ORGAN TOXICITY AND MECHANISMS



Coffee consumption, metabolic syndrome and clinical severity of psoriasis: good or bad stuff?

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Abstract

Despite the wide consumption of coffee, its anti-inflammatory effect on clinical severity of psoriasis is still debatable. The aim of this study was to evaluate the association between the coffee consumption and clinical severity of psoriasis in a sample of patients stratified according to the presence of the metabolic syndrome (MetS) and smoking. This cross-sectional case–control observational study was conducted on 221 treatment-naïve psoriatic patients. Lifestyle habits, anthropometric measures, clinical and biochemical evaluations were obtained. Clinical severity of psoriasis was assessed by Psoriasis Area and Severity Index (PASI) score. Data on energy caloric intake and coffee consumption were collected using a 7-day food diary record. The coffee consumption was analyzed as coffee intake (consumers and non-consumers) and daily servings (range 0–4 servings/day). Coffee consumers have a lower PASI score vs non-consumers (p < 0.001). The lowest PASI score and MetS prevalence were found in patients consuming 3 cups of coffee/day (p < 0.001), which was also the most common daily serving (34.8%), whereas the highest PASI score was found among those drinking ≥ 4 cups/day. Grouping the case patients according to smoking and MetS, the best odds of PASI score was observed in those drinking 3 cups of coffee per day and no smokers, after adjusting for total energy intake (OR 74.8; p < 0.001). As a novel finding, we reported a negative association between coffee intake, MetS prevalence and clinical severity of psoriasis. The evaluation of the anti-inflammatory effect of coffee on clinical severity of psoriasis, whose metabolic risk increases along with its clinical severity, could be of great importance from a public health perspective.

Keywords Coffee consumption \cdot Clinical severity of psoriasis \cdot PASI score \cdot Metabolic syndrome \cdot Cigarette smoking \cdot Nutritionist

Introduction

Coffee is one the most consumed beverage in the World, just after water and tea (Ludwig et al. 2014). It is estimated that the coffee consumption worldwide is about 50 million cups; in particular, per capita consumption for Italy, where coffee is almost prepared and consumed in the Italian style (i.e., by espresso or moka), is 5.6 kg (International Coffee Council 2017). Long-term intake of coffee, whose most basic component is caffeine, has demonstrated to exert a

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number of potential benefits on human health (Grosso et al. 2017; Tajik et al. 2017; Hall et al. 2015), through its effects on different systems, including the immune system (Gökcen and Şanlier 2017; Sharif et al. 2017). Coffee consumption has reported to have pronounced antioxidant activity, resulting in a decreased inflammatory state (Li et al. 2012), due to the powerful anti-oxidants such as polyphenols containing chlorogenic acid and caffeic acid, diterpenes comprising cafestol and kahweol, lactones, niacin, and trigonelline, which is the precursor of niacin (Baspinar et al. 2017). Long-term intake of coffee reduces the activation in vitro Nuclear Factor Kappa B (NF- κ B) (Shin et al. 2017). NF- κ B is a family of transcription factors controlling apoptosis and pro-inflammatory cytokine expression, in a dose-dependent manner, via the inhibition of the oxidative stress due to reactive oxygen species (ROS) accumulation (Chu et al. 2013; Akash et al. 2014; Khan et al. 2016). Although several studies have

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been conducted to elucidate the effects of coffee consumption on various diseases, it has also been reported that coffee consumption could prevent several inflammation-driven, chronic diseases, including cardiovascular diseases (Montagnana et al. 2012), type 2 diabetes (Bae et al. 2014; Floegel et al. 2012), neurodegenerative diseases such as Parkinson's and Alzheimer's diseases (Madeira et al. 2017), non-alcoholic fatty liver disease and its progression to hepatic fibrosis and cirrhosis (Liu et al. 2015; Wijarnpreecha et al. 2017). In addition, growing interest has been focused on the inverse association of coffee consumption with the Metabolic Syndrome (MetS) (Baspinar et al. 2017).

Psoriasis is a chronic immune-mediated inflammatory skin disease. Psoriasis lesions are characterized by hyperproliferation of epidermal keratinocytes associated with inflammatory cellular infiltrate in both dermis and epidermis (Barrea et al. 2017). Of interest is that psoriasis is associated with an increased metabolic risk in a manner that varies with the severity of psoriasis (Ganzetti et al. 2016; Gisondi et al. 2015), as well as with non-alcoholic fatty liver disease (Balato et al. 2015a). According to recent literature data, psoriatic patients show a greater prevalence of obesity (Fleming et al. 2015) and MetS (Voiculescu et al. 2014), which confers a higher cardiovascular risk (Shahwan and Kimball 2015). Among the environmental risk factors for psoriasis, evidence is accumulating that nutrition plays a major role per se in the pathogenesis of psoriasis (Barrea et al. 2016a). In particular, specific nutrients, such as monounsaturated fatty acids, omega 3 (Guida et al. 2014), and vitamin D (Barrea et al. 2017), or healthy dietary patterns, such as the Mediterranean diet (Barrea et al. 2015a), could contribute to reduce the clinical severity of psoriasis, also adjusting for known confounders, such as body weight and MetS (Barrea et al. 2015b). The association of circulating vitamin D levels with chronic autoimmune diseases (Altieri et al. 2017) and clinical psoriasis severity has been largely reported (Lee and Song 2018). In addition, specific parameters of body composition commonly used as expression of the nutritional status, such as phase angle, are associated with the clinical severity of psoriasis (Barrea et al. 2016b).

Considering the evidence linking coffee consumption and inflammation, the anti-inflammatory effect of coffee could be relevant in the pathogenesis of psoriasis. However, only few studies investigated the association between coffee consumption and psoriasis and there is still considerable uncertainty, especially regarding its possible contribution to the clinical severity of psoriasis (Sharif et al. 2017). On the one side, in a cohort study on 968 subjects, there was no evidence for the association between consumption of coffee and incidence of psoriasis (Li et al. 2012). This lack of association was also confirmed in a case–control study on 94 twins pairs (Duffy et al. 1993). On the other side, both in vivo and in vitro studies supported the anti-inflammatory and immunosuppressant activities of coffee in psoriasis (Gökcen and Şanlier 2017; Swanson et al. 2007; Li et al. 2012). In particular, Swanson et al. (2007) demonstrated in an observational study conducted on 65 psoriatic patients that coffee consumption did not aggravate this pathological condition (Swanson et al. 2007), while Li et al. (2012) found that coffee improved the efficacy of psoriasis pharmacological treatments, such as methotrexate and sulfasalazine (Li et al. 2012). However, it is important to remember that smoking per se may increase the risk of psoriasis (Setty et al. 2007), and could represent the major confounder underlying the association between coffee intake and risk of psoriasis in age-adjusted models (Li et al. 2012). Indeed, it is well-known that cigarette smoking and coffee consumption are strongly associated (Swanson et al. 1994; Hewlett and Smith 2006; Ware et al. 2017), and several observational studies showed that coffee consumers are more likely to be smokers than non-consumers (Hewlett and Smith 2006; Ware et al. 2017; Freedman et al. 2012).

Besides the association between coffee and presence/ absence of psoriasis, data supporting this association based on a more detailed coffee consumption and the clinical severity of psoriasis are still lacking. In addition, no studies have investigated the association between coffee consumption and MetS in the clinical setting of psoriasis, in particular considering the confounding effect of cigarette smoking. The aim of this observational study was to evaluate the association between coffee consumption and clinical severity of psoriasis in a sample of treatment-naïve psoriatic patients, stratified according to categories of MetS and cigarette smoking.

Methods

Design and setting

This is a cross-sectional case–control observational study carried out at the Department of Clinical Medicine and Surgery of the University of Naples Federico II (Italy), Unit of Endocrinology; from October 2015 to March 2017. The work has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans, and it has been approved by the Ethical Committee of the University of Naples "Federico II" Medical School (n. 265/15). The purpose of the protocol was explained to both the patients and the controls, and written informed consent was obtained. The study was conducted without support from the pharmaceutical industry.

