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Psoriasis: a Skin Disease Associated With Increased Cardiovascular Risk☆

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Abstract Psoriasis and psoriatic arthritis are associated with increased risk of cardiovascular events and cardiovascular mortality. Alongside classic risk factors for atherosclerosis, the severity of psoriatic skin disease also influences cardiovascular risk in these patients. In both cases, endothelial dysfunction and increased intima-media thickness in the carotid artery are indicators of subclinical cardiovascular disease. Active treatment of the psoriasis and management of traditional cardiovascular risk factors are essential in order to reduce cardiovascular morbidity in these patients. Clinical practice guidelines on the management of cardiovascular risk will define a new integrated approach to the care of patients with psoriasis and psoriatic arthritis.

PALABRAS CLAVE
Psoriasis;
Artritis psoriásica;
Enfermedad cardiovascular;
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Manejo clínico

Psoriasis: una enfermedad cutánea relacionada con riesgo cardiovascular elevado

Resumen La psoriasis y la artritis psoriásica se asocian con un mayor riesgo de eventos cardiovasculares y de mortalidad cardiovascular. Además de los factores clásicos de aterosclerosis, la gravedad de la afección cutánea influye en el aumento del riesgo cardiovascular en estos pacientes. En ambos procesos se observa la presencia de disfunción endotelial y un grosor aumentado de la íntima-media de la arteria carótida, como expresión de enfermedad cardiovascular subclínica. El tratamiento activo de la enfermedad y el manejo de los factores de riesgo cardiovascular clásicos son fundamentales para disminuir la morbilidad cardiovascular

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en estos pacientes. El establecimiento de guías clínicas para el manejo del riesgo cardiovascular abrirá, en el futuro, un nuevo abordaje clínico integral del paciente con psoriasis y la artritis psoriásica.

Psoriasis is a chronic inflammatory skin disease that affects between 1% and 3% of the population, with the highest prevalence in the white population.[1] The authors of a study carried out in the United States estimated the prevalence of heart disease in patients with psoriasis to be 14.3%, somewhat higher than in the general population (11.3%).[2] This difference could be attributed to the higher incidence of metabolic syndrome and other traditional cardiovascular risk factors in these patients. However, the higher prevalence of heart disease in patients with psoriasis has been shown to be independent of body mass index, and in a recent study obesity was not an independent risk factor for acute myocardial infarction in this setting.[3]

Psoriasis is now thought to be an independent risk factor for coronary artery disease and acute myocardial infarction.[3] The risk of developing ischemic heart disease and cerebrovascular disease has been reported to be higher in patients with moderate to severe psoriasis than in the general population.[4,5] Using the Framingham risk score, Kimball et al.[4] estimated the 10-year risk of coronary heart disease and stroke in 1591 patients with moderate to severe psoriasis. In the patients with a PASI score between 10 and 20, the 10-year risk of coronary heart disease and stroke was 12.3% and 8.3%, respectively, and the corresponding figures in patients with a PASI score greater than 20 were 12.2% and 8.7%, respectively. While the level of risk did not differ greatly according to the PASI score, estimated cardiovascular risk was significantly higher in both groups of patients than in the general population, with a risk that was 28% greater risk for coronary heart disease and 11.8% greater for stroke. In another study the presence of psoriasis, even in mild forms but especially in severe cases, was found to be an independent risk factor for stroke.[5]

The hypothesis that the severity of psoriasis is a significant factor in the development of cardiovascular disease is also supported by the evidence of a correlation between PASI scores and insulin secretion.[6] Insulin resistance is a hallmark of metabolic syndrome, and a statistically significant correlation has been observed in patients with psoriasis between PASI scores and serum levels of resistin (a cytokine known to be increased in insulin resistance).[6] The implications of these findings are that the more severe the psoriasis the higher the risk of cardiovascular complications and that a chronic inflammatory state is of pathogenic importance in the development of vascular disease in these patients.

