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Ventricular Tachycardia and Sudden Cardiac Death in Connective Tissue Diseases: Can Cardiovascular Magnetic Resonance Play a Role?

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Abstract

Ventricular tachycardia (VT) and sudden cardiac death (SCD) are deleterious manifestations of cardiac involvement in connective tissue diseases (CTD). In rheumatoid arthritis (RA), the commonest cause of SCD is coronary artery disease that may lead to acute coronary syndrome and VT. In systemic lupus erythematosus (SLE), VT is due either to coronary artery disease or to acute myocarditis. VT/SCD can be also assessed in polymyostis (PM) and dermatomyositis (DM). Finally, VT was described in 7-13%, while SCD in 5-21% of unselected SSc patients.

Cardiovascular magnetic resonance (CMR) has been already used as screening tool in CTDs, because of its capability to evaluate noninvasively and without radiation, function, inflammation, perfusion defects and fibrosis. Apart of the impaired ventricular function, which can be by itself a predisposing factor for VT/SCD, the commonest causes that can potentially lead to VT/SCD in CTDs are myocarditis, coronary artery disease with ischemic type fibrosis, microvascular disease, nonischemic type fibrosis and heart failure.

The detection of perfusion defects by CMR can be served as a tool to select those patients, who should undergo x ray coronary angiography and/or angioplasty. The location and extent of myocardial scar can guide further electrophysiologic study and/or intervention. On the other hand, in those with myocarditis, microvascular disease and/or heart failure, a modification in both cardiac and rheumatic medication may be recommended after evaluation of CMR findings.

CMR in CTDs with VT/SCD may guide risk stratification, rheumatic and cardiac therapeutic decision making and therefore it should be included as a reliable adjunct in the evaluation of these patients.

Keywords: Ventricular tachycardia; Sudden cardiac death; Cardiovascular magnetic resonance; Myocardial fibrosis

Introduction

Ventricular tachycardia (VT) and sudden cardiac death (SCD) are deleterious manifestations of cardiac involvement in connective tissue diseases (CTD) [1]. However, multicenter studies about VT and SCD in CTDs are still missing.

In rheumatoid arthritis (RA), the commonest cause of SCD is atherosclerotic coronary artery disease (CAD) that may lead to acute coronary syndrome and VT [1]. Additionally, VT was detected after low dose methotrexate [2] and intravenous infusion of infliximab [3]. Finally, giant cell myocarditis (GCM), a rare, frequently fatal cardiac inflammation of unknown origin, characterized by degeneration and necrosis of myocardial fibers, can be also presented as VT with or without congestive heart failure (CHF), during the course of RA, with poor prognosis, despite partial responsiveness to immunosuppressive medications [4].

In systemic lupus erythematosus (SLE), although supraventricular tachycardia is the commonest finding, VT is not uncommon and is mainly due to CAD [1]. Chloroquine plays a protective role in the unexpected high rate of cardiac arrhythmias and conduction disturbances, observed in SLE [2]. Acute myocarditis and ventricular arrhythmia can be also documented at the initial presentation of SLE in children. Early diagnosis and a combination treatment for heart failure, arrhythmias and immunosuppression may lead to a favorable prognosis [3]. Acute myocarditis in SLE may present with VT as a first manifestation [4]. Long QT syndrome with atrioventricular block and VT can be also developed in neonates of mothers with SLE [5]. Finally, the chronic use of antimalarial drugs may lead to potentially lethal VT [6]. In the current era of implanted devices, an implantable defibrillator is a necessary adjunct to medical treatment in CTDs with lethal arrhythmias [7].

In systemic sclerosis (SSc), the most frequent arrhythmias are premature ventricular contractions (PVCs), appearing as monomorphic, single PVCs, bigeminy, trigeminy or pairs. Non-sustained VT was described in 7-13%, while SCD was reported in 5-21% of unselected SSc patients [8].

