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REVIEW

The emerging role of cardiovascular magnetic resonance imaging in the assessment of cardiac involvement in juvenile idiopathic arthritis

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Abstract

Juvenile idiopathic arthritis (JIA) is the commonest rheumatic disease in childhood and presents several subtypes according to the ILAR classification. JIA, specifically in its systemic form, may seriously damage various structures of the cardiovascular system. Other JIA phenotypes are also of interest, as cardiovascular disease (CVD) is underestimated and understudied, but chronic systemic inflammation and risk factors remained important contributors for CVD development. The currently applied non-invasive modalities, although they are important for the initial evaluation of JIA patients, frequently fail to detect the silent, subclinical forms of CVD. Cardiovascular magnetic resonance (CMR), due to its multifaceted capability in the detection of cardiovascular disease, can offer early, reproducible, non-invasive information about cardiovascular disease in JIA, allowing risk stratification and timely initiation /modification of cardiologic and anti-rheumatic treatment. However, lack of availability/expertise and high cost still hamper its application in the clinical cardio-rheumatic practice. The aim of the current article is to present an overview of CVD in JIA emphasizing the emerging role of CMR in early diagnosis and treatment follow-up of CVD in JIA patients.

Keywords Juvenile rheumatoid arthritis · Cardiac magnetic resonance · Vasculitis · Myocarditis · Coronary artery disease · Fibrosis

Introduction

Juvenile idiopathic arthritis (JIA) is a heterogeneous group of chronic inflammatory arthritides with onset in patients under the age of 16 years. It is the most common rheumatic disease in childhood with a prevalence of 0.1% [1, 2]. JIA presents several subtypes with the most recently used classification by the ILAR [3] including oligo-articular JIA (the most common form), poly-articular JIA, poly-articular JIA with positive rheumatoid factor, enthesitis related arthritis, psoriatic arthritis (the latter two compose the spondylarthropathies) and systemic JIA [4]. JIA remission is usually achieved using new therapeutic approaches, but for many patients long-term immunomodulatory treatment is needed. According to the literature one-third of adults with JIA have persistent active disease, specifically those with poly-articular type [5, 6]. Sustained systemic inflammation accelerates atherosclerosis and therefore JIA patients are at increased risk of cardiovascular disease (CVD) [7]. The increased incidence of CVD in adult inflammatory arthritis creates a strong interest to further evaluate the CVD risk in JIA. However, there are some peculiarities characterizing the JIA including the following:

1. Juvenile idiopathic arthritis is a disease with significant differences in clinical presentation, prognosis and degree of systemic inflammation between subtypes and therefore atherosclerosis may not be present to the same degree in all subtypes

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2. The largest cohort studies of JIA include patients in childhood when clinical manifestations of CVD are unusual
3. Published data about CVD in JIA have been collected only from children and adolescents and their correlation to CVD presented later in the adult life remains unknown. However, there are studies supporting that the disease severity was associated with triglycerides level and atherogenic index and could be improved using anti TNF-α treatment with a beneficial effect on the cardiovascular risk in JIA patients [8].

Cardiac disease in systemic onset juvenile arthritis

Systemic onset juvenile arthritis (SoJIA) is characterized by high-spiking day fever, arthritis and evanescent rashes. The diagnosis of SoJIA is often challenging, because various infective diseases and/or other autoimmune, inflammatory diseases, specifically Kawasaki disease (KD) may share common clinical characteristics. The cardiac manifestations in SoJIA include coronary arteritis, myopericarditis, vasculitis, congestive heart failure, valvular abnormalities, pulmonary hypertension and conduction system abnormalities. Coronary artery dilatation, wall irregularities or thickening with or without myo-pericarditis are not unusual during SoJIA and should be differentiated from KD. The differential diagnosis between SoJIA and KD is based on persistent arthritis. Furthermore, in SoJIA biologic treatments are usually needed to achieve remission [9].

Myocarditis can be found in up to 5% of SoJIA, with recurrence in up to 60% of them. The rapid evolution of systemic symptoms combined with elevated cardiac biomarkers, electrocardiographic changes, lack of segmental wall-motion abnormalities on echocardiogram with or without pericarditis and elevated inflammatory markers, suggesting SoJIA flare-up, leads to the diagnosis of myocarditis [10]. The conventional therapy for acute myocarditis in SoJIA is to support the LV function using a standard therapeutic regimen including an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, a β-blocker, and a diuretic, if needed. In deteriorated patients despite optimal medical treatment, mechanical circulatory support should be considered as a bridge to transplantation or recovery. In patients with biopsy-proven, virus-negative inflammatory cardiomyopathy, immunosuppressive therapy is effective and safe in combination with supportive treatment for cardiac function [11, 12]. Children with SoJIA may develop myocarditis with consequent cardiomyopathy and congestive heart failure as a complication of the underlying disease process. Congestive heart failure as a presenting manifestation of SoJIA is rather unusual and can be controlled with intensive immunosuppressive therapy. Intravenous gamma globulin has been associated with recovery of left ventricular (LV) function and a trend toward better survival rates in children with acute myocarditis, due to SoJIA [13].

