Adherence to the Mediterranean diet model and psoriatic disease (skin, joint and metabolic expression of psoriasis)

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Abstract

Psoriasis is a chronic disease, characterized by systemic inflammation with skin, joint and metabolic involvement. The most common tools to evaluate the severity of each disease is respectively the Psoriasis Area Severity Index (PASI) and the Disease Activity Index for Psoriatic Arthritis (DAPSA). The association between psoriasis and obesity and the role of visceral fat in producing an inflammatory state have been demonstrated. The Mediterranean Diet (MD) has been recommended as a model of healthy diet on the basis of scientific evidence and considered as an adjuvant therapy for all patients affected by chronic inflammatory diseases. Our study evaluated the association between adherence to MD (assessed with the Predimed questionnaire) and psoriatic disease severity. 80 patients (40 with psoriasis and 40 with psoriatic arthritis) were evaluated for disease severity (PASI, DAPSA) and were assessed for Metabolic Syndrome according to the International Diabetes Federation (IDF) definition. To evaluate adherence to the MD, each patient was administered the Predimed questionnaire which includes 14 questions. Our study shows a correlation between low adherence to MD and a high expression of psoriasis, considering cutaneous, joint symptoms and the metabolic profile.

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Introduction

Scientific evidence has demonstrated that the diet plays a primary role in protecting health at every age. Other studies have shown that there is a major risk of chronic degenerative, cardiovascular and neoplastic diseases in patients affected by inflammatory diseases like psoriasis and psoriatic arthritis. Psoriasis is a chronic immune-mediated disease associated with a disorder in the regulation of T Helper lymphocytes. The main histopathological features of psoriasis include epidermal hyperproliferation with abnormal differentiation and dermo-epidermal inflammatory infiltrate. The most common tool to evaluate psoriasis severity is PASI (Psoriasis Area Severity Index): it combines the severity of skin lesions (in terms of erythema, scaling and thickness) and the affected body surface in a single score between 0 and 72. Psoriatic Arthritis (PsA) is a chronic inflammatory disease, characterized by pain, swelling and joint stiffness, ligament and tendon inflammation and impaired physical function, which affects from 6 to 42% of psoriatic patients. In most cases skin lesions precede the onset of arthritis by about 10 years. In general arthritis occurs around 40 years of age and is distributed between men and women. There are many tools to evaluate the degree of PsA activity, but the most common is the DAPSA score (Disease Activity Index for Psoriatic Arthritis). It includes the level of pain perceived by the patient (Pt-Pain in cm VAS), the overall evaluation of the patient (PtGA in cm VAS), the number of painful and swollen joints (painful joints TJC 68 and swollen joints SJC6 8) and inflammatory markers (Protein C Reactive PCR mg/dL).[1,2] Obesity is generally classified according to the Body Mass Index (BMI), defined as the ratio between weight (in kg) and height (in square meters). Actually, the adipose tissue, in particular perivisceral abdominal fat, is considered not only as energy reserve but as an endocrine organ because it can produce inflammatory factors such as cytokines (TNF-α, IL-6, IL-10, IL-1β), hormones (leptin, adiponectin, adipsin, resistin, visfatin), acute phase proteins (PAI-1, fibrinogen, PCR) and non-esterified fatty acids. These substances can have a proinflammatory effect, inducing dyslipidaemia, insulin resistance and pro thrombotic status. In recent years the association between psoriasis and obesity has been widely demonstrated. When analyzing the role of adipocytokines, produced by the adipose tissue, it is important to understand how psoriasis and obesity are linked and can influence each other. Psoriatic patients can have

