Dietary inflammatory potential and psoriatic arthritis

Scientific abstract

Background & objectives: Recently, diet has gained increasing attention as a lifestyle factor that may influence disease activity in psoriatic arthritis (PsA). Patients with PsA seek to understand the association between diet and their health. We aim to assess the dietary intake of patients with PsA, evaluate dietary components with inflammatory potential, and quantify the associations between adherence to a pro-inflammatory diet and PsA disease activity. Secondary objective includes evaluating the feasibility of using a food frequency questionnaire among this population. *Methods*: This cross-sectional study will include 60 patients with PsA from the DEPAR cohort. Participants will complete a food frequency questionnaire to assess their diet (calorie intake, macronutrients, micronutrients) and the inflammatory potential will be calculated using the dietary inflammatory index. Disease activity assessment will include: Disease Activity index for PsA (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), and minimal disease activity. *Expected Results*: Description of the diet of PsA patients based on the pro- and anti-inflammatory components. Strength of the association between adherence to a pro-inflammatory diet and PsA disease activity. *Significance for psoriatic disease*: Assessing the diet of patients with PsA and understanding the effect of dietary inflammatory potential on disease activity promotes the integration of dietary assessment and modification into the PsA management plan, and empowers patients to make informed dietary choices for better self-management of their condition.

Lay abstract

Background & Objectives: There has been growing interest in how diet might affect psoriatic arthritis (PsA), a condition that causes joint pain and skin problems. This study looks at what people with PsA eat, especially foods that may promote or reduce inflammation, and how their diet relate to their disease symptoms. It will also test how easy it is to use a food questionnaire to collect this information. *Methods*: We will ask 60 patients with PsA to fill out a food frequency questionnaire about what they usually eat. We will then look at how many calories and nutrients they consume, and use a special tool called the dietary inflammatory index to rate how likely their diet is to promote inflammation. We will also measure how active their disease is using standard scoring tools: Disease Activity Index for PsA (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), and minimal disease activity. *Expected Results*: We expect that each patient diet will be rated as either more inflammatory or less inflammatory. We also expect that people with more inflammatory diets will have more active PsA symptoms. *Significance for psoriatic disease:* If we understand how diet affects PsA, doctors can give dietary advice to help people better manage their condition. This could also help patients understand how diet can affect their health and make food choices that may improve their symptoms and quality of life.

Background

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis with a heterogenous clinical presentation, affecting around 20% of patients with psoriasis [1]. The pathophysiology of PsA results from a complex interplay between genetic predisposition and environmental triggers [2, 3]. Increased disease activity can adversely affect the physical health and quality of life of the patients [4, 5]. Recently, diet has gained increasing attention as a lifestyle factor that may influence disease activity in PsA; however, the existing literature remains limited [6, 7]. Understanding the role of diet in PsA disease activity would provide a foundation for future interventions aimed at improving patient outcomes.

Diet can influence the immune system through the macronutrient and micronutrient composition and total calorie intake (energy intake). Nutrients play a role in supporting immune cells function and modulating the immune response [8]. Vitamins A, C and D, and zinc are examples of nutrients that support immune cell function [8]. Amino acids such as L-arginine and L-tryptophan are required for optimal macrophage activity [8]. In addition, nutrients can influence insulin signaling, which in turn plays a role in regulating immune cell function [9-11]. On the other hand, saturated fats stimulate toll-like receptor 4 (TLR4) in immune cells, which activates the NF-κB signaling pathway and increases pro-inflammatory cytokine production [12]. Excess calorie intake, the other element from diet, is a key factor in the development of obesity which is observed in around 30% of patients with PsA [13-16]. Obesity is characterized by chronic low-grade inflammation, is associated with impaired immune function, and imposes mechanical stress on the joints [17, 18]. Both dietary composition and calorie intake can influence the gut microbiome. For instance, diet high in saturated fats increases Gram-negative bacteria such as *Proteobacteria* and *Bacteroides,* leading to gut dysbiosis [19]. Gut dysbiosis disrupts the intestinal barrier, allowing bacterial endotoxins to enter the bloodstream, activate the immune system, and trigger the release of pro-inflammatory cytokines [20]. In PsA, these alterations in immune function could translate to clinical features such as joint inflammation, skin lesions, and enthesitis, which are markers of disease activity.

