



**Editorial for "Regional Myocardial Remodeling
Characteristics Correlates with Cardiac Events in
Sarcoidosis"**

Journal:	<i>Journal of Magnetic Resonance Imaging</i>
Manuscript ID	JMRI-20-0143
Wiley - Manuscript type:	Editorial
Classification:	Heart < Cardiovascular and interventional imaging < Clinical Science, Functional cardiac imaging < Cardiovascular and interventional imaging < Clinical Science, Contrast enhancement (cardiovascular) < Cardiovascular and interventional imaging < Clinical Science
Manuscript Keywords:	sarcoidosis, cardiac magnetic resonance, prognosis

SCHOLARONE™
Manuscripts

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Title: Extending the Role of Cardiac Magnetic Resonance in Sarcoidosis Risk Stratification – Editorial on “regional myocardial remodelling characteristics correlates with cardiac events in sarcoidosis”

Kenneth Chan, MRCP¹

¹Cardiovascular Medicine,
Radcliffe Department of Medicine,
University of Oxford, Oxford, UK

Kenneth.chan@cardiov.ox.ac.uk

Keywords: sarcoidosis; cardiac magnetic resonance; prognosis

1
2
3 Sarcoidosis is an infiltrative granulomatous disorder with cardiac involvement in about 5% of
4
5 the cases.¹ Cardiac sarcoidosis could manifest as heart failure, conduction abnormalities or
6
7 cardiac arrhythmias which carries significant mortality risk.² Thus detection of cardiac sarcoid
8
9 and recognising adverse features could guide interventions such as implantable cardiac
10
11 defibrillator (ICD) to halt the risk of sudden cardiac death from ventricular arrhythmias. Based
12
13 on observational studies, the 2017 American Heart Association/American College of
14
15 Cardiology/Heart Rhythm Society guideline has a class IIa recommendation (reasonably
16
17 beneficial) to perform cardiac MR or PET scan in patients with left ventricular (LV) ejection
18
19 fraction greater than 35% with a view to identify patients who might benefit from ICD
20
21 implantation.³
22
23
24
25
26
27

28 The current study reported in the *Journal* explored the prognostic role of MR in cardiac
29
30 sarcoidosis. This retrospective observational study investigated cardiac events in 132 patients
31
32 with cardiac sarcoid over a median of 40.7 months. In this cohort of patient with preserved
33
34 LV systolic function, the study focused on LV geometric changes including regional
35
36 myocardial wall thickness (RMWT) in interventricular septum/lateral wall. Although only
37
38 composite endpoint (cardiac mortality, new onset arrhythmia, heart failure hospitalization,
39
40 device implantation) was presented, this study highlighted several important observations.
41
42 First, LV hypertrophy was independently predictive of clinical endpoints. Perhaps it is not
43
44 surprising more hypertrophic heart is corresponded to more severe infiltrative
45
46 cardiomyopathy, particularly in this very hypertrophic cohort (mean LV mass index 108g/m²
47
48 and 87g/m² respectively in patients with and without endpoint), but LVMI has not been able
49
50 to reach statistical significance in previous studies.⁴ Second, 4 types of regional LV
51
52 remodelling were observed. Type I (no remodelling), II (concentric remodelling), III
53
54 (concentric LV hypertrophy) IV (eccentric LVH). The latter 3 types confers progressively
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

higher risk of adverse clinical endpoints, with all patients having type IV remodelling having clinical events in the follow up period. Most interestingly, regional rather than global LV remodelling parameters showed greater clinical predictive value, where RWMT showed a hazard ratio of 3.5 for clinical end points, compared to 1.01 using LVMI. Cardiac sarcoidosis is an infiltrative cardiomyopathy, hence focal or patchy rather than diffuse pathological process could be expected. Recent analysis of pathological images from autopsy/cardiac transplant cases described a characteristic multifocal, epicardial, septal and right ventricular (RV) free wall involvement in the myocardium.⁵ This support the notion that regional myocardial changes could more accurately represent disease activity and influence patient clinical outcomes.

The presence of late gadolinium enhancement (LGE) on MR has been established as a prognostic marker in cardiac sarcoidosis, with a hazard ratio of ~20-30 for adverse cardiac events in previous studies.⁶ There is also a dosage response, where 1% LGE burden increasing the hazard of death or ventricular tachycardia (VT) by 8%.⁴ LGE could help quantifying areas of focal myocardial fibrosis which are substrates for ventricular arrhythmias. The presence of LGE on patients with MR features of cardiac sarcoidosis could therefore aid selecting patients who could benefit from ICD implantation.⁷ Having an ICD in these patients was associated with lower rate of sudden cardiac death in 3-year follow up.⁸ In patients with preserved LV systolic function, patients without LGE showed reassuring prognosis.⁴ The current study observed an increase in regional wall LGE in early hypertrophic remodelling stages (type II and III), but decrease in later eccentric stage (type IV). Therefore it is possible that regional wall thickness increase with the disease activity at early stage, and the myocardium that were replaced by fibrous scarring tissue become burnt out as disease further progress, leading to regression of thickness.