an increase in leptin, resistin and visfatin, but a reduction of adiponectin. Leptin and resistin are pro-inflammatory adipocytokines that activate endothelial cells, promoting neo-angiogenesis, keratinocyte production and endothelial smooth muscle cells migration. Consequently, in obese patients they would have a pro-atherogenic effect, also stimulating the production of TNF alfa, that is a key cytokine in psoriatic plaque.[3,4] Visfatin has also a pro-inflammatory effect and is mainly involved in the development of insulin resistance linked to obesity. On the other hand, adiponectin, that induces an anti-inflammatory effect, is decreased in obese psoriatic patients. Moreover, cytokines, responsible for insulin-resistance in obese patients, such as TNF-alpha, IL-1, IL-6, IL-7 and VEGF, play a key role also in the development of psoriasis. For this reason, many psoriatic patients can become obese, in particular when the cutaneous disease is severe and uncontrolled. Obesity increases their cardiovascular risk, induced by chronic systemic inflammation, and triggers treatment resistance.[5] In fact many studies have demonstrated that weight loss often improves psoriasis, as occurs in the patients undergoing gastric bypass with consequent weight loss and cutaneous remission.[6,7] An Italian case-control study showed that the metabolic syndrome is significantly more common in psoriatic patients than in controls (30.1% *vs*. 20.6%); both diseases are also associated with an increased cardiovascular risk.[8,9] Psoriatic patients, also with normal BMI, have an increased predisposition to develop diabetes as well as other metabolic disorders. The pathogenetic link between psoriasis and diabetes seems to be related to the production of inflammatory cytokines, such as TNF alpha, IL-17, IL-18, IL-6 and VEGF, that induce insulin resistance. In fact, also young people suffering from Diabetes I have an increased risk of psoriasis compared to healthy subjects. The improper activation of these molecules leads to hyperglycemia, insulin resistance and increased glycated hemoglobin, as well as to a progression of psoriatic lesions.[10-12] Dyslipidemia can be found in a high percentage of psoriatic patients and is also associated to psoriasis severity. The Mediterranean Diet (MD) has been recommended as a model of healthy diet on the basis of scientific evidence for many years. In particular, the Mediterranean nutritional model is not considered a specific diet program, but it represents rather a set of eating healthy habits. According to MD, it is recommended to eat natural and fresh food, such as seasonal fruit and vegetables, cereals, fish and legumes and to use extra virgin olive oil as condiment. On the contrary, the consumption of animal fats should be limited. What distinguishes MD is both the quality and the balance of nutrients in the food consumed. MD can be considered an adjuvant therapy for all the patients affected by chronic inflammatory diseases, like psoriasis, because it contains a daily high percentage of monounsaturated and polyunsaturated fatty acids, vitamins and minerals, which have anti-inflammatory and antioxidant properties and a protective effect on the cardiovascular system. In particular, the nutritional therapy with a high content of ω-3 fatty acids, which are found especially in vegetable oils, oily fish and fish oil, has proved a valid support to the pharmacological treatment of chronic inflammatory rheumatic diseases.[13] Similar anti-inflammatory properties have been recognized for monounsaturated fatty, acids like oleic acid (series ω-9) contained in extra virgin olive, the main ingredient of the Mediterranean nutritional model. The oleic acid introduced with the diet is able to reduce the competition in the body between fatty acids ω-6 and ω-3 favoring the incorporation of the latter in cell membranes. Moreover, olive oil is rich in phenolic substances, in particular tyrosolol, hydroxytyrosolol and oleuropein, which play a protective role against oxidative stress, that characterizes systemic inflammation in rheumatic diseases.[14-15] Recently, a new molecule, called olecantal, has been identified in olive oil, which is able to inhibit COX-1 and COX-2 enzymes in the prostaglandines biosynthetic pathway, similarly to ibuprofen.[16] Furthermore, the presence of fruit and vegetables in MD ensures adequate intake of antioxidant vitamins, such as vitamin C and vitamin E, whose deficiency has been associated with an increased risk of developing inflammatory arthritis.[17] Therefore, it may be interesting to assess the adherence to MD in patients affected by chronic inflammatory diseases like psoriasis and psoriatic arthritis. The PREDIMED score (Figure 1) is an adherence index to MD, introduced first in

