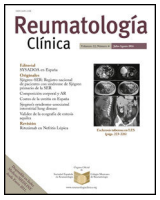
Reumatol Clin. 18 (2022) 387–392

Sociedad Española de Reumatología - Colegio Mexicano de Reumatología

Reumatología Clínica

www.reumatologiaclinica.org



Original Article

Psoriatic arthritis: interaction between cardiometabolic diseases and inflammatory burden of the disease☆

José Andrés Lorenzo Martín,[a,*] Estefanía Pardo Campo,[b] Marina Pino Martinez,[b] María Colazo Burlato,[a] Manuel Rubén Queiro Silva[b]

[a] *Hospital Universitario de Burgos, Burgos, Spain*
[b] *Hospital Universitario Central de Asturias, Oviedo, Spain*

ARTICLE INFO

Article history:
Received 16 July 2020
Accepted 26 May 2021
Available online 17 November 2021

Keywords:
Psoriatic arthritis
Metabolic disease
Cardiovascular disease
Anti-TNFα
Inflammation

ABSTRACT

Background and objetives: Psoriatic arthritis is accompained by several cardiometabolic comorbidities. Obesity causes a low-grade systemic inflammation and is a negative predictor of treatment response. We wanted to evaluate if there are interactions between metabolic status, inflammatory parameters and disease activity; and whether metabolic or cardiovascular diseases have any association with the reduction of the inflammatory burden by treating the psoriatic arthritis.
Material and methods: We have carried out a cross-sectional descriptive study of 160 patients with psoriatic arthritis. Sociodemographic, clinical and analytical variables were collected, as well as the presence of dactylitis and enthesitis; and HAQ, DAPSA and Minimal Disease Activity criteria. Chi-square test and the H of Kruskall Wallis were used to carry out comparisons, considering $P < .05$ as statistically significant. To establish correlations, Pearson correlation coefficient was used.
Results: BMI and waist circumference correlate with CRP and ESR (significance: < .05) although the correlation strenght is low (Pearson <.4), but there is no such relationship with DAPSA or meeting MDA criteria. Using biologic therapies is associated with a lower prevalence of cardiovascular events ($P = 0.047$; OR: 0.12, 95% CI: 0.01-0.9) and enthesitis ($P = .008$; OR: 0.3, CI 95%: 0.16-0.56); and normal levels of CRP ($P = .029$; OR: 0.25, 95% CI: 0.07-0.87) and ESR ($P = 0.024$; OR: 0.36, 95% CI: 0.16-0.82) when comparing to conventional therapies.
Discussion and conclusions: Anti-TNFα treatment could reduce cardiovascular risk in patients with psoriatic arthritis. There may be higher levels of CRP and ESR in obese individuals without this necessarily implying higher disease activity.

Published by Elsevier España, S.L.U.

Artritis psoriásica: interacción entre enfermedades cardiometabólicas y la actividad inflamatoria de la enfermedad

Palabras clave:
Artritis psoriásica
Enfermedad metabólica
Enfermedad cardiovascular
Anti-TNFα
Inflamación

RESUMEN

Antecedentes y objetivos: La artritis psoriásica se acompaña de una serie de comorbilidades cardiovasculares y metabólicas. La obesidad transcribe un estado de inflamación sistémica de bajo grado. Además, es un predictor negativo de la respuesta al tratamiento. Nuestro objetivo es evaluar si existen interacciones entre el estado metabólico, los parámetros inflamatorios y la actividad de la enfermedad. También queremos comprobar si las enfermedades metabólicas o cardiovasculares tienen alguna asociación con la reducción de la carga inflamatoria mediante el tratamiento de la enfermedad.

☆ Please cite this article as: Lorenzo Martín JA, Pardo Campo E, Pino Martinez M, Colazo Burlato M, Queiro Silva MR. Artritis psoriásica: interacción entre enfermedades cardiometabólicas y la actividad inflamatoria de la enfermedad. Reumatol Clin. 2022;18:387–392.

* Corresponding author.
E-mail address: andrew_1_andres@outlook.com (J.A. Lorenzo Martín).

