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Mediterranean diet and Psoriatic Arthritis activity: a multicenter cross-sectional study

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Abstract

Diet is a modifiable factor implicated in chronic systemic inflammation, and the mediterranean dietary pattern is considered to be a healthy model in terms of morbidity and mortality. The main aim of this study was to evaluate the adherence to the mediterranean diet in patients with Psoriatic Arthritis (PsA) and its impact on disease activity. A cross-sectional observational study was conducted in a cohort of 211 consecutive PsA patients. We evaluated PsA activity by disease activity index for PSoriatic Arthritis (DAPSA) and composite psoriatic disease activity index (CPDAI). The NCEP-ACT III criteria were used to identify subjects with MetS, and in each subject, we evaluated body mass index (BMI). A validated 14-item questionnaire for the assessment of adherence to the mediterranean diet (PREDIMED) was recorded for all the enrolled subjects. Patients showed a median age of 55 (48–62) and disease duration was 76 (36–120) months. 27.01% of patients were classified as having MetS. The median of the mediterranean diet score (MDS) was 7 (6–9). A moderate adherence to mediterranean diet was found in 66.35% of the entire cohort; 15.64% and 18.01% of the patients showed low- and high adherence to the dietary pattern, respectively. We found a negative association between DAPSA and adherence to mediterranean diet ($B = -3.291$; 95% CI − 5.884 to − 0.698). DAPSA was positively associated with BMI ($B = 0.332$; 95% CI 0.047–0.618) and HAQ ($B = 2.176$; 95% CI 0.984–3.368). Results from our study evidenced that in PsA patients, higher levels of disease activity as measured by DAPSA correlated with low adherence to mediterranean diet, suggesting potential benefit of antinflammatory properties of this dietary pattern.

Keywords Body mass index · C-reactive protein · DAPSA · Mediterranean diet · Psoriatic Arthritis

Introduction

Psoriatic arthritis (PsA) is an inflammatory arthropathy associated with psoriasis and heterogenous manifestations [1, 2]. Among those, atherosclerosis, obesity, and metabolic syndrome (MetS) have been described as possible phenotypic aspects of the underlining inflammatory process [3–5].

However, high severity of PsA and increased prevalence of cardiovascular (CV) disease and its risk factors have also been explained by unhealthy lifestyle and nutritional aspects [6].

Diet is a modifiable factor implicated in chronic systemic inflammation, as well in psoriatic disease. Nevertheless, the relationship between dietary pattern and PsA incidence and severity has been scarcely studied [7, 8]. Particularly, it has been demonstrated that PsA patients have an excessive consumption of calories, lipids, fatty acids, and cholesterol [9]. Furthermore, very low energy diet along with short-term weight loss treatment has been found to be associated with significant positive effects on articular and entheseal severity in PsA patients with obesity [10].

Intermittent fasting (Ramadan fasting) has been reported to be associated with beneficial effects on PsA disease activity, expressed by disease activity index for Psoriatic Arthritis (DAPSA) and bath ankylosing spondylitis disease activity index (BASDAI), enthesitis, and dactylitis, independently by weight loss [11]. This has been

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hypothesized related to impact of fasting on proinflammatory mechanisms [11].

Moreover, obese PsA patients under biological therapy receiving hypocaloric diet with a weight loss > 5% had more frequently a minimal disease activity than those with weight loss < 5% [12].

Among dietary patterns, the Mediterranean diet is considered to be a healthy model in terms of morbidity and mortality [13]. It is characterized by a high intake of fruits, vegetables, legumes cereals, and fish, which are rich in vitamins, anti-oxidant, and anti-inflammatory nutrients. This dietary pattern comprises also low–moderate intake of dairy products, eggs, and poultry as well as low consumption of sweets, red meat, and wine. The main source of dietary fat is represented by monounsaturated fatty acids' compounds contained by the extra virgin olive oil (EVOO) [14].

Main results of studies on Mediterranean diet and psoriasis suggest an independent inverse association between compliance with the Mediterranean diet and psoriasis occurrence, severity, and quality of life [15–18].

To our knowledge, there are no studies investigating correlation between adherence to the Mediterranean diet and severity of PsA.

