



Subclinical Atherosclerosis in Psoriatic Arthritis Patients and its Correlation with Disease Activity and Severity. A review

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ABSTRACT

Background: Psoriatic arthritis (PsA) is a chronic, seronegative spondyloarthritis (SpA) that impacts up to 30% of patients with psoriasis. PsA may impact the spine (axial disease), sacroiliac joints, and peripheral joints (peripheral disease). Atherosclerosis is regarded as a significant cardiovascular risk factor. In PsA patients, the precise mechanism of increased early atherosclerosis remains unclear. Chronic inflammation can exacerbate atherosclerosis by causing endothelial dysfunction, both directly and indirectly. The goal of the trial was to ascertain the correlation between the severity and activity of psoriatic arthritis and subclinical atherosclerosis in patients through the use of flow-mediated dilatation (FMD) and carotid intima media thickness (CIMT).

Keywords: Atherosclerosis, psoriatic arthritis, severity, flow mediated dilatation.

Introduction

Psoriasis is an autoimmune inflammatory disease that is diagnosed using the Classification Criteria for Psoriatic Arthritis (CASPAR). It is imperative that physicians diagnose PsA at an early stage, as the risk of poor long-term physical function and joint erosions increases when the diagnosis is delayed by even a mere six months. Prompt treatment initiation is facilitated by early diagnosis, which enhances clinical outcomes and joint damage mitigates and both disease severity (Krakowski *et al.*, 2019).

In PsA patients, atherosclerosis is a prevalent condition that results from the accumulation of a sticky substance known as plaque within the arteries. Atherosclerosis is a gradual process that occurs as blood cells, fat, cholesterol, and other substances in the blood combine to form plaque. The accumulation of plaque results in the constriction of arteries. As a result, the body's oxygen-rich blood supply to vital organ tissues is diminished (Peluso *et al.*, 2019). Inflammation is a critical factor in all stages of the atherosclerotic process, which is why it is typically classified as a chronic inflammatory disease. Throughout the initiation and development of atherosclerosis, inflammation serves as a widespread foundation for the pathological changes (Zhu *et al.*, 2018). Secondary autoimmune atherosclerosis, which was previously known as accelerated atherosclerosis, and primary simple atherosclerosis, which develops with age, are the two primary categories into which atherosclerosis is classified (Sima *et al.*, 2018). Atherosclerosis is the primary cause of cardiovascular disease in autoimmune rheumatic diseases (AIRDs) (Hedar *et al.*, 2021).

The atherogenic process is believed to be accompanied by flow-mediated inflammatory changes in endothelial cells (ECs). ECs express a diverse array of inflammatory factors when activated, such as monocyte chemoattractant protein-1, IL-8, intercellular adhesion molecule-1 (ICAM-1), vascular adhesion molecule-1 (VCAM-1), E-selectin, and P-selectin. This attracts lymphocytes and monocytes, which bind to the endothelium and infiltrate the arterial wall, resulting in inflammation (Zhu *et al.*, 2018).

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In addition to vascular smooth muscle cells (VSMCs), macrophages, tumor necrosis factor (TNF- α) and dendritic cells (DCs), other cytokines and cells are also involved in this process. Oxidized LDL (oxLDL) is produced by the modification of a significant quantity of low-density lipoprotein (LDL). The development of atherosclerotic plaques is facilitated by the accumulation of this oxLDL in the vascular internal wall (Chistiakov, *et al.*, 2018; Ranjit *et al.*, 2007).

Smoking, diabetes, obesity, high blood pressure, and physical inactivity are all considered significant risk factors for cardiovascular disease (CVD). Atherosclerosis is also included in this mix. Furthermore, there is valuable information regarding the influence of related factors, such as gender, age, blood triglyceride and high-density lipoprotein (HDL) cholesterol levels, and psychosocial issues (Hajar, 2017).

Coronary artery, Cerebrovascular disease and peripheral artery disease are most frequently caused by atherosclerosis. Significant stenosis is the result of the accumulation of vessel-occluding plaques in the subendothelial intimal layer of large- and medium-sized arteries over time, which disrupts blood flow (Wolf and Ley, 2019).

Dyslipidemia was detected in 55.8% of participants with psoriasis, indicating a high risk of the condition. Additionally, the danger of dyslipidemia rises as the severity of psoriasis increases. Consequently, it is crucial to conduct routine serum lipid tests on all psoriatic patients in order to detect dyslipidemia at an early stage and prevent complications such as cardiovascular disease. Cardiovascular disease (CVD) accounted for 31% of all global deaths in 2015, resulting in an estimated 17.9 million deaths and affecting an estimated 422.7 million individuals (Song *et al.*, 2020; Mozaffarian, 2017).

