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Clinical Research

Similarities in Coronary Function and Myocardial Deformation Between Psoriasis and Coronary Artery Disease: The Role of Oxidative Stress and Inflammation

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See editorial by Mancini, pages 242-243 of this issue.

ABSTRACT

Background: Psoriasis has been associated with increased risk for coronary artery disease (CAD). We investigated the presence of vascular and subclinical left ventricular (LV) dysfunction in patients with psoriasis compared with patients with CAD.

Methods: We compared 59 patients with psoriasis without evidence of CAD (psoriasis area and severity index [PASI], 11.5 ± 8) with 59 patients with angiographically documented CAD and 40 controls. We measured (1) the carotid-femoral pulse wave velocity (PWVc) and central augmentation index (CAI), (2) coronary flow reserve (CFR) by Doppler echocardiography, (3) flow-mediated dilation (FMD) of the brachial artery and carotid intima media thickness (IMT), (4) LV global longitudinal strain (GLS) and GLS rate (GLSR) using speckle tracking echocardiography, and (5) malondialdehyde (MDA) and interleukin-6 (IL-6) levels.

Results: Patients with psoriasis had higher PWVc, CAI, IMT, MDA, and IL-6 levels and lower FMD, CFR, GLS, and GLSR than did controls ($P < 0.05$), but they had values of these markers that were similar to those of patients with CAD ($P > 0.05$) after adjustment for athero-

RÉSUMÉ

Introduction : Le psoriasis est associé à l'augmentation du risque de coronaropathie (CP). Nous avons étudié la présence de la dysfonction vasculaire et de la dysfonction ventriculaire gauche (VG) infraclinique chez les patients souffrant de psoriasis par rapport aux patients souffrant de CP.

Méthodes : Nous avons comparé 59 patients souffrant de psoriasis sans signe de CP (indice d'étendue et de gravité du psoriasis [PASI : *psoriasis area and severity index*], 11,5 ± 8) à 59 patients souffrant de CP démontrée par angiographie et à 40 témoins. Nous avons mesuré : 1) la vitesse de l'onde de pouls carotido-fémorale (VOPcf) et l'indice d'augmentation de la pression centrale (IApc); 2) la réserve coronarienne (RC) par échocardiographie Doppler; 3) la dilatation de l'artère brachiale induite par le flux (DIF) et l'épaisseur de l'intima-média de la carotide (EIMc); 4) la déformation longitudinale globale (DLG) du VG et le taux de déformation longitudinale globale (TDLG) par échocardiographie *Speckle Tracking* (suivi de pixel); 5) les concentrations de malondialdéhyde (MDA) et d'interleukine 6 (IL-6).

Psoriasis is an immune-mediated disease affecting about 3% of the adult general population[1] and has been associated with atherosclerosis and increased cardiovascular risk.[2,3] Psoriasis and coronary artery disease (CAD) share common pathophysiological mechanisms, including inflammation, oxidative stress, and common genetic susceptibility.[3]

Established prognostic markers of vascular integrity and function—namely, carotid-femoral pulse wave velocity (PWV), central augmentation index (CAI),[4-7] carotid intima media thickness (IMT),[6] coronary flow reserve (CFR) as assessed by Doppler echocardiography, and brachial artery flow-mediated dilation (FMD),[8-10]— have been found to be impaired in patients with psoriasis.[7,11-13] Longitudinal myocardial deformation of the left ventricle, as assessed by

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sclerotic risk factors: (PWVc [m/s], 10.4 ± 1.8 vs 8.6 ± 1.5 vs 10.3 ± 2, respectively; CFR, 2.4 ± 0.1 vs 3.4 ± 0.6 vs 2.6 ± 0.6, respectively; GLS [%], −16.2 ± 4 vs −21.9 ± 1.6 vs −16.6 ± 4.5, respectively; GLSR [L/sec], −0.85 ± 0.2 vs −1.2 ± 0.12 vs −0.9 ± 0.4, respectively; MDA [nM/L], 1.68 vs 1.76 vs 1.01, respectively; IL-6 [pg/mL], 2.26 vs 2.2 vs 1.7, respectively; $P < 0.05$ for all comparisons). PASI was related to IMT ($r = 0.67$; $P < 0.01$). Decreased GLS was associated with increased MDA, IL-6, PWVc, CAI, and reduced CFR ($P < 0.05$).

Conclusions: Psoriasis and CAD present similar vascular and LV myocardial dysfunction, possibly because of similar underlying inflammatory and oxidative stress processes. Vascular dysfunction in psoriasis is linked to abnormal LV myocardial deformation.