Although prominent in the systemic form of SoJIA, CVD has been described as less of a problem in the other disease subtypes. Few examples limited to case reports, case series or small cohorts of patients were presented with abnormal LV relaxation [14] or aortic abnormalities in patients with Poly-articular JIA [15, 16], ERA and juvenile ankylosing spondylitis [17]. The reason for the limited evidence may be the lack of clinically overt cardiac involvement in JIA. Furthermore, there are no reports or recommendations for routine cardiac screening in patients with JIA.

Cardiovascular magnetic resonance can provide accurate, reproducible and operator independent information about cardiovascular (CV) function and myocardial tissue characterization, including inflammation, stress perfusion defects and fibrosis. It has been recently applied as a useful adjunct in the diagnosis and treatment evaluation of various types of CVD in autoimmune rheumatic diseases (ARDs) [18].

The aim of the current article is to present an overview of CVD in JIA emphasizing the emerging role of cardiovascular magnetic resonance (CMR) in early diagnosis and treatment follow-up of CVD in JIA patients.

Research strategy

A MedLine, Embase and Scopus search was performed according to published guidance on narrative reviews [19] using the following terms: juvenile rheumatoid arthritis, rheumatoid arthritis, cardiovascular involvement, myocarditis, cardiac magnetic resonance. Original research papers and review articles focusing on the cardiac disease evaluated by CMR in patients with JIA up to December 2017 were selected to be included in this review. Publications not in English and data from ongoing research were excluded.

Why CVD risk should be considered in JIA?

Cardiovascular disease is an important cause of mortality and morbidity in patients with RA and also other forms of adult inflammatory arthritis. Therefore, EULAR has published guidelines recommending that cardiovascular risk is assessed annually in RA patients [20]. In addition to aggressive management of traditional cardiovascular risk factors, the guidelines emphasize the importance of controlling disease activity in order to reduce the CVD risk in these diseases [20].

Although JIA presents similarities with adult onset disease, there are still not available guidelines. Thus far, it has

been documented that abnormal lipid levels and atherogenic indices were associated with disease activity in JIA and improved significantly following effective anti-rheumatic treatment [21]. In addition, traditional risk factors including hypertension, dyslipidaemia and lack of physical activity are more apparent in JIA, compared to age-matched healthy controls. Furthermore, it should be considered that clinically overt CVD may not be presented until adulthood. It is also unclear, if the risk is the same for all subtypes of JIA or only for those with sustained inflammation. Therefore, based on the existing data, it seems reasonable to recommend CVD risk assessment in JIA, particularly in those with sustained inflammation [22].

Why should we consider cardiovascular magnetic resonance as a tool in JIA?

Cardiovascular magnetic resonance is a non-invasive imaging modality without ionizing radiation, capable of providing accurate and reproducible information about CV function and myocardial tissue characterization including assessment of inflammation, stress perfusion defects and/or fibrosis. CMR can differentiate patients with myocardial ischemia and/or subendocardial/transmural fibrosis due to either macro- or micro-vascular coronary artery disease [23, 24] from patients with epicardial, diffuse and/or segmental myocardial fibrosis secondary due to inflammation and/or cardiomyopathies [23, 24]. Furthermore, CMR can also evaluate pulmonary arterial hypertension (PAH), peri-myocardial disease and coronary artery disease acuity [25], extent and disease acuity of vascular inflammation [25] and the causal pathophysiologic processes behind silent or overt heart failure and rhythm disturbances [26, 27]. Apart from its use as gold standard for CV structure and function, CMR is ideal for tissue characterization. The signal intensity of CMR images is based on the magnetic properties of hydrogen nuclei in the patient's body. The two most commonly used indices are longitudinal relaxation time (T1) and transverse relaxation time (T2). T2 imaging offers qualitative and/or semiquantitative information about myocardial oedema using the ratio of myocardial vs skeletal muscle signal intensity. Recently, a true quantitative approach of myocardial oedema using T2 mapping has been proposed. T1 imaging can be used for perfusion evaluation (first-pass assessment) or for fibrosis assessment 15 min post-gadolinium injection (late gadolinium enhanced imaging: LGE). The clinical superiority of CMR compared to echocardiography is the use of LGE for the detection of replacement myocardial fibrosis, due to myocardial infarction (MI), myocarditis or cardiomyopathies (Fig. 1). LGE is based on the differences of signal intensity between scarred and normal myocardium to generate image contrast. This technique, although of great utility for detecting replacement myocardial fibrosis, is not capable to visualize diffuse myocardial fibrosis. To overcome this limitation, T1 mapping (native or pre-contrast and post-contrast) and extracellular volume fraction (ECV) measurement has been developed and enables identification of diffuse myocardial fibrosis, undetectable by the currently used circulating biomarkers [28]. The use of T1/T2 mapping indices has demonstrated that patients with autoimmune rheumatic diseases (ARDs) have higher T1 and T2 mapping values (more diffuse fibrosis and myocardial oedema) compared to controls, with most significant differences between patients and controls in native T1 and T2 mapping values, which are independent of the presence of LGE [29]. Using all these parameters together, CMR offers an excellent tool for assessment of the various aspects of CVD in JIA [29].