Material y método: Hemos realizado un estudio descriptivo transversal de 160 pacientes con artritis psoriásica. Se recogieron variables sociodemográficas, clínicas y analíticas. También se registró la presencia de dactilitis y entesitis, el HAQ, DAPSA y si se cumplen o no los criterios MDA. La prueba de chi-cuadrado y la H de Kruskall Wallis se utilizaron para realizar comparaciones, considerando p < 0,05 como estadísticamente significativo. Para establecer correlaciones, se utilizó el coeficiente de correlación de Pearson.
Resultados: El IMC y el perímetro abdominal se correlacionan con la PCR y la VSG (significación < 0,05) aunque la fuerza de correlación es baja (Pearson < 0,4), pero no con DAPSA o con cumplir los criterios de MDA. El uso de terapias biológicas se asocia con una menor prevalencia de eventos cardiovasculares (p = 0,047; OR: 0,12; IC 95%: 0,01-0,9) y de entesitis (p = 0,008; OR: 0,3; IC 95%: 0,16-0,56). También se asocia a unos niveles normales de PCR (p = 0,029; OR: 0,25; IC 95%: 0,07-0,87) y VSG (p = 0,024; OR: 0,36; IC 95%: 0,16-0,82) cuando se compara con las terapias convencionales.
Discusión y conclusiones: El tratamiento anti-TNFα podría reducir el riesgo cardiovascular en pacientes con artritis psoriásica. Puede haber niveles más altos de PCR y VSG en personas obesas sin que esto implique necesariamente una mayor actividad de la enfermedad.

Publicado por Elsevier España, S.L.U.

Introduction

Psoriatic arthritis (PsA) is a chronic arthritis associated with psoriasis. The prevalence is .58% (95% CI: .14-.49) in our setting (Spain) according to data from the EPISER registry[1].

It is a very heterogeneous disease, with multiple facets in addition to musculoskeletal manifestations[2]. PsA is accompanied by several cardiovascular and metabolic comorbidities that increase the risk of a major cardiovascular event (MACE)[3,4]. However, the occurrence of MACE is not exclusively due to common risk factors such as hypertension, dyslipidaemia, diabetes mellitus or obesity. The inflammatory nature of the disease also plays an important role[5]. Acute phase reactants, such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR),which are used in the follow-up of chronic arthritis, have been associated with arterial wall stiffness[6] and the increase in cardiovascular risk[7,8].

Obesity is highly prevalent in people with psoriasis and with PsA, compared with health individuals[4]. Being overweight causes low grade systemic inflammation and is associated with higher levels of CRP and ESR[9], which may lead to errors when assessing obese patients.

When considering the interaction between obesity and disease, there is evidence that obesity is a negative predictor of both the effectiveness and persistence of an adequate response to biological and non-biological treatment in patients with PsA[10]. However, this interaction is bidirectional: proinflammatory cytokines involved in the onset and maintenance of immune-mediated disease also promote metabolic syndrome[11]. Therefore, there are studies that suggest that treatment of inflammatory arthropathies could improve the metabolic profile and cardiovascular risk of this type of patient[12], although the evidence is not very clear, at least in PsA[13].

Our study is twofold in its aim. On the one hand, we want to test whether there are interactions between the patient's metabolic status, inflammatory parameters and the disease assessed by different tools (Disease Activity in Psoriatic Arthritis [DAPSA], Minimal Disease Activity [MDA] and HAQ index). On the other hand, we want to assess whether metabolic or cardiovascular diseases have any association with the reduction of inflammatory burden by PsA treatment.

Material and method

We conducted a descriptive cross-sectional study of 160 patients with PsA from a rheumatology department of a tertiary hospital in north-eastern Spain during a period from June 2018 to March 2019. Outpatients of both sexes over 18 years of age, diagnosed with PsA according to the Classification Criteria for Psoriatic Arthritis (CASPAR), were included. Patients with and without disease-modifying treatments were included. No patients were excluded. An additional consultation was performed with all patients for data collection.

The study procedures included the collection of sociodemographic, clinical, analytical and radiographic variables. For the prescription of systemic medications, as well as for the assessment of therapeutic targets, the updated recommendations for the management of PsA given by the Spanish Society of Rheumatology were followed.