Résultats : Les patients souffrant de psoriasis avaient des VOPcf, IApc, EIMc, et des concentrations de MDA et de IL-6 plus élevés et des DIF, RC, DLG et TDLG plus faibles que les témoins ($P < 0,05$), mais les valeurs de ces marqueurs étaient similaires à celles des patients souffrant de CP ($P > 0,05$) après l'ajustement des facteurs de risque d'athérosclérose : (VOPcf [m/s], 10,4 ± 1,8 *vs* 8,6 ± 1,5 *vs* 10,3 ± 2, respectivement; RC, 2,4 ± 0,1 *vs* 3,4 ± 0,6 *vs* 2,6 ± 0,6, respectivement; DLG [%], −16,2 ± 4 *vs* −21,9 ± 1,6 *vs* −16,6 ± 4,5, respectivement; TDLG [l/sec], −0,85 ± 0,2 *vs* −1,2 ± 0,12 *vs* −0,9 ± 0,4, respectivement; MDA [nM/l], 1,68 *vs* 1,76 *vs* 1,01, respectivement; IL-6 [pg/ml], 2,26 *vs* 2,2 *vs* 1,7, respectivement; $P < 0,05$ pour toutes les comparaisons). Le PASI était associé à la EIMc ($r = 0,67$; $P < 0,01$). La diminution de la DLG était associée à l'augmentation du MDA, de la IL-6, de la VOPcf, du IApc, et à la réduction de la RC ($P < 0,05$).

Conclusions : Le psoriasis et la CP présentent des dysfonctions vasculaire et myocardique ventriculaire gauche similaires, possiblement en raison des processus de stress inflammatoire et oxydatif sous-jacents similaires. La dysfonction vasculaire lors de psoriasis est liée à la déformation anormale du myocarde VG.

speckle tracking echocardiography, is a major determinant of adverse left ventricular (LV) remodelling and prognosis after myocardial infarction.[14] Abnormal PWV and CFR are related to increased inflammatory and oxidative stress burden as well as impaired longitudinal LV function in hypertensive patients and those with rheumatoid arthritis.[9,15,16] However, the oxidative stress burden, myocardial deformation abnormalities, and the impact of vascular dysfunction on LV myocardial deformation have not been clearly defined in patients with psoriasis.

We hypothesized that (1) markers of vascular and LV function are impaired in patients with psoriasis compared with controls but are similar to those in patients with CAD and (2) vascular and coronary microcirculatory dysfunction has a negative impact on LV function in patients with psoriasis on the basis of a similar inflammatory and oxidative stress burden.

Thus in the present study, we investigated (1) vascular structure and function as assessed by carotid IMT, PWV, augmentation index, FMD of the brachial artery, and CFR of the left anterior descending artery; (2) LV myocardial deformation as assessed by 2-dimensional speckle tracking echocardiography; (3) oxidative stress as assessed by malondialdehyde (MDA) levels, and inflammatory burden as assessed by interleukin 6 (IL-6) levels in patients with psoriasis compared with patients with CAD and controls.

Methods

Study population

We studied 59 patients with psoriasis matched by age and sex with 59 patients with angiographically documented CAD ($\geq$ 70% luminal diameter stenosis) and preserved ejection fraction (EF) > 50%.

Forty participants with age, sex, and atherosclerotic risk factors similar to those of the patients with psoriasis—with normal electrocardiograms, echocardiograms, treadmill test results, and stress echocardiograms—were selected as a control group with low risk for obstructive CAD from participants attending the cardiology outpatient clinic.

The psoriasis area and severity index (PASI) was calculated in all patients.[17] All patients with psoriasis received treatment with cyclosporine 2.5-3 mg/kg daily. The disease duration from initial diagnosis until inclusion in the study was 61.3 ± 15 months. All patients had plaque-type psoriasis, and no one had psoriatic arthritis or inflammatory bowel syndrome. Exclusion criteria for patients with psoriasis were presence of wall motion abnormalities and EF $\leq$ 50%, psoriatic arthritis, history of acute coronary syndrome, familial hyperlipidemia, diabetes mellitus, chronic obstructive pulmonary disease or asthma, moderate or severe valvular heart disease, primary cardiomyopathies, and malignant tumours. CAD was excluded in patients with psoriasis by the absence of clinical history, angina, and reversible myocardial ischemia as assessed by a treadmill test and stress echocardiography.

Regarding the group of patients with CAD, we included 59 patients who fulfilled all the following criteria: (1) exercise and stress-related angina, (2) evidence of reversible ischemia during a treadmill exercise test and stress echocardiography, and (3) angiographically documented stenosis of $\geq$ 70% in 1 or several of the major coronary arteries within 1 year before inclusion in the study. All participants attended our preventive medicine laboratory. Exclusion criteria were a history of ST-elevation myocardial infarction, presence of wall motion abnormalities or EF of $\leq$ 50%, or both, to exclude the presence of transmural scar compromising myocardial deformation indices. Other exclusion criteria were history of acute coronary syndrome without ST-segment elevation within the past year, familial hyperlipidemia, diabetes mellitus, chronic obstructive pulmonary disease or asthma, moderate or severe valvular heart disease, and malignant tumours. We performed vascular and LV function assessment on the same day in all patients and controls. The study protocol was approved by our institute's ethics committee, and written informed consent forms were obtained from all patients.