For this reason, we conducted a multicentric cross-sectional observational study to evaluate the adherence to the Mediterranean diet in patients with PsA and its impact on disease activity.

Patients and methods

A multicentric cross-sectional observational study has been conducted in a cohort of PsA patients of five Rheumatology Units from the University of Naples Federico II, Naples (Italy); University of L'Aquila, L'Aquila (Italy); Università Campus Bio-Medico, Rome (Italy); University of Rome Tor Vergata, Rome (Italy); and Sant'Andrea Hospital, Sapienza University of Rome, Rome (Italy).

Consecutive PsA patients attending the five outpatient Rheumatology Units were enrolled from January 2019 to May 2019. The study was approved on 22/06/2015 by the Federico II Naples Hospital Local Ethics Committee (protocol no: 15-126) and was conducted in conformity with the Declaration of Helsinki and its later amendments. A written informed consent for the anonymous use of data was obtained from all participants.

Inclusion criteria were both sexes, age > 18 years, and the fulfilment of CASPAR (Classification criteria for Psoriatic Arthritis) criteria [19, 20]. The exclusion criteria were: (1) current use of corticosteroids, (2) recent use of at least 6 months of corticosteroids, and (3) endocrinopathies and use of progestins.

In detail, the following data were recorded for each PsA patient: age, gender, vital signs, PsA duration, previous and/or actual treatments, and current comorbidities.

Assessment of disease activity

To measure PsA activity, the composite disease severity scores, DAPSA, and composite psoriatic disease activity index (CPDAI) were assessed.

For DAPSA, we summed the following variables: Tender and Swollen Joints Count (TJC68, SJC66), patient global assessment (PtGA), patient pain on a 10 cm visual analogue scale (VAS), and C-reactive protein (CRP) [21, 22]. We measured CPDAI score by the use of 68 TJC and 66 SJC, dactylitis (count of digit involved), enthesitis [leeds enthesitis index (LEI)], skin involvement by psoriasis severity index (PASI) and dermatology life quality index questionnaire (DLQI), health assessment questionnaire (HAQ), and axial involvement by BASDAI [23].

We also assessed axial involvement by the use of the single measure bath ankylosing spondylitis functional index (BASFI).

Assessment of metabolic parameters

Anthropometric parameters recorded were height and weight. In each subject, weight and height were used to calculate the BMI [weight (kg) divided by height squared (m2), kg/m2]. The degree of obesity was established according to a scale based on BMI cut-off points: 25 ≤ 30 kg/m2 (overweight), 30–34.9 kg/m2 (grade I obesity), 35–39.9 kg/m2 (grade II obesity), and ≥ 40 kg/m2 (grade III obesity or severe obesity), respectively.

For the definition of MetS, we used the following parameters: serum concentrations of total cholesterol (TC), HDL-C, TG and plasma glucose concentration, and systolic and diastolic blood pressure. Patients with a blood pressure ≥ 140/90 mmHg or those on anti-hypertensive drugs were considered as high blood pressure sufferers. Then, the NCEP-ACT III criteria were used to identify subjects with MetS [24].

A validated 14-item questionnaire for the assessment of adherence to the Mediterranean Diet (PREDIMED) [25] was recorded for all the enrolled subjects during a face-to-face interview between the patient and a rheumatologist. Briefly, for each item was assigned score 1 and 0; PREDIMED score was calculated as follows: 0–5, lowest adherence; 6–9, moderate adherence; ≥ 10–14, highest adherence.

Statistical analysis

Continuous data were described by median (25–75th Pctl), while categorical variables were described as percentages

(%). The Shapiro–Wilk test has been used to test the normality of data. Fisher's exact test has been used for analysis of contingency table, while Kruskal–Wallis has been used to compare ranks. Using DAPSA as dependent variable, a multiple linear regression analysis model was set up considering for multivariable analysis every variable with $p < 0.1$ in univariate analysis. For all the analysis, STATA v.14 has been used.

Results

On the basis of the inclusion and exclusion criteria, 211 subjects were included in the study.

Main demographic, anthropometric and clinical characteristics of the study population are reported in Table 1.