Population study

The study has been conducted on 221 adult treatmentnaïve patients out of 359 unselected Caucasian subjects of both genders affected by psoriasis attending the Psoriasis Care Center of the Outpatient Clinic of the Section of Dermatology, University of Naples Federico II. To improve the power of the study, we increased the homogeneity of the patient sample by including treatment-naïve adult patients only. In particular, exclusion criteria were the following:

- diagnosis of psoriasis lasting < 6 months or subjects receiving any systemic treatment for psoriasis including acitretin, ciclosporin, methotrexate, phototherapy or biologics for at least 3 months (52 patients) or diagnosis of pustular (five patients), erythrodermic (three patient) or psoriatic arthritis (18 patients);
- 2. pregnancy or lactation in the past 6 months (three patients);
- history of excessive alcohol use according to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-V diagnostic criteria (four patients);
- 4. neoplastic, metabolic, hepatic, and cardiovascular disorder or other concurrent medical illness (i.e., renal disease, and malabsorptive disorders) (nine patients);
- 5. occasional or current of use of medications (whether prescribed or over the counter) or energy drinks and beverages containing high concentrations of caffeine,

such as Coca-Cola, red bull, guaranà, green tea, cacao, (23 patients);

6. decaffeinated coffee consumers (21 patients).

Two hundred twenty-one healthy subjects were chosen as controls among hospital volunteers and employees from the same geographical area. Controls were matched by age, sex and body mass index (BMI) and a full medical history, including drug use, was collected. The flow chart of study subjects is shown in Fig. 1.

Power size justification

The power size was calculated based on the following assumptions: 95% confidence interval (2-sided), and 221 psoriatic patients. In addition, we assumed that the prevalence rate was 0.22 between the sample participants with consumption of coffee (99 psoriatic patients, > 3 cups coffee per day) and with the total population subjects (442 participants). Based on these assumptions, the calculated power size was 91%. The effect size calculation between < 3 cups coffee per day (122 patients) and > 3 cups coffee per day (99 patients) in psoriatic patients sample was 0.44 by test for two proportion (Table 1).

Lifestyle habits

Lifestyle habits, including smoking and physical activity level, have been investigated by a standard questionnaire.

Fig. 1 Flow chart of study design



Table 1 Power size justificat	ion
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Power size Effect size		
Parameters Values Parameters	Values	
n 221 n (> 3 cups coffee per day) 9	99	
PR 0.22 n (<3 cups coffee per day)	122	
α 0.05 α 0	0.05	
$1-\beta$ 0.91 $1-\beta$ ().91	
ES).44	

PR prevalent rate, α I type-error; $1 - \beta$ power size, *ES* effect size

Subjects smoking at least one cigarette per day were considered current smokers, while former smokers were the subjects who stopped smoking at least one year before the interview. The remaining participants were defined as noncurrent smokers. Physical activity levels were expressed according to whether the participant habitually engaged in at least 30 min/day of aerobic exercise (YES/NO).

Assessment of coffee consumption

The daily caloric intake and coffee consumption data were collected using a 7-day food diary record (Welch et al. 2001; Goulet et al. 2004). Information on coffee brewing (instant coffee or espresso by Italian coffeepot) and use of additives, such as cream, milk, etc., was obtained. These data were carried out during a face-to-face interview between the patient and a certified nutritionist. On day one of the diary, nutritionists trained to standardized protocols provided participants with instructions on how to complete the diary at the health check and asked participants to recall the previous day's intake. Participants prospectively completed the remaining 6 days and returned the records to the nutritionist. Data were processed using a commercial software (Terapia Alimentare Dietosystem® DS-Medica, http://www.dsmed ica.info). This database was able to calculate the total energy intake, expressed in kilocalories (kcal).

The coffee consumption was analyzed in two separate models: (1) coffee intake (consumers and non-consumers) and (2) daily servings of coffee (range 0–4 servings/day). In particular, the first category: non-consumers; the second category: 1 cup coffee per day; the third category: 2 cups coffee per day; the fourth category: 3 cups coffee per day; the fifth category: more than 4 cups of coffee per day.

Anthropometric measurements and blood pressure

All anthropometric measurements were taken with subjects wearing only light clothes and without shoes. In each subject, weight and height were measured to calculate the BMI [weight (kg) divided by height squared (m²), kg/m²]. Height was measured to the nearest 1 cm using a wall-mounted

stadiometer (Seca 711; Seca, Hamburg, Germany). Body weight was determined to the nearest 50 g using a calibrated balance beam scale (Seca 711; Seca, Hamburg, Germany). BMI was classified according to WHO's criteria with normal weight: 18.5-24.9 kg/m²; overweight, 25.0-29.9 kg/ m²; grade I obesity, 30.0–34.9 kg/m²; grade II obesity, 35.0–39.9 kg/m²; grade III obesity \geq 40.0 kg/m² (WHO 2000). Waist circumference (WC) was measured to the closest 0.1 cm using a non-stretchable measuring tape at the natural indentation or at a midway level between lower edge of the rib cage and iliac crest if no natural indentation was visible, according to the National Center for Health Statistics (NCHS) (NCHS 2014). In all individuals, systolic (SBP) and diastolic (DBP) blood pressure were measured three times, two min apart, with a random zero sphygmomanometer (Gelman Hawksley Ltd., Sussex, UK) after the subject had been sitting for at least 10 min. The average of the second and third reading was recorded.

Biochemical measurements

Samples were collected in study population between 8 and 10 a.m. after an overnight fast of at least 8 h and stored at -80 °C until processed. All biochemical analyses including fasting plasma glucose, total cholesterol, triglycerides, were performed with a Roche Modular Analytics System in the Central Biochemistry Laboratory of our Institution. Low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol were determined by direct method (homogeneous enzymatic assay for the direct quantitative determination of LDL and HDL cholesterol). C-reactive protein (CRP) levels were determined with a nephelometric assay with CardioPhase high-sensitive from Siemens Health-care Diagnostics (Marburg, Germany).

Criteria to define metabolic syndrome

According to the National Cholesterol Education Program (NCEP)-Adult Treatment Panel (ATP III) definition, MetS is present if three or more of the following five criteria are met: WC over 102 and 88 cm (in male and female, respectively), blood pressure over 130/85 mmHg, fasting triglyceride level over 150 mg/dl, fasting HDL cholesterol level less than 40 and 50 mg/dl (in male and female, respectively) and fasting glucose over 100 mg/dl (NCEP-ATP III 2001).

Psoriasis Area and Severity Index (PASI)

The classic Psoriasis Area and Severity Index (PASI) score assesses the extent and severity of psoriasis. The extent of psoriasis is measured by the body area involved and the severity of erythema, induration and desquamation of the plaques. The body area involved is the percentage of area involved in a particular body region. For calculating classic PASI, the body is divided into four body regions: head, upper extremities, trunk and lower extremities. These four body regions correspond to approximately 10, 20, 30 and 40% of the total body surface area (BSA), respectively.

The PASI score is a validated and widely used tool for measuring psoriasis severity. The sum of the PASI scores for all four body regions is the total classic PASI score. The total classic PASI score ranges from 0 to 72 (Frediksson and Pettersson 1978; Spuls et al. 2010). To prevent rate biases, the dermatologists who evaluated the PASI score were blinded to the design of the study.

Statistical analysis

Results are expressed as mean ± standard deviation (SD) or as median plus range according to variable distributions evaluated by Kolmogorov–Smirnov test (p < 0.001). To correct for skewed distributions, CRP levels values were logarithmically transformed and back-transformed for presentation in tables. Differences between groups were analyzed by paired t test or Wilcoxon signed-rank test, when appropriate. A Chi-square (χ^2) test was used to test the significance of differences in frequency distribution. Differences in coffee consumption (yes/ no) and PASI score among smoking and MetS categories, were analyzed by unpaired t test for independent samples. When more than two groups were compared, analyses of variance (ANOVA) or Kruskal-Wallis test were performed, as appropriate, followed by Bonferroni post hoc analysis. Proportional Odds Ratio (OR) models, 95% Interval Confidence (IC), and Akaike Information Criterion (AIC), were performed to assess the association among quantitative variables (consumer and non-consumers of coffee). Multinomial logistic regression, probability, OR, IC and AIC, was performed to model the relationship between the PASI score and the five groups of daily servings of coffee (range 0-4 servings/day). In these analyses, we entered only those variables that had a p value < 0.05 in the univariate analysis. To avoid multicollinearity, variables with a variance inflation factor (VIP)>10 were excluded. Values $\leq 5\%$ were considered statistically significant. Data were stored and analyzed using the MedCalc® package (Version 12.3.0 1993-2012 MedCalc Software bvba, MedCalc Software, Mariakerke, Belgium). Proportional odds model and multinomial logistic regression were carried out using the R Project for Statistical Computing 2014 (http://www.R-proje ct.org).