1
2
3 So how does MR assessment of regional myocardial remodelling help in the diagnostic
4
5 algorithm of cardiac sarcoidosis? Perhaps the strength of MR is in early detection of cardiac
6
7 sarcoidosis and screening alternative diagnosis to account for patients' symptoms. Changes
8
9 in regional wall thickness and LGE are sometimes not necessarily specific for cardiac
10
11 sarcoidosis and abnormal MR scans could then be followed up by FDG-PET to detect areas
12
13 of myocardial inflammation in conjunction with localised LGE. Current guidelines suggests
14
15 MR/FDG-PET imaging to guide ICD implantation in patients with impaired LV systolic
16
17 function.³ In patients with preserved LV function (ejection fraction $\geq 55\%$), steroid therapy has
18
19 been shown to reduce LV remodelling.⁹ Therefore recognising early phenotype, such as
20
21 regional myocardial remodelling, could help to identify opportunities for treatment before
22
23 irreversible scarring occurs. Further studies is needed to investigate the temporal relationship
24
25 between regional myocardial remodelling and LGE development in disease progression.
26
27 More granular clinical end points, rather than composite cardiovascular outcomes, could also
28
29 be helpful to guide clinical decision making by delineating the risk of regional myocardial
30
31 remodelling in predisposing ventricular arrhythmias, conduction abnormalities, and
32
33 development of heart failure.
34
35
36
37
38
39
40
41
42

43 **Acknowledgements**

44
45 K.C is supported by NIHR Academic Clinical Fellowship.
46
47

48 **Conflict of interest**

49
50
51 None
52
53
54
55
56
57
58
59
60

References

1. Birnie DH, Nery PB, Ha AC, Beanlands RS. Cardiac sarcoidosis. *Journal of the American College of Cardiology*. 2016;68:411-421

2. Nordenswan HK, Lehtonen J, Ekstrom K, Kandolin R, Simonen P, Mayranpaa M, Vihinen T, Miettinen H, Kaikkonen K, Haataja P, Kerola T, Rissanen TT, Kokkonen J, Alatalo A, Pietila-Effati P, Utriainen S, Kupari M. Outcome of cardiac sarcoidosis presenting with high-grade atrioventricular block. *Circulation. Arrhythmia and electrophysiology*. 2018;11:e006145

3. Al-Khatib SM, Stevenson WG, Ackerman MJ, Bryant WJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field ME, Fonarow GC, Gillis AM, Granger CB, Hammill SC, Hlatky MA, Joglar JA, Kay GN, Matlock DD, Myerburg RJ, Page RL. 2017 aha/acc/hrs guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: Executive summary: A report of the american college of cardiology/american heart association task force on clinical practice guidelines and the heart rhythm society. *Journal of the American College of Cardiology*. 2018;72:1677-1749

4. Murtagh G, Laffin LJ, Beshai JF, Maffessanti F, Bonham CA, Patel AV, Yu Z, Addetia K, Mor-Avi V, Moss JD, Hogarth DK, Sweiss NJ, Lang RM, Patel AR. Prognosis of myocardial damage in sarcoidosis patients with preserved left ventricular ejection fraction: Risk stratification using cardiovascular magnetic resonance. *Circulation. Cardiovascular imaging*. 2016;9:e003738

5. Okasha O, Kazmirczak F, Chen KA, Farzaneh-Far A, Shenoy C. Myocardial involvement in patients with histologically diagnosed cardiac sarcoidosis: A systematic review and meta-analysis of gross pathological images from autopsy or cardiac transplantation cases. *Journal of the American Heart Association*. 2019;8:e011253

6. Hulten E, Agarwal V, Cahill M, Cole G, Vita T, Parrish S, Bittencourt MS, Murthy VL, Kwong R, Di Carli MF, Blankstein R. Presence of late gadolinium enhancement by cardiac magnetic resonance among patients with suspected cardiac sarcoidosis is associated with adverse cardiovascular prognosis: A systematic review and meta-analysis. *Circulation. Cardiovascular imaging*. 2016;9:e005001

7. Greulich S, Deluigi CC, Gloekler S, Wahl A, Zurn C, Kramer U, Nothnagel D, Bultel H, Schumm J, Grun S, Ong P, Wagner A, Schneider S, Nassenstein K, Gawaz M, Sechtem U, Bruder O, Mahrholdt H. Cmr imaging predicts death and other adverse events in suspected cardiac sarcoidosis. *JACC. Cardiovascular imaging*. 2013;6:501-511

8. Nadel J, Lancefield T, Voskoboinik A, Taylor AJ. Late gadolinium enhancement identified with cardiac magnetic resonance imaging in sarcoidosis patients is associated with long-term ventricular arrhythmia and sudden cardiac death. *European heart journal cardiovascular Imaging*. 2015;16:634-641

9. Chiu CZ, Nakatani S, Zhang G, Tachibana T, Ohmori F, Yamagishi M, Kitakaze M, Tomoike H, Miyatake K. Prevention of left ventricular remodeling by long-term corticosteroid therapy in patients with cardiac sarcoidosis. *The American journal of cardiology*. 2005;95:143-146