Dietary inflammatory index (DII) is a literature-based tool developed by Shivappa et al., to assess the inflammatory potential of diet from maximally anti-inflammatory to maximally pro-inflammatory [21]. A total of 45 food components are considered in the DII based on their effect on six inflammatory markers: CRP, TNF-α, interleukin (IL)-1β, IL-4, IL-6 and IL-10. DII has been widely investigated to evaluate its effect on health-related outcomes such as increased risk for metabolic syndrome, cardiovascular disease, irritable bowel disease, colorectal cancer, obesity and mortality [22-29]. DII has been also associated with higher disease activity in rheumatoid arthritis [30]. However, to best of our knowledge, the effect of DII on PsA outcomes is currently unknown, even though PsA patients tend to have higher BMI and are more prone to cardiovascular disease [13-15, 31]. We hypothesize that patients with PsA consume pro-inflammatory and anti-inflammatory diets, and that adherence towards a pro-inflammatory diet would be associated with higher disease activity. Therefore, we aim to i) assess dietary intake of adult patients with PsA (calorie intake, macronutrients, micronutrients), ii) evaluate the dietary components with inflammatory potential using the DII, and iii) quantify the associations between DII scores and PsA disease activity scores. Secondary objectives include evaluating the feasibility of using food frequency questionnaire to assess dietary intake among patients with PsA, for further implementation in larger cohorts.

Methods

Population and setting

This cross-sectional pilot study will include 60 patients with PsA. Patients will be included from an ongoing multi-center prospective cohort study in the southwest region of the Netherlands, the Dutch South West Psoriatic Arthritis (DEPAR) study. The DEPAR study was approved by the Medical Ethics Committee of Erasmus Medical Center Rotterdam, the Netherlands (MEC-2012-549). All participants provide written consent upon inclusion.

The inclusion criteria for DEPAR are: patients diagnosed with PsA according to the treating physician, at least 18 years of age, have sufficient knowledge of the Dutch language and they must

not have been treated with disease-modifying antirheumatic drugs (DMARDs) at the time of inclusion.

Dietary assessment
Participants will be asked to complete a validated food frequency questionnaire (FFQ) to assess their habitual diet. Data from the FFQ will be used to assess the intake of calories, macronutrients and micronutrients. Using this information, the DII for each participant will be calculated as described by Shivappa et al. [21]. Briefly, a z-score is calculated for each food component using the formula: z-score= (reported daily intake - global daily mean intake)/global daily standard deviation). The z-score is then converted into percentile. This percentile is doubled, and a value of 1 is subtracted from the score to center the values around 0 and bound them between -1 and +1. These values are then multiplied by the "overall food parameter-specific inflammatory effect score" provided by Shivappa et al.. Finally, the DII score is calculated by summing-up the individual DII scores of each food component. The score ranges between -8.87 (maximally anti-inflammatory) to +7.98 (maximally pro-inflammatory).

Disease activity
Disease activity will be assessed using composite scores: Disease Activity index for PsA (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), and minimal disease activity.

Feasibility
Feasibility will be assessed based on the FFQ completion and participation rates, and by conducting interviews with a cross-section of patients (2 groups of 6 patients each).

Statistical analysis
Descriptive statistics will be used to analyze characteristics of the study population and dietary intake. Crude and multivariable regression models will be used to analyze the associations between DII and disease activity.

Project timeline

Task	MREC & FFQ implementation	Inclusion	Outcome analysis & reporting
Month	M1- M2	M3 - M6	M7 - M8

Preferred start date: July 2025

Expected results
Description of the diet of PsA patients by evaluating the intake of proinflammatory and anti-inflammatory dietary components. Strength of the association between adherence to a pro-inflammatory diet and PsA disease activity.

Significance for psoriatic disease
Diet provides a non-pharmacological approach to manage PsA. Assessing the patient diet and its inflammatory potential and understanding how it is associated with PsA disease activity, promotes the integration of dietary assessment and modifications as part of a comprehensive management plan to improve patient outcomes. In addition, this knowledge will empower patients to make informed decisions about their dietary choices, promoting a better self-management of their condition.

