leisure time, forming the basis on which a physical activity level was calculated[16].

Laboratory analysis. All patients donated blood samples. Overnight fasting blood samples were drawn for measurement of cholesterol (mmol/l), high-density lipoprotein (HDL) and low-density lipoprotein cholesterol (mmol/l), triglycerides (mmol/l), erythrocyte sedimentation rate (ESR; Westergren, mm/h), serum IgA antibodies against transglutaminase, serum IgA, and serum levels of S-25-dihydroxyvitamin D (calcidiol). Antibodies against transglutaminase were analyzed because an undiagnosed celiac disease may affect nutritional uptake and laboratory results, and it has been suggested to play a role in the etiology of AS[17]. Calcidiol, i.e., 25(OH) vitamin D, was measured because it has also been considered to have a role in the etiology of AS[18]. All analyses were performed using routine laboratory protocols at the University Hospital of Umeå.

Blood samples were stored and analyzed later for high-sensitivity C-reactive protein (hsCRP, mg/l; Immundiagnostik AG ELISA kit). Interleukin 1ß (IL-1ß), interleukin 1 receptor antagonist (IL-1ra), IL-6, IL-17, interferon-γ (IFN-γ), monocyte chemotactic protein (MCP), and TNF-α were measured using multiplex detection kits (Bio-Rad, Hercules, CA, USA). Analyses of cytokines were performed according to the manufacturers' descriptions.

To assess dietary fatty acid intake over longer and shorter terms, we performed analyses of adipose tissue and plasma phospholipid content. Adipose tissue samples were taken from the upper left buttock with a Vacutainer needle according to the method described by Beynen and Katan[19]. Tissue samples were collected and stored in cryotubes at –80°C before further analysis. Blood samples were taken into EDTA anticoagulant and were centrifuged at 2500–3000 g for 10 min after resting for 30 min, then the plasma was frozen at –80°C.

Plasma phospholipids were separated by thin layer chromatography and selected as the most feasible fraction by which to analyze long-chain fatty acids. Plasma phospholipids and adipose tissue were analyzed by gas chromatography (TR-Fame column; 30 m × 0.32 mm ID × 0.25 μm film gas chromatography column; Thermo Electron Corp., Waltham, MA, USA) as described[19a].

The activity of delta-5-desaturase (D5D) was estimated by calculating the sum of AA and EPA divided by DGLA in plasma phospholipids. Delta-6-desaturase (D6D) was calculated as the ratio between LA and DGLA, since the elongation step that converts LA to gamma-linolenic acid (18:3n6), the actual precursor to DGLA, is not rate-limiting.

Statistical analysis. To accommodate a missing value in the BASDAI and BASFI scores, the respective value was calculated as the mean of the remaining appropriate questions. Laboratory test results below the detectable limit were assigned a value of zero.

Statistical differences between groups were tested with an independent sample t test for continuous data, Mann-Whitney U test for ordinal and non-normally distributed data, and Fisher's exact test and chi-square test for categorical data. Spearman rank correlation test was used to test the relationship of disease activity and data on food consumption. Pearson product-moment correlation coefficient test was used for continuous normally distributed data. In the analysis of fatty acids, patients were also stratified into 1 group with high disease activity (BASDAI ≥ 4) and 1 with low disease activity (BASDAI < 4). Multiple linear regression modeling comprising variables selected on the basis of univariate analyses and the scientific rationale was used to predict plasma phospholipid content of AA. Results were considered statistically significant at a 2-tailed p value ≤ 0.05. Statistical calculations were performed with PASW 18.0 for Macintosh.

RESULTS

Clinical characteristics of 66 patients in the study are described in Table 1. Four patients had a concurrent diagnosis of inflammatory bowel disease (IBD). Among the women there were significantly more smokers and a greater age ($p < 0.05$ and $p < 0.01$, respectively). All patients exhibited normal levels of serum IgA antibodies against transglutaminase and calcidiol (< 10 U/ml and 25–220 nmol/l, respectively), although 2 patients showed slightly elevated results for antibodies against transglutaminase (8.6 and 10.0 U/ml; data not

Table 1. Demographic data and inflammatory status for 66 patients with ankylosing spondylitis.