Results

The study population consisted of 221 psoriatic patients, aged 21–59 years (57.5%, 127 males). Their mean value of PASI score was 8.13 ± 6.64 . All case patients completed

the 7-day food diary record. Mean total energy intake was 2747.39 ± 544.26 . Table 2 reports the anthropometric measurements, the clinical characteristics and lifestyle habits of the case patients and the subjects matched for age, sex and BMI, serving as control group. As expected, psoriatic patients presented worse anthropometric measurements and metabolic profile, and higher CRP levels compared to the control group (p < 0.001). Among psoriatic patients, there were more smokers than in controls, whereas there were no differences in their physical activity. Figure 2 shows that the prevalence of the single metabolic risk factors and MetS were significantly higher among case patients than controls (p < 0.001).

The coffee intake in two groups is shown in Fig. 3. No significant differences were found in the coffee intake between case patients and control group; in particular, coffee drinkers were 190 (86.0%) among case patients vs 176 among controls (79.6%); $\chi^2 = 2.69$, p = 0.101; in addition, the coffee preparation method was not different, as in both groups, the coffee drinkers did not consume instant coffee or used additives, such as cream, milk, etc. Considering the daily servings of coffee in psoriatic patients, the majority of psoriatic patients consumed 3 cups coffee per day (77 patients, 34.8%) (Fig. 4).

Table 3 summarizes the anthropometric measurements and clinical characteristics stratified according to the daily servings of coffee. The best anthropometric measurements and metabolic profile, in particular a lower number of Mets parameters (p < 0.001), were observed in subgroup of psoriatic patients consuming 3 cups coffee per day. In Fig. 5 were reported the PASI score and CRP levels in psoriatic patients grouped according to coffee intake or daily servings of coffee. The coffee consumers have lower PASI score $(7.02 \pm 6.05 \text{ vs } 14.90 \pm 6.13)$ and CRP levels $(3.92 \pm 4.23 \text{ vs } 5.75 \pm 5.99 \text{ ng/ml})$ compared to non-consumers (p < 0.001). Again, the lowest PASI score (2.89 ± 2.06) and CRP levels $(2.49 \pm 3.22 \text{ ng/ml})$ were found among psoriatic patients consuming 3 cups coffee per day (n = 77), while the highest PASI score (19.76 ± 5.15) and CRP levels $(8.60 \pm 5.76 \text{ ng/ml})$ were found among those drinking ≥ 4 cups per day.

In Table 4, mean PASI score values were reported according to coffee intake, smoking and MetS categories. Across all categories, coffee drinkers showed an overall lower PASI score compared to non-consumers, with the lowest PASI score in the category no smoking and no MetS (p < 0.001). In Table 5, mean of PASI score values were shown according to the daily servings of coffee, smoking and MetS categories. Across all daily servings of coffee, in the category no smoking and no MetS, the psoriatic patients drinking 3 cups coffee per day showed the lowest PASI score, while case patients drinking \geq 4 cups per day have the highest PASI score. Table 2Anthropometricmeasurements, clinicalcharacteristics and lifestylehabits of the case patients andthe subjects matched for age,sex and BMI, serving as controlgroup

Parameters	Psoriatic patients, $n = 221$	Control group, $n = 221$	p values
Age (years)	37.0 (21.0–59.0)	36.0 (20.0-49.0)	0.508
Gender, males $(n, \%)$	127, (57.5%)	127, (57.5%)	$\chi^2 = 0.009, p = 0.923$
BMI (kg/m ²)	30.4 ± 5.8	29.7 ± 7.3	0.295
Normal weight $(n, \%)$	43, 19.5%	67, 30.3%	$\chi^2 = 6.40, p = 0.011$
Overweight (n, %)	68, 30.8%	63, 28.5%	$\chi^2 = 0.17, p = 0.677$
Obesity I (n, %)	64, 29.0%	46, 20.8%	$\chi^2 = 3.49, p = 0.062$
Obesity II (n, %)	36, 16.3%	19, 8.6%	$\chi^2 = 5.32, p = 0.021$
Obesity III (n, %)	10, 4.5%	26, 11.8%	$\chi^2 = 6.80, p = 0.009$
WC (cm)	108.0 (69.0-156.0)	97.0 (61.0–147.0)	< 0.001
SBP (mmHg)	130.0 (100.0–165.0)	120.0 (90.0-165.0)	0.003
DBP (mmHg)	80.0 (50.0-100.0)	75.0 (50.0-100.0)	< 0.001
Fasting glucose (mg/dl)	104.0 (65.0–199.0)	94.0 (59.0–198.0)	0.002
Total cholesterol (mg/dl)	205.6 ± 50.0	190.9 ± 54.4	0.003
HDL cholesterol (mg/dl)	39.0 (22.0–79.0)	44.0 (26.0–71.0)	0.007
LDL cholesterol (mg/dl)	135.7 ± 45.9	123.1 ± 51.2	0.008
Triglycerides (mg/ml)	163.3±75.4	141.3 ± 41.9	< 0.001
CRP levels (ng/ml) ^a	2.8 (0.10-30.24)	0.9 (0.10-3.98)	< 0.001
Physical activity			
Sedentary (n, %)	154, 69.7%	149, 67.4%	$\chi^2 = 0.17$
Moderate $(n, \%)$	67, 30.3%	72, 32.6%	p = 0.682
Smoking			
Yes (<i>n</i> , %)	126, 57.0%	97, 43.9%	$\chi^2 = 7.09$
No (<i>n</i> , %)	95, 43.0%	124, 56.1%	p = 0.008

The psoriatic patients exhibited statistically significant differences compared to controls for BMI, WC, blood pressure, metabolic profiles, CRP levels and smoking habit

Results are expressed as mean \pm SD or as median plus range according to variable distributions evaluated by Kolmogorov–Smirnov test

^aCRP levels was logarithmically transformed and back-transformed for presentation in table. Differences between groups were analyzed by paired *t* test or Wilcoxon signed-rank test, when appropriate. The Chi-square (χ^2) test was used to determine the significance of differences in physical activity and smoking habit between the two groups. A *p* value in bold type denotes a significant difference (p < 0.05)

BMI body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *CRP* C-reactive protein

Correlation studies

In Table 6 was reported a bivariate proportional odds ratio model performed to assess the association of coffee intake with anthropometric measures, metabolic and inflammatory profile, and lifestyle habits. Coffee intake was associated positively with HDL cholesterol and physical activity, and negatively with triglycerides, inflammatory profile, MetS presence, and smoking. Table 7 shows the multinomial logistic regression model performed to assess the association among five different servings of coffee consumption with the PASI score adjusted for total energy intake. Grouping the case patients according to smoking and MetS, the best odds of PASI score was observed in those drinking 3 cups coffee per day with no smoking and without MetS, independently for total energy intake (OR 74.8, p < 0.001).