VT and SCD can be also assessed during polymyostis (PM) and dermato-myositis (DM), although their incidence has been poorly defined [9-13].

How can Cardiovascular Magnetic Resonance Imaging Clarify the Pathophysiologic Background of VT/SCD in CTDs?

VT in CTDs can be due to various pathologies including myocardial inflammation, myocardial ischemia due to obstructive disease of epicardial coronary arteries, coronary artery spasm, microvascular disease and myocardial scar, either of ischemic or non-ischemic origin.

CMR has been already used as the ideal screening tool in CTDs, because of the advantage to evaluate noninvasively and without radiation, function, inflammation, perfusion defects and fibrosis [14-18]. Apart of the impaired ventricular function, which can be by itself a predisposing factor for VT/SCD, the commonest pathophysiologic processes, detected by CMR that can potentially lead to VT/SCD in CTDs, are the following:

Myocardial inflammation

Myocardial inflammation (myocarditis) in CTDs can be due either to the disease per se or to infectious causes [19]. CMR is the ideal technique for the evaluation of inflammation involving the heart. Myocarditis usually has a subclinical course, which cannot be easily detected with standard blood inflammatory indices (ESR, CRP etc.) and can potentially lead to dilated cardiomyopathy and heart failure [20]. It may remain undetectable by the routine used imaging techniques, because these techniques are unable to distinguish various tissue changes, such as edema, cell infiltration, fibrosis that may occur without concurrent changes in left ventricular ejection fraction, the most often evaluated parameter by echocardiography. According to the current experience, in myocarditis, due to infectious causes, a decrease in left ventricular ejection fraction was not evident during the course of the disease, while an increase in cardiac troponin was found in only 20% of cases [20]. Myocardial biopsy, considered as the gold standard for diagnosis of myocarditis, is an invasive procedure and according to ACC/ AHA guidelines should be kept only for patients with unexplained new-onset heart failure < 2 weeks associated with a normal-sized or dilated left ventricle in addition to haemodynamic compromise and cannot be used for screening or follow-up tool [20]. Furthermore its diagnostic value is limited due to a number of reasons, such as sampling error, variation in observer expertise etc. [20].

CMR contributes to the diagnosis of myocarditis using 3 types of images: T2-weighted (T2-W), early T1- weighted (T1-W) images taken 1 min (EGE) and delayed enhanced images (LGE) taken 15 minutes after the injection of contrast agent. T2-W is an indicator of tissue water content, which is increased during inflammation and/or necrosis. However, the differentiation between necrosis and inflammation needs other parameters, such as EGE and LGE. Myocardial necrosis in the acute phase of myocarditis plays a major role in LGE formation, but also severe oedema could increase the gadolinium distribution and cause LGE. A combined CMR approach using T2-W, early and late gadolinium enhancement has a sensitivity of 76%, a specificity of 95.5% and a diagnostic accuracy of 85% for the detection of myocardial inflammation [19-21]. Initial NYHA functional class >II and LGE are independent predictive factors of MACE during long-term follow-up after acute myocarditis [22]. Furthermore, according to recent data, in consecutive patients suspected for no ischemic cardiomyopathy, LGE volume and sustained VT were independent predictors of severe cardiac inflammation [23]. CMR becomes more valuable, if we take under consideration that in postmyocarditis patients with only epicardial scar, the automatic voltage mapping may miss the electrical VT substrate. In these cases, LGE is absolutely necessary to optimize the scar delineation and facilitate ablation [24,25]. Finally, giant cell myocarditis (GCM) has a characteristic CMR pattern of LGE, cine-MRI and myocardial strain that are related to the clinical and pathology findings. In GCM, LGE reflects areas of fibrosis, inflammation and oedema that are specific for this type of myocarditis; additionally, the diffuse LV hypokinesis and the impaired longitudinal strain reflect the area with extensive nonspecific cellular infiltration [26]. Finally, a mixture of ischemic and no ischemic LGE patterns is typical of GCM [27].