Characteristic	All Patients, n = 66	Men, n = 51	Women, n = 15
Age, yrs, mean (SD)	47.7 (10.0)	46.3 (10.5)	52.3 (6.1)**
Disease duration, yrs, mean (SD)	17.0 (10.8)	16.5 (10.4)	18.6 (12.3)
Physical activity level, mean (SD)	1.76 (0.12)	1.75 (0.13)	1.77 (0.08)
Body mass index, kg/m^2, mean (SD)	27.3 (10.8)	27.8 (5.3)	25.5 (3.2)
Smokers, n (%)	8 (12)	3 (6)	5 (27)*
Ex-smokers, n (%)	20 (30)	16 (31)	4 (33)
BASDAI, median (IQR)	3.8 (2.1–4.9)	3.5 (2.1–4.9)	4.6 (2.7–6.4)
BASFI, median (IQR)	2.3 (1.1–3.7)	2.0 (1.1–3.5)	3.7 (1.1–4.9)
ESR, mm/h, mean (SD)	14.9 (10.6)	13.7 (10.3)	19.1 (10.6)
hsCRP, mg/l, mean (SD)	4.2 (2.5)	4.6 (2.5)	2.9 (2.0)*

* $p < 0.05$, ** $p < 0.01$; p values denote statistically significant differences between men and women. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; ESR: erythrocyte sedimentation rate (Westergren); hsCRP: high-sensitivity C-reactive protein.

shown) and 7 patients exhibited slightly depressed levels of calcidiol (< 50 nmol/l).

All PUFA, except ALA, showed correlations between the calculated dietary intake and their content in adipose tissue (Table 2). The dietary intake of long-chain omega-3 fatty acids EPA and DHA correlated with quantities measured in the plasma phospholipids ($r_s = 0.42$, $p < 0.01$, and $r_s = 0.53$, $p < 0.001$, respectively). Shorter PUFA and omega-6 PUFA did not correlate to quantities measured in plasma phospholipids. Total dietary intake of SFA did not correlate to measured quantities in plasma phospholipids or adipose tissue.

There was no correlation between dietary fat intake and disease activity assessed by BASDAI (Table 3). ESR correlated negatively with dietary total PUFA and omega-3 LCPUFA ($r_s = –0.25$ and $r_s = –0.27$, respectively, $p < 0.05$). There were no correlations among the cytokines measured, calcidiol, antibodies against transglutaminase, and disease activity as assessed by BASDAI, ESR, or hsCRP (data not shown).

The plasma phospholipid content of AA correlated significantly with the BASDAI score ($r_s = 0.39$, $p < 0.01$). Separating the patients into 2 groups according to disease activity revealed significantly higher levels of AA among

Table 2. Proportions of polyunsaturated fatty acids in dietary intake of fats, in plasma phospholipids, and in gluteal adipose tissue among 66 patients with ankylosing spondylitis. Data expressed as mean (SD).

	Diet	Plasma Phospholipids	Adipose Tissue
Linoleic acid (%)	13.3 (5.7)	20.9 (2.1)	10.3 (1.0)*
Alpha-linolenic acid (%)	2.5 (0.8)	0.16 (0.14)	1.0 (0.2)
Arachidonic acid (%)	0.13 (0.06)	8.5 (1.3)	0.3 (0.09)*
Eicosapentaenoic acid (%)	0.14 (0.09)	1.5 (0.7)**	0.12 (0.04)***
Docosahexaenoic acid (%)	0.27 (0.20)	3.6 (1.2)***	0.2 (0.1)***

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. P values denote statistically significant correlation according to Spearman rank test between dietary intake and plasma phospholipids, or adipose tissue, respectively.

Table 3. Correlations between dietary intake, calculated as percentage of energy intake, and measures of disease activity among 66 patients with ankylosing spondylitis. Spearman rank correlation test.