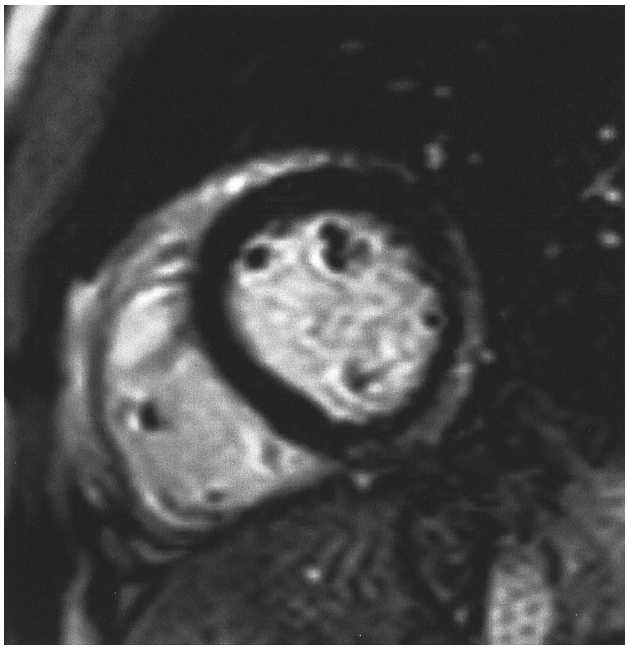

Fig. 1 Subepicardial LGE in the inferolateral wall of LV, due to myocardial inflammation in a JIA patient

Compared to echocardiography, the cornerstone of cardiac imaging, CMR has some important advantages. It is operator and acoustic window independent, more accurate and reproducible than echocardiography and can perform tissue characterization, which is of great value for the early detection of myocardial inflammation/fibrosis in JIA and can not be achieved by echocardiography. A summary of CMR advantages compared to other non-invasive imaging modalities is presented in Table 1.

Table 1 Summary of CMR advantages against other non-invasive imaging modalities

	Radiation	Cost	Cardiac function	Myocardial perfusion	Coronary arteries	Tissue characterization
Echo	−	Low	++	+	−	−
Nuclear	+	High	++	++	−	−
CT	+	High	+	−	+++	−
CMR	−	High	+++	+++	++	+++

Echo echocardiography, *nuclear* nuclear techniques, *CT* computed tomography, *CMR* cardiovascular magnetic resonance

How can CMR indices interpret the pathophysiologic phenomena occurring in the myocardium of JIA patients?

A protocol for cardiac evaluation of JIA should ideally include:

Tissue characterization

1. *Oedema imaging* T2 ratio of cardiac over skeletal muscle and T2 mapping are the most commonly used CMR indices for oedema imaging. A T2 ratio > 1.9 and a T2 mapping > 58 msec are considered as values indicative of myocardial oedema [30, 31].
2. *Lake Louise (LL) criteria* LL criteria have been established through the *Journal of American College Cardiology* (JACC) White Paper as a diagnostic approach about how to noninvasively diagnose myocarditis [32]. According to LL criteria, for the diagnosis of myocarditis an integrated CMR protocol, including oedema (T2 ratio > 1.9), cellular infiltration (early gadolinium enhancement—EGE > 4) and myocardial necrosis evaluation (positive late gadolinium enhancement—LGE), should be applied. The best diagnostic performance of CMR was obtained when "any-two" of the three sequences were positive in the same patient yielding a sensitivity of 76% and a specificity of 95.5% [32]. A pericardial effusion, detected by CMR, might serve as a new criterion for the non-invasive diagnosis of myocarditis in patients with recent onset of clinical symptoms and normal LV function [33].
3. *Fibrosis assessment* Cardiac fibrosis may be presented in various forms including:

(a) Diffuse interstitial fibrosis

This form represents fibrosis with a diffuse distribution within the interstitium [34]. It has been already described in hypertension, diabetes mellitus, aging heart, idiopathic dilated cardiomyopathy, left ventricular pressure and volume-overload states and in the remote non-infarcted area in patients with myocardial infarction [34].