Coronary artery disease with ischemic type fibrosis

CMR can detect myocardial ischemia, due to atherosclerotic disease (CAD) of the epicardial coronary arteries or due to disease of small intramyocardial coronary arteries. Myocardial ischemia can be detected by two different ways:

- Observation of wall motion abnormalities using the stress factor dobutamine, as in stress echo, but without the limitation of acoustic window. Compared to stress echo, dobutamine stress CMR has better sensitivity (86% vs 74%) and specificity (86% vs 70%) [28,29].
- Evaluation of myocardial perfusion using the first pass of a T1-shortening contrast agent (first-pass gadolinium) [30,31]. Data, acquired during intravenous vasodilator-stress usually adenosine, delineate the underperfused regions and are indicators of myocardial ischemia. The spatial resolution of CMR myocardial perfusion is 2- 3 mm. It is superior to other imaging modalities, such as nuclear techniques and therefore, CMR can easily reveal subendocardial ischemia missed by these techniques [32,33]. The recent MR-IMPACT study in 234 patients reported improved detection of epicardial coronary artery stenosis by CMR compared with SPECT in the first multi-centre, multi-vendor comparison [34].

Myocardial scar, due to CAD, is either subendocardial or transmural and follows the distribution of the occluded epicardial coronary artery. The amount of fibrotic tissue, as assessed by LGE, is an independent predictor for future cardiac events [35].

Micro vascular disease (MVD)

Micro vascular cardiac disease is a common finding in CTDs [14-17]. Vasodilator stress CMR, using myocardial perfusion reserve index (MPRI) has a good correlation with the invasive coronary reactivity testing (CRT) and has been proposed as a reliable index to detect MVD [36].

Non-ischemic type fibrosis

In contrary to ischemic type fibrosis that follows the distribution of obstructed epicardial coronary artery, the non-ischemic type is patchy, intramyocardial or subepicardial and is not related with the distribution of epicardial coronary arteries. It can be found in any kind of myocarditis (infective or autoimmune) and in small vessels vasculitis either primary or secondary [14-17]. Additionally, diffuse subendocardial fibrosis, detected by CMR, is a common finding in CTDs and carries increased risk for future cardiac events and heart failure [14-17,37,38]. The quantification of the LGE extent may facilitate risk stratification in patients with indication for implantable

cardioverter-defibrillator (ICD) for the primary prevention of SCD [39].

Heart failure

Heart failure is a common cause predisposing to VT/SCD [40]. However, in CTDs, heart failure with preserved ejection fraction (LVPEF) is more common than overt left ventricular failure [41]. In a study of sarcoid patients, it was documented that patients with LGE were at significant risk for VT/SCD, even if they had preserved left ventricular ejection fraction. In these patients, increased LGE burden and right ventricular dysfunction identified those at highest risk of death/VT [41]. Additionally, RV involvement in CTDs facilitate the development of VT/SCD [42].

Clinical Implications of CMR Findings

The routine non-invasive evaluation of CTDs includes clinical, ECG and echocardiographic assessment. However, cardiac involvement in CTDs remains clinically silent until the latest stages of the disease; ECG findings maybe non-specific and echocardiography is an operator depended technique, limited by acoustic window and unable to perform tissue characterization [43].

Recently, CMR has been proposed as the ideal diagnostic adjunct for CTDs [43]. The detection of stress myocardial perfusion defects by CMR is more reliable compared with SPECT and can be used to select those patients, who should undergo X-ray coronary angiography and potentially angioplasty [44]. Additionally, the location and extent of myocardial scar can guide further electrophysiologic evaluation and/or intervention [38,42,45]. It was also documented that in those with myocardial inflammation, microvascular disease and/or heart failure, a modification of both cardiac and rheumatic medication may be recommended after the CMR evaluation [15,16,19,37,44,45]. However, all CMR advantages are usually hampered by the increased cost, lack of availability and expertise. Additionally, the use of CMR in patients with pacemakers/defibrillators demands CMR conditionel devices, because otherwise these patients cannot be scanned. Finally, renal failure is also an important contraindication for paramagnetic contrast agent use in these patients.