References

1 Karmacharya P, Chakradhar R, Ogdie A. The epidemiology of psoriatic arthritis: A literature review. Best Pract Res Clin Rheumatol 2021;35(2):101692.
2 Carvalho AL, Hedrich CM. The Molecular Pathophysiology of Psoriatic Arthritis-The Complex Interplay Between Genetic Predisposition, Epigenetics Factors, and the Microbiome. Front Mol Biosci 2021;8:662047.
3 Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. The Lancet 2018;391(10136):2273-84.
4 Gudu T, Gossec L. Quality of life in psoriatic arthritis. Expert Rev Clin Immunol 2018;14(5):405-17.
5 Walsh JA, Ogdie A, Michaud K, et al. Impact of key manifestations of psoriatic arthritis on patient quality of life, functional status, and work productivity: Findings from a real-world study in the United States and Europe. Joint Bone Spine 2023;90(3):105534.
6 Leite BF, Morimoto MA, Gomes CMF, et al. Dietetic intervention in psoriatic arthritis: the DIETA trial. Advances in Rheumatology 2022;62(1):12.
7 Öteleş S, Ayan G, Ekici M, Ünal E, Bilgiç P, Kalyoncu U. The dietary acid load is associated with disease severity in psoriatic arthritis. Modern Rheumatology 2023;34(5):1019-26.
8 Munteanu C, Schwartz B. The relationship between nutrition and the immune system. Front Nutr 2022;9:1082500.
9 Makhijani P, Basso PJ, Chan YT, et al. Regulation of the immune system by the insulin receptor in health and disease. Front Endocrinol (Lausanne) 2023;14:1128622.
10 Clegg DJ, Gotoh K, Kemp C, et al. Consumption of a high-fat diet induces central insulin resistance independent of adiposity. Physiol Behav 2011;103(1):10-6.
11 Pektas MB, Koca HB, Sadi G, Akar F. Dietary Fructose Activates Insulin Signaling and Inflammation in Adipose Tissue: Modulatory Role of Resveratrol. Biomed Res Int 2016;2016:8014252.
12 Rocha DM, Caldas AP, Oliveira LL, Bressan J, Hermsdorff HH. Saturated fatty acids trigger TLR4-mediated inflammatory response. Atherosclerosis 2016;244:211-5.
13 Giles JT, Ogdie A, Gomez Reino JJ, et al. Impact of baseline body mass index on the efficacy and safety of tofacitinib in patients with psoriatic arthritis. RMD Open 2021;7(1).
14 McInnes IB, Ferraccioli G, D'Agostino MA, et al. Body mass index and treatment response to subcutaneous abatacept in patients with psoriatic arthritis: a post hoc analysis of a phase III trial. RMD Open 2019;5(1):e000934.
15 Vallejo-Yagüe E, Burkard T, Micheroli R, Burden AM. Minimal disease activity and remission in patients with psoriatic arthritis with elevated body mass index: an observational cohort study in the Swiss Clinical Quality Management cohort. BMJ Open 2022;12(9):e061474.
16 WHO. Obesity and overweight. In; 2024.
17 de Heredia FP, Gómez-Martínez S, Marcos A. Obesity, inflammation and the immune system. Proceedings of the Nutrition Society 2012;71(2):332-8.
18 Wang T, He C. Pro-inflammatory cytokines: The link between obesity and osteoarthritis. Cytokine & Growth Factor Reviews 2018;44:38-50.
19 Singh RK, Chang H-W, Yan D, et al. Influence of diet on the gut microbiome and implications for human health. Journal of Translational Medicine 2017;15(1):73.

20 Zhao Ma, Chu J, Feng S, et al. Immunological mechanisms of inflammatory diseases caused by gut microbiota dysbiosis: A review. Biomedicine & Pharmacotherapy 2023;164:114985.
21 Shivappa N, Steck SE, Hurley TG, Hussey JR, Hébert JR. Designing and developing a literature-derived, population-based dietary inflammatory index. Public Health Nutr 2014;17(8):1689-96.
22 Shivappa N, Godos J, Hébert JR, et al. Dietary Inflammatory Index and Colorectal Cancer Risk-A Meta-Analysis. Nutrients 2017;9(9).
23 Shivappa N, Godos J, Hébert JR, et al. Dietary Inflammatory Index and Cardiovascular Risk and Mortality-A Meta-Analysis. Nutrients 2018;10(2).
24 Ji M, Hong X, Chen M, Chen T, Wang J, Zhang N. Dietary inflammatory index and cardiovascular risk and mortality: A meta-analysis of cohort studies. Medicine (Baltimore) 2020;99(20):e20303.
25 Tan QQ, Du XY, Gao CL, Xu Y. Higher Dietary Inflammatory Index Scores Increase the Risk of Diabetes Mellitus: A Meta-Analysis and Systematic Review. Front Endocrinol (Lausanne) 2021;12:693144.
26 Garcia-Arellano A, Martínez-González MA, Ramallal R, et al. Dietary inflammatory index and all-cause mortality in large cohorts: The SUN and PREDIMED studies. Clin Nutr 2019;38(3):1221-31.
27 Eslampour E, Ghanadi K, Aghamohammadi V, et al. "Association between dietary inflammatory index (DII) and risk of irritable bowel syndrome: a case-control study". Nutr J 2021;20(1):60.
28 Hariharan R, Odjidja EN, Scott D, et al. The dietary inflammatory index, obesity, type 2 diabetes, and cardiovascular risk factors and diseases. Obes Rev 2022;23(1):e13349.
29 Bakhshimoghaddam F, Chaharlang R, Mansoori A, Dehghanseresht N. Dietary inflammatory index and its association with risk of metabolic syndrome and its components: a systematic review and Meta-analysis of Observational studies. Journal of Health, Population and Nutrition 2024;43(1):87.
30 Tandorost A, Kheirouri S, Moludi J, Seyedmardani S. Association of Dietary Inflammatory Index (DII) with disease activity and inflammatory cytokines in the patients with rheumatoid arthritis. Int J Clin Pract 2021;75(11):e14792.
31 Polachek A, Touma Z, Anderson M, Eder L. Risk of Cardiovascular Morbidity in Patients With Psoriatic Arthritis: A Meta-Analysis of Observational Studies. Arthritis Care Res (Hoboken) 2017;69(1):67-74.