(b) Replacement fibrosis

The replacement fibrosis is due to the replacement of myocytes after cell damage. It appears immediately after the loss of myocytes' integrity and may present either a localized distribution (ischemic cardiomyopathy, myocarditis, hypertrophic cardiomyopathy, autoimmune diseases) or a diffuse distribution (chronic renal insufficiency, toxic cardiomyopathies) [34].

Replacement fibrosis can be detected by CMR using late gadolinium enhancement (LGE). LGE is based on the combination of an increased distribution of the contrast agent and a prolonged washout, due to decreased capillary density within the myocardial scar tissue [34]. This causes T1 shortening that appears as bright signal in T1 images post-gadolinium (bright is dead) [34].

Although LGE is the most accurate index to estimate myocardial replacement fibrosis, its sensitivity is limited for the assessment of diffuse interstitial fibrosis, because image contrast in LGE relies on the difference in signal intensity between fibrotic and "normal" myocardium, and this does not occur in diffuse fibrosis (33). Recent technical innovations allowed to perform myocardial T1 mapping. Compared to LGE images, T1 mapping enables direct myocardial signal quantification and provides a better characterization of myocardial tissue composition on a global or regional level. The pre-contrast (native) mean T1 value of normal myocardium is of 977 ± 63 ms and the post-contrast values 10–15 min after gadolinium injection of normal myocardium is 483 ± 20 ms, measured at 1.5 T. T1 mapping is the ideal tool to quantify diffuse myocardial fibrosis and improve the accuracy of LGE in myocardial scar detection [34]. Post-contrast T1 mapping is mainly used to calculate the extracellular volume fraction (ECV) in combination with pre-contrast T1 mapping. ECV is a marker of myocardial tissue remodelling and provides a physiologically meaningful measurement. Normal ECV values of 25.3 ± 3.5%, measured in 1.5 T, have been reported in healthy individuals [35].

Function and valvular assessment

Cardiovascular magnetic resonance measures ventricular volumes and ejection fraction without contrast agent providing 3-dimensional images of the heart, also feasible with 3D echocardiography. While CMR ejection fraction and volumes are more accurate and reproducible than other imaging modalities, they present a good correlation with them [36]. CMR allows the best follow-up of individual patients with respect to changes in ventricular volumes, mass and function. In a direct comparison of reproducibility between CMR and echocardiography has been shown that for an 80% power and a p value of 0.05, the sample size required was 505 patients using 2D echo, but only 14 patients using CMR [37]. Finally, CMR is the best technique to perform valvular regurgitation and timely intervention in JIA patients with valvular diseases [38].

Coronary artery evaluation

Cardiovascular magnetic resonance allows non-invasive, non-radiating assessment of coronary arteries. The major comparative advantage of CMR is the possibility of a combined scanning protocol, including coronary artery anatomy, cardiac function, inflammation and stress myocardial perfusion/fibrosis in the same study, providing valuable information for patients with coronary artery and myocardial disease, such as those with JIA.

Coronary MRA has been currently used for visualization of anomalies of the origin and course of the coronary arteries (class I indication), as well as to visualize coronary bypass grafts (class II indication) and may potentially be used to exclude CAD in selected patients [39].

There is only one study about coronary arteries in RA using coronary magnetic resonance angiography, which did not include coronary artery wall assessment [40]. However, the evaluation of right coronary artery wall by CMR in asymptomatic older subjects showed increased coronary atherosclerosis in subjects with type 2 diabetes as well as coronary calcification. Coronary wall CMR may contribute to the non-invasive assessment of subclinical coronary atherosclerosis in older, high-risk patient groups [41, 42].

Stress myocardial perfusion evaluation

Cardiovascular magnetic resonance can also detect myocardial ischemia using either dobutamine or adenosine stress test, but the most commonly used technique is the evaluation of myocardial perfusion by using the first pass of a bolus of a T1-shortening contrast agent (first-pass gadolinium) [43, 44]. Data acquired during intravenous vasodilator-stress (usually adenosine) delineate the underperfused regions, associated with myocardial ischemia. The spatial resolution of CMR myocardial perfusion imaging of 2–3 mm is superior to other imaging modalities, such as nuclear techniques, so that subendocardial ischemia can be more reliably identified [45, 46]. Recently, the CE-MARC study has documented the high diagnostic accuracy and superiority of CMR over SPECT [47]. Finally, stress myocardial perfusion CMR has a high negative predictive value for adverse cardiac events [48].