According to the dominant joint pattern in the last 5 years of follow-up, patients were diagnosed as having oligoarticular forms of PsA if they had a maximum of 4 inflamed joints; polyarthritis if they had 5 or more inflamed joints, and the ASAS criteria for axial spondyloarthritis were followed for the definition of axial forms. The presence of dactylitis or enthesitis was also collected, whether present at the time of data collection or recorded in the previous medical history. Distal interphalangeal joint involvement was recorded as another feature of PsA, but not as a specific joint pattern.

Both the DAPSA index, which focuses on joint involvement, and the MDA, a binary measure of disease status covering important domains of PsA (including joints, skin and entheses), have been shown to have construct validity and are easy to perform in clinical practice. We used them to assess both disease activity (DAPSA) and treatment goals (MDA and DAPSA remission) in the present work. Patients were considered to be in MDA when they met at least 5 of the following criteria: painful joint count ≤ 1; swollen joint count ≤ 1; Psoriasis Area and Severity Index ≤ 1 or body surface area $\leq 3\%$; patient's visual analogue pain scale score ≤ 15; patient's overall visual analogue disease activity scale score ≤ 20; HAQ score $\leq .5$; and number of painful entheses ≤ 1. The DAPSA score was calculated by summing the number of tender and swollen joints, pain on the visual analogue scale, patient global assessment and CRP. Clinical DAPSA was calculated without the contribution of CRP. DAPSA and clinical DAPSA ≤ 4 scores identified a state of remission. We used the Spanish version of the HAQ disability questionnaire to assess patients' quality of life.

Cardiometabolic risk factors (obesity, diabetes, hypertension, dyslipidaemia and smoking) and adverse cardiovascular events (angina, myocardial infarction, stroke and peripheral arterial ischaemia) were recorded for all patients. Cardiometabolic risk factors were only recorded if they were present at the time of the visit. Normal values for CRP and ESR are set at .5 mg/dl and 20 mm/h respectively, according to our laboratory cut-off points.

Descriptive statistics are expressed as percentages, means or medians, and the interquartile range (IQR) is indicated where appropriate. For comparisons between qualitative variables we used the chi-squared test, and for quantitative variables, Student's

t-test, Mann-Whitney U test and Kruskall Wallis H test, depending on the normality or non-normality of the distribution of the variables, considering p < .05 as statistically significant. We also used odds ratio (OR) to measure the association between treatment and different outcomes or events, such as MACE, DAPSA, MDA, CRP and ESR. To establish correlations between BMI, waist circumference, CRP, ESR, DAPSA, HAQ and MDA, Pearson's correlation coefficient was used. Meeting MDA criteria is a qualitative value, so it was recorded as a binary value: 0 = does not meet criteria; 1 = meets criteria, so a negative relationship with this variable indicates an association with meeting MDA criteria. IBM SPSS Statistics 19.0 software was used for data analysis.

Results

Our series included 77 women and 83 men. The mean age was 54 years (IQR: 44.25-64.75) and the mean duration of the disease was 10.6 years (IQR: 4-15). Regarding anthropometric data, the mean BMI of our patients was 28.3 (IQE: 24.53-30.88) and the mean waist circumference was 101.1 cm (IQR: 92.25-108.75) in our series, although we did not differentiate between men and women.

Approximately one third of our series suffered from a cardiovascular risk factor, the most common being high blood pressure (28%), dyslipidaemia (25%) and obesity (33%), followed by a tobacco habit (24%).

The oligoarticular pattern was the most frequent in our series (44%), followed by the polyarticular pattern (26%) and the mixed pattern (23%), with the exclusively axial form being the least frequent (7%). Twenty five per cent of our series had enthesitis and involvement of distal interphalangeal joints. Forty one per cent of the subjects had dactylitis. Erosions were present in 12% of the study population, and 3% presented with uveitis.

The DAPSA median was 6 (IQR: 2-12), whilst the acute phase reactants were negative in the majority of our series: CRP median: .2 (IQR: .1-.6); ESR media: 6,5 (IQR: 3-15). HAQ median .25 (IQR: 0-.6). Sixty six per cent of our sample met with the MDA criteria.