Psoriatic arthritis (PsA) is a chronic inflammatory joint disease associated with psoriasis that affects 0.3% to 1% of the population.[7] In 85% of patients with PsA, joint involvement is preceded by psoriatic skin lesions. Patients with PsA are usually seronegative for rheumatoid factor, a finding that can serve to differentiate between PsA and rheumatoid arthritis. PsA is currently classified as a rheumatic disease and included in the group of spondyloarthropathies.[8] As in rheumatoid arthritis, which is the prototype of a chronic inflammatory disease associated with accelerated atherosclerosis and a high incidence of cardiovascular disease,[9] higher mortality has been observed in PsA than in the general population primarily owing to the increased risk of cardiovascular disease in these patients.[10] In a study that compared 3066 patients with PsA and a matched group of controls (1:4 ratio), Han et al.[11] observed a higher prevalence of peripheral vascular disease, congestive heart failure, atherosclerosis, ischemic heart disease, and cerebrovascular disease in patients with PsA compared to the control group. The same authors also observed an increased incidence of the traditional cardiovascular risk factors, such as hypertension, diabetes mellitus, and dyslipidemia, in the patients with PsA.

It has been observed that the high cardiovascular mortality in rheumatoid arthritis is due to the concurrence of traditional cardiovascular risk factors,[12] a chronic inflammatory state,[13] and certain genetic factors.[13,14] It is therefore conceivable that the same factors may be responsible for the high cardiovascular morbidity and mortality observed in patients with PsA.

Subclinical atherosclerosis—diagnosed on the basis of increased intima-media thickness in the common carotid artery—has also been reported in association with the following chronic inflammatory rheumatic diseases: ankylosing spondylitis[15] (a spondyloarthropathy like PsA), psoriasis without joint involvement,[16] and PsA.[17,18] Patients with all these diseases were found to have increased carotid artery intima-media thickness compared to control groups matched for age, sex, and traditional cardiovascular risk factors.

This association may provide very significant prognostic information in patients with these chronic inflammatory diseases since, as previously noted, a direct correlation has been found between common carotid artery intima-media thickness and the development of cardiovascular complications in both the general population and in patients with rheumatoid arthritis.[19]

A correlation has also been reported in PsA between common carotid artery intima-media thickness and the presence of traditional risk factors for atherosclerosis.[18] Two studies in the past decade in patients with PsA with no clinical evidence of cardiovascular disease and no traditional cardiovascular risk factors have confirmed the increased prevalence of subclinical atherosclerosis in this population. Subclinical disease was manifest by the presence of endothelial dysfunction, a condition that represents the initial phase in the development of atherosclerosis,[20] or by increased carotid intima-media thickness.[21] However, no association has been observed between the severity of joint involvement in PsA and subclinical atherosclerosis[20,21] or

cardiovascular events.[22] This lack of evidence would appear to be an indication that, in PsA, the severity of the patient's skin condition may be more predictive of the development of vascular disease than the joint involvement.

In line with the studies showing a correlation between the severity of psoriasis and cardiovascular events,[4,5] Gladman et al.[22] found in patients with PsA that, in addition to known risk factors for atherosclerosis, the severity of skin involvement was predictive of cardiovascular disease.

The implication of the evidence discussed above is that chronic inflammation may play a key role in the accelerated development of atherosclerosis in patients with psoriasis and PsA. However, while chronic inflammation itself may be the key factor in the development of cardiovascular disease, we should not forget the additive effect in this process of traditional cardiovascular risk factors.

In view of this evidence, clinicians treating patients with psoriasis and PsA should routinely take active steps to reduce cardiovascular risk in these patients, and the first step in this process should be to determine cardiovascular risk in every patient. Unfortunately, there are at present no guidelines dealing specifically with the management of cardiovascular risk in these patients. We should, therefore, envisage the future development of comprehensive cardiovascular risk charts specifically adapted to these diseases. Given the close correlation between the severity of skin disease and the development of cardiovascular events, these tables should take into account the clinical assessment of the patient's psoriasis and the treatments prescribed as well as the traditional risk factors.

