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Cardiovascular disease in inflammatory rheumatic diseases

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A B S T R A C T

Chronic inflammatory rheumatic diseases (IRD), including rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis, are prevalent conditions worldwide, with a considerable burden on healthcare systems. They are associated with increased cardiovascular (CV) morbidity and mortality. In this review, we focused on the epidemiology, traditional CV risk factors, genetics, and the link between chronic inflammation, atherosclerosis, and CV disease. Remarkably, patients with IRD have higher vulnerability to atheromatous plaques. The risk of unstable plaques is higher in patients with rheumatoid arthritis than in controls. Active disease is a characteristic ascribed to vulnerability and rupture of plaques and a cause of thrombosis in IRD. Management of CV risk in patients with IRD includes optimal control of disease activity. CV risk stratification by applying risk charts is also essential. Imaging techniques might be useful to determine the actual CV risk of patients with IRD who are included in the category of intermediate or moderate CV risk.

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Introduction

Treatment strategies and outcome of inflammatory rheumatic diseases (IRD) have considerably changed since the application of tight control of the disease and advent of biologic therapies, which are always adjusted to specific therapeutic targets. Presently, patients with chronic IRD die more frequently because of infectious complications and certain comorbidities than because of the disease itself. Within the general comorbidity of IRD, cardiovascular (CV) disease (CVD) is the most relevant.

In this chapter, we will focus on the CV morbidity of the most prevalent IRD: rheumatoid arthritis (RA) and spondyloarthritis, particularly on ankylosing spondylitis (AS) and psoriatic arthritis (PsA). Other diseases included in the group of spondyloarthritis, such as undifferentiated spondyloarthritis and nonradiographic axial spondyloarthritis, are not discussed in this review because of the lack of consistent data on the CV comorbidities in these entities.

The current knowledge on CVD in patients with IRD has been updated. Therefore, a PubMed search of the most relevant literature was performed, particularly studies published in English over the last 10 years.

Epidemiology of cardiovascular disease in inflammatory rheumatic diseases

Standardized mortality ratios (SMRs) in patients with IRD are higher than those in the general population (1.3–2.3 in RA, 1.6–1.9 in AS, and 0.8–1.6 in PsA, respectively). This increased and often premature mortality is mainly due to CV events [1]. A recent cross-sectional study on individuals periodically followed-up at rheumatology outpatient clinics has shown that despite having low disease activity, the prevalence of CVD in patients with IRD remains elevated compared with individuals without IRD [2]. Another recent population-based study has confirmed that CV mortality among patients with RA in the past 15 years was higher than that in the general population [3]. In this regard, a meta-analysis showed that CV mortality in RA was 50% higher than that in the general population [4], with a 59% increase due to ischemic heart disease (IHD) and a 52% increase due to cerebrovascular accidents (CVA) [4]. The risk of myocardial infarction (MI) and CVA was increased by 68% and 41%, respectively, in patients with RA compared to the general population [5]. Moreover, the risk of MI in RA corresponds to the overall risk of MI observed in non-RA subjects who are on average 10 years older [6]. Interestingly, this increased risk of CVD in RA is comparable to that observed in type 2 diabetes mellitus (DM) [7,8].

Importantly, the presentation of cardiac symptoms in RA is often different from that seen in the general population. It is not uncommon to see RA patients with unrecognized coronary symptoms that are misdiagnosed as mechanical or atypical chest pain that later develops into heart failure more frequently than the general population [9]. This is the result of a process of accelerated atherogenesis that represents the common pathogenic link between CV comorbidity and IRD [5].

In addition to higher mortality ratios than the general population, AS and PsA patients also have an increased rate of CV mortality [10]. Several studies have shown that IHD, CVA, and peripheral arterial disease (PAD) are more common in patients with AS or PsA than in the general population [11,12]. Dutch investigators confirmed that the prevalence of MI was more in patients with AS than in the general population [13]. With respect to this, a meta-analysis of seven longitudinal studies revealed a significant increase in MI [odds ratio (OR) 1.60, 95% confidence interval (CI) 1.32–1.93] in AS patients compared to the general population [14]. A significantly increased incidence of stroke was also found (OR 1.50, 95% CI 1.39–1.62) [14].

Estimation of the CV risk attributed to PsA is more difficult because of the potential CV burden that skin disease itself confers to patients with PsA [15]. Indeed, patients with severe psoriasis have greater global and CV mortality than the general population with a SMR of 1.52 (95% CI 1.44–1.60) [16]. In a population-based cohort study comparing patients with psoriasis, PsA, and RA, after adjustment for traditional CV risk factors (CVRFs), the number of major adverse CV events was more in PsA patients not receiving any disease-modifying antirheumatic drug (DMARD) [hazard ratio (HR) 1.24, 95% CI 1.03–1.49], patients with RA (non-DMARD users: HR 1.39, 95% CI 1.28–1.50; DMARD users: HR 1.58, 95% CI 1.46–1.70), patients with psoriasis not using DMARDs (HR 1.08, 95% CI 1.02–1.15), and patients with severe psoriasis using DMARDs (HR 1.42, 95% CI 1.17–1.73) [17].

A Danish nationwide cohort study reported a significantly increased overall mortality in patients with psoriasis [risk ratio (RR) 1.74, 95% CI 1.32–2.30], particularly arising from CVD (RR 1.84, 95% CI

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