	Dietary Intake, %, median (IQR)	Correlations to Measures of Disease Activity BASDAI	ESR	hsCRP
Fat	36.0 (32.3–39.0)	0.10	–0.21	0.04
Protein	14.7 (13.6–15.6)	–0.17	–0.06	0.01
Carbohydrate	46.0 (42.1–49.6)	–0.12	0.22	0.10
Saturated fatty acids	14.4 (12.6–16.4)	–0.01	0.00	0.10
Linoleic acid	4.3 (3.4–5.3)	0.11	–0.24	–0.10
Alpha-linolenic acid	0.85 (0.68–1.03)	0.06	–0.22	0.00
Polyunsaturated fatty acids	5.4 (4.3–6.5)	0.10	–0.25*	–0.11
Long-chain omega-3 fatty acids	0.13 (0.09–0.18)	0.06	–0.27*	–0.17

* $p < 0.05$. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ESR: erythrocyte sedimentation rate (Westergren); hsCRP: high-sensitivity C-reactive protein; IQR: interquartile range.

patients with higher disease activity (9.0% compared to 8.1% in patients with lower disease activity; $p < 0.01$; Table 4). In the male cohort there was a significant correlation between AA and BASDAI ($r_s = 0.40$, $p < 0.01$), but only a trend to correlation between D5D and BASDAI ($r_s = 0.26$, $p = 0.06$). Among female patients a correlation was seen between D5D and BASDAI ($r_s = 0.55$, $p = 0.03$), but not between AA and BASDAI. Considering the estimated D6D activity, no significant correlation to BASDAI was found in either sex or the patient group as a whole (data not shown). Body mass index showed no correlations with levels of AA in plasma phospholipids, but did so with levels of its precursor DGLA ($r = 0.46$, $p < 0.001$; data not shown). Body mass index was also inversely correlated to the estimated D5D activity ($r = –0.44$, $p < 0.001$; data not shown). Plasma levels of SFA, for example palmitic acid (16:0), did not correlate with BASDAI scores.

In adipose tissues, the composition of fatty acids did not correlate with disease activity assessed by BASDAI, ESR, or hsCRP (data not shown).

Multiple linear regression modeling revealed that a higher plasma phospholipid content of AA was related to lower plasma phospholipid content of LA, to lower age, to lower alcohol consumption, and to a higher BASDAI score (Table 5). Intake of fish and vegetables correlated positively with HDL cholesterol ($r_s = 0.40$, $p < 0.01$, and $r_s = 0.35$, $p < 0.01$, respectively; Table 6), known to be beneficial for cardiovascular health. In addition, high fish intake was associated with lower plasma levels of triglycerides ($r_s = –0.26$, $p < 0.05$).

DISCUSSION

The correlation between plasma phospholipid levels of AA and the BASDAI scores was the most interesting observation in our study. Plasma AA may therefore be a potential biomarker for disease activity in AS, as it might reflect a dynamic process involved in the inflammation associated with AS. The finding of increased D5D activity suggests there may be an enhanced biosynthesis of AA, with a consequent increased incorporation into phospholipids, possibly related to higher disease activity in patients with AS. The higher level of AA in more affected patients is also interesting in the context of the recent findings that NSAID act as inhibitors of new bone formation in patients with AS[20]. Among healthy adults it has been shown that bone remodeling is triggered by the eicosanoid PGE_2, which is derived from AA and released from osteocytes and mature osteoblasts[21]. Although the importance of AA and PGE_2 in bone remodeling is established[22], the significance of LCPUFA in bone metabolism has been suggested to be more extensive than is currently recognized[23].

Table 4. Plasma phospholipid content of AA, DGLA, EPA, and estimated activity of D5D among 66 patients with ankylosing spondylitis with low and high disease activity according to BASDAI. Data expressed as mean (SD).