Questions	Criteria for 1 point
1. Do you use olive oil as main culinary fat?	Yes
2. How much olive oil do you consume in a given day (including oil used for frying, salads, out-of-house meals, etc.)?	≥4 tbsp
3. How many vegetable servings do you consume per day? (1 serving : 200 g [consider side dishes as half a serving])	≥2 (≥1 portion raw or a a salad)
4. How many fruit units (including natural fruit juices) do you consume per day?	≥3
5. How many servings of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? (1 serving: 100–150 g)	<1
6. How many servings of butter, margarine, or cream do you consume per day? (1 serving: 12 g)	<1
7. How many sweet or carbonated beverages do you drink per day?	<1
8. How much wine do you drink per week?	≥7 glasses
9. How many servings of legumes do you consume per week? (1 serving : 150 g)	≥3
10. How many servings of fish or shellfish do you consume per week? (1 serving 100–150 g of fish or 4–5 units or 200 g of shellfish)	≥3
11. How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard?	<3
12. How many servings of nuts (including peanuts) do you consume per week? (1 serving 30 g)	≥3
13. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage?	Yes
14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomato and onion, leek, or garlic and simmered with olive oil)?	≥2

Figure 1. Validated 14-item Questionnaire of Mediterranean diet adherence (Predimed).

2013 and used in many clinical studies. It is simple to use in adults and provides information on how far the patient's diet deviates from MD.[18,19]

On the basis of this questionnaire it is possible to evaluate the association between adherence to MD and various inflammatory diseases. However, up to now few data are available about adherence to MD and psoriatic disease.[20]

Objectives

Even though the association between abdominal obesity, perivisceral fat and insulin resistance, which are the key elements of metabolic syndrome, and psoriasis has been widely demonstrated, the role of MD and its anti-inflammatory and antioxidant effect in the treatment of psoriatic patients is not well known. The aim of this study was to evaluate the association between adherence to MD (evaluated with the Predimed questionnaire) and the psoriatic disease.

Materials and Methods

Eligible patients were >18 years old with psoriasis and/or psoriatic arthritis and were consecutively examined at the Dermopathic Institute of the Immaculate in Rome. To be included, patients had to be on any systemic treatment (including acitretin, cyclosporine, methotrexate and biological drugs) for at least 12 months before the start of study or not to be on any treatment. The key exclusion criteria included patients who had started any systemic therapy for less than 12 months. A control group of patients visited at our hospital for other cutaneous diseases was also progressively enrolled. For each enrolled patient (including the control group), anamnestic, demographic and clinical data were recorded upon entry to the study, including age, sex, BMI and waist circumference. The metabolic status of each patient was assessed by collecting the following tests: HDL cholesterol, triglycerides, glycemia. Also, the use of any hypolipidemic or antihypertensive therapy was recorded. The metabolic syndrome was assessed according to the definition of the International Diabetes Federation (IDF) and corresponds to the presence of visceral obesity plus two other criteria among hypertrglyceridemia, low HDL cholesterol, hypertension and hyperglycemia, including diabetes.[21] The severity of psoriasis and psoriatic arthritis was evaluated using the PASI Index and the DAPSA Index. To evaluate adherence to the Mediterranean diet, each patient was administered the Predimed questionnaire, a 14-question questionnaire. Patients were asked to answer the questionnaires taking into account the eating habits adopted in the last 12 months. The Predimed score was calculated on the basis of a 10-point scale: 0-5 low adherence, 6-9 medium adherence, equal to or more than 10 high adherence.

The study was approved by the Local Ethical Committee and conducted in accordance with the Declaration of Helsinki guidelines.

Results

We enrolled 80 consecutive patients with psoriasis (40/80) or psoriatic arthritis (40/80) who met our inclusion and exclusion criteria. The study population included 39 males and 41 females, aged between 18 and 79 (range 18-79). The mean PASI score was 7.62 (mild psoriasis) and the mean DAPSA was 27.5 (arthritis with moderate activity). The control group was comparable to the study group and included 80 patients, 29 males and 51 females, aged between 20 and 85. The mean BMI of the patients enrolled was 29.55, while in the control group it was 24.14, which confirms a higher incidence of overweight/obesity in the psoriatic patient group than in the control group. Visceral obesity and metabolic syndrome were also more represented in the psoriatic group than in the control group (Figure 2).