Currently, there are no CMR studies about JIA. However, CMR studies in RA showed evidence of myocardial inflammation/fibrosis that were correlated with RA disease activity and myocardial changes known to precede the development of clinically overt heart failure (HF) [49]. Furthermore, in active RA, local myocardial scars visible as LGE and/or prolonged myocardial T1 relaxation times suggesting diffuse inflammation or fibrosis are common findings [50]. Finally, a reduction of the CMR stress perfusion index known as myocardial perfusion reserve index (MPRI) was common in patients with both primary (PRP) and secondary Raynaud phenomenon (SRP) including RA patients, but it was more severe in SRP, even if Raynaud phenomenon (RP) patients were under treatment with calcium blockers. Occult fibrosis was also found in those SRP with the reduced MPRI, but not in PRP [51].

CMR disadvantages

Although CMR is an excellent diagnostic modality, it is not widely used due to the following reasons:

1. Lack of availability/expertise
2. Long examination and processing time
3. High cost
4. Lack of training between referring physicians.

Proposed CMR indications for JIA

1. Baseline cardiac evaluation of all SoJIA, even if they do not have cardiac symptoms and the echocardiogram is normal.
2. CMR for all JIA presenting with resting tachycardia (evidence of inflammation), atypical/typical chest discomfort/pain, fatigue, shortness of breath, even if the echocardiogram is normal and the underlying disease seems quiescent.
3. CMR for all JIA presenting with evidence of heart failure and/or arrhythmia for further risk stratification and potential treatment modification.

Proposed CMR protocol for JIA

1. Bi-ventricular function and wall-motion assessment

2. T2-imaging or native T1-mapping to assess oedema (disease acuity)
3. LGE to assess replacement myocardial fibrosis that may occur even in those JIA patients with normal LV function
4. ECV to assess diffuse myocardial fibrosis, missed by LGE
5. Coronary artery assessment (stenosis, ectasia and/or wall thickening).

The above information provided by CMR may influence risk stratification and both cardiologic and anti-rheumatic medication. According to ESC guidelines, every morphologic or functional change in myocardium, detected by any diagnostic technique, should prompt early treatment with ACE-inhibitors and b-blocker, even if LV ejection fraction remains normal [52]. Furthermore, the detection of myocardial oedema, indication of active myocardial involvement, demands intensive immunosuppressive treatment, even if the patient remains oligo-asymptomatic and the underlying disease seems quiescent. However, clear indications for CMR in JIA are still missing. Therefore, further research is needed, before definitive conclusions about the role of CMR in JIA can be drawn (18).

Conclusion

Juvenile idiopathic arthritis, specifically in patients with the systemic form of the disease, may seriously damage various structures of the cardiovascular system. Other JIA phenotypes are a population of interest, as CVD is underestimated and understudied, but chronic systemic inflammation and risk factors have important value. CMR, due to its multifaceted capability to detect cardiovascular disease, can offer early, reproducible, non-invasive information about cardiovascular disease in JIA, allowing risk stratification and timely initiation /modification of cardiologic and anti-rheumatic treatment. However, lack of availability/expertise and high cost still hamper its application in the clinical cardio-rheumatic practice.

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Compliance with ethical standards

Conflict of interest There is no conflict of interest for any of the authors

Research involving human participants and/or animals N/A. It is a review study.