Conclusions

CMR, by identifying various pathologic processes taking place in CTDs with VT/SCD, is an important player in the assessment of pathophysiologic background of VT/SCD and may guide risk stratification, suggest a change in rheumatic and/or cardiac treatment and be used as a powerful adjunct in the routine diagnostic evaluation of these patients.

References:

1. Seferović PM, Ristić AD, Maksimović R, Simeunović DS, Ristić GG, et al. (2006) Cardiac arrhythmias and conduction disturbances in autoimmune rheumatic diseases. Rheumatology (Oxford) 45: 39-42.
2. Borek G, Jenzer HR, Frey LD, Locher JT (1992) Repetitive exercise induced ventricular tachycardia in a patient with rheumatoid arthritis taking low dose methotrexate. J Rheumatol 19: 1004-1005.
3. Lazzerini PE, Acampa M, Hammoud M, Maffei S, Capecchi PL, et al. (2008) Arrhythmic risk during acute infusion of infliximab: a prospective, single-blind, placebo-controlled, crossover study in patients with chronic arthritis. J Rheumatol 35: 1958-1965.
4. Rosenstein ED, Zucker MJ, Kramer N (2000) Giant cell myocarditis: most fatal of autoimmune diseases. Semin Arthritis Rheum 30: 1-16.
5. Teixeira RA, Borba EF, Pedrosa A, Nishioka S, Viana VS, et al. (2014) Evidence for cardiac safety and antiarrhythmic potential of chloroquine in systemic lupus erythematosus. Europace 16: 887-892.
6. Huang CN, Yu HH, Chiu SN, Lee JH, Wang LC, et al. (2013) Acute myocarditis and ventricular fibrillation as initial presentation of pediatric systemic lupus erythematosus. Rheumatol Int 33: 1093-1096.
7. Chen CY, Wang FL, Lin CC (2006) Chronic hydroxychloroquine use associated with QT prolongation and refractory ventricular arrhythmia. Clin Toxicol 44: 173-175.
8. Couto N, Ladeira R, Pimenta J (1993) Regression of tachycardiomyopathy after implant of pacemaker with antitachycardial function. Arq Bras Cardiol 60: 31-33.
9. Jindal G, Singh S, Suri D, Rawat A, Rohit M (2012) Recurrent ventricular tachycardia in a child with juveniledermatomyositis - an unusual association. Int J Rheum Dis 15: e26-27.
10. Dilaveris P, Pietri P, Tsiachris D, Gatzoulis K, Stefanadis C (2012) Inducible ventricular tachycardia due to dermatomyositis-related cardiomyopathy in the era of implantable cardioverter-defibrillator therapy. Circulation 125: 967-969.
11. Cuilleret FJ, Agraou B, Kyndt X, Cuilleret V, Agraou H, et al. (2003) Cardiac effects of dermatomyositis. A case report. Arch Mal Coeur Vaiss 96: 919-922.