The patient population was Caucasian (100%) with a large preponderance of females (62.09%) and a median age of 55 (48–62). Disease duration (namely, time from diagnosis of PsA) was 76 (36–120) months. According to NCEP-ACT III criteria, 27.01% of patients were classified as having MetS.

Conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) were used by 41.71% of the patients, and particularly, 28.44% were receiving methotrexate, 9.48% sulfasalazine, 1.42% cyclosporine A, and 2.37% leflunomide. Biologic DMARDs (bDMARDs) or the phosphodiesterase-4 (PDE-4) inhibitor, apremilast, were used by 60.66% of the patients and particularly, 0.9% infliximab, 9.48% etanercept, 16.11% adalimumab, 0.95% certolizumab pegol, 13.74% golimumab, 9.48% ustekinumab, 3.32% secukinumab, and 6.64% apremilast.

Table 1 Main demographic, anthropometric, and clinical characteristics of the study population

Entire population ($n = 211$)	
Age, years	55 (48–62)
F/M (%)	62.09/37.91
BMI	26.56 (23.55–30.08)
MetS (%)	27.01
Disease duration, months	76 (36–120)
HAQ	0.88 (0.25–1.38)
BASFI	3 (1–5)
DAPSA	16.33 (7.3–24.1)
CPDAI	3 (2–6)
CRP, mg/dl	0.4 (0.14–0.91)
csDMARD (%)	41.71
bDMARD or apremilast (%)	60.66
MDS	7 (6–9)

Data expressed as median (25–75th percentile) or percentages (%)

BASFI bath ankylosing spondylitis function index, *bDMARDs* biologic disease-modifying anti-rheumatic drugs, *BMI* body mass index, *CPDAI* composite psoriatic disease activity index, *CRP* C-reactive protein, *csDMARDs* conventional synthetic disease-modifying anti-rheumatic drugs, *DAPSA* disease activity in Psoriatic Arthritis score, *F* female, *HAQ* health assessment questionnaire, *MetS* metabolic syndrome, *M* male, *MDS* mediterranean diet score

The measures of PsA activity showed a median DAPSA value of 16.33 (7.3–24.1) and CPDAI of 3 (2–6).

The median of the mediterranean diet score (MDS) was 7 (6–9). A moderate adherence to Mediterranean Diet was found in 66.35% of the entire cohort; 15.64% and 18.01% of the patients showed low and high adherences to the dietary pattern, respectively.

There were no significant differences in any of the variables between males and females.

A significant difference in age among classes of adherence to Mediterranean diet (low, moderate, or high adherence) was found ($p = 0.04$). Particularly, we found a significant difference in age between patients in low adherence to Mediterranean diet [51 (45–58) years] compared with patients with high adherence [58 (52–62) years] ($p = 0.01$).

Using the Kruskal–Wallis test, no significant difference in CRP levels among the three classes of adherence to Mediterranean diet has been demonstrated ($p = 0.2$) (Table 2).

Results of the univariate and multivariate linear regression analyses examining the factors associated with disease activity as measured by DAPSA are shown in Table 3. Intriguingly, the adjusted linear regression model showed a negative association between DAPSA and adherence to Mediterranean diet intended as classes (B = − 3.291; 95% CI − 5.884 to − 0.698). Moreover, DAPSA were negatively associated with male sex ($B = -4.999$; 95% CI − 8.120 to − 1.877) and the treatment with bDMARDs or apremilast ($B = -5.326$; 95% CI − 8.381 to − 2.271), whereas it was positively associated with BMI $B = 0.332$; 95% CI 0.047–0.618) and HAQ ($B = 2.176$; 95% CI 0.984–3.368).

Discussion

The aim of the study was to investigate the correlation between adherence to the Mediterranean diet and PsA activity, as measured by DAPSA and CPDAI. In particular, the study was conducted highlight possible PsA activity differences between patients grouped according to the class of adherence to Mediterranean diet.

Our cohort was represented by more than 200 patients, mainly represented by females (62%). Enrolled patients showed a long disease duration (above 6 years) and above 27% of patients were classified as having MetS.