Discussion

The present study evidenced a negative association between coffee intake, MetS prevalence and clinical severity of psoriasis in a sample of treatment-naïve psoriatic patients. According to the current literature supporting the inflammatory link between psoriasis and with MetS, we confirmed that among psoriatic patients, there was a greater presence of MetS compared to age, sex and BMI-matched control group (Rodríguez-Zúñiga and García-Perdomo 2017). As novel findings, we evidenced that psoriatic patients who consumed coffee presented lower clinical severity and better anthropometric measurements and metabolic profile compared to non-consumers, independently of gender and total energy intake calculated by the 7-day food diary record. Of interest is that stratifying the study group of psoriatic patients according to the daily servings of coffee, smoking habits



Fig. 2 Frequency of metabolic risk factors and prevalence of the MetS in psoriatic patients and control group. The psoriatic patients exhibited statistically significant differences in all the MetS parameters compared to controls: WC (71.5 vs 51.1%; $\chi^2 = 18.5$, p < 0.001), SBP/DBP (43.9 vs 28.5%; $\chi^2 = 10.7$, p = 0.001), triglycerides (59.7 vs 25.8%; $\chi^2 = 50.6$, p < 0.001), HDL-C (62.0 vs 30.8%; $\chi^2 = 42.7$, p < 0.001); fasting glucose (59.3 vs 43.4%; $\chi^2 = 10.5$, p = 0.002) and MetS presence/absence (64.3 vs 31.2%; $\chi^2 = 47.0$, p < 0.001), respectively. The MetS is defined according to the NCEP ATP III definition



Fig. 3 Coffee intake in psoriatic patients and control group. No significant differences were found in the coffee intake between case patients and control group. Coffee drinkers were 190 (86.0%) among case patients vs 176 among controls (79.6%); $\chi^2 = 2.69$, p = 0.101. Results are expressed as percentage. The Chi-square (χ^2) test was used to test the significance of differences in the frequency of coffee consumers between the two groups. A *p* value in bold type denotes a significant difference (p < 0.05)

(Expert Panel on Detection 2001). Results are expressed as percentage. The Chi-square (χ^2) test was used to determine the significance of differences in the frequencies between the two groups. A *p* value in bold type denotes a significant difference (p < 0.05). WC waist circumference, SBP systolic blood pressure, DBP diastolic blood pressure, HDL-C high-density lipoprotein cholesterol, MetS metabolic syndrome, NCEP ATP III National Cholesterol Education Program Adult Treatment Panel

and presence/absence of MetS, the category of patients consuming of 3 cups of coffee per day, no smokers and without MetS, presented the lowest PASI score compared to the other categories, independently of total energy intake.

Psoriasis is a common, chronic, immune-mediated skin disease with systemic pro-inflammatory activation, where both environmental and genetic factors contribute to its pathogenesis (Ahdout et al. 2012). The treatment of environmental modifiable risk factors, such as diet and nutrition, and modulation of the systemic inflammatory response are important therapeutic goals in the integrated management of psoriatic patients (Trojacka et al. 2015; Balato et al. 2015b). Among the risk factors for psoriasis, evidence is accumulating that nutrition plays a major role per se in psoriasis pathogenesis and dietary factors can affect both drug's pharmacokinetics and pharmacodynamics (Kim and Lee 2013). Single food components have been suggested to play a role in etiology and pathogenesis of psoriasis (Wolters 2006; Millsop et al. 2014).

Coffee is among the most widely consumed pharmacologically active beverages, and its consumption has become a regular part of daily life worldwide. Coffee is one of the major contributors of caffeine to the diet (Mitchell et al. 2015). Caffeine, which represents no more than 1% of the

Fig. 4 Daily servings of coffee in psoriatic patients. The daily servings of coffee consumption (range 0-4 servings/ day) were analyzed. The first category: non-consumers; the second category: 1 cup coffee per day; the third category: 2 cups coffee per day; the fourth category: 3 cups coffee per day; the fifth category: more than 4 cups of coffee per day. Results are expressed as percentage. The majority of the 190 coffee drinking patients (77 patients) consumed 3 cups coffee per day (34.8%)



Table 3 Anthropometric measures and metabolic profile of psoriatic patients according to daily servings of coffee (0-4 servings/day)

Parameters	Daily servings of coffee consumption (cups per day)					
	0 cups	1 cup	2 cups	3 cups	\geq 4 cups	p value
	<i>n</i> =31, 14.0%	<i>n</i> =32, 14.5%	n=59, 26.7%	<i>n</i> =77, 34.8%	n=22, 10.0%	
Age (years)	36.0 (21.0–50.0)	39.0 (23.0–50.0)	37.0 (24.0–59.0)	36.0 (21.0–59.0)	36.5 (21.0–54.0)	0.449
BMI (kg/m ²)	30.9 ± 5.4	30.8 ± 5.6	29.3 ± 4.6	29.4 ± 6.1	35.5 ± 5.7	< 0.001
WC (cm)	109.0 (72.0-149.0)	109.5 (81.0–149.0)	105.0 (69.0–142.0)	98.0 (69.0-142.0)	134.5 (106.0–156.0)	< 0.001
SBP (mmHg)	135.0 (100.0–150.0)	135.0 (100.0–150.0)	125.0 (100.0–155.0)	120.0 (110.0–165.0)	140.0 (110.0–160.0)	< 0.001
DBP (mmHg)	80.0 (60.0-100.0)	85.0 (60.0-100.0)	80.0 (50.0-95.0)	75.0 (60.0–95.0)	85.0 (60.0-100.0)	0.002
Fasting glucose (mg/dl)	104.0 (70.0–196.0)	112.5 (68.0–190.0)	101.0 (65.0–149.0)	102.0 (68.0–197.0)	121.5 (71.0–199.0)	0.024
Total cholesterol (mg/ dl)	213.4 ± 50.6	207.5 ± 42.7	207.1 ± 44.9	188.6 ± 46.3	247.0 ± 59.9	< 0.001
HDL cholesterol (mg/ dl)	35.0 (24.0-63.0)	38.5 (22.0–79.0)	43.0 (23.0-64.0)	46.0 (26.0–79.0)	31.5 (24.0–51.0)	< 0.001
LDL cholesterol (mg/ dl)	139.4 ± 47.6	139.6 ± 41.3	137.9 ± 42.6	116.9±43.0	180.0 ± 42.0	< 0.001
Triglycerides (mg/ml)	194.5 ± 68.4	158.9 ± 64.7	155.4 ± 75.6	137.9 ± 68.0	236.0 ± 68.0	< 0.001
MetS (number param- eters)	3.4 ± 1.2	3.6 ± 1.1	2.7 ± 1.4	2.2 ± 1.5	4.2 ± 0.8	< 0.001
Energy intake (kcal)	2739.9 ± 504.8	2720.3 ± 523.6	2629.9 ± 513.9	2757.9 ± 550.0	3075.6 ± 597.5	0.027

The best anthropometric measurements and metabolic profile, in particular a lower number of MetS parameters (p < 0.001) were observed in the subgroup of psoriatic patients consuming 3 cups coffee per day

Results are expressed as mean \pm SD or as median plus range according to variable distributions evaluated by Kolmogorov–Smirnov test. Differences between groups were analyzed by ANOVA or Kruskal–Wallis test, when appropriate. A *p* value in bold type denotes a significant difference (*p* < 0.05)

BMI body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *MetS* metabolic syndrome

total coffee composition, is a biologically active natural metabolite with widely recognized therapeutic effects (Montagnana et al. 2012). Caffeine exerts a number of biological effects, acting also on inflammation and immune system (Festugato 2011; Hall et al. 2015). Caffeine is able to reduce the migration of monocytes and neutrophils, blood cells closely involved in mediating of inflammation and activation of adaptive immune system (Sharif et al. 2017). This interesting role of caffeine in immunosuppression, and specifically in autoimmune diseases, is also explained by the inhibition of the release of pro-inflammatory cytokines and Th1/Th2 cell proliferation. At high doses, caffeine is able to



Fig. 5 The PASI score and CRP levels in psoriatic patients grouped according to coffee intake (yes/no) and daily servings of coffee (range 0–4 servings/day). The coffee consumers (n=190) have lower PASI score (7.02±6.05 vs 14.90±6.13) and CRP levels (3.92±4.23 vs 5.75±5.99 ng/ml) compared to non-consumers (n=31) (p<0.001). The lowest PASI score (2.89±2.06) and CRP levels (2.49±3.22 ng/ml) were found among psoriatic patients consuming 3 cups coffee per day (n=77), while the highest PASI score (19.76±5.15) and CRP levels (8.60±5.76 ng/ml) were found among those drinking≥4 cups per day. One cup coffee per day (n=32): PASI score (9.45±3.44) and CRP levels (3.84±4.41 ng/ml); 2 cups coffee per day (n=59): PASI score (6.34±3.16) and CRP levels (4.06±3.93 ng/ml). Results are expressed as mean±SD. CRP levels was logarithmically transformed and back-transformed for presentation in figure. Differences between two groups were analyzed by paired t test, while the differences