12. Adler M, Banerjeee S, Stratton R (2002) Ventricular tachycardia as a presenting feature of dermatomyositis. Heart 88: 443.
13. Mavrogeni SI, Bratis K, Karabela G, Spiliotis G, Wijk KV, et al. (2015) Cardiovascular Magnetic Resonance Imaging clarifies cardiac pathophysiology in early, asymptomatic diffuse systemic sclerosis. Inflamm Allergy Drug Targets 14: 29-36.
14. Mavrogeni S, Sfikakis PP, Dimitroulas T, Koutsogeorgopoulou L, Karabela G, et al. (2016) Imaging patterns of cardiovascular involvement in mixed connective tissue disease evaluated by cardiovascular magnetic resonance. Inflamm Allergy Drug Targets.
15. Rodríguez-Reyna TS, Morelos-Guzman M, Hernández-Reyes P, Montero-Duarte K, Martínez-Reyes C, et al. (2015) Assessment of myocardial fibrosis and microvascular damage in systemic sclerosis by magnetic resonance imaging and coronary angiotomography. Rheumatology (Oxford) 54: 647-654.
16. Ntusi NA, Piechnik SK, Francis JM, Ferreira VM, Rai AB, et al. (2014) Subclinical myocardial inflammation and diffuse fibrosis are common in systemic sclerosis--a clinical study using myocardial T1-mapping and extracellular volume quantification. J Cardiovasc Magn Reson 16: 21.
17. Mavrogeni S, Spargias K, Markussis V, Kolovou G, Demerouti E, et al. (2009) Myocardial inflammation in autoimmune diseases: investigation by cardiovascular magnetic resonance and endomyocardial biopsy. Inflamm Allergy Drug Targets 8: 390-397.
18. Dennert R, Crijns HJ, Heymans S (2008) Acute viral myocarditis. Eur Heart J 29: 2073-2082.
19. Abdel-Aty H, Boye P, Zagrosek A, Wassmuth R, Kumar A, et al. (2005) Diagnostic performance of cardiovascular magnetic resonance in patients with suspected acute myocarditis: comparison of different approaches. J Am Coll Cardiol 45: 1815-1822.
20. Chopra H, Arangalage D, Bouleti C, Zarka S, Fayard F, et al. (2016) Prognostic value of the infarct- and non-infarct like patterns and cardiovascular magnetic resonance parameters on long-term outcome of patients after acute myocarditis. Int J Cardiol 212: 63-69.
21. Pöyhönen P, Holmström M, Kivistö S, Hänninen H (2014) Late gadolinium enhancement on CMR and sustained ventricular tachycardia predict severe cardiac inflammation. Acta Cardiol 69: 637-647.
22. Berte B, Sacher F, Cochet H, Mahida S, Yamashita S, et al. (2015) Postmyocarditis ventricular tachycardia in patients with epicardial-only scar: a specific entity requiring a specific approach. J Cardiovasc Electrophysiol 26: 42-50.