In our series there are 50 patients being treated with synthetic disease-modifying drugs (S-DMARDs): 43 patients with methotrexate, 6 patients with leflunomide and 1 patient with sulfasalazine. There are 89 individuals receiving treatment with biologic therapies (b-DMARDs): 67 patients with anti-TNF (iTNF), 18 patients with ustekinumab and 4 patients with secukinumab. The remaining 21 patients do not receive any specific treatment due to good disease control. All these data are presented in Table 1.

BMI and waist circumference positively correlated with the CRP and the ESR (bilateral significance <.05), although the degree of correlation is low (Pearson < .4). We found no relationship between BMI or waist circumference and DAPSA or meeting with MDA criteria. There was also a correlation between the CRP and the ESR with DAPSA and fulfilment of the MDA criteria (Bilateral significance: < .05). These data are contained in Table 2.

When assessing the relationship between metabolic diseases, acute phase reactants, DAPSA and HAQ; we found that high blood pressure was associated with higher ESR values (Mann-Whitney U, p = .019) and HAQ (Mann-Whitney U, p = .049), while hyperuricaemia was associated with higher CRP levels (Mann-Whitney U, p = .026). We found no association with the rest of metabolic diseases. These data are contained in Table 3.

If we check the associations between treatment and the different diseases that make up the metabolic syndrome, we find that the treatment of PsA does not modify any of them. However, these diseases were recorded qualitatively (present or not present). Blood pressure, blood glucose, cholesterol, triglycerides and uric acid values were not collected.

The use of bDMARDs was associated with a lower prevalence of MACE in comparison to sDMARDs (p = .047; OR: .12; 95% CI:.01-.9). We also found a lower prevalence of enthesitis (p = .008; OR: .3; 95% CI:.16-.56), and a higher possibility of having lower DAPSA (p = .03; OR: .28; 95% CI:.11-.72) or meeting with the MDA criteria (p = .001; OR: 3,65; 95% CI:1.63-8.13), and greater probability of having normal CRP (p = .029; OR: .25; 95% CI:.07-.87) and ESR (p = .024; OR: .36; 95% CI:.16-.82) levels in the group which received treatment with bDMARDs compared with the group which received sDMARDs.

Discussion

Metabolic diseases and cardiovascular risk are two aspects that are often overlooked in the routine management of PsA patients, although it is well documented that these patients tend to have an unfavourable profile in both areas.

Our results indicate that there is a positive correlation between anthropometric measures (BMI and waist circumference) and acute phase reactants (CRP and ESR), but when compared with DAPSA or MDA criteria, there is no such relationship. This indicates that in obese patients we may find elevated acute phase reactants without necessarily being associated with increased disease activity.

If we evaluate the association between treatment and the different metabolic diseases in our patients, we find that treatment of the disease is not associated with a lower prevalence of hypertension, dyslipidaemia, diabetes or hyperuricaemia. Nor are there differences in the prevalence of these metabolic diseases between the different treatment groups (sDMARDs versus bDMARDs). On the other hand, we found a lower prevalence of enthesitis and cardiovascular events in the bDMARDs group compared to the sDMARDs group. These results are consistent with other studies in which enthesitis was associated with increased cardiovascular risk in patients with PsA[14]. There are also differences in CRP and ESR levels, where we found that treatment with B-CSF is more frequently associated with normal levels of both acute phase reactants compared to those receiving treatment with S-CSF, which may also explain the difference in the prevalence of cardiovascular events between these groups[7,8].

Out of all the metabolic diseases included in our study, only hypertension and hyperuricaemia were associated with higher values of CRP, ESR or HAQ, but diabetes or dyslipidaemia were not, probably due to the data collection protocol.

Obesity involves excess adipose tissue, which has classically been regarded as an energy reserve tissue. However, this is a misperception. Adipose tissue acts as an endocrine organ in that it produces anti-inflammatory and pro-inflammatory cytokines, called adipokines[15]. In situations where calorie supply exceeds the body's needs, the adipocyte initially hypertrophies to maintain normal adipose tissue function and allows the formation of new adipocytes (hyperplasia). This phenomenon is directly related to the degree of obesity.[15] If excessive calorie intake is perpetuated over time, triglyceride accumulation will occur only through adipocyte hypertrophy and not hyperplasia, resulting in impaired regulation of the synthesis of anti-inflammatory and pro-inflammatory cytokines[15]. In particular, some of the adipokines that are synthesised to a greater extent are tumour necrosis factor alpha (TNF), interleukin-6, monocyte chemoattractant protein 1 and plasminogen activator inhibitor[16].