inhibit the Cyclic Adenosine MonoPhosphate (cAMP) phosphodiesterase, resulting in increased cAMP levels, which acts as immunomodulator and stimulates the release of antiinflammatory cytokines (Sharif et al. 2017), in particular in immune cells (Festugato 2011). In addition, caffeine acts as a receptor antagonist of adenosine (Gökcen and Şanlier 2017). However, coffee is a complex mixture of chemicals and, beyond caffeine, it also contains thousands of different chemicals, including carbohydrates, lipids, nitrogenous compounds, vitamins, minerals, alkaloids, and phenolic compounds with different functional properties (Spiller 1984; Bae et al. 2014). Several mechanisms have been proposed to explain the role of bioactive compounds of coffee on systemic inflammation. Coffee habitual consumption, in human and in animal models, can reduce the levels of interleukin (IL)-1 β , IL-6, tumor necrosis factor (TNF)- α and

among more than two groups were analyzed by ANOVA, followed by Bonferroni post hoc analysis. A *p* value in bold type denotes a significant difference (p < 0.05). *PASI* Psoriasis Area Severity Index; *CRP* C-reactive protein, *NF-* κ *B* nuclear factor kappa B, *ROS* reactive oxygen species, *MetS* metabolic syndrome, *BMI* body mass index, *kcal* kilocalories, *WC* waist circumference, *NCHS* National Center for Health Statistics, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *CRP* C-reactive protein, *NCEP-ATP III* National Cholesterol Education Program-Adult Treatment Panel, *PASI* Psoriasis Area and Severity Index, *BSA* body surface area, *SD* standard deviation, *OR* odds ratio, *IC* interval confidence, *AIC* Akaike information criterion, *cAMP* Cyclic Adenosine MonoPhosphate, *IL* interleukin, *TNF* tumor necrosis factor, *INF* interferon

CRP levels; on the other hand, it can increase anti-inflammatory markers, such as adiponectin, IL-4 and IL-10 levels (Akash et al. 2014). Probably, this anti-inflammatory effect might be specifically linked to the polyphenols contained in coffee. These polyphenols, in particular chlorogenic acid and its metabolites, are able to inhibit in vitro the activation of NF-kB in a dose-dependent manner, acting against the oxidative stress due to ROS accumulation and inhibiting pro-inflammatory mediators synthesis and release (in particular, TNF- α , IL-1 β and -6, and Interferon (INF)- γ), while caffeic acid causes a decreasing in nitrite levels and inhibition of inflammation pathways (Hall et al. 2015). Interestingly, in coffee specific polysaccharides are present (such as arabinogalactan proteins) which act as immunomodulatory agents, stimulating splenocytes and peritoneal macrophages proliferation, resulting in improving dermatitis and allergic

Parameters	PASI score			
	n	$Mean \pm SD$	p value	
Smoking				
Coffee consumption	103	10.8 ± 5.9	< 0.001	
No coffee consumption	23	17.6 ± 4.7		
No smoking				
Coffee consumption	87	2.6 ± 1.7	< 0.001	
No coffee consumption	8	7.2 ± 0.9		
MetS				
Coffee consumption	116	9.1 ± 6.4	< 0.001	
No coffee consumption	26	15.7 ± 6.2		
No MetS				
Coffee consumption	74	3.8 ± 3.5	< 0.001	
No coffee consumption	5	10.6 ± 3.6		
No smoking/no MetS				
Coffee consumption	51	1.9 ± 1.3		
No coffee consumption	3	8.1 ± 0.9	< 0.001	

 Table 4
 Differences of clinical severity of psoriasis according to coffee intake, smoking and MetS categories

Across all categories, coffee drinkers showed an overall lower PASI score compared to non-consumers, with the lowest PASI score in the category no smoking and no MetS. Results are expressed as mean \pm SD according to variable distributions evaluated by Kolmogorov–Smirnov test. Differences between two groups were analyzed by *t* test for independent samples. A *p* value in bold type denotes a significant difference (*p* < 0.05)

PASI Psoriasis Area Severity Index, MetS metabolic syndrome, SD standard deviation

reactivity (Gökcen and Şanlier 2017). As support for its antiinflammatory effects, an in vitro study suggested that coffee extract was able to exert anti-inflammatory and immunosuppressant activity (Gökcen and Şanlier 2017).

No previous studies have investigated in psoriatic patients the association between daily servings of coffee and clinical severity of the disease in treatment-naïve patients, after adjustment for known confounders, such as smoking habit and MetS. Out of 3 studies evaluating the association between coffee consumption and psoriasis, 2 of them used these variables as dichotomous ones (yes/no), thus providing only a rough estimate of coffee intake and psoriasis (Duffy et al. 1993; Swanson et al. 2007); in addition, the clinical severity of psoriasis was not taken into consideration. Coffee consumption has often been measured by items on dietary questionnaires and interviews and, with respect to measuring coffee consumption, studies have noted sufficiently repeatability (Sääksjärvi et al. 2010). By contrast, 7-day food record, considered the "gold standard" of self-administered food frequency questionnaires, allows a more accurate measurement of the real total energy intake, and of single foods and beverages, such as coffee, compared to those obtained by retrospective food frequency questionnaires (Thompson
 Table 5
 Differences of clinical severity of psoriasis according to the daily servings of coffee, smoking and MetS categories

Parameters	n	PASI score	p values
Smoking		12.0 ± 6.2	< 0.001
1 cup coffee per day	23	10.9 ± 3.0	-
2 cups coffee per day	37	8.4 ± 1.6	-
3 cups coffee per day	21	5.5 ± 1.7	-
≥4 cups coffee per day	22	19.8 ± 5.2	-
No smoking		3.0 ± 2.1	< 0.001
1 cup coffee per day	9	5.8 ± 0.4	-
2 cups coffee per day	22	2.8 ± 1.6	-
3 cups coffee per day	56	1.9 ± 1.1	-
\geq 4 cups coffee per day	0	-	-
MetS		10.3 ± 6.8	< 0.001
1 cup coffee per day	27	9.6 ± 3.5	-
2 cups coffee per day	38	6.9 ± 2.8	-
3 cups coffee per day	30	3.9 ± 2.4	-
\geq 4 cups coffee per day	21	19.8 ± 5.3	-
No MetS		4.2 ± 3.9	< 0.001
1 cup coffee per day	5	8.6 ± 3.5	
2 cups coffee per day	21	5.2 ± 3.4	
3 cups coffee per day	47	2.2 ± 1.5	
\geq 4 cups coffee per day	1	19.6	
No smoking/No MetS			< 0.001
1 cup coffee per day	0	_	
2 cups coffee per day	11	2.3 ± 1.4	
3 cups coffee per day	40	1.7 ± 1.1	
\geq 4 cups coffee per day	0	-	

Results are expressed as mean \pm SD, according to variable distributions evaluated by Kolmogorov–Smirnov test. Differences between groups were analyzed by ANOVA. A *p* value in bold type denotes a significant difference (*p* < 0.05)

Across all daily servings of coffee, in the category no smoking and no MetS, the psoriatic patients drinking 3 cups coffee per day showed the lowest PASI score, while case patients drinking \geq 4 cups per day have the highest PASI score

PASI Psoriasis Area Severity Index, MetS metabolic syndrome, SD standard deviation

and Subar 2013; Hoidrup et al. 2002). In the third study, Li et al. (2012) reported that the risk of psoriasis was moderately elevated with increasing coffee consumption in an ageadjusted model, although this trend became not significant after adjusting for smoking, whereas the decaffeinated coffee was not significantly associated with this risk. Although these authors provided a detailed description of caffeine intake, which was calculated according to the method of the US Department of Agriculture food composition data, in this study all the caffeinated beverages were included, with a possible misleading effect due to their high sugar and energy ratio (Li et al. 2012). In addition, in this study, the diagnosis of psoriasis, although confirmed using the Psoriasis Screening Tool questionnaire, was ascertained by self-report on

 Table 6
 Bivariate proportional odds ratio model performed to assess

 the association of coffee intake with anthropometric measures, metabolic and inflammatory profile, and lifestyle habits

