



# Autoimmune and inflammatory diseases

## Enfermedades autoinmunes e inflamatorias

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### INTRODUCTION

The prevalence of autoimmune diseases (AI) is around 4%. It is more common in women (78-80%), with a higher incidence of cardiovascular disease (CVD), which is considered an emerging or gender-specific cardiovascular risk factor (CVR). There is an increased immune and inflammatory response, suggesting an involvement of the sex chromosome and sex hormones. Risk factors (RF) and poor lifestyles, immune system disorders, chronic systemic inflammation, endothelial dysfunction, increased oxidative stress, and accelerated atherosclerosis (atherosclerotic cardiovascular disease - ACVD) at the coronary artery level and microvessels. The risk of developing ACVD shows a linear relationship with the activity and severity of AI, higher in women < 40 and with SLE. The risk of ACVD in rheumatoid arthritis (RA) is 1.5 to 2, psoriatic arthritis (PSA) 1.5 to 1.7, systemic lupus erythematosus (SLE) 2 to 3, and 2 to 12 in vasculitis. They can present valvular, pericardial disease, myocarditis, fibrosis, heart failure (HF), and arrhythmias. RA and SLE are more likely to develop left ventricular hypertrophy (LVH) (RR 6.5 and 4, respectively).<sup>1-3</sup> Nonsteroidal anti-inflammatory drugs (NSAID) and corticosteroids reduce inflammation and cause dyslipidemia, hyperglycemia, obesity, and hypertension. Biological immunosuppressants as anti-TNF (adalimumab, etanercept, infliximab) and non-TNF (abatacept, anakinra, and rituximab) reduce CVR (< 30%) (suppress inflammatory state and improve endothelial function), the same as disease-modifying drugs (DMD)

(hydroxychloroquine, methotrexate, and sulfasalazine).<sup>1,4</sup>

In women with intermediate CVR (according to the risk calculator for CVD of the American Heart College), the existence of AI should be considered a «risk increaser or potentiator». The available tools underestimate the existing CVR by 12 to 20%.<sup>1,4</sup> The Interamerican Society of Cardiology (SIAC),<sup>4</sup> in the guide on primary prevention of cardiovascular disease in women, recommends:

1. Calculation of CVR and controlling CVRF (recommendation class IIb, evidence level A).
2. Healthy lifestyles (recommendation class I, evidence level B).
3. Apply in RA a correction factor of 1.5 on the risk calculation score and search for subclinical atherosclerosis (recommendation class IIa, evidence level B).
4. Regular blood pressure measurement is recommended, and if necessary, implement treatment (recommendation class I, evidence level B).

### TREATMENT, MONITORING, AND PREVENTION OF CARDIOVASCULAR DISORDERS

The drugs used in AI pose a high risk of complications and systemic and CV adverse effects<sup>1,5,6</sup> (Table 1).

### NON-INVASIVE CARDIOVASCULAR IMAGING

Noninvasive imaging methods assess disease activity, treatment effects, and complications.<sup>7</sup>

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Table 1: Pharmacological therapy, secondary and adverse effects.

| Drug   | Indications                   | Mechanisms of injury  | Alterations and metabolic and cardiovascular risks  |
|--|-------------------------------|---|---|
| Nonsteroidal anti-inflammatory drugs<br>Glucocorticoids            | All inflammatory diseases     | Direct endothelial damage, decreased nitric oxide and bleeding<br>Inhibition of the hypothalamic-pituitary-adrenal axis, premature atherosclerosis, water retention, insulin resistance | Arterial hypertension<br>MI, CVE, AF, HF<br>Osteoporosis, obesity, high blood pressure, MI, CVE, HF, arrhythmias (AF, flutter), DVT, PE |
| Antimalarials drugs (hydroxychloroquine)<br>Cyclophosphamide       | SLE, RA, SS<br>SLE, SSc       | QT prolongation, electrolyte imbalances<br>Direct drug toxicity   | Arrhythmias (torque de pointes, ventricular tachycardia), cardiotoxicity<br>Cardiotoxicity, premature ovarian failure, cytopenias       |
| Metotrexato  | RA, myopathies<br>SS, SLE, TA | Increased LDL, hyperhomocysteinemia, folate inhibitor   | Elevated liver enzymes, exacerbation of rheumatic nodules, nephropathy, hypercholesterolemia  |
| Anti-CD20 (rituximab)<br>JAK inhibitors (baricitinib, tofacitinib) | SLE, SS<br>SLE, RA            | Ventricular remodeling<br>Hypercoagulability  | HF<br>MI, CVE, DVT, PE, hypercholesterolemia  |
| Anti-TNF alfa (etanercept, infliximab)                             | RA, TA                        | Left ventricular dysfunction  | HF worsening  |

MI = myocardial infarct. CVE = cerebral vascular event. AF = atrial fibrillation. DVT = deep vein thrombosis. PE = pulmonary thromboembolism. SLE = systemic lupus erythematosus. RA = rheumatoid arthritis. SS = Sjogren's syndrome. SSc = systemic sclerosis. TA = Takayasu arthritis. HF = heart failure.

Echocardiography shows valvular involvement (30-70%), pulmonary arterial hypertension (20-30%), pericardial effusion (30%), mobility alterations, and subclinical systolic/diastolic dysfunction (30%).<sup>3,7-9</sup> Single photon emission tomography (SPECT) and positron emission tomography (PET), nuclear magnetic resonance (NMR), and computed tomography (CT) allow an anatomical assessment of the coronary tree and great vessels (inflammation) and functional (ischemia).<sup>10</sup>

### CONCLUSIONS

Autoimmune diseases confer high cardiovascular risk in women. The calculation of the CVR and intensification of the CVRF are essential. CV imaging is helpful in the diagnosis of complications and follow-up. Management requires multidisciplinary intervention to reduce cardiovascular morbidity and mortality.

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