At time of evaluation, we found low/moderate disease activity as evaluated by CPDAI [3 (2–6)] and DAPSA [16.33 (7.3–24.1)]. These results were expected as 60% of patients

Table 2 Psoriatic arthritis patients' characteristics according to the class of adherence to Mediterranean diet

	Low adherence ($n=33$)	Moderate adherence ($n=140$)	High adherence ($n=38$)	*P*
Age (years)	51 (45–58)	55 (48–61)	58 (52–62)	0.04
F/M (%)	45.45/54.55	63.50/36.50	70.73/29.27	0.07
Disease duration, months	75 (40–132)	84 (34–144)	60 (36–96)	0.3
BMI	26.57 (22.79–29.67)	26.57 (23.47–30.5)	26.45 (24.2–31.14)	0.6
HAQ	0.88 (0.38–1.5)	1 (0.25–1.38)	0.75 (0.35–1.25)	0.8
BASFI	2.75 (1–4.3)	2.9 (1.4–5.2)	3.5 (1–5)	0.8
DAPSA	19 (10.1–26.3)	16.44 (7–24.1)	12.52 (7.15–21.4)	0.3
CPDAI	3 (2–6)	4 (2–5)	3 (2–5)	0.6
CRP mg/dl	0.65 (0.15–1.15)	0.4 (0.15–0.98)	0.23 (0.14–0.55)	0.2
MetS (%)	21.21	25.55	36.59	0.3
csDMARD (%)	18.18	65.91	15.91	0.6
bDMARD or apremilast (%)	14.06	67.97	17.97	0.7

Data expressed as median (25–75th percentile) or percentages (%)

BASFI bath ankylosing spondylitis function index, *bDMARDs* biologic disease-modifying anti-rheumatic drugs, *BMI* body mass index, *CPDAI* composite psoriatic disease activity index, *CRP* C-reactive protein, *csDMARDs* conventional synthetic disease-modifying anti-rheumatic drugs, *DAPSA* disease activity in Psoriatic Arthritis score, *F* female, *HAQ* health assessment questionnaire, *MetS* metabolic syndrome, *M* male

Table 3 Multiple linear regression analysis showing the association of the Disease Activity in Psoriatic Arthritis Score (DAPSA) with the variables, sex, BMI, class of adherence, HAQ, and treatment with bDMARD or small molecules. For multivariate analysis: constant 17.959 (95% CI 8.331–27.587), $p<0.001$

	Univariate		Multivariate	
	B (95% CI)	*p*	B (95% CI)	*p*
Age	− 0.021 (− 0.169 to 0.127)	0.781		
Male sex	− 5.456 (− 8.767 to -2.145)	0.001	− 4.999 (− 8.120 to − 1.877)	0.002
Disease duration	− 0.004 (− 0.026 to 0.017)	0.681		
BMI	0.352 (0.060 to 0.644)	0.018	0.332 (0.047 to 0.618)	0.023
Class of adherence to Mediterranean diet	− 2.659 (− 5.476 to 0.158)	0.064	− 3.291 (− 5.884 to − 0.698)	0.013
HAQ	2.795 (1.552 to 4.038)	< 0.001	2.176 (0.984 to 3.368)	< 0.001
Metabolic Syndrome	1.173 (− 2.531 to − 4.878)	0.533		
Treatment with csDMARDs	− 1.059 (− 4.395 to 2.277)	0.532		
Treatment with bDMARD or small molecules	− 6.287 (− 9.546 to − 3.027)	0.000	− 5.326 (− 8.381 to − 2.271)	0.001

bDMARDs biologic Disease-modifying anti-rheumatic drugs, *BMI* Body Mass Index, *csDMARDs* conventional synthetic disease-modifying anti-rheumatic drugs, *HAQ* health assessment questionnaire, *PsA* psoriatic arthritis

were taking bDMARDs or apremilast treatment and the remaining population was taking csDMARDs' therapy.

When we assessed the adherence to the Mediterranean Diet by the PREDIMED questionnaire, a moderate or high adherence to Mediterranean Diet was found in more than half of the enrolled patients. Low adherence to the dietary pattern was found in above 15.64% of the cohort and this correlated with a high PsA activity, as measured by DAPSA.