Parameters	OR	p value	95% CI	AIC
Gender		0.272		182.01
Male	0.65		0.26-1.04	
Female	1.53		1.14-1.92	
Age (years)	1.02	0.370	0.99-1.04	182.40
BMI (kg/m ²)	0.98	0.596	0.98 - 1.05	182.93
WC (cm)	0.99	0.681	0.98 - 1.00	183.04
SBP (mmHg)	0.98	0.418	0.97 - 1.00	182.56
DBP (mmHg)	1.00	0.825	0.98 - 1.02	183.16
Fasting glucose (mg/dl)	0.99	0.049	0.98-1.01	182.44
Total cholesterol (mg/dl)	0.99	0.046	0.99-1.00	182.32
HDL cholesterol (mg/dl)	1.04	0.047	1.02-1.06	178.82
LDL cholesterol (mg/dl)	0.99	0.036	0.99-1.01	176.24
Triglycerides (mg/ml)	0.99	0.016	0.99-1.00	177.58
CRP levels (ng/ml) ^a	0.92	0.044	0.89–0.96	179.43
PASI score	0.85	< 0.001	0.82 - 0.88	150.31
MetS				
Yes	0.30	0.018	2.81-3.83	176.48
No	3.31		0.21-0.81	
Physical activity		0.007		166.27
Sedentary	0.06		14.94–16.99	
Moderate	15.96		0.96-1.09	
Smoking		0.041		178.65
Yes	2.42		1.99-2.86	
No	0.41		0.02-0.85	

Coffee intake was associated positively with HDL cholesterol and physical activity, and negatively with triglycerides, inflammatory profile, MetS presence, and smoking. Proportional odds model were carried out using the R Project for Statistical Computing 2014 (http://www.R-project.org)

OR odds ratio, *CI* confidence interval, *AIC* Akaike information criterion, *BMI* body mass index, *WC* waist circumference, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *CRP* C-reactive protein, *PASI* Psoriasis Area Severity Index, *MetS* metabolic syndrome

^aCRP levels was logarithmically transformed and back-transformed for presentation in table

questionnaires, and there were no indications on the clinical severity of the disease or medication use (treatment-naïve/ on treatment). Interestingly, the authors also reported that coffee improved the efficacy of psoriasis pharmacological treatment, such as methotrexate and sulfasalazine (Li et al. 2012).

It is, however, important to consider that the cross-sectional studies reported have examined the effects of longterm coffee consumption, while the effect observed in the initial consumption of coffee, and the effect following recurring consumption could be different. In particular, during the acute inflammatory state, caffeine had been reported to exert a pro-inflammatory activity, resulting in increased inflammatory markers levels, including TNF- α and β , IL-6 and INF-y. Interestingly, these pro-inflammatory cytokines, exert in psoriasis a clear mitogen activity for keratinocytes (Festugato 2011). Nevertheless, although several studies reported pro-inflammatory effects of caffeine, others underlined a converse effect, anti-inflammatory by increasing IL-10 (Sharif et al. 2017) and inhibiting TNF- α production in vitro (Hall et al. 2015). As a support for these findings, the use of topical formulation of caffeine on plaque psoriasis resulted in a significant improvement in psoriasis area and severity index in a double-blinded placebo controlled study which demonstrated (Vali et al. 2005). In this respect, our study evidenced that the coffee intake exerted a beneficial effect on psoriasis clinical severity and this effect was also dose-related. In fact, we found out that CRP levels and PASI score decreased as much as the coffee's daily consumption increases. However, this relationship was lost when the subjects took more than 4 cups daily and this could be explained by a possible pro-inflammatory effect of excessive coffee intake, as previously reported (Lopez-Garcia et al. 2006; Zampelas et al. 2004; Corrêa et al. 2013). In particular, Zampelas et al. (2004), in a cross-sectional survey enrolled a large number of adults aimed to investigate the association between coffee consumption and inflammatory markers, and found that coffee consumption < 200 ml/day was related to higher plasma concentrations of IL-6, CRP levels, and TNF- α , lending support to the hypothesis that compounds in this beverage could contribute to increased inflammation (Zampelas et al. 2004). This relation could explain, in part, the effect of increased coffee consumption on the clinical severity of psoriasis that we observed in our study.

We are aware that there are some limitations in the current study. First, the cross-sectional nature of this study did not allow determine whether any cause-and-effect relationship exists between coffee intake and clinical severity of psoriasis. Second, in this study, we did not include the psoriatic patients who consumed the decaffeinated coffee. Therefore, we cannot determine the relative contribution of caffeine or polyphenols to our results. Third, the sample size is relatively small and a larger group of patients would have been more informative. However, for greater statistical accuracy, we calculated the power size justification, which was of 91% and the effect size calculation between <3 cups coffee per day and >3 cups coffee per day of coffee in psoriatic patients sample was 0.44 by test for two proportion. Further strengths of this study include that the diagnosis of psoriasis was not self-reported, but clinically evaluated using the PASI score by an experienced dermatologist, and the possible interference of the anti-psoriatic agents was controlled by including only treatment-naïve patients; in addition, the nutritional status was evaluated using the 7-day food diary record, by an experienced nutritionist. This method, which is considered as the "gold standard" in **Table 7** Multinomial logistic regression model performed to assess the association among five different servings of coffee (0 to \geq 4 cups coffee per day) with the PASI score, after adjusting for the total energy intake

Parameters	n	Probability	<i>p</i> value	OR	AIC	95% CI
Smoking	126					
0 cup coffee per day	23	(intercept)	(intercept)	(intercept)	250.66	
1 cup coffee per day	23	- 0.45	< 0.001	0.61		0.47-0.75
2 cups coffee per day	37	- 0.63	< 0.001	1.01		0.85 - 1.17
3 cups coffee per day	21	- 0.83	< 0.001	1.81		1.57-2.06
≥4 cups coffee per day	22	0.07	< 0.001	0.07		0.01-0.13
No smoking	95					
0 cup coffee per day	8	(intercept)	(intercept)	(intercept)	107.53	
1 cup coffee per day	9	- 0.95	< 0.001	9.71		9.70-9.72
2 cups coffee per day	22	- 0.95	< 0.001	74.2		74.28-74.30
3 cups coffee per day	56	- 0.95	< 0.001	74.8		74.80-74.82
\geq 4 cups coffee per day	_	_	_	_		_
MetS	142					
0 cup coffee per day	26	(intercept)	(intercept)	(intercept)	322.38	
1 cup coffee per day	27	- 0.25	< 0.001	0.28		0.21-0.36
2 cups coffee per day	38	- 0.39	< 0.001	0.49		0.41-0.58
3 cups coffee per day	30	- 0.59	< 0.001	0.91		0.77 - 1.05
≥4 cups coffee per day	21	- 0.13	< 0.001	0.12		0.07-0.18
No MetS	79					
0 cup coffee per day	5	(intercept)	(intercept)	(intercept)	132.83	
1 cup coffee per day	5	- 0.18	< 0.001	0.20		0.01-0.39
2 cups coffee per day	21	- 0.40	< 0.001	0.52		0.35-0.69
3 cups coffee per day	47	- 0.65	< 0.001	1.05		0.85-1.25
\geq 4 cups coffee per day	1	_	-	_		_
No smoking/No MetS	54					
0 cup coffee per day	3	(intercept)	(intercept)	(intercept)	225.29	
1 cup coffee per day	_	-	_	-		_
2 cups coffee per day	11	- 0.47	0.004	0.57		0.44-0.69
3 cups coffee per day	40	- 0.72	< 0.001	1.12		0.96-1.28
\geq 4 cups coffee per day	-	-	-	-		-

Grouping the case patients according to smoking and MetS, the best odds of PASI score was observed in those drinking 3 cups coffee *per* day no-smoking, independently for total energy intake (OR 74.8, p < 0.001)

A p value in bold type denotes a significant difference (p < 0.05). Multinomial logistic regression were carried out using the R Project for Statistical Computing 2014 (http://www.R-project.org)

PASI Psoriasis Area Severity Index, OR odds ratio, AIC Akaike information criterion, CI confidence interval, MetS metabolic syndrome

validation studies of different types of self-administered food frequency questionnaires, allowed to better characterize the coffee intake as daily servings and total energy intake. Moreover, in spite of the wide variability in the coffee preparation methods reported across the other studies, and consequently in caffeine content, all the participants in this study have the same geographical origin and consumed coffee in the Italian style.