On the other hand, the average adherence to the Mediterranean model evaluated using the Predimed score was 6.9 in psoriatic patients and 7.8 in the control group. Patients were divided into three groups according to MD adherence, assessed with the PREDIMED score: poor adherence if the score was between 0-5, medium adherence between 5-10, high adherence if the score was >10. An inverse relationship between MD adherence and metabolic, cutaneous and articular expression of psoriatic disease was found. In patients with a Predimed score 0-5, which means poor adherence to MD, mean waist circumference, mean values of metabolic syndrome, DAPSA, PASI and BMI were found significantly higher than in patients with a Predimed score >5 (Figures 3 and 4).

Discussion

In recent years the association between psoriasis and obesity has been widely demonstrated. Obesity is the main cause of insulin resistance and chronic, low-grade inflammation, which characterizes the metabolic syndrome. In particular, visceral adipose tissue is no longer considered just a deposit of energy, but a real endocrine organ. It can release numerous cytokines and bioactive peptide molecules, the adipocytokines, which are thought to be as a link between psoriasis, obesity, insulin resistance and other inflammatory comorbidities.[22,23] In obese patients there is an abnormal formation of fat deposits with hypertrophic and hyperplastic adipocytes, which increase demand for oxygen, with consequent cellular hypoxia, activation of stress pathways and release of cytokines and pro-inflammatory chemokines. These cytokines activate the chemotaxis of macrophages in the adipose tissue. The macrophages are located around the necrotic adipocytes and secrete additional pro-inflammatory cytokines, thus amplifying the inflammatory process. Among all the pro inflammatory cytokines, TNF-α and IL-6 play a key role. TNF-α, which is a central pro-inflammatory cytokine also in the pathogenesis of psoriasis, induces the secretion of IL-6,

	Psoriatic patients 80 pts. 39M 41F 40 Pso 40 PsA	Controls 80 pts. 29M 51F
Mean BMI	29.55	24.14
Under weight	0%	2.5%
Normal	23.75%	51.2%
Over weight	38.75%	34.6%
Obesity I° grade	23.75%	6.4%
Obesity II° grade	8.75%	2.5%
Obesity III° grade	5%	2.5%
Visceral obesity	80 %	69%
Metabolic syndrome	62.5%	30%

Figure 2. Body mass index (BMI), visceral obesity and metabolic syndrome in psoriatic patients and in the control group.

which stimulates the hepatic synthesis of C-reactive protein.[24,25] A direct correlation between BMI and the risk of psoriasis has been demonstrated. In healthy patients a moderate increase in BMI (between 26 and 29) determines a slight increase in the risk of psoriasis onset, while obesity (BMI>29) doubles this risk. In addition, the presence of obesity in psoriatic patients has been related to severe psoriasis.[26] Obesity is also over-represented in patients with psoriatic arthritis and it is often associated with high disease activity, reduced drug efficacy and increased cardiovascular risk. Several studies have reported a high prevalence of obese (BMI ≥30) in patients with psoriatic arthritis.[27] Also in our study the mean BMI was 29.5, thus confirming a high prevalence of overweight in patients affected by psoriatic disease. More than 60% of enrolled patients were in the overweight-obesity grade I band with 38.75% overweight and 23.75% first-degree obesity. The mean BMI and its distribution in the overweight-obesity group were similar in the two groups of psoriasis and psoriatic arthritis. In the control group, the mean BMI was significantly lower and most patients were in the normal-weight or overweight range (18-29), confirming that obesity is a frequent comorbidity in the psoriatic patient. In our study visceral obesity was present in 64/80 patients (80%); 50 patients (62.5%) had metabolic syndrome, defined as visceral obesity with