	Low Disease Activity BASDAI < 4, n = 36	High Disease Activity BASDAI ≥ 4, n = 30
AA (%)	8.06 (1.28)	8.98 (1.15)**
DGLA (%)	2.82 (0.70)	2.68 (0.67)
EPA (%)	1.46 (0.65)	1.64 (0.75)
D5D	3.58 (1.08)	4.29 (1.47)*

* $p < 0.05$, ** $p < 0.01$. p values denote statistically significant difference between the groups. AA: arachidonic acid; DGLA: dihomo-gamma-linolenic acid; EPA: eicosapentaenoic acid; D5D: estimated delta-5-desaturase activity; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

Table 5. Variables associated with content of arachidonic acid in plasma phospholipids among 66 patients with ankylosing spondylitis in a multiple linear regression model.

Variable	Standardized ß (95% CI)	p
BASDAI, mm	0.02 (0.01–0.03)	< 0.01
Linoleic acid, %*	–0.31 (–0.42– –0.19)	< 0.001
Alcohol consumption, g/mo	–0.10 (–0.16– –0.04)	< 0.01
Age, yrs	–0.03 (–0.05– –0.01)	< 0.05
Overall model, adjusted $r^2 = 0.51$		

* Plasma phospholipid content of linoleic acid (18:2n6). BASDAI: Bath Ankylosing Spondylitis Disease Activity Index.

The capacity to endogenously produce LCPUFA is believed to decrease with increasing age[24,25]. Alcohol consumption has been shown to inhibit endogenous production of LCPUFA, probably through the inhibition of D5D and D6D activity[26]. However, the BASDAI results still showed a strong relationship to the plasma content of AA with adjustment for these variables in a multiple regression model. Endogenous production of LCPUFA is suggested to be higher among premenopausal women[27]. Among our female cohort we found there was a significant correlation between BASDAI and the estimated D5D activity, but not between BASDAI and AA. This may be because of the small number of women (n = 15), or because, compared with the men, the women had increased utilization of AA from phospholipids.

Our findings are consistent with results from studies of patients with related diseases. In IBD, an abnormal plasma LCPUFA pattern has been described, with increased omega-3 and decreased omega-6 fatty acid levels compared with controls[28,29]. The abnormalities were suggested to be caused by increased PUFA biosynthesis in combination with an increased LCPUFA utilization of mainly AA. Similar abnormalities in fatty acids have been described in patients with psoriasis[30]. The genetic influence on endogenous production of LCPUFA has also been discussed recently. The activity of the D5D and D6D enzymes, which are encoded by the fatty acid desaturase genes 1 and 2 (FADS-1 and -2), have been suggested to influence both cardiovascular and inflammatory diseases[31,32].

Humans have the capacity to form the necessary AA from a wide range of dietary intake of LA[7]. Therefore, to lessen dis-

Table 6. Correlations between dietary intake, calculated as percentage of energy intake (E%) as well as consumption frequencies, and atherogenic lipids among 66 patients with ankylosing spondylitis. Spearman rank correlation test. Data are E% unless otherwise indicated.

Dietary Intake	Median (IQR)	Correlations to Atherogenic Lipid Factors		
		TG	Cholesterol	HDL
Fat	36.0 (32.3–39.0)	–0.36**	0.15	0.16
Protein	14.7 (13.6–15.6)	–0.01	–0.00	–0.14
Carbohydrate	46.0 (42.1–49.6)	0.38**	–0.30*	–0.33**
Saturated fatty acids	14.4 (12.6–16.4)	–0.38**	–0.05	0.16
Linoleic acid	4.3 (3.4–5.3)	–0.05	0.22	–0.06
Alpha-linolenic acid	0.85 (0.68–1.03)	–0.10	0.08	–0.09
Polyunsaturated fatty acids	5.4 (4.3–6.5)	–0.08	0.21	–0.03
Long-chain omega-3 fatty acids	0.13 (0.09–0.18)	–0.25*	0.25*	0.26*
Milk and soured milk, servings/mo	76.9 (37.4–99.6)	–0.44**	–0.21	0.22
Meat and meat products, servings/mo	22.2 (17.1–30.4)	–0.21	0.04	0.16
Fish, servings/mo	4.5 (2.2–8.4)	–0.26*	0.20	0.40**
Vegetables, servings/mo	38.9 (23.6–57.2)	0.07	0.14	0.35**
Fruit, servings/mo	38.5 (20.7–67.8)	–0.01	0.09	0.31*