Conclusions

Caffeine is the most frequently consumed pharmacologically active substance globally. Because of its wide consumption in the population, the evaluation of the anti-inflammatory effect of coffee on clinical severity of psoriasis, whose metabolic risk increases along with its clinical severity, could be of great importance from a public health perspective. The novel association between coffee consumption, MetS prevalence and clinical severity of psoriasis suggests that a growing cooperation among nutritionists, endocrinologists and dermatologists might provide a combination key in the complex management of the psoriatic patients and may encourage further studies to evaluate the effects of the changes in coffee intake on psoriasis. Future studies comparing long-term consumption of caffeinated coffee and decaffeinated coffee containing bioactive components, such as polyphenols, on clinical severity in psoriatic patients may be of interest.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

References

- Ahdout J, Kotlerman J, Elashoff D, Kim J, Chiu MW (2012) Modifiable lifestyle factors associated with metabolic syndrome in patients with psoriasis. Clin Exp Dermatol 37(5):477–483. https://doi.org /10.1111/j.1365-2230.2012.04360.x
- Akash MS, Rehman K, Chen S (2014) Effects of coffee on type 2 diabetes mellitus. Nutrition 30(7–8):755–763. https://doi.org/10.1016/j. nut.2013.11.020
- Altieri B, Muscogiuri G, Barrea L, Mathieu C, Vallone CV, Mascitelli L, Bizzaro G, Altieri VM, Tirabassi G, Balercia G, Savastano S, Bizzaro N, Ronchi CL, Colao A, Pontecorvi A, Della Casa S (2017) Does vitamin D play a role in autoimmune endocrine disorders? A proof of concept. Rev Endocr Metab Disord 18(3):335– 346. https://doi.org/10.1007/s11154-016-9405-9
- Bae JH, Park JH, Im SS, Song DK (2014) Coffee and health. Integr Med Res 3(4):189–191. https://doi.org/10.1016/j.imr.2014.08.002
- Balato N, Napolitano M, Ayala F, Patruno C, Megna M, Tarantino G (2015a) Nonalcoholic fatty liver disease, spleen and psoriasis: new aspects of low-grade chronic inflammation. World J Gastroenterol 21(22):6892–6897. https://doi.org/10.3748/wjg.v21. i22.6892
- Balato N, Megna M, Palmisano F, Patruno C, Napolitano M, Scalvenzi M, Ayala F (2015b) Psoriasis and sport: a new ally? J Eur Acad Dermatol Venereol 29(3):515–520. https://doi.org/10.1111/ jdv.12607

- Barrea L, Balato N, Di Somma C, Macchia PE, Napolitano M, Savanelli MC, Esposito K, Colao A, Savastano S (2015a) Nutrition and psoriasis: is there any association between the severity of the disease and adherence to the Mediterranean diet?. J Transl Med 13:18. https://doi.org/10.1186/s12967-014-0372-1
- Barrea L, Macchia PE, Tarantino G, Di Somma C, Pane E, Balato N, Napolitano M, Colao A, Savastano S (2015b) Nutrition: a key environmental dietary factor in clinical severity and cardiometabolic risk in psoriatic male patients evaluated by 7-day food-frequency questionnaire. J Transl Med 13:303. https://doi. org/10.1186/s12967-015-0658-y
- Barrea L, Nappi F, Di Somma C, Savanelli MC, Falco A, Balato A, Balato N, Savastano S (2016a) Environmental risk factors in psoriasis: the point of view of the nutritionist. Int J Environ Res Public Health. https://doi.org/10.3390/ijerph13070743
- Barrea L, Macchia PE, Di Somma C, Napolitano M, Balato A, Falco A, Savanelli MC, Balato N, Colao A, Savastano S (2016b) Bioelectrical phase angle and psoriasis: a novel association with psoriasis severity, quality of life and metabolic syndrome. J Transl Med 14(1):130. https://doi.org/10.1186/s12967-016-0889-6
- Barrea L, Savanelli MC, Di Somma C, Napolitano M, Megna M, Colao A, Savastano S (2017) Vitamin D and its role in psoriasis: an overview of the dermatologist and nutritionist. Rev Endocr Metab Disord 18(2):195–205. https://doi.org/10.1007/ s11154-017-9411-6
- Baspinar B, Eskici G, Ozcelik AO (2017) How coffee affects metabolic syndrome and its components. Food Funct 8(6):2089–2101. https ://doi.org/10.1039/c7fo00388a
- Chu YF, Hu K, Hatzold T, Black RM, Chen D (2013) Flaking process increases the NF-κB inhibition activity and melanoidin extractability of coffee. Food Sci Nutr 1(5):363–368. https://doi. org/10.1002/fsn3.19
- Corrêa TA, Rogero MM, Mioto BM, Tarasoutchi D, Tuda VL, César LA, Torres EA (2013) Paper-filtered coffee increases cholesterol and inflammation biomarkers independent of roasting degree: a clinical trial. Nutrition 29(7–8):977–981. https://doi. org/10.1016/j.nut.2013.01.003
- Duffy DL, Spelman LS, Martin NG (1993) Psoriasis in Australian twins. J Am Acad Dermatol 29(3):428–434
- Expert Panel on Detection (2001) Evaluation, and treatment of high blood cholesterol in adults: executive summary of the third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). JAMA 285(19):2486–2497
- Festugato M (2011) Pilot study on which foods should be avoided by patients with psoriasis. An Bras Dermatol 86(6):1103–1108
- Fleming P, Kraft J, Gulliver WP, Lynde C (2015) The relationship of obesity with the severity of psoriasis: a systematic review. J Cutan Med Surg 19(5):450–456. https://doi.org/10.1177/12034 75415586332
- Floegel A, Pischon T, Bergmann MM, Teucher B, Kaaks R, Boeing H (2012) Coffee consumption and risk of chronic disease in the European Prospective Investigation into Cancer and Nutrition (EPIC)-Germany study. Am J Clin Nutr 95(4):901–908. https:// doi.org/10.3945/ajcn.111.023648
- Frediksson T, Pettersson U (1978) Severe psoriasis oral therapy with a new retinoid. Dermatologica 157:238–244
- Freedman ND, Park Y, Abnet CC, Hollenbeck AR, Sinha R (2012) Association of coffee drinking with total and cause-specific mortality. N Engl J Med 366(20):1891–1904. https://doi.org/10.1056/ NEJMoa1112010
- Ganzetti G, Campanati A, Molinelli E, Offidani A (2016) Psoriasis, non-alcoholic fatty liver disease, and cardiovascular disease: Three different diseases on a unique background. World J Cardiol 8(2):120–131. https://doi.org/10.4330/wjc.v8.i2.120