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References

1. Ravelli A, Martini A (2007) Juvenile idiopathic arthritis. Lancet 369:76778
2. Symmons DP, Jones M, Osborne J et al (1996) Pediatric rheumatology in the United Kingdom: data from the British Pediatric Rheumatology Group National Diagnostic Register. J Rheumatol 23:197580
3. Petty RE, Southwood TR, Manners P et al (2004) International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol 31:3902
4. Nigrovic PA, Raychaudhuri S, Thompson SD (2018) Review: genetics and the classification of arthritis in adults and children. Arthritis Rheumatol 70(1):7–17
5. Minden K, Niewerth M, Listing J et al (2002) Long-term outcome in patients with juvenile idiopathic arthritis. Arthritis Rheum 46:2392401
6. Zak M, Pedersen FK (2000) Juvenile chronic arthritis into adulthood: a long-term follow-up study. Rheumatology 39:198–204
7. Bohr AH, Fuhlbrigge RC, Pedersen FK, de Ferranti SD, Muller K (2016) Premature subclinical atherosclerosis in children and young adults with juvenile idiopathic arthritis. A review considering preventive measures. Pediatr Rheumatol Online J 14(1):3
8. Yeh KW, Lee CM, Chang CJ, Lin YJ, Huang JL (2014) Lipid profiles alter from pro-atherogenic into less atherogenic and pro-inflammatory in juvenile idiopathic arthritis patients responding to anti TNF-α treatment. PLoS One 9(6):e90757
9. Lefèvre-Utile A, Galeotti C, Koné-Paut I (2014) Coronary artery abnormalities in children with systemic-onset juvenile idiopathic arthritis. Jt Bone Spine 81(3):257–259
10. Movva R, Brown SB, Morris DL, Figueredo VM (2013) Anakinra for myocarditis in juvenile idiopathic arthritis. Tex Heart Inst J 40(5):623–625
11. Kuhl U, Pauschinger M, Schwimmbeck PL, Seeberg B, Lober C, Noutsias M et al (2003) Interferon-beta treatment eliminates cardiotropic viruses and improves left ventricular function in patients with myocardial persistence of viral genomes and left ventricular dysfunction. Circulation 107(22):2793–2798
12. Schultheiss HP, Kuhl U, Cooper LT (2011) The management of myocarditis. Eur Heart J 32(21):2616–2625
13. Drucker NA, Colan SD, Lewis AB, Beiser AS, Wessel DL, Takahashi M et al (1994) Gamma-globulin treatment of acute myocarditis in the pediatric population. Circulation 89(1):252–257
14. Bharti BB, Kumar S, Kapoor A, Agarwal A, Mishra R, Sinha N (2004) Assessment of left ventricular systolic and diastolic function in juvenile rheumatoid arthritis. J Postgrad Med 50(4):262–265 **(discussion 266-7)**
15. Bultink IE, Lems WF, Dijkmans BA, van Soesbergen RM, Lindeman J (2002) Severe aortic regurgitation in RF positive polyarticular JIA. Ann Rheum Dis 61(3):282–283
16. Aubert S, Hayem G, Aumont MC, Brochet E, Acar C (2007) Valve repair for mitral insufficiency secondary to idiopathic juvenile polyarthritis. J Heart Valve Dis 16(3):324–327
17. Jiménez-Balderas FJ, García-Rubi D, Pérez-Hinojosa S, Arellano J, Yáñez P, Sanchez ML, Camargo-Coronel A, Zonana-Nacach A (2001) Two-dimensional echo Doppler findings in juvenile and adult onset ankylosing spondylitis with long-term disease. Angiology 52(8):543–548
18. Mavrogeni SI, Sfikakis PP, Dimitroulas T, Koutsogeorgopoulou L, Katsifis G, Markousis-Mavrogenis G, Kolovou G, Kitas GD (2018) Can cardiovascular magnetic resonance prompt early cardiovascular/rheumatic treatment in autoimmune rheumatic diseases? Current practice and future perspectives. Rheumatol Int 38(6):949–958