TNFα is a central protein in the pathophysiology of inflammatory arthropathies and the therapeutic target of many biological treatments. It is also a link between immune-mediated diseases, obesity and other associated conditions such as insulin resistance, dyslipidaemia and atherosclerosis[10]. Evidence suggests that interventions such as diet or physical activity that lead to a decrease in body weight may also decrease TNFα[17]. There is also an estab-

Table 1
Population characteristics.

	N (%)	Mean	Median	Interquartile range
Sex				
Man	77 (48)			
Woman	83 (52)			
Age		54.4	56	(44.25-64.75)
Duration of the PsA (years)		10.6	8	(4.00-15.00)
BMI		28.3	27.55	(24.53-30.88)
Waist circumference (cm)		101.1	101	(92.25-108.75)
DM	18 (11)			
HBP	44 (28)			
Dyslipidaemia	40 (25)			
Hyperuricaemia	9 (6)			
Obesity	52 (33)			
Tobacco habit	38 (24)			
Cardiovascular events	9 (6)			
Joint pattern				
Oligo	71 (44)			
Poli	41 (26)			
Axial	11 (7)			
Mixed	37 (23)			
Dactylitis	65 (41)			
Enthesitis	40 (25)			
Distal interphalangeal joints	40 (25)			
Uveitis	4 (3)			
Erosions	19 (12)			
CRP			.2	(.10-.60)
ESR			6.5	(3.00-15.00)
HAQ			.25	(.00-.63)
DAPSA			6	(2.00-12.00)
MDA				
No	54 (34)			
Yes	106 (66)			
No treatment	21 (13.1)			
sDMARDs				
Methotrexate	43 (26.9)			
Leflunomide	6 (3.7)			
Sulfasalazine	1 (.6)			
bDMARDs				
iTNF	67 (41.9)			
Ustekinumab	18 (11.3)			
Secukinumab	4 (2.5)			

Table 2
Correlations.

		Waist circumference	CRP	ESR	HAQ	DAPSA	MDA
BMI	Pearson	.792	.192	.365	.262	.114	−.085
	Significance	**.000**	**.015**	**.000**	**.001**	.151	.287
Waist circumference	Pearson		.192	.212	.153	.006	.094
	Significance		**.015**	**.007**	.053	.941	.236
CRP	Pearson			.647	.184	.295	−.208
	Significance			.000	.020	.000	.008
ESR	Pearson			1.000	.299	.344	−.356
	Significance				.000	.000	.000
HAQ	Pearson				1,000	.659	−.609
	Significance					.000	.000
DAPSA	Pearson					1,000	−.781
	Significance						.000
MDA	Pearson						
	Significance						

Statistically significant data in bold.

Table 3
Relationship between metabolopathies and acute phase reactants, DAPSA and HAQ (Mann-Whitney U test).

	CRP (p-value)	ESR (p-value)	DAPSA (p-value)	HAQ (p-value)
Diabetes mellitus	.292	.728	.512	.320
Hypertension	.467	.019	.424	.049
Dyslipidemia	.930	.161	.321	.067
Hyperuricaemia	.026	.077	.850	.735

lished relationship between obesity and PsA. This relationship is bidirectional: obesity involves the synthesis of cytokines such as TNF or vascular endothelial growth factor, which promote the onset of arthritis in predisposed subjects; in fact, excess body weight is considered an independent risk factor for PsA. On the other hand, proinflammatory cytokines involved in the pathophysiology of PsA favour obesity[18].

CRP and ESR are 2 acute phase reactants that are commonly used in the daily practice of the rheumatologist. CRP is associated with poorer blood glucose and blood pressure control and is often higher in smokers[7]. ESR is an independent predictor of cardiovascular risk, which can be useful for assessing risk even in a non-high-risk population[8]. Both ESR and CRP are associated with higher BMI and waist circumference[7,8]. Obesity leads to higher levels of these acute phase reactants, which is partly due to TNF and interleukin-[19]. This relationship between BMI and acute phase reactants is present in subjects with and without PsA or rheumatoid arthritis (RA)[20], indicating that excess CRP in obese individuals does not necessarily imply increased disease activity[21]. Our results reflect that there is an association between anthropometric data and acute phase reactants, but no such association with disease activity as measured by DAPSA and MDA. Therefore, our results suggest that in obese patients higher CRP and/or ESR values do not necessarily imply higher disease activity.