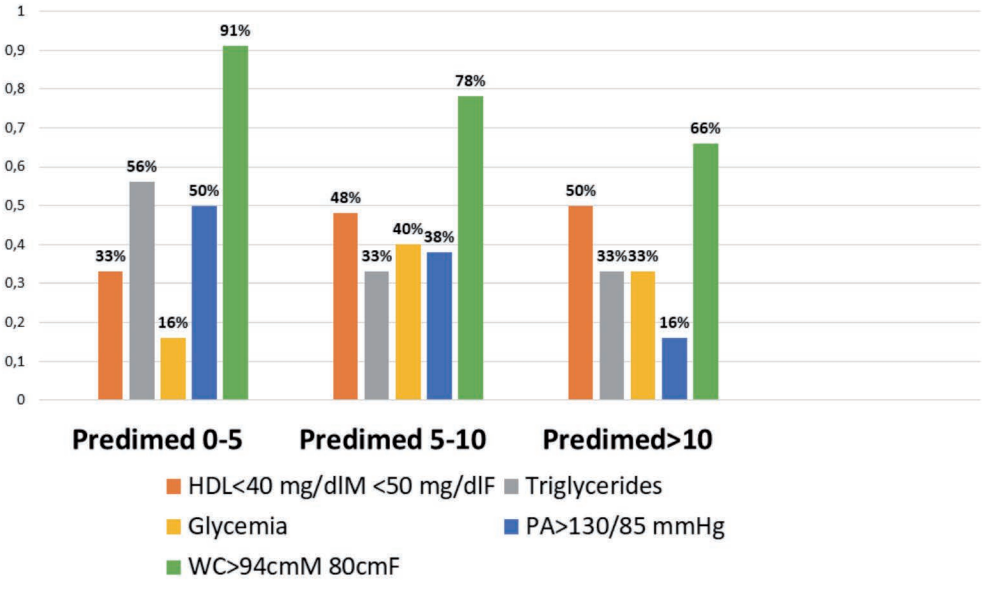

Figure 3. Correlation between PREDIMED body mass index and metabolic syndrome. HDL, high density lipoprotein; WC, waist circumference.

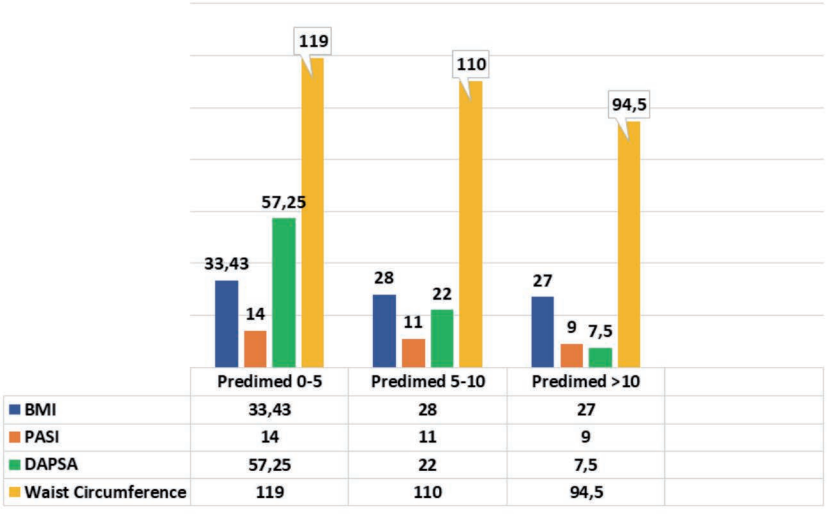

Figure 4. Correlation between PREDIMED body mass index (BMI) Psoriasis Area Severity Index (PASI) - Disease Activity Index for Psoriatic Arthritis (DAPSA) and waist circumference.