19. Gasparyan AY, Ayvazyan L, Blackmore H, Kitas GD (2011) Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. Rheumatol Int 31(11):1409–1417
20. Peters MJ, Symmons DP, McCarey D et al (2010) EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis 69:32531
21. Shen CC, Yao TC, Yeh KW, Huang JL (2013) Association of disease activity and anti-rheumatic treatment in juvenile idiopathic arthritis with serum lipid profiles: a prospective study. Semin Arthritis Rheum 42(6):590–596
22. Coulson EJ, Ng WF, Goff I, Foster HE (2013) Cardiovascular risk in juvenile idiopathic arthritis. Rheumatology 52(7):1163–1171
23. Mavrogeni S, Sfikakis PP, Gialafos E, Bratis K, Karabela G, Stavropoulos E, Spiliotis G, Sfendouraki E, Panopoulos S, Bournia V, Kolovou G, Kitas GD (2014) Cardiac tissue characterization and the diagnostic value of cardiovascular magnetic resonance in systemic connective tissue diseases. Arthritis Care Res (Hoboken) 66:104–112
24. Mavrogeni S, Markousis-Mavrogenis G, Koutsogeorgopoulou L, Dimitroulas T, Bratis K, Kitas GD, Sfikakis P, Tektonidou M, Karabela G, Stavropoulos E, Katsifis G, Boki KA, Kitsiou A, Filaditaki V, Gialafos E, Plastiras S, Vartela V, Kolovou G (2017) Cardiovascular magnetic resonance imaging pattern at the time of diagnosis of treatment naïve patients with connective tissue diseases. Int J Cardiol 236:151–156
25. Mavrogeni SI, Kitas GD, Dimitroulas T, Sfikakis PP, Seo P, Gabriel S, Patel AR, Gargani L, Bombardieri S, Matucci-Cerinic M, Lombardi M, Pepe A, Aletras AH, Kolovou G, Miszalski T, Van Riel P, Semb A, Gonzalez-Gay MA, Dessein P, Karpouzas G, Puntman V, Nagel E, Bratis K, Karabela G, Stavropoulos E, Katsifis G, Koutsogeorgopoulou L, Van Rossum A, Rademakers F, Pohost G, Lima JAC (2016) Cardiovascular magnetic resonance in rheumatology: current status and recommendations for use. Int J Cardiol 217:135–148
26. Mavrogeni S, Sfikakis PP, Karabela G, Stavropoulos E, Spiliotis G, Gialafos E, Panopoulos S, Bournia V, Manolopoulou D, Kolovou G, Kitas G (2014) Cardiovascular magnetic resonance imaging in asymptomatic patients with connective tissue disease and recent onset left bundle branch block. Int J Cardiol 171:82–87
27. Kobayashi Y, Kobayashi H, Giles JT, Hirano M, Nakajima Y, Takei M (2016) Association of tocilizumab treatment with changes in measures of regional left ventricular function in rheumatoid arthritis, as assessed by cardiac magnetic resonance imaging. Int J Rheum Dis 19:1169–1174
28. Mayr A, Kitterer D, Latus J, Steubing H, Henes J, Vecchio F, Kaesemann P, Patrascu A, Greiser A, Groeninger S, Braun N, Alscher MD, Sechtem U, Mahrholdt H, Greulich S (2016) Evaluation of myocardial involvement in patients with connective tissue disorders: a multi-parametric cardiovascular magnetic resonance study. J Cardiovasc Magn Reson 18:1–13
29. Mavrogeni S, Markousis-Mavrogenis G, Koutsogeorgopoulou L, Kolovou G (2017) Cardiovascular magnetic resonance imaging: clinical implications in the evaluation of connective tissue diseases. J Inflamm Res 10:55–61
30. Abdel-Aty H, Boyé P, Zagrosek A, Wassmuth R, Kumar A, Messroghli D, Bock P, Dietz R, Friedrich MG, Schulz-Menger J (2005) Diagnostic performance of cardiovascular magnetic resonance in patients with suspected acute myocarditis: comparison of different approaches. J Am Coll Cardiol 45(11):1815–1822
31. Maceira AM, Monmeneu JV, Igual-Muñoz B, Lopez-Lereu PM, Garcia PM, Cosin J (2015) Reference values for regional and global myocardial T2 mapping with cardiovascular magnetic resonance at 1.5T and 3T. J Cardiovasc Magn Reson 17(Suppl 1):P12
32. Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, White JA, Abdel-Aty H, Gutberlet M, Prasad S, Aletras A, Laissy JP, Paterson I, Filipchuk NG, Kumar A, Pauschinger M, Liu P, International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis (2009) Cardiovascular magnetic resonance in myocarditis: a JACC White Paper. J Am Coll Cardiol. 53(17):1475–1487
33. Ong P, Athansiadis A, Hill S, Kispert EM, Borgulya G, Klingel K, Kandolf R, Sechtem U, Mahrholdt H (2011) Usefulness of pericardial effusion as new diagnostic criterion for noninvasive detection of myocarditis. Am J Cardiol. 108:445–452
34. Nathan M, Ying LC, Pierre C, Blumke D, Lima J (2011) Assessment of myocardial fibrosis with cardiac magnetic resonance. J Am Coll Cardiol 57(8):891–903
35. Sado DM, Flett AS, Banypersad SM, White SK, Maestrini V, Quarta G, Lachmann RH, Murphy E, Mehta A, Hughes DA, McKenna WJ, Taylor AM, Hausenloy DJ, Hawkins PN, Elliott PM, Moon JC (2012) Cardiovascular magnetic resonance measurement of myocardial extracellular volume in health and disease. Heart 98:1436–1441
36. Schalla S, Nagel E, Lehmkuhl H, Klein C, Bornstedt A, Schnackenburg B et al (2001) Comparison of magnetic resonance realtime imaging of LV function with conventional magnetic resonance imaging and echocardiography. Am J Cardiol 87:95–99
37. Bottini PB, Carr AA, Prisant M et al (1995) Magnetic resonance imaging compared to echo/phy to assess LV MASS in the hypertensive patient. Am J Hypertens 8:221–226
38. Mavrogeni SI, Kitas GD, Dimitroulas T, Sfikakis PP, Seo P, Gabriel S, Patel AR, Gargani L, Bombardieri S, Matucci-Cerinic M, Lombardi M, Pepe A, Aletras AH, Kolovou G, Miszalski T, van Riel P, Semb A, Gonzalez-Gay MA, Dessein P, Karpouzas G, Puntmann V, Nagel E, Bratis K, Karabela G, Stavropoulos E, Katsifis G, Koutsogeorgopoulou L, van Rossum A, Rademakers F, Pohost G, Lima JA (2016) Cardiovascular magnetic resonance in rheumatology: current status and recommendations for use. Int J Cardiol 217:135–148
39. Chiribiri A, Botnar RM, Nagel E (2013) Magnetic resonance coronary angiography: where are we today? Curr Cardiol Rep 15(2):328
40. Mavrogeni S, Manoussakis MN, Karagiorga TC, Douskou M, Panagiotakos D, Bournia V, Cokkinos DV, Moutsopoulos HM (2009) Detection of coronary artery lesions and myocardial necrosis by magnetic resonance in systemic necrotizing vasculitides. Arthritis Rheum 61(8):1121–1129
41. Terashima M, Nguyen PK, Rubin GD, Meyer CH, Shimakawa A, Nishimura DG, Ehara S, Iribarren C, Courtney BK, Go AS, Hlatky MA, Fortmann SP, McConnell MV (2010) Right coronary wall CMR in the older asymptomatic advance cohort: positive remodeling and associations with type 2 diabetes and coronary calcium. J Cardiovasc Magn Reson 12:75
42. Kim WY, Astrup AS, Stuber M, Tarnow L, Falk E, Botnar RM, Simonsen C, Pietraszek L, Hansen PR, Manning WJ, Andersen NT, Parving HH (2007) Subclinical coronary and aortic atherosclerosis detected by magnetic resonance imaging in type 1 diabetes with and without diabetic nephropathy. Circulation 115(2):228–235
43. Schwitter J (2006) Myocardial perfusion imaging by cardiac magnetic resonance. J Nucl Cardiol 13:841–854 **(21)**
44. Schwitter J, Nanz D, Kneifel S, Bertschinger K, Buchi M, Knusel PR, Marincek B, Luscher TF, von Schulthess GK (2001) Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. Circulation 103:2230–2235
45. Plein S, Ryf S, Schwitter J, Radjenovic A, Boesiger P, Kozerke S (2007) Dynamic contrast-enhanced myocardial perfusion MRI accelerated with k-t sense. Magn Reson Med 58:777–785

