PSORIASIS AS CARDIOVASCULAR RISK FACTOR

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Summary

Psoriasis is no longer perceived as a mere skin disease but rather a systematic chonic inflammatory disease that carries with it substantial risk in increasing morbidity and mortality rates due to cardiovascular events. Current clinical practice guidelines only address managing traditional risk factors therefore an interdisciplinary approach and a protocol that would evaluate cardiovascular risk for these patientsis needed. Managing psoriasis is a priority and the necessity for monitoring associated risks, consulting new research findings and ghiding treatments by widely accepted protocols, is ever increasing.

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Psoriasis is a chronic, inflammatory autoimmune disease that affects approximately 5% of the total population. There are multiple types of psoriasis and in 90% of cases, plaque psoriasis or psoriasis vulgaris, is observed; other types of psoriasis that are frequently diagnosed are, guttate psoriasis, inverse psoriasis and erythrodermic or nummular (discoid) eczema plaques (1). The ethiopathogenesis of the disease may lead to associated comorbidities such as obesity, atherosclerosis, hypertension, metabolic syndrome and dyslipidemia due to a constant out put of proinflammatory cytokines (2). There are other dermatologic and non-dermatologic diseases that can be associated with psoriasis such as, nonalcoholic steatohepatitis, celiac disease, osteoporosis, chronic obstructive bronchitis, amyloidosis, bullous pemphigoid and vitiligo (3,4,5).

The exact mechanisms by which psoriasis occurs are not yet fully elucidated but the presence of chronic inflammation which is brought about by oxidative stress as well as free radicals can be considered elements that favour the formation of atherosclerotic plaques along the blood vessels (6). It is important to note that an increase in endothelial nitric oxide and an increased secretion of endothelin-1 can lead to insulin resistance. This is caused by reduced insulin sensitivity in the tissue due to a prolongued or chronic exposure of proinflammatory cytokines (7). The risk of cardiovascular events in patients that suffer from psoriasis is great and can be attributed to the correlation between the molecular and metabolic modifications that appear during etiopathogenic processes. Thus, the greater the disease's severity, the greater the cardiovascular risk.

In order to evaluate the severity of psoriasis, dermatologists use widely accepted methods from the following:

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- PASI (Psoriasis Area of Severity Index), according to the American Academy of Dermatology and is the most common index used in clinical trials
- BSA (Body Surface Area)
- SPI (Salford Psoriasis Index)
- DIDS (Dermatology Index of Disease Severity)
- DLQI (Dermatology Life Quality Index)
- PQLQ (Psoriasis Quality of Life Questionnaire)
- PDI (Psoriasis Disability Index)

Even though there are multiple indices that are used for disease evaluation, no one index comprises the ensemble of all the modifications that can be expected in psoriasis such as: skin damage, associated symptomatology, joint damage, quality of life or associated disease risk.

It has been demonstrated that 1% of patients suffering from psoriasis, approximately 40% of the total population, does not follow through with the treatment advised by their doctor (8). The question, therefore, is how many patients under treatment are actually abiding by the treatment plan offered to them by their medical practitioner? The problems that can arise from negligence are the systemic diseases than may ensue; for example, if the patient suffers only from minor skin lesions and is not bothered by any aspect of the disease, it becomes more difficult to treat and thereafter quantify the extent to which the patient suffers from the disease, locally and systemically.

On the other hand, for the patients that have undergone treatment for psoriasis, to what extent does the treatment affect other organs? Some treatments, such as biological therapy, can be more harmful than beneficial for patients with associated diseases such as heart failure, as noted by the FDA (Food and Drug Administration).

Diabetes, insulin resistance and atherosclerosis can be linked to proteins such as adipokines, leptin, adiponectin, TNF alfa and interleukin 6, found in adipocytes (9). Visfatin, an adipokine discovered by Fukuhara et al in 2005, is a marker that can evaluate cardiovascular risk in humans as well as in mice (10). Visfatin also acts as a marker for detecting the atherosclerotic process and endothelial dysfunction (11,12).

Visfatin can activate endothelial cells by activating the k-B nuclear factor and by stimulating intercellular adhesion molecules such as ICAM-1, VCAM-1, E-selectin which in turn stimulate vascular inflammation (13). According to some authors, serum Visfatin levels positively correlate with inflammatory markers such as IL-6 or CRP and are now called "the universal chronic inflammation marker." Visfatin also affects monocytes and enothelial cells by increasing IL 1 beta production, alongside increasing IL-6 levels. Visfatin also increases chemokines such as CXCL8, CXCL10, CXCL20 and TNF alfa, the latter being located on human keratinocytes (14).

Nicotinamide adenine dinucleotide phosphate (NADPH) is a superoxid anion that plays a role in the regeneration of proinflammatory enzymes that are associated with enothelial dysfunction. Some authors are divided as to NADPH's and Visfatin's role in increasing cardiovascular risk; Boini et al suggest that Visfatin activates NADPH oxidase while other authors suggest that Visfatin can activate the renin–angiotensin system and failure to adequately do so increases cardiovascular risk (15,16).

Some representative prospective and retrospective epidemiological surveys, indicate that psoriasis andpsoriatic arthritis patients, as compared to healthy people, exhibit an increased prevalence of ischemic heart disease, myocardial infarction, hypertension, dyslipidemia or diabetes (17,18).

There are a number of studies that try to accentuate the link between cardiovascular risk and psoriasis. It is standard procedure to determine patients' glycemia, cholesterol levels, triglycerid levels, CPR and blood pressure, especially in patients with psoriasis. Is a standard blood work-up sufficient to determine an increase in cardiovascular risk in patients with psoriasis or should medical practitioners search for a marker to more accurately determine cardiovascular risk? Could Visfatin be such a marker?

Since a multidisciplinary approach is taken in treating patients with psoriasis (dermatologist, rheumatologist, GP and psychologist), a protocol that would evaluate cardiovascular risk based on

the chronic inflammatory response could revolutionise how this disease is managed and can lead to earlier detection of cardiovascular risk factors and thus, can improve the quality of life of psoriasis sufferers.

Supposing that patients with psoriasis are prone to developing cardiovascular diseases, it is insufficient to conclude that even though Visfatin has a role in inducing atherosclerosis, endothelial dysfunction as well as blood vessel bed lesions, supplimentary studies are needed to clarify the link between cardiovascular disease and serum markers that can predict the disease's evolution (19).

There are studies that contradict one another with regard to the role systemic therapies play in protecting the patient from developing associated diseases; upholding the contrary is even more difficult than correlating systematic therapies to overall associated risk (20). Thus, the question of, to what extent does systematic therapy affect other implicated organs?

Psoriasis is no longer perceived as a mere skin disease but rather a systematic chonic inflammatory disease that carries with it substantial risk in increasing morbidity and mortality rates due to cardiovascular events. A growing number of patients are left untreated or are not compliant and can go on to suffer cardiovascular afflictions due to the inflammatory reaction rendered by the skin lesions.

Managing psoriasis is a priority and the necessity for monitoring associated risks, consulting new research findings and ghiding treatments by widely accepted protocols, is ever increasing.

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Conflict of interest
NONE DECLARED

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