the association of more two other criteria among the usual ones (hypertriglyceridemia, low HDL values, hyperglycemia, hypertension or DMT2). As regards metabolic parameters, no difference in prevalence was observed in the psoriasis group compared to the psoriatic arthritis group. In the control group, instead, visceral obesity was found in 69% of patients and metabolic syndrome in 30%. Metabolic syndrome, a frequent comorbidity of psoriasis, increases cardiovascular risk. Patients with psoriasis have an increased predisposition to develop metabolic disorders and type 2 diabetes. In particular the risk of developing type 2 diabetes in psoriatic patients is independent from BMI, although it is certainly higher in obese than in normal BMI patients. Even young people with type 1 diabetes have an increased risk of developing psoriasis compared to healthy subjects: the pathogenetic link would be related to the production of inflammatory cytokines, in particular TNF alpha, IL-17, IL-18, IL-6 and VEGF. The improper activation of these molecules leads to hyperglycemia, insulin resistance and increased glycated hemoglobin, as well as to a progression of psoriatic lesions. Dyslipidemia is a well-known cardiovascular risk factor and it is found in a good percentage of psoriatic patients, significantly related to psoriasis severity. The efficacy of the diet on the reduction of visceral fat in psoriatic patients has been widely proved: over six months a reduction of <5% of body weight can reduce the cardiovascular risk and a 5-10% reduction can prevent or promote the remission of type II diabetes mellitus. The loss of >10% body weight reduces serum levels of inflammatory cytokines such as TNF alpha, IL-6, MCP-1, Protein C reactive, leptin, resistin and increases levels of anti-inflammatory mediators like adiponectin and IL-10.[25,28] Remission of psoriasis after a 4-week low-calorie diet (855 Kcal. per day) and after gastric bypass surgery has also been reported. Other studies have shown that a low-calorie diet (640 Kcal) reduces systemic inflammation as well as disease activity of psoriatic arthritis. Recently, a systematic review, analyzing 55 studies, has reported a significant reduction in severity of psoriasis and/or psoriatic arthritis after a low-calorie diet in overweight and obese patients.[29] Despite the large bulk of data available on the efficacy of low-calorie diet in the improvement of inflammatory diseases, few data have been reported on the adherence and the efficacy of the MD diet in psoriatic patients. In our study, adherence to the MD was 6.9 based on the PREDIMED score (*versus* 7.8 in the control group), which represents a medium adherence, despite most of the patients enrolled were from central and southern Italy. In particular, the use of 4 teaspoons or more of extra virgin olive oil per day turned out to be common in psoriatic patients. However, none of the patients declared to eat fresh or preserved red meat daily, while the consumption of legumes, fruit, vegetables and fish was very limited. Consequently, the reduced daily assumption of fruit and vegetables does not allow the adequate intake of antioxidant vitamins such as vitamin C and vitamin E, whose deficiency has been associated with an increased risk of developing inflammatory arthritis. In the same way, a low consumption of fish reduces the intake of polyunsaturated fatty acids, especially ω-3, and monounsaturated fatty acids which have a significant anti-inflammatory effect. Even though our study was carried out on a limited number of patients, it showed a direct relationship between adherence to MD and the metabolic, cutaneous and articular expression of psoriatic disease. The mean values of waist circumference and all the components of the metabolic syndrome, DAPSA, PASI and BMI are significantly higher in patients with Predimed score 0-5 (with poor adherence to MD). A progressive improvement of the Predimed score determines a progressive reduction in metabolic parameters (waist circumference, BMI) and activity diseases scores (DAPSA, PASI).

Conclusions

Psoriasis is a chronic recurrent disease, characterized by a chronic systemic inflammation with a skin, joint and metabolic expression which determines a high social impact and high cardiovascular risk. Weight loss with a low-calorie diet has proven effective in improving the severity of psoriatic disease. On the other hand, the adherence to MD in psoriatic patients seems to be rather low, despite it has been little investigated. In particular, most psoriatic patients do not eat adequate quantities of fruit, vegetables and fish, which could provide useful antioxidant nutrients with an anti-inflammatory effect. Even if our study was carried out on a limited number of patients, it seems to confirm the association between psoriasis and high BMI. It also highlighted a correlation between low adherence to MD and high expression of psoriasis, considering not only cutaneous and joint symptoms, but also the metabolic profile. Similarly, these parameters improve with increased adherence to MD assessed with the Predimed questionnaire. Even though it would be necessary to confirm these data with other studies on a larger number of patients, our study shows how a correct diet, which is not only low-calorie, but also anti-inflammatory and antioxidant such as the Mediterranean diet, can be considered an essential therapeutic tool in the psoriatic patient. In fact, the MD has been demonstrated to have beneficial effects on psoriatic disease in all its various aspects by reducing the systemic inflammation. For this reason the MD should play a key role in the treatment of psoriatic patients.

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