ΚΑΡΔΙΑΓΓΕΙΑΚΗ ΜΑΓΝΗΤΙΚΗ ΤΟΜΟΓΡΑΦΙΑ ΣΤΑ ΡΕΥΜΑΤΟΛΟΓΙΚΑ ΝΟΣΗΜΑΤΑ

Σοφία Μαυρογένη MD, FESC
Ωνάσειο Καρδιοχειρουργικό Κέντρο, Αθήνα
Rheumatic diseases with heart involvement

- Rheumatoid arthritis (RA) and seronegative arthritis
- Systemic lupus erythematosus (SLE)
- Vasculitis (VSC)
- Idiopathic inflammatory myopathies (IM)
- Systemic sclerosis (scleroderma) (SSc)
- Sjogren syndrome (SS)
- Sarcoidosis (SRC)
Cardiac disease in ARDs

- **Valvular Disease**
  - Echo +++
  - Nuclear -
  - CT -
  - CMR ++

- **Coronary artery lesions**
  - Echo =
  - Nuclear -
  - CT ++
  - CMR +

- **Diffuse myocardial fibrosis**
  - Echo -
  - Nuclear -
  - CT ±
  - CMR +++

- **Replacement myocardial fibrosis**
  - Echo -
  - Nuclear ±
  - CT ±
  - CMR +++

- **Perfusion Defects**
  - Echo =
  - Nuclear ±
  - CT ±
  - CMR +++

- **Myocardial Oedema**
  - Echo -
  - Nuclear -
  - CT -
  - CMR +++

- **LV Function**
  - Echo ++
  - Nuclear +
  - CT ++
  - CMR +++

- **RV Function**
  - Echo +
  - Nuclear +
  - CT ++
  - CMR +++
Is there a place for CMR in RD?

- RD usually have a silent or oligo-symptomatic cardiac presentation
- **Tissue characterisation** can not be performed by echo, nuclear, CT
- **Acuity** of heart involvement can not be detected by echo, nuclear, CT
- **Great vessels angiography** can not be assessed by echo, nuclear
- CMR is operator independent, reproducible, nonradiating = **ideal for serial evaluation**
- **Stress CMR**, nonradiating, without the limitations of acoustic window and/or breast artifacts, is **ideal for CAD and microvascular disease**

Mavrogeni S et al. Semin Arthr Rheumatism 2011
Edema and fibrosis imaging by CMR: How can the experience of Cardiology be best utilized in rheumatological practice?

- Transmitting the CMR experience from Cardiology into Rheumatology is of value because:
  - Heart disease has atypical clinical presentation in RD
  - CMR detects early myocardial tissue changes
  - CMR identifies cardiac disease acuity and various patterns of heart involvement
  - CMR documents heart lesion severity and aid therapeutic decisions

Oedema Imaging in ARDs
Fibrosis Imaging in ARDs

A. LGE in PAH

B. Extensive intramyocardial fibrosis

C. Transmural fibrosis

D. Localised subendocardial fibrosis

E. Subepicardial fibrosis

F. Diffuse subendocardial fibrosis

LGE pattern in ARDs
T1 mapping in ARDs
Myocardial perfusion-fibrosis pattern in systemic sclerosis assessed by cardiac magnetic resonance

Mavrogeni et al. Int J Cardiol 2012
CMR in myocardial inflammation in ARDs: An appraisal of the diagnostic strengths and limitations of the Lake Louise criteria.

- Of the 3 Lake Louise indices, EGE and LGE may be affected by co-existing disease processes or be present due to a fibrotic ARD like SSc.
- T2-ratio is the only uniformly robust measurement across ARDs.
- The introduction of T1/T2 mapping and ECV allowed the quantification of intramyocardial fibrosis missed by LGE and the detection of myocardial oedema respectively, both commonly found in ARDs.
- The inclusion of T1/T2 mapping and ECV may better describe diffuse oedema and fibrosis;
- Further investigation pertaining to their implementation in ARD assessment algorithms through multicenter studies is needed.

Mavrogeni S et al. Int J Cardiol 2017
KAWASAKI DISEASE: MRA vs. QCA

Mavrogeni et al. JACC 2004
CMR evaluation of cardiac involvement during the convalescence of Kawasaki disease

- Coronary ectasia and myocardial inflammation are common findings during the convalescence of KD.
- Myocardial infarction and coronary aneurysms can be occasionally found although the early start of immunoglobulin.
- A single CMR in KD during convalescence may provide important diagnostic information on myocardial inflammation and/or infarction and coronary anatomy.

Mavrogeni et al. JACC Imag 2011
Detection of coronary artery lesions and myocardial necrosis by CMR in systemic necrotizing vasculitides

- CMR assessment of patients with systemic vasculitis reveals:
  - Coronary ectatic disease in the majority of patients with MPA and PAN, as well as in several patients with WG.
  - Myocardial necrosis can be detected in MPA and CSS.