46. Gebker R, Jahnke C, Paetsch I, Kelle S, Schnackenburg B, Fleck E, Nagel E (2008) Diagnostic performance of myocardial perfusion MR at 3 T in patients with coronary artery disease. Radiology 247:57–63
47. Greenwood JP, Maredia N, Younger JF, Brown JM, Nixon J, Everett CC, Bijsterveld P, Ridgway JP, Radjenovic A, Dickinson CJ, Ball SG, Plein S (2012) Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. Lancet 379:453–460
48. Gargiulo P, Dellegrottaglie S, Bruzzese D, Savarese G, Scala O, Ruggiero D, D'Amore C, Paolillo S, Agostoni P, Bossone E, Soricelli A, Cuocolo A, Trimarco B, Filardi PP (2013) The prognostic value of normal stress cardiac magnetic resonance in patients with known or suspected coronary artery disease: a meta-analysis. Circ Cardiovasc Imaging 6(4):574–582
49. Kobayashi H, Kobayashi Y, Yokoe I, Akashi Y, Takei M, Giles JT (2017) Magnetic resonance imaging-detected myocardial inflammation and fibrosis in rheumatoid arthritis: associations with disease characteristics and N-terminal Pro-brain natriuretic peptide levels. Arthritis Care Res (Hoboken) 69(9):1304–1311
50. Holmström M, Koivuniemi R, Korpi K, Kaasalainen T, Laine M, Kuuliala A, Leirisalo-Repo M, Kupari M, Kivistö S (2016) Cardiac magnetic resonance imaging reveals frequent myocardial involvement and dysfunction in active rheumatoid arthritis. Clin Exp Rheumatol 34(3):416–423
51. Mavrogeni S, Bratis K, Koutsogeorgopoulou L, Karabela G, Savropoulos E, Katsifis G, Raftakis J, Markousis-Mavrogenis G, Kolovou G (2017) Myocardial perfusion in peripheral Raynaud's phenomenon. Evaluation using stress cardiovascular magnetic resonance. Int J Cardiol 228:444–448
52. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P; Authors/Task Force Members; Document Reviewers (2016) 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 18(8):891–975