Obesity is also associated with a worse response to treatment in both RA and PsA, especially if the patient is receiving anti-TNFα therapy[22]. However, the underlying mechanisms of this phenomenon are not fully understood. One possible explanation is that the production of TNF and interleukin-6 by adipocytes in situations of obesity, together with the disease activity itself, creates an increased inflammatory burden[23]. There is also a hypothesis that obese patients have a greater volume of distribution, generating a lower peak of the drug in the blood, which is related to lower effectiveness and also facilitates the synthesis of antipharmacological antibodies[23].

Given the implications of TNFα in metabolic diseases, it is logical to assume that biologic therapies may have a positive impact on a patient's metabolic profile, although there is no clear evidence in this regard. Some studies have found that individuals treated with infliximab, adalimumab or etanercept show a trend towards a smaller waist circumference, decreased insulin resistance, triglyceride levels and baseline blood glucose levels, and higher HDL levels[11,12]. These findings appear to be similar in other immune-mediated diseases, such as RA[24], psoriasis[25] or inflammatory bowel disease[26], thus highlighting the role of TNF as an intermediary between inflammatory and metabolic diseases. However, there are other studies that do not find this relationship, at least in patients with PsA[13]. Methotrexate use has been associated with an improvement in lipid profile and basal blood glucose, but there is no such association with insulin resistance[27]. In any case, the benefit related to metabolic disease, if any, seems to be more evident in patients treated with anti-TNF than in those receiving methotrexate[12]. With respect to cardiovascular disease, anti-TNF treatment may reduce the risk of cardiovascular events, although this association is more evident in patients with RA[29] than in patients with psoriasis or PsA[28,29]. Our data show no association between anti-TNFα treatment and metabolic diseases, probably due to the data collection protocol, but they do indicate that the use of bDMARDs could reduce the prevalence of cardiovascular events when compared with those receiving treatment with conventional therapies.

Among the limitations of our study are those inherent to a cross-sectional study. The fact that we did not find a relationship with metabolic status could be due to the fact that we only took into account whether or not the patient was diagnosed with any of the metabolic diseases included in the study. Blood pressure, cholesterol, triglycerides, blood glucose or uric acid values were not recorded. Therefore, there could be some relationship between the metabolic profile and the treatment received; and it was not found due to the data collection protocol. The correlations we have obtained have a low or very low degree of association, probably due to the baseline situation of the patients in terms of disease activity and CRP and ESR values (Table 1).

Conclusions

There is a lower prevalence of enthesitis and cardiovascular events, and lower CRP and ESR levels in the group of patients treated with biologic therapies compared to those treated with methotrexate or other conventional therapies. Our results are consistent with other studies that find enthesitis to be an independent cardiovascular risk factor in PsA. Therefore, our data strengthen the available evidence suggesting that anti-TNF therapy may reduce cardiovascular risk in patients with PsA. This could be due to a greater decrease in inflammatory burden compared to conventional therapies.

Our results show no association between biological therapies and a favourable metabolic profile, although this could be due to the data collection protocol.

The data from our series also indicate that higher CRP and ESR levels may be present in obese individuals, without necessarily implying higher disease activity, so that the assessment of these patients should be more thorough.

Conflict of interests

The authors have no conflict of interests to declare.