* $p < 0.05$, * $p < 0.01$. TG: serum triglycerides; HDL: serum high-density lipoprotein; IQR: interquartile range.

ease activity in AS the diet probably needs to either (1) outnumber the substrate for AA, i.e., LA with ALA, because they share the same enzymatic pathways[33,34]; or (2) have a very high intake of EPA, which will compete with AA for eicosanoid production[34] and also inhibit the endogenous production of AA[35], or do both. Neither of these possibilities is easily achieved through dietary changes. From this we conclude that any further study on the effect of diet in AS that aims at altering disease activity through use of LCPUFA should incorporate rather radical changes, such as study of an Inuit diet or high-dose supplementation of highly concentrated n-3 fatty acids. We found support for this in our previous study on omega-3 supplementation in AS[36], where a significant effect on disease activity was found only in patients with high-dose supplementation of 4.55 grams per day. This need for high-dose supplementation or radical changes of fat intake to achieve effects on chronic inflammatory diseases has been discussed[37,38].

Although the dietary PUFA were related to a decreased ESR, and the content of phospholipid AA in plasma was closely related to the perceived symptoms as assessed by BASDAI, the dietary fat intake within the variations of a Western diet had no effect on the BASDAI indices in our group of patients with AS. There were, however, correlations between diet and blood lipids such as HDL. It is well documented that lifestyle factors such as diet can influence blood lipids in the general population[39]. Thus our findings may have implications for preventive strategies targeting the increased cardiovascular morbidity described in AS[2,40], a topic suitable for further studies.

A strength of our study was the inclusion of a well-defined cohort of patients with a verified diagnosis of AS. We excluded patients treated with TNF-α inhibitors, comprising about 14% of the patients at the clinic[41]. This was done because TNF-α inhibitors are reported to affect lipid metabolism[42]. According to Swedish guidelines, treatment with TNF-α inhibitors can be introduced if BASDAI score is > 4 and conventional treatment has failed[43]. This may have created a bias toward patients with less active disease; however, 30 of the patients still had BASDAI ≥ 4. We also used a BASDAI value of 4 to separate and compare the patients with high and low disease activity. This is in accord with the consensus for classification of inflammatory, active AS disease[44]. It is also close to the 3.9 cutoff value that has been shown to discriminate between poorly and well controlled disease[45]. A limitation of our study was the lack of a healthy control group; however, the primary objective was to investigate whether dietary PUFA were correlated with disease activity in patients with AS, and a healthy control group was not considered necessary to achieve this. Since the inflammatory processes of AS are dynamic processes that use PUFA, the cross-sectional design introduces some limitations. For example, use of AA from phospholipids, which occurs in any inflammatory condition, may have affected our measured levels of AA and our calculated D5D values. However, these circumstances should dilute the significance, rather than create false-positive results.

Our primary goal was to assess the relationship between dietary fat intake and disease activity in patients with AS. Although the overall dietary intake of PUFA was related to a decreased ESR, there was no effect on disease activity measured by BASDAI. In a previous study we found that the diet of AS patients from northern Sweden may influence gastric symptoms[41]. In our present study, diet was found to be correlated to blood plasma lipid levels and therefore may affect cardiovascular risks. Together these findings suggest that dietary habits among patients with AS in Western populations may be more important for future comorbidity than for AS disease activity. Finally, our finding that the plasma phospholipid con-

tent of AA correlates with disease activity may reflect a dynamic process involved in the inflammation associated with AS. This requires further investigation.

ACKNOWLEDGMENT

We gratefully acknowledge Ann-Cathrin Kallin for skillful assistance with the sampling and administration of patients; and Catharina Ericsson and Siv Tengblad for assistance with the laboratory analyses.

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