The diagnosis of atherosclerosis is based on the presence of carotid plaque and an increase in carotid intima-media thickness, which was proportional to age and was more prevalent in men than in women. The scope of this diagnosis is restricted to individuals among the ages of 30 and 79 (Zhu *et al.*, 2012). It is well-established that AIRDs are associated with atherosclerotic CVD (Hollan *et al.*, 2013). This is associated with the elevated expression of prothrombotic mediators, upregulation of oxidative stress, proinflammatory cytokines, and abnormal vascular tone in these patients (Salmon and Roman 2008). In addition to conventional atherosclerotic risk factors such as hypertension, hyperlipidemia, and diabetes mellitus, rheumatic disease mechanisms are involved in the development and progression of atherosclerotic CVD in all vascular beds. Patients with rheumatic diseases are primarily affected by the extent, duration, and control of the disease process, which in turn influences the progression of atherosclerotic CVD. However, the risk of atherosclerotic cardiovascular disease is elevated in all patients with rheumatic diseases. (Mahtta *et al.*, 2020). Furthermore, the factors that significantly contribute to the development of premature atherosclerosis in patients with autoimmune rheumatic disease are currently unknown (Prasad *et al.*, 2015).

AIRDs' mortality rate is elevated. The primary causes of mortality in autoimmune diseases are active diseases, infections, and/or cardiovascular diseases. Furthermore, the morbidity and mortality rates of cardiovascular diseases in these patients may be at least two to three times higher than those of the general population. In reality, cardiovascular diseases are responsible for up to 30–50% of the mortality associated with rheumatological autoimmune diseases. Chronic systemic inflammation, a complication of autoimmune diseases, and the subsequent release of cytokines accelerate the atherosclerosis process. This acceleration may be attributable to the disease, its treatment, or its complications (Buleu *et al.*, 2019). Each relapse and recurrent acute inflammation significantly exacerbates the disease's prognosis, particularly in terms of the occurrence of cardiovascular events (Szekanecz *et al.*, 2016; Minno *et al.*, 2012).

Assessment of Atherosclerosis

1-Radiological assessment by Musculoskeletal ultrasound

In recent decades, the atherosclerotic disease process has been assessed through the utilization of advancements in all major non-invasive imaging technologies. Ultrasound is distinguished from other imaging modalities by its low cost and widespread availability. (Steinl and Kaufmann, 2015)

According to the report, the total plaque area or volume and the number of visualized plaques are independent predictors of future cardiovascular mortality and coronary events. Protrusions of the intima-media can be identified as established atherosclerotic lesions using anatomical B-mode ultrasound imaging (Steinl and Kaufmann, 2015).

The development of plaques that are large enough to be observed with ultrasound occurs at a relatively late stage in the progression of atherosclerosis. However, high-resolution ultrasound can be used to measure intima media thickness (CIMT) increases in the carotid arteries that occur prior to plaque formation. In numerous large observational trials, an increase in CIMT has been identified as a risk factor for cardiovascular events. Consequently, preliminary evaluations of the efficacy of novel therapies that target atherosclerosis may also be facilitated by CIMT measurements, which are advantageous in population trials. (Nambi *et al.*, 2010).

A single longitudinal measurement of CIMT was taken manually for both sides just prior to the bifurcation of the common carotid artery. Atherosclerosis is defined as a CIMT score exceeding 0.9 mm.

The International Brachial Artery Reactivity Task Force evaluates flow-mediated dilatation (FMD) of the brachial artery through a technique report.

Using the formula flow-mediated dilation at brachial artery $=[(Df-Di)/Di] \times 100$, flow mediated dilation was calculated. Endothelial dysfunction was defined at a flow-mediated dilation at brachial artery less than 11.1% (Babalic *et al.*, 2022).

DI: Diameter at rest DF: Diameter post deflation

This technique used to detect the elasticity of brachial artery, as there is impaired FMD in long standing PsA with atherosclerosis which indicate endothelial dysfunction.

Doppler studies were conducted to assess the CIMT and brachial flow-mediated dilatation. (Harris *et al.*, 2010).

2-Laboratory Assessment of Atherosclerosis

The lipid measurements for LDL cholesterol, triglycerides, HDL cholesterol, VLDL, and total cholesterol were obtained from serum samples that were fasted for approximately 10 hours (Yilmazer *et al.*, 2015).

Conclusions

The CIMT is a fundamental tool to detect early subclinical atherosclerosis in PsA patients especially in individuals with other cardiovascular risk factors like, hypertension, high BMI, smoking, high disease activity and with longer duration of the disease.

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