The univariate analysis failed in demonstrating an association between disease activity and the adherence to Mediterranean diet. Despite this, in a multivariate model adjusted for sex, BMI, HAQ, and type of pharmacological treatment, we found that a higher PsA activity, as measured by DAPSA, was associated with low adherence to Mediterranean diet. The calculation of DAPSA included CRP; however, in this study, CRP levels were not significant different among the classes of adherence.

Our findings are concordant with results from studies showing an inverse association between compliance with the Mediterranean diet and psoriasis severity, and inflammatory state [15–18, 26].

However, further studies are needed for evaluating the impact of Mediterranean Diet on inflammatory parameters in PsA patients. Until today, the current study represents the first one focusing on Mediterranean Diet in PsA. Evidence to support the association between lower inflammation and other specific dietary patterns is limited [27]. Among those, an intermittent fasting has been reported to be associated with

positive effects on PsA severity as measured by DAPSA; in addition, a very low energy diet with short-term weight loss showed a significant positive effect on articular and entheseal severity in obese PsA patients [10, 11]. Weight loss achieved by diet, or also in concomitance of physical exercise, has been reported more effective than anti-inflammatory therapy alone in improving the symptoms and systemic inflammation with significant reductions in the serum levels of CRP and several proinflammatory molecules in obese PsA patients [28].

Our study also showed that DAPSA resulted positively associated with BMI, sustaining the possible link between the severity of the disease, metabolic manifestations and dietary pattern [29]. This is in line with recent evidences in which PsA inflammation and obesity are considered as strictly interconnected [30, 31]. However, the underlying mechanisms linking obesity and PsA severity have not yet been completely clarified. Indeed, if on one hand, obesity has been reported a factor associated with a systemic low-grade inflammation, on the other hand, elevated BMI could sustain an elevated articular biomechanical stress with an increased inflammatory response [32, 33]. It is plausible that these two mechanisms could concur to promote inflammatory processes in psoriatic disease [32, 33].

Diet is a modifiable factor implicated in chronic systemic inflammation. Mediterranean diet is considered to be a healthy model in terms of morbidity and mortality [13, 14]. Several studies have evidenced the anti-inflammatory effects of the Mediterranean diet, as it could be reducing circulating proinflammatory cytokines [34–38].

The anti-inflammatory properties on arthritis could be explained by different mechanisms, mainly represented by effects of several compounds of Mediterranean Diet, such as oleic acid, monounsaturated fatty acids, polyphenol extract, anti-oxidant agents, and the inhibitor of cyclooxygenase-2, resveratrol [39, 40]. Furthermore, dietary fiber favoring beneficial effects on gut microbiota could have a role in improving the regulation of gut immune responses [41–45].

Results from our study open a new research area on the possible anti-inflammatory role of the Mediterranean dietary pattern in PsA. It has been yet highlighted that lifestyle interventions as well dietary modification should be implemented for PsA patients [46].

In 2018, the Medical Board of the National Psoriasis Foundation proposed evidence-based dietary recommendations for adults with psoriasis and PsA. In these recommendations, it is suggested dietary weight reduction with a hypocaloric diet in overweight and obese PsA patients. It is recommended also that adults with PsA supplement their standard medical therapies with dietary interventions to reduce disease severity [47].

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommends that all PsA patients should be encouraged to achieve and maintain a healthy body weight [48] and an appropriate dietary pattern, by Mediterranean Diet, could represent a useful strategy for this aim.

Furthermore, the identification of PsA patients with a high inflammatory pattern and cardiometabolic manifestations could represent a key step to implement preventive approaches, such as dietary modifications along with appropriate pharmacological strategies. The whole diet approach seems particularly promising to reduce the inflammation associated with MetS and this can be a promising strategy also in psoriatic disease [49].

The main limitations of the study were represented by the absence of patients naïve to cs- and bDMARDs and by the cross-sectional design that does not allow to fully establish if adherence to the Mediterranean diet is related to the severity of the disease.