- Gisondi P, Galvan A, Idolazzi L, Girolomoni G (2015) Management of moderate to severe psoriasis in patients with metabolic comorbidities. Front Med (Lausanne) 2:1. https://doi.org/10.3389/ fmed.2015.00001
- Gökcen BB, Şanlier N (2017) Coffee consumption and disease correlations. Crit Rev Food Sci Nutr. https://doi.org/10.1080/10408 398.2017.1369391
- Goulet J, Nadeau G, Lapointe A, Lamarche B, Lemieux S (2004) Validity and reproducibility of an interviewer-administered food frequency questionnaire for healthy French-Canadian men and women. Nutr J 3:13. https://doi.org/10.1186/1475-2891-3-13
- Grosso G, Godos J, Galvano F, Giovannucci EL (2017) Coffee, caffeine, and health outcomes: an umbrella review. Annu Rev Nutr 37:131–156. https://doi.org/10.1146/annurev-nutr-071816-064941
- Guida B, Napoleone A, Trio R, Nastasi A, Balato N, Laccetti R, Cataldi M (2014) Energy-restricted, n-3 polyunsaturated fatty acids-rich diet improves the clinical response to immuno-modulating drugs in obese patients with plaque-type psoriasis: a randomized control clinical trial. Clin Nutr 33(3):399–405. https://doi.org/10.1016/j. clnu.2013.09.010
- Hall S, Desbrow B, Anoopkumar-Dukie S, Davey AK, Arora D, McDermott C, Schubert MM, Perkins AV, Kiefel MJ, Grant GD (2015) A review of the bioactivity of coffee, caffeine and key coffee constituents on inflammatory responses linked to depression. Food Res Int 76(Pt 3):626–636. https://doi.org/10.1016/j.foodr es.2015.07.027
- Hewlett P, Smith A (2006) Correlates of daily caffeine consumption. Appetite 46(1):97–99. https://doi.org/10.1016/j.appet.2005.10.004
- Hoidrup S, Andreasen AH, Osler M, Pedersen AN, Jorgensen LM, Jorgensen T, Schroll M, Heitmann BL (2002) Assessment of habitual energy and macronutrient intake in adults: comparison of a seven day food record with a dietary history interview. Eur J Clin Nutr 56(2):105–113. https://doi.org/10.1038/sj.ejcn.1601292
- International Coffee Council (2017). Trends in Coffee Consumption in Selected Importing Countries. http://www.ico.org/documents/ icc-109-8e-trends-consumption.pdf. Accessed 13 Dec 2017
- Khan FA, Maalik A, Murtaza G (2016) Inhibitory mechanism against oxidative stress of caffeic acid. J Food Drug Anal 24(4):695–702. https://doi.org/10.1016/j.jfda.2016.05.003
- Kim CR, Lee JH (2013) An observational study on the obesity and metabolic status of psoriasis patients. Ann Dermatol 25(4):440–444. https://doi.org/10.5021/ad.2013.25.4.440
- Lee YH, Song GG (2018) Association between circulating 25-hydroxyvitamin D levels and psoriasis, and correlation with disease severity: a meta-analysis. Clin Exp Dermatol. https://doi.org/10.1111/ ced.13381
- Li W, Han J, Qureshi AA (2012) No association between coffee and caffeine intake and risk of psoriasis in US women. Arch Dermatol 148(3):395–397. https://doi.org/10.1001/archdermatol.2011.2933
- Liu F, Wang X, Wu G, Chen L, Hu P, Ren H, Hu H (2015) Coffee consumption decreases risks for hepatic fibrosis and cirrhosis: a metaanalysis. PLoS One 10(11):e0142457. https://doi.org/10.1371/ journal.pone.0142457
- Lopez-Garcia E, van Dam RM, Qi L, Hu FB (2006) Coffee consumption and markers of inflammation and endothelial dysfunction in healthy and diabetic women. Am J Clin Nutr 84(4):888–893
- Ludwig IA, Clifford MN, Lean ME, Ashihara H, Crozier A (2014) Coffee: biochemistry and potential impact on health. Food Funct 5:1695–1717. https://doi.org/10.1039/c4fo00042k
- Madeira MH, Boia R, Ambrósio AF, Santiago AR (2017) Having a coffee break: the impact of caffeine consumption on microgliamediated inflammation in neurodegenerative diseases. Mediators Inflamm 2017:4761081. https://doi.org/10.1155/2017/4761081
- Millsop JW, Bhatia BK, Debbaneh M, Koo J, Liao W (2014) Diet and psoriasis, part III: role of nutritional supplements. J Am Acad Dermatol 71(3):561–569. https://doi.org/10.1016/j.jaad.2014.03.016
- Deringer

- Mitchell DC, Hockenberry J, Teplansky R, Hartman TJ (2015) Assessing dietary exposure to caffeine from beverages in the U.S. population using brand-specific versus category-specific caffeine values. Food Chem Toxicol 80:247–252. https://doi. org/10.1016/j.fct.2015.03.024
- Montagnana M, Favaloro EJ, Lippi G (2012) Coffee intake and cardiovascular disease: virtue does not take center stage. Semin Thromb Hemost 38(2):164–177. https://doi. org/10.1055/s-0032-1301414
- National Center for Health Statistics (NCHS) (2011) Anthropometry Procedures Manual. National Health and Nutrition Examination Survey (NHANES). https://www.cdc.gov/nchs/data/nhanes/nhane s_11_12/Anthropometry_Procedures_Manual.pdf. Accessed 15 Nov 2017
- Rodríguez-Zúñiga MJM, García-Perdomo HA (2017) Systematic review and meta-analysis of the association between psoriasis and metabolic syndrome. J Am Acad Dermatol 77(4):657–666. e8. https://doi.org/10.1016/j.jaad.2017.04.1133
- Sääksjärvi K, Knekt P, Männistö S, Heliövaara M (2010) Self-administered questionnaire is a reliable measure of coffee consumption. J Epidemiol 20(5):363–369
- Setty AR, Curhan G, Choi HK (2007) Smoking and the risk of psoriasis in women: nurses' health study II. Am J Med 120(11):953–959. https://doi.org/10.1016/j.amjmed.2007.06.020
- Shahwan KT, Kimball AB (2015) Psoriasis and cardiovascular disease. Med Clin North Am 99(6):1227–1242. https://doi.org/10.1016/j. mcna.2015.08.001
- Sharif K, Watad A, Bragazzi NL, Adawi M, Amital H, Shoenfeld Y (2017) Coffee and autoimmunity: more than a mere hot beverage! Autoimmun Rev 16(7):712–721. https://doi.org/10.1016/j.autre v.2017.05.007
- Shin HS, Satsu H, Bae MJ, Totsuka M, Shimizu M (2017) Catechol groups enable reactive oxygen species scavenging-mediated suppression of PKD-NFkappaB-IL-8 signaling pathway by chlorogenic and caffeic acids in human intestinal cells. Nutrients. https ://doi.org/10.3390/nu9020165
- Spiller MA (1984) The chemical components of coffee. Prog Clin Biol Res 158:91–147
- Spuls PI, Lecluse LL, Poulsen ML, Bos JD, Stern RS, Nijsten T (2010) How good are clinical severity and outcome measures for psoriasis?: quantitative evaluation in a systematic review. J Invest Dermatol 130(4):933–943. https://doi.org/10.1038/jid.2009.391
- Swanson JA, Lee JW, Hopp JW (1994) Caffeine and nicotine: a review of their joint use and possible interactive effects in tobacco withdrawal. Addict Behav 19(3):229–256
- Swanson DL, Barnes SA, Mengden Koon SJ, el-Azhary RA (2007) Caffeine consumption and methotrexate dosing requirement in psoriasis and psoriatic arthritis. Int J Dermatol 46(2):157–159. https://doi.org/10.1111/j.1365-4632.2006.02954.x
- Tajik N, Tajik M, Mack I, Enck P (2017) The potential effects of chlorogenic acid, the main phenolic components in coffee, on health: a comprehensive review of the literature. Eur J Nutr. https://doi. org/10.1007/s00394-017-1379-1
- Thompson FE, Subar AF (2013) Chap. 1—dietary assessment methodology. In: Ferruzzi AMCJBG (eds) Nutrition in the prevention and treatment of disease, 3rd edn. Academic, London, pp 5–46
- Trojacka E, Zaleska M, Galus R (2015) Influence of exogenous and endogenous factors on the course of psoriasis. Pol Merkur Lekarski 38(225):169–173
- Vali A, Asilian A, Khalesi E, Khoddami L, Shahtalebi M, Mohammady M (2005) Evaluation of the efficacy of topical caffeine in the treatment of psoriasis vulgaris. J Dermatolog Treat 16(4):234–237. https://doi.org/10.1080/09546630510011801
- Voiculescu VM, Lupu M, Papagheorghe L, Giurcaneanu C, Micu E (2014) Psoriasis and metabolic syndrome—scientific evidence and therapeutic implications. J Med Life 7(4):468–471

- Ware JJ, Tanner JA, Taylor AE, Bin Z, Haycock P, Bowden J, Rogers PJ, Davey Smith G, Tyndale RF, Munaf

 ô MR (2017) Does coffee consumption impact on heaviness of smoking? Addiction 112(10):1842–1853. https://doi.org/10.1111/add.13888
- Welch AA, McTaggart A, Mulligan AA, Luben R, Walker N, Khaw KT, Day NE, Bingham SA (2001) DINER (data into nutrients for epidemiological research)—a new data-entry program for nutritional analysis in the EPIC-Norfolk cohort and the 7-day diary method. Public Health Nutr 4(6):1253–1265
- Wijarnpreecha K, Thongprayoon C, Ungprasert P (2017) Coffee consumption and risk of nonalcoholic fatty liver disease: a systematic

review and meta-analysis. Eur J Gastroenterol Hepatol 29(2):e8-e12. https://doi.org/10.1097/MEG.00000000000776

- Wolters M (2006) The significance of diet and associated factors in psoriasis Hautarzt. 57(11):999–1004. https://doi.org/10.1007/ s00105-006-1164-1
- World Health Organ Tech Rep Ser (2000) Obesity: preventing and managing the global epidemic. Rep WHO Consult 894:1–253
- Zampelas A, Panagiotakos DB, Pitsavos C, Chrysohoou C, Stefanadis C (2004) Associations between coffee consumption and inflammatory markers in healthy persons: the ATTICA study. Am J Clin Nutr 80(4):862–867

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