References

1. Seoane-Mato D, Sánchez-Piedra C, Fernández LS, Mascaró FS, García FJB, Ruiz FP, et al. Prevalencia de enfermedades reumáticas en población adulta en España (estudio EPISER 2016). Objetivos y metodología. Reumatol Clin. 2019;15:90–6, http://dx.doi.org/10.1016/j.reuma.2017.06.009.
2. Peluso R, Iervolino S, Vitiello M, Bruner V, Lupoli G, Di Minno MND. Extra-articular manifestations in psoriatic arthritis patients. Clin Rheumatol. 2015;34:745–53, http://dx.doi.org/10.1007/s10067-014-2652-9.
3. Queiro R, Lorenzo A, Pardo E, Brandy A, Coto P, Ballina J. Prevalence and type II diabetes-associated factors in psoriatic arthritis. Clin Rheumatol. 2018;37:1059–64, http://dx.doi.org/10.1007/s10067-018-4042-1.
4. Queiro R, Lorenzo A, Pardo E, Brandy A, Coto P, Ballina J. Obesity in psoriatic arthritis: Comparative prevalence and associated factors. Medicine (Baltimore). 2019;98:e16400, http://dx.doi.org/10.1097/MD.0000000000016400.
5. Gladman DD, Ang M, Su L, Tom BDM, Schentag CT, Farewell VT. Cardiovascular morbidity in psoriatic arthritis. Ann Rheum Dis. 2009;68:1131–5, http://dx.doi.org/10.1136/ard.2008.094839.
6. Muhammad IF, Borné Y, Östling G, Kennbäck C, Gottsäter M, Persson M, et al. Acute phase proteins as prospective risk markers for arterial stiffness: The Malmö Diet and Cancer cohort. PLoS One. 2017:12, http://dx.doi.org/10.1371/journal.pone.0181718.
7. Fonseca FAH, de Oliveira Izar MC. High-sensitivity C-reactive protein and cardiovascular disease across countries and ethnicities. Clinics (Sao Paulo). 2016;71:235–42, http://dx.doi.org/10.6061/clinics/2016(04)11.
8. Godsland IF, Bruce R, Jeffs JAR, Leyva F, Walton C, Stevenson JC. Inflammation markers and erythrocyte sedimentation rate but not metabolic syndrome factor score predict coronary heart disease in high socioeconomic class males: The HDDRISC study. Int J Cardiol. 2004;97:543–50, http://dx.doi.org/10.1155/2011/273105.
9. Karczewski J, Śledzińska E, Baturo A, Jończyk I, Maleszko A, Samborski P, et al. Obesity and inflammation. Eur Cytokine Netw. 2018;29:83–94, http://dx.doi.org/10.1684/ecn.2018.0415.
10. Galíndez E, Carmona L. Is obesity in psoriatic arthritis associated with a poorer therapeutic response and more adverse effects of treatment with an anchor drug? Reumatol Clin. 2016;12:307–12, http://dx.doi.org/10.1016/j.reuma.2015.12.005.
11. Maruotti N, d'Onofrio F, Cantatore FP. Metabolic syndrome and chronic arthritis: Effects of anti-TNF-α therapy. Clin Exp Med. 2015;15:433–8, http://dx.doi.org/10.1007/s10238-014-0323-4.
12. Costa L, Caso F, Atteno M, Del Puente A, Darda MA, Caso P, et al. Impact of 24-month treatment with etanercept, adalimumab, or methotrexate on metabolic syndrome components in a cohort of 210 psoriatic arthritis patients. Clin Rheumatol. 2014;33:833–9, http://dx.doi.org/10.1007/s10067-013-2369-1.