Among advantages of our study, DAPSA represents a valid composite disease activity measure, and in comparison with CPDAI, it is recognized to better correlate with subclinical inflammatory severity [50–53]. Furthermore, we excluded patients with endocrinopathies and current or recent treatment with glucocorticoids and progestins, for avoiding factors interfering with components of MetS and dietary intake.

On the basis of our findings, we hypothesized that Mediterranean diet could be considered a healthy model for PsA patients, but further studies are needed.

These could evaluate the relation between the adherence to Mediterranean Diet and PsA activity also by the use of other validated questionnaires, such as the MedDietScore, the Mediterranean Lifestyle (MEDLIFE) index, and the questionnaire derived from the Spanish EPIC Cohort Study (Relative Mediterranean Diet Score) [54–57].

Conclusion

In conclusion, results from our cohort have evidenced that high PsA activity, as measured by DAPSA, is associated with low adherence to Mediterranean Diet, suggesting that PsA patients could benefit of antinflammatory properties of this dietary pattern.

Further studies on larger sample size and naive patients are advocated to identify a possible impact of Mediterranean dietary pattern on disease severity.

Author contribution All authors made substantial contributions to the conception or design of the work, the acquisition, and interpretation of data. All authors contributed to the critical review and revision of the manuscript and approved the final version. All the authors agreed to be accountable for all aspects of the work. *FC* study design, data acquisition, statistical analysis, interpretation of data, writing of the

first draft of the paper, review, and acceptance; *LN* study design, data acquisition, statistical analysis, interpretation of data, writing of the first draft of the paper, review, and acceptance; *FC* study design, data acquisition, interpretation of data, review, and acceptance; *APD* study design, data acquisition, interpretation of data, review, and acceptance; *MSC* study design, data acquisition, interpretation of data, review, and acceptance; *MT* study design, data acquisition, interpretation of data, review, and acceptance; *DC* study design, data acquisition, interpretation of data, review, and acceptance; *PR* study design, data acquisition, interpretation of data, review, and acceptance; *MC* study design, statistical analysis interpretation of data, review, and acceptance; *AA* study design, data acquisition, interpretation of data, review, and acceptance; *BL* study design, data acquisition, interpretation of data, review, and acceptance; *RP* study design, data acquisition, interpretation of data, review, and acceptance; *AA* study design, data acquisition, interpretation of data, review, and acceptance; *RG* study design, data acquisition, interpretation of data, review, and acceptance; *RS* study design, data acquisition, interpretation of data, review, and acceptance; *LC* study design, data acquisition, interpretation of data, writing of the first draft of the paper, review, and acceptance.

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Data availability All data relevant to the study are included in the article.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest in this work. Francesco Caso: conflict of interest and relationships with pharma agencies—none; Luca Navarini: conflict of interest and relationships with pharma agencies—none; Francesco Carubbi: conflict of interest and relationships with pharma agencies—none; Andrea Picchianti-Diamanti: conflict of interest and relationships with pharma agencies—none; Maria Sole Chimenti: conflict of interest and relationships with pharma agencies—none; Marco Tasso: conflict of interest and relationships with pharma agencies—none; Damiano Currado: conflict of interest and relationships with pharma agencies—none; Piero Ruscitti: conflict of interest and relationships with pharma agencies—PR received speaker honoraria and/or grants from BMS, MSD, Ely Lilly, SOBI and Pfizer outside this work; Massimo Ciccozzi: conflict of interest and relationships with pharma agencies—none; Antonio Annarumma: conflict of interest and relationships with pharma agencies—none; Bruno Laganà: conflict of interest and relationships with pharma agencies—none; Roberto Perricone: conflict of interest and relationships with pharma agencies—none; Antonella Afeltra: conflict of interest and relationships with pharma agencies—none; Roberto Giacomelli: conflict of interest and relationships with pharma agencies—RG received speaker honoraria and/or grants from Abbvie, Roche, Actelion, BMS, MSD, Ely Lilly, SOBI and Pfizer outside this work; Raffaele Scarpa: conflict of interest and relationships with pharma agencies—RS received speaker honoraria and/or grants from Abbvie, Celgene, MSD, Ely Lilly, Novartis, and Pfizer; Luisa Costa: conflict of interest and relationships with pharma agencies—none.

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