Mini Review

The risk of cardiovascular disease in patients with rheumatoid arthritis: A discussion of the link, response to treatment, and the path forward

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Introduction

Increased risk of Cardiovascular Disease (CVD) in patients with Rheumatoid Arthritis (RA) has been well established for decades and bolstered by countless studies since the 1950's [1,2]. Numerous papers have explored the pathogenesis and have demonstrated that the systemic inflammation caused in RA increases arterial stiffness, which may result from loss of elasticity and stenosis [3,4]. The inflammation also impairs cholesterol efflux and leads to destabilization of coronary plaque, increasing the risk of rupture and infarction [5,6]. Studies have further demonstrated that active RA causes an imbalance in the dilatation and vasoconstriction of the endothelium, and enhanced residence of reactive oxygen species and proinflammatory factors within the endothelial walls, leading to barrier permeability and leakage of inflammatory mediators into the Cardiovascular (CV) tissue [7,8].

Epidemiology of cardiovascular disease in rheumatoid arthritis

The elevated risk of developing CVD is associated with significant morbidity and mortality as well as high healthcare related costs [9]. Prior research has shown a mortality that is 1.5 times higher in patients with RA compared with the general population and that CVD is the leading source of mortality, accounting for 30–40% of deaths [10]. Despite more aggressive strategies of early RA treatment, increased premature mortality persists [11].

Impact of rheumatoid arthritis disease management on cardiovascular risk

Multiple studies have shown that effectively combatting RA decreases the risk of clinical CVD [12]. Dampening of articular inflammation has been shown to improve arterial stiffness [13]. Moreover, disease control results in lowered levels of N-terminal pro-brain natriuretic peptide (NT-proBNP), homeostasis model assessment–estimated insulin resistance, total cholesterol, and high-density lipoprotein cholesterol (TC/HDL-C), all validated biomarkers of CVD [14,15].

The Cardiovascular Inflammation Reduction Trial showed that treatment with methotrexate (MTX), the gold standard choice for initial therapy in RA, in particular, reduces the risk of congestive heart failure (CHF) related hospitalizations [16]. MTX also reduces all-cause CVD. Furthermore, studies have illustrated its role in reducing levels of high sensitivity C-reactive protein, interleukin (IL) 6, and tumor necrosis factor α (TNF-α) [17]. MTX also helps to restore vascular endothelial vasodilation, most likely as a result of its potent anti-inflammatory effects [18].

Role of cytokine inhibitors in lowering cardiovascular risk

The cardioprotective effect provided by use of MTX is enhanced by the use of anti-TNF-α agents in treating patients with RA. Use of TNF-α blocking agents is associated with a

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