13. Channual J, Wu JJ, Dann FJ. Effects of tumor necrosis factor-α blockade on metabolic syndrome components in psoriasis and psoriatic arthritis and additional lessons learned from rheumatoid arthritis. Dermatol Ther. 2009;22:61–73, http://dx.doi.org/10.1111/j.1529-8019.2008.01217.
14. Lorenzo A, Pardo E, Charca L, Pino M, Queiro R. Enthesitis and joint erosions are disease traits associated with cardiovascular risk in psoriatic arthritis. Clin Rheumatol. 2020, http://dx.doi.org/10.1007/s10067-020-05088-2.
15. Flores-Lázaro JR, Rodríguez-Martínez E, Rivas-Arancibia S. Consecuencias metabólicas de la alteración funcional del tejido adiposo en el paciente con obesidad. Rev Med Hosp Gen Mex. 2011;74:157–65.
16. Izaola O, de Luis D, Sajoux I, Domingo JC, Vidal M. Inflammation and obesity (lipoinflammation). Nutr Hosp. 2015;31:2352–8, http://dx.doi.org/10.3305/nh.2015.31.6.8829.
17. Miller EG, Sethi P, Nowson CA, Dunstan DW, Daly RM. Effects of progressive resistance training and weight loss versus weight loss alone on inflammatory and endothelial biomarkers in older adults with type 2 diabetes. Eur J Appl Physiol. 2017;117:1669–78, http://dx.doi.org/10.1007/s00421-017-3657-2.
18. Cañete JD, Mease P. The link between obesity and psoriatic arthritis. Ann Rheum Dis. 2012;71:1265–6, http://dx.doi.org/10.1136/annrheumdis-2012-201632.
19. Strober B, Teller C, Yamauchi P, Miller JL, Hooper M, Yang Y-C, et al. Effects of etanercept on C-reactive protein levels in psoriasis and psoriatic arthritis. Br J Dermatol. 2008;159:322–30, http://dx.doi.org/10.1111/j.1365-2133.2008.08628.x.
20. Russolillo A, Iervolino S, Peluso R, Lupoli R, Di Minno A, Pappone N, et al. Obesity and psoriatic arthritis: from pathogenesis to clinical outcome and management. Rheumatology (Oxford). 2013;52:62–7, http://dx.doi.org/10.1093/rheumatology/kes242.
21. George MD, Giles JT, Katz PP, England BR, Mikuls TR, Michaud K, et al. Impact of obesity and adiposity on inflammatory markers in patients with rheumatoid arthritis. Arthritis Care Res (Hoboken). 2017;69:1789–98, http://dx.doi.org/10.1002/acr.23229.
22. Singh S, Facciorusso A, Singh AG, Casteele NV, Zarrinpar A, Prokop LJ, et al. Obesity and response to anti-tumor necrosis factor-α agents in patients with select immune-mediated inflammatory diseases: A systematic review and meta-analysis. PLoS One. 2018:13, http://dx.doi.org/10.1371/journal.pone.0195123.
23. Højgaard P, Glintborg B, Kristensen LE, Gudbjornsson B, Love TJ, Dreyer L. The influence of obesity on response to tumour necrosis factor-α inhibitors in psoriatic arthritis: results from the DANBIO and ICEBIO registries. Rheumatology (Oxford). 2016;55:2191–9, http://dx.doi.org/10.1093/rheumatology/kew326.
24. Naghashian F, Hosseinzadeh-Attar MJ, Akhlaghi M, Yekaninejad MS, Aryaeian N, Derakhshanian H. The relationship between anthropometric status and rheumatoid arthritis. Exploring the role of nesfatin and asymmetric dimethylarginine. Acta Reumatol Port. 2019;44:126–31.
25. Adalimumab therapy improves insulin sensitivity in non-diabetic psoriatic patients: A 6-month prospective study. ACR Meeting Abstracts [acceso 21 Abr 2020]. Available from: https://acrabstracts.org/abstract/adalimumab-therapy-improves-insulin-sensitivity-in-non-diabetic-psoriatic-patients-a-6-month-prospective-study/.
26. Paschou SA, Kothonas F, Lafkas A, Myroforidis A, Loi V, Terzi T, et al. Favorable effect of anti-TNF therapy on insulin sensitivity in nonobese, nondiabetic patients with inflammatory bowel disease. Int J Endocrinol. 2018;2018:6712901, http://dx.doi.org/10.1155/2018/6712901.
27. Marks JL, Edwards CJ. Protective effect of methotrexate in patients with rheumatoid arthritis and cardiovascular comorbidity. Ther Adv Musculoskelet Dis. 2012;4:149–57, http://dx.doi.org/10.1177/1759720X11436239.
28. Yang Z, Lin N, Li L, Li Y. The effect of TNF inhibitors on cardiovascular events in psoriasis and psoriatic arthritis: An updated meta-analysis. Clinic Rev Allerg Immunol. 2016;51:240–7, http://dx.doi.org/10.1007/s12016-016-8560-9.
29. Armstrong AW, Brezinski EA, Follansbee MR, Armstrong EJ. Effects of biologic agents and other disease-modifying antirheumatic drugs on cardiovascular outcomes in psoriasis and psoriatic arthritis: A systematic review. Curr Pharm Des. 2014;20:500–12, http://dx.doi.org/10.2174/13816128200414021312350 5.