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Heart involvement in rheumatoid arthritis: Multimodality imaging and the emerging role of cardiac magnetic resonance

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ABSTRACT

Objectives: Patients with rheumatoid arthritis (RA) exhibit a high risk of cardiovascular disease (CVD). CVD in RA can present in many guises, commonly detected at a subclinical level only.
Methods: Modern imaging modalities that allow the noninvasive assessment of myocardial performance and are able to identify cardiac abnormalities in early asymptomatic stages may be useful tools in terms of screening, diagnostic evaluation, and risk stratification in RA.
Results: The currently used imaging techniques are echocardiography, single-photon emission computed tomography (SPECT), and cardiac magnetic resonance (CMR). Between them, echocardiography provides information about cardiac function, valves, and perfusion; SPECT provides information about myocardial perfusion and carries a high amount of radiation; and CMR—the most promising imaging modality—evaluates myocardial function, inflammation, microvascular dysfunction, valvular disease, perfusion, and presence of scar. Depending on availability, expertise, and clinical queries, "right technique should be applied for the right patient at the right time."
Conclusions: In this review, we present a short overview of CVD in RA focusing on the clinical implication of multimodality imaging and mainly on the evolving role of CMR in identifying high-risk patients who could benefit from prevention strategies and early specific treatment targeting the heart. Advantages and disadvantages of each imaging technique in the evaluation of RA are discussed.

Introduction

Rheumatoid arthritis (RA) is a common inflammatory autoimmune disorder of the joints that affects ~1% of the population. RA is a chronic, incurable condition and has a significant impact on quality of life resulting in a high socioeconomic burden [1]. Apart from synovial tissue destruction and remodeling, RA also presents with extra-articular manifestations such as vasculitis, lung disease, and cardiac complications, which include amongst others pericarditis, myocarditis, valvular disease, and most importantly, ischemic heart disease and heart failure [2–4]. RA patients have a reduced life expectancy mainly due to increased cardiovascular morbidity compared to the general population [5] and as demonstrated by a recent meta-analysis the majority of deaths are due to cardiovascular disease (CVD) [6]. Although several reports indicate that traditional CVD factors such as hypertension [7], dyslipidemia [8], insulin resistance [9], body composition alterations [10], and sedentarity [11] are important contributors, they are not sufficient to explain the entire magnitude of the enhanced CVD risk in this population [12]. High-intensity systemic inflammation, RA disease characteristics, and their complex interplay with the aforementioned classic risk factors may also contribute to the increased CVD morbidity and mortality [13–18].

It has been shown that CVD in RA shares similarities with CVD in diabetes mellitus in terms of clinical presentation [19] and the presence of preclinical atherosclerosis [20]. Compared with non-diabetic controls, non-diabetic patients with RA and non-RA patients with type 2 diabetes mellitus have the same risk of developing CVD according to a nationwide Danish study [21]. Similar to what occurs in diabetes mellitus, patients with RA are less likely to report symptoms of angina, may have silent myocardial infarction, and experience higher fatality rates and worse outcome from acute coronary syndromes compared to general population [22]. The incidence of congestive heart failure is also increased in patients with RA and contributes to CVD increased mortality and morbidity [23]. These findings emphasize the

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necessity of a more detailed screening of cardiac involvement during RA before heart disease and/or failure become clinically overt or progress to irreversible stages.

In that respect, the utilization of biochemical markers [24,25] and modern imaging modalities [26,27] for the noninvasive CVD assessment and risk stratification for RA patients has attracted the interest of rheumatologists, cardiologists, and radiologists. The currently available data suggest that there is room for the introduction of novel diagnostic protocols based on imaging methods; however, such strategies need to be validated in large, well-controlled studies. This article aims to present a short overview of CVD disease in RA, focusing on the clinical implication of multimodality imaging and mainly on the evolving role of cardiac magnetic resonance imaging (CMR) in identifying patients at high risk who could benefit from prevention strategies and early specific treatment targeting the heart.

Methods

The search was performed using as inclusion criteria the available literature about (a) indications of different imaging techniques in Cardiology, describing also advantages and disadvantages, (b) pathophysiology of heart involvement during the course of RA, and (c) evidence of different imaging techniques performance in the evaluation of heart disease in RA.