23. Maccabelli G, Tsiachris D, Silberbauer J, Esposito A, Bisceglia C, et al. (2014) Imaging and epicardial substrate ablation of ventricular tachycardia in patients late after myocarditis. Europace 16: 1363-1372.
24. Sujino Y, Kimura F, Tanno J, Nakano S, Yamaguchi E, et al. (2014) Cardiac magnetic resonance imaging in giant cell myocarditis: intriguing associations with clinical and pathological features. Circulation 129: e467-469.
25. Azarine A, Guillemain R, Bruneval P (2009) Different focal delayed gadolinium-enhancement patterns using cardiacmagnetic resonance in a case of diffuse giant cell myocarditis. Eur Heart J 30: 1485.
26. Nagel E, Lehmkuh HB, Bocksch W (1999) Noninvasive diagnosis of ischemia-induced wall motion abnormalities with the use of high-dose dobutamine stress MRI: comparison with dobutamine stress echocardiography. Circulation 99: 763-770.
27. Wahl A, Paetsch I, Roethemeyer S, Klein C, Fleck E, et al. (2004) High-dose dobutamine-atropine stress cardiovascular magnetic resonance for follow-up after coronary revascularization procedures in patients with wall motion abnormalities at rest. Radiology 233: 210 –216.
28. Hundley WG, Hamilton CA, Thomas MS, Herrington DM, Salido TB, et al. (1999) Utility of fast cine magnetic resonance imaging and display for the detection of myocardial ischemia in patients not well suited for second harmonic stress echocardiography. Circulation 100: 1697–1702.
29. Danias PG (2001) Gadolinium-enhanced cardiac magnetic resonance imaging: expanding the spectrum of clinical applications. Am J Med 110: 591-592.
30. Schwitter J (2006) Myocardial perfusion imaging by cardiac magnetic resonance. J Nucl Cardiol 13: 841–854.
31. Schwitter J, Nanz D, Kneifel S, Bertschinger K, Buchi M, et al. (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.
32. Schwitter J, Wacker CM, van Rossum AC, Lombardi M, Al-Saadi N, et al. (2008) MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial. Eur Heart J 29: 480-489.
33. Kwong RY, Chan AK, Brown KA, Chan CW, Reynolds HG, et al. (2006) Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. Circulation 113: 2733-2743.
34. Thomson LE, Wei J, Agarwal M, Haft-Baradaran A, Shufelt C, et al. (2015) Cardiac magnetic resonance myocardial perfusion reserve index is reduced in women with coronary microvascular dysfunction. A National Heart, Lung, and Blood Institute-sponsored study from the Women's Ischemia Syndrome Evaluation. Circ Cardiovasc Imaging 8.
35. Mavrogeni S, Karabela G, Gialafos E, Stavropoulos E, Spiliotis G, et al. (2013) Cardiac involvement in ANCA (+) and ANCA (-) Churg-Strauss syndrome evaluated by cardiovascular magnetic resonance. Inflamm Allergy Drug Targets 12: 322-327.
36. Mavrogeni S, Sfikakis PP, Gialafos E, Karabela G, Stavropoulos E, et al. (2013) Diffuse, subendocardial vasculitis. A new entity identified by cardiovascular magnetic resonance and its clinical implications. Int J Cardiol 168: 2971-2972.
37. Neilan TG, Coelho-Filho OR, Danik SB, Shah RV, Dodson JA, et al. (2013) CMR quantification of myocardial scar provides additive prognostic information in nonischemic cardiomyopathy. JACC Cardiovasc Imaging 6: 944-954.
38. Klein L, Hsia H (2014) Sudden cardiac death in heart failure. Cardiol Clin 32: 135-144.
39. Murtagh G, Laffin LJ, Beshai JF, Maffessanti F, Bonham CA, et al. (2016) Prognosis of Myocardial Damage in Sarcoidosis Patients With Preserved Left Ventricular Ejection Fraction: Risk Stratification Using Cardiovascular Magnetic Resonance. Circ Cardiovasc Imaging 9: e003738.
40. Mavrogeni S, Sfikakis PP, Karabela G, Stavropoulos E, Kolovou G, et al. "All roads lead to Rome" ventricular tachycardia due to right ventricle involvement in autoimmune and non-autoimmune disease. Int J Cardiol 173: 126-127.
41. Mavrogeni SI, Kitas GD, Dimitroulas T, Sfikakis PP, Seo P, et al. (2016) Cardiovascular magnetic resonance in rheumatology: Current status and recommendations for use. Int J Cardiol 217: 135-148.
42. Greenwood JP, Maredia N, Younger JF, Brown JM, Nixon J, et al. (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.
43. Bisbal F, Fernández-Armenta J, Berruezo A, Mont L, Brugada J (2014) Use of MRI to guide electrophysiology procedures. Heart 100: 1975-1984.
44. Apte M, McGwin G Jr, Vilá LM, Kaslow RA, Alarcón GS, et al. (2008) LUMI- NA Study Group. Associated factors and impact of myocarditis in patients with SLE from LUMINA, a multiethnic US cohort. Rheumatology (Oxford) 47: 362-367.
45. Mavrogeni S, Sfikakis PP, Gialafos E, Bratis K, Karabela G, et al. (2014) Cardiac tissue characterization and the diagnostic value of cardiovascular magnetic resonance in systemic connective tissue diseases. Arthritis Care Res (Hoboken) 66: 104-112.