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Metabolic abnormalities in patients with inflammatory rheumatic diseases

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A B S T R A C T

Patients with rheumatoid arthritis (RA) experience an increased cardiometabolic risk factor burden that is substantially driven by systemic inflammation. This occurs less consistently in patients with ankylosing spondylitis (AS). Psoriatic arthritis most strongly associates with excess adiposity and metabolic risk. RA patients also often have systemic inflammation-induced proinflammatory high-density lipoprotein (HDL) cholesterol particles and lean/muscle mass loss in association with increased adiposity, a condition termed rheumatoid cachexia, which further enhances cardiovascular risk. The presence of proinflammatory HDL and lean mass loss was also reported in patients with AS. Individualized aerobic and resistance exercise programs can improve body composition and metabolic risk factor profiles in RA and AS. Future studies should assess how long-term lifestyle changes can be effectuated and if these can influence cardiovascular events in inflammatory rheumatic diseases. Herein, we review the current evidence on metabolic abnormalities in inflammatory arthritis. We propose management strategies and a research agenda.

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Introduction

The increased risk of cardiovascular disease (CVD) in rheumatoid arthritis (RA) is now well documented. In a meta-analysis of 14 studies among 41,490 patients with RA, the pooled relative risk (RR) for incident CVD was 1.48 (95% confidence interval (CI) 1.36 to 1.62) with a significantly increased risk of myocardial infarction (MI) and cerebrovascular accidents of 68% and 41%, respectively [1]. Likewise, a meta-analysis of 24 mortality studies among 111,758 RA patients revealed that the weighted standardized mortality rate (SMR) for CVD death was 1.59 (95% CI 1.46 to 1.73) with a significantly increased risk of death from ischemic heart disease (IHD) and cerebrovascular accidents of 59% and 52%, respectively [2]. Recently, Fransen et al. [3] reported in a meta-analysis of 13 studies that compared to the general population, the RR of a CVD event is 2.59 (95% CI 1.77 to 3.79) and 1.27 (95% CI 1.16 to 1.38) in RA patients <50 years compared to those aged ≥50 years. This indicates that the increased risk of CVD events is particularly high in young RA patients. Although less extensively investigated, patients with other types of inflammatory arthritis including ankylosing spondylitis (AS) and psoriatic arthritis (PsA) are likely to experience a similarly increased burden of comorbid CVD. Indeed, two further recent meta-analyses revealed a significant 60% and 50% increased risk of incident MI and stroke, respectively, in AS, and 68% for MI and 22% for cerebrovascular disease in PsA [4,5].

The mechanisms underlying the enhanced risk of atherosclerotic CVD in inflammatory arthritis are currently under investigation. Studies have consistently shown that besides a range of genetic factors [6], disease characteristics and traditional CVD risk factors are independently associated with increased atherosclerosis and cardiovascular events [7–10] in inflammatory arthritis. Studies in this area have focused predominantly on systemic inflammation as a disease feature. Importantly, systemic inflammation can augment atherogenesis not only through its direct effects on the vasculature but also by its adverse impact on traditional CVD risk factors [11–14]. Indeed, the traditional cardiovascular risk factor burden is increased in inflammatory arthritis and its substantial contribution to CVD events is increasingly recognized [15].

Traditional CVD risk factors comprise mainly the metabolic abnormalities of obesity, impaired glucose metabolism, dyslipidemia, and high blood pressure [16]. Apart from their individual contribution to atherosclerosis, these risk factors interrelate and thereby cluster into the metabolic syndrome (MetS), the presence of which enhances the risk of atherosclerotic CVD twofold in the non-RA population [16]. In addition, in nondiabetic persons, MetS increases the risk of type 2 diabetes fivefold. Metabolic risk factors can be favorably modified by lifestyle intervention [16].

In this chapter, we review metabolic abnormalities in RA, AS, and PsA (summarized in Table 1). We conducted a Medline search up to August 2016 using the terms “metabolic factors,” “obesity,” “body composition,” “insulin resistance,” “lipids,” “diabetes,” “hypertension,” “metabolic syndrome,” “diet” and “physical activity,” and combined each with “rheumatoid arthritis,” “ankylosing spondylitis,” and “psoriatic arthritis.” We concentrated on recent systematic reviews and meta-analyses. We propose management strategies aimed at reducing the metabolic risk factor burden in inflammatory arthritis (summarized in Table 2) and propose a research agenda.

Table 1
Metabolic risk factor profiles in patients with RA, AS, and PsA.

Metabolic factor	RA	AS	PsA
BMI	unaltered or increased	unaltered	markedly increased
Body fat	increased	unaltered or reduced	increased
Lean mass	reduced	unaltered or reduced	unaltered
Insulin resistance	increased	unaltered	increased
Diabetes	increased	unaltered	increased
HDL cholesterol	reduced	reduced	reduced
Triglycerides	unaltered or increased	unaltered	increased
Proinflammatory HDL particles	increased	increased	unknown
Hypertension	unaltered or increased	unaltered	increased
Metabolic syndrome prevalence	increased	increased	increased

RA: rheumatoid arthritis; AS: ankylosing spondylitis; PsA: psoriatic arthritis; BMI: body mass index; HDL: high density lipoprotein.

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