Pathophysiology of heart involvement in RA

Pericarditis–myocarditis–endocarditis

Pericarditis is the most common heart problem caused by RA. The postmortem incidence of pericarditis in patients with RA is reported to be in the range of 11–50% [4,28]. During the last few decades, echocardiography has allowed the antemortem detection of pericardial effusions and other sequelae of pericarditis in about One-Third of patients with RA; however, the actual number of people with pericarditis symptoms and clinical evidence is much smaller, about 2% [29,30]. The onset of pericarditis seems to bear no relationship to the duration of arthritis, though it is more frequent in middle-aged males with active disease. It typically occurs in rheumatoid factor-positive patients, one-third of whom may have rheumatoid nodules and other extra-articular features of RA [31]. The prognosis of rheumatoid pericarditis is generally good, and treatment with oral steroids and non-steroidal anti-inflammatory drugs (NSAIDs) seems to be appropriate for the majority of patients. Whether pericarditis contributes to the overall cardiac morbidity and mortality is unknown; cardiac tamponade or constrictive pericarditis is very rare. In a small number of patients (2–5%), pericarditis represents the first clinical manifestation of RA, and a diagnostic approach with a full risk factor evaluation including serologic and immunologic investigations in individuals with new-onset pericardial effusions may result in early diagnosis and better clinical outcome [32]. The potential beneficial impact of aggressive strategies of RA management with conventional and biologic disease-modifying anti-rheumatic agents (DMARDs) on pericardial involvement in RA remains unclear.

Myocarditis is a rare but well-recognized form of rheumatoid cardiac inflammatory disease that assumes one of two different histological patterns: a granulomatous form that is considered specific for RA and a nonspecific form that may also be observed in other disorders [33]. When present, the granulomas show a predilection for the left ventricle and are morphologically identical to the subcutaneous nodules of RA [34]. This differs from the nonspecific inflammatory pattern, which is composed predominantly of lymphocytes, plasma cells, and histiocytes and involves the collagenous interstitium of the heart [35,36]. Both forms of RA-associated myocarditis have been implicated in fatal arrhythmias and secondary cardiomyopathy resulting in heart failure [37]. Drugs commonly used in the treatment of RA, such as corticosteroids and anti-malarials, have very rarely been associated with cardiac injury [38]. Although postmortem studies reported a high prevalence of RA myocarditis, particularly of the nonspecific type [34], it seldom becomes clinically apparent, and it is not usually included in the differential diagnosis of RA patients presenting with chronic heart failure. This is probably the result of the application of echocardiography in the routine evaluation for cardiac systolic function, as this technique is not able to detect the presence of an inflammatory process in the myocardium. The introduction of CMR, as the imaging modality of choice for myocarditis detection, is expected to further clarify this issue [39].

The prevalence of RA valvular heart disease is variable in the literature varying from 3% to 70% [4]. This high variability may be due to different genetic background of the studied population and different methods used for the detection of valvular disease. Mitral valve insufficiency appears to be the most common abnormality followed by aortic valve insufficiency [40]. In some studies, the occurrence of valvular heart disease is associated with male gender and the presence of rheumatoid nodules, age, disease duration, and degree of inflammatory activity [41], but such relationships have not been confirmed in other series [42]. Rheumatoid granuloma and other nonspecific valvular lesions could be detected within cusps, causing regurgitation, but may also result in fibrosis and calcification [4]. Although most patients are asymptomatic, the possibility of bacterial endocarditis, the formation of thrombus originating from the valvular inflammatory material, and the infrequent evolution of lesions to valve rupture with hemodynamic consequences require diligent surveillance, mainly in patients with more severe valvular disease [43].

Coronary artery disease

RA patients are at increased risk of suffering from CVD events which tend to occur approximately a decade earlier than age- and sex-matched controls [44]. Furthermore, they are twice more likely to develop myocardial infarction irrespective of age, history of prior CVD events, and traditional risk factors [45,46]. These observations have prompted some experts to consider RA as a coronary heart disease equivalent [47] and a novel risk factor for cardiovascular disease [48]. Structural and morphological variables of subclinical atherosclerosis such as carotid intima–media thickness [49] and coronary artery calcification [50] have been found to be worse in patients with prolonged arthritis than in patients of the same age with more recent disease onset, indicating that long-standing RA promotes atherosclerosis. Associations between acute phase reactants and morphologic features of premature atherosclerosis have also been established in some [51,52] but not all [53] the studies assessing carotid intima–media thickness and endothelial function in RA patients [20,54–63]. Atherosclerosis is now considered to be associated with chronic inflammatory mechanisms and shares significant pathophysiologic similarities with RA. For example, the recruitment of autoreactive and inflammatory cells, the cytokines synthesis, and the structural abnormalities observed during the development, progression, and rupture of atheromatous plaques are reminiscent of similar changes seen in chronic rheumatoid synovitis [64,65].

In RA, inflammation precedes atherosclerotic changes. It appears that parameters predisposing to enhanced CVD mortality are present very early during the natural history of the disease as rheumatoid factor-positive subjects are at highest risk of suffering from myocardial infarction, heart failure, and/or valvular