From the dermatological standpoint, a treatment aimed at reducing the severity of skin disease would also reduce the inflammatory burden. In these patients, it is also important to monitor known modifiable cardiovascular risk factors, such as obesity, hypertension, and dyslipidemia, and to check blood sugar levels regularly because of the increased risk of diabetes mellitus. Proper control of these factors may be of greater importance in patients with a long history of psoriasis or PsA in whom the presence of sustained chronic inflammation in conjunction with poor control of cardiovascular risk factors could lead to a higher atherogenic burden. In this regard, a direct correlation between the duration of PsA and the presence of an abnormally thick common carotid artery intima-media was detected in a recent study.[21]

If, once again, we take rheumatoid arthritis as a model for chronic inflammatory disease, we find that a consensus group of European experts has recommended stratifying cardiovascular risk in patients with rheumatoid arthritis using the Systematic Coronary Risk Evaluation (SCORE) risk charts.[23] On the basis of the available evidence, the 2 key aspects of the management of cardiovascular risk in rheumatoid arthritis are the use of SCORE risk charts adapted to each population group and clinical assessment of disease severity. It is very possible that this approach could also prove useful for the management of cardiovascular risk in patients with psoriasis and PsA. However, its usefulness has not yet been demonstrated and no consensus has been reached on clinical guidelines relating to this important aspect of the management of these patients.

In view of the higher incidence of dyslipidemia and hypertension in patients with psoriasis and PsA, treatment with statins and/or antihypertensive agents should be considered in accordance with the Spanish guidelines on the management of cardiovascular risk based on the SCORE risk chart, adapted to a southern European population, as a guide. The Third European Joint Task Force on cardiovascular prevention in clinical practice recommended the SCORE model as a tool for predicting cardiovascular risk. The model predicts cardiovascular mortality at 10 years on the basis of age, sex, systolic blood pressure, total cholesterol, and smoking status. In view of the geographical variability of cardiovascular risk in Europe, 2 SCORE models have been developed: 1 for high-risk and 1 for low-risk countries. The main difference between the SCORE risk function and the Framingham-DORICA model is that the SCORE chart estimates risk for all atherothrombotic cardiovascular manifestations, including stroke, heart failure, and peripheral arterial disease, and not just coronary heart disease. Moreover, several studies have suggested that the Framingham-DORICA tables tend to underestimate cardiovascular risk in Spain, especially in hypertensive patients with other cardiovascular risk factors; the SCORE risk charts are, therefore, the recommended instrument for use in this country.[24,25]

Given that the prevalence of cardiovascular disease in patients with psoriasis and PsA is high, cardiovascular risk should be assessed in these patients by identifying factors inherent in these chronic inflammatory diseases that have been shown to be associated with the development of accelerated atherogenesis and cardiovascular events. We would therefore consider the presence of a PASI > 10 to be a prognostic factor signaling the need for more rigorous management of the skin symptoms on the part of the dermatologist.

As a first step, clinicians who assess patients with psoriasis or PsA should also define a primary cardiovascular risk prevention strategy, based initially on making general recommendations to the patient regarding lifestyle, such as the need for regular moderate physical activity, a heart healthy diet, weight and blood pressure control, as well as tobacco cessation when appropriate. Furthermore, in accordance with the SCORE guidelines, treatment with statins and/or antihypertensive drugs should be initiated in patients with high cardiovascular risk (SCORE $\geq$ 5%).

In summary, the risk of cardiovascular morbidity and mortality is higher in patients with psoriasis and PsA than in the population in general. The presence of severe psoriasis is a significant predictor of cardiovascular risk in these patients. In addition to treating the cutaneous manifestations in patients with psoriasis and the rheumatic process in patients with PsA, clinicians must also monitor and appropriately manage the traditional risk factors for atherogenesis.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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