Mavrogeni et al Arthr Rheum 2009
Imaging patterns of HEART FAILURE in rheumatoid arthritis evaluated by CMR

- In RA with HF, CMR revealed
  - Acute myocarditis
  - Chronic myocarditis
  - Myocardial infarction
  - Dilated Cardiomyopathy
  - Diffuse subendocardial fibrosis.

- The correlation of LGE with inflammatory indexes and disease activity emphasizes the role of inflammation in HF development in RA.

- In non RA with HF, CMR revealed
  - Dilated Cardiomyopathy
  - Myocardial infarction

Mavrogeni S et al. Int J Cardiol 2013
Diffuse Myocardial Fibrosis and Inflammation in RA: Insights From CMR T1 Mapping

- Subclinical CV disease is frequent in RA, including focal and diffuse myocardial fibrosis and inflammation, which are associated with impaired strain and RA disease activity.

- CMR T1 mapping provides potential added value as a biomarker for disease monitoring and study of therapies.

Ntutsi NA et al. JACC CI 2015
Heart failure imaging patterns in systemic lupus erythematosus. Evaluation using CMR

CMR in SLE with HF, using the combination of function- oedema-fibrosis imaging, can identify

• acute myocarditis,
• dilated cardiomyopathy,
• myocardial infarction,
• vasculitis and
• valvular heart disease.

• The correlation of LGE with the inflammatory profile emphasizes the role of inflammation in both ischemic and nonischemic HF in SLE.

• The assessment of heart disease acuity and characteristics of myocardial fibrosis can potentially facilitate individualized CVD risk stratification in SLE.

Mavrogeni S et al. Int J Cardiol 2014
The diagnostic role of CMR in detecting myocardial inflammation in SLE. Differentiation from viral myocarditis.

- After CMR evaluation in a population of suspected infective myocarditis (IM) and active SLE, we proved that:
  - High T2 and EGE were the main characteristics of both IM and SLE.
  - LGE was positive in the majority of IM, but in minority of active SLE.
  - EMB identified myocarditis in >half of CMR positive patients.
  - PCR was positive in almost all IM, but unusual in SLE.

- Due to subclinical presentation of SLE myocarditis and the limitations of endomyocardial biopsy, CMR is the best alternative for assessment of myocardial inflammation in SLE.

Mavrogeni S et al. *Lupus* 2013
Complementary role of cardiovascular imaging and laboratory indices in early detection of cardiovascular disease in SLE

- An algorithm for CVD evaluation in SLE includes
  - clinical evaluation
  - laboratory evaluation
  - ECG
  - Echo and
  - CMR in patients with
  - inconclusive findings,
  - persistent cardiac symptoms despite normal standard evaluation,
  - new onset of life-threatening arrhythmia/HF and/or
  - tool to select SLE patients for Cardiac Catheterization.

Mavrogeni S et al Lupus 2017
CMR imaging predicts death and other adverse events in suspected CARDIAC SARCOIDOSIS

- In a population of sarcoid patients with nonspecific symptoms, LGE was the best independent predictor of potentially lethal events, as well as other adverse events.

- These data support the necessity for future large, longitudinal follow-up studies to definitely establish LGE as an independent predictor of cardiac death in sarcoidosis.

Greulich S et al. JACC Cardiovasc Imaging 2013
INFLAMMATORY MYOPATHIES (IM)

- Polymyositis / Dermatomyositis are inflammatory myopathies that may be complicated by myocarditis.

- To diagnose myocarditis in IM remains a challenge, due to:
  - high risk for death and
  - lack of standardized diagnostic criteria.

- Currently, IM myocarditis diagnosis is based on ECG, laboratory and echocardiographic findings, but these criteria are of limited value.

- CMR unveils silent myocardial involvement in PM/DM.

Mavrogeni et al. JACC Imag 2011
Cardiac tissue characterization and the diagnostic value of CMR in connective tissue diseases

• CMR in symptomatic CTDs can assess disease acuity and various imaging patterns including vasculitis, myocarditis and myocardial infarction; therefore, it can be part of CTDs diagnostic algorithm

• **Stress studies** in CTDs with negative CMR detected CAD in **20%** of cases

Mavrogeni et al. *Arthr Care Research* 2014
CMR in Rheumatology: Current Status and Recommendations for use

- The *International Consensus Group on CMR in Rheumatology* was formed in January 2012 aiming to achieve consensus among CMR and rheumatology experts in developing initial recommendations on the current state-of-the-art use of CMR in CTDs. The present report outlines the recommendations of participating CMR and rheumatology experts with regards to:

  - (a) *indications for use of CMR* in RA, spondyloarthropathies, SLE, vasculitis of small, medium, large vessels, myositis, sarcoidosis and SSc;
  
  - (b) *CMR protocols, terminology* for reporting CMR and diagnostic CMR criteria for assessment and quantification of CV involvement in CTDs;
  
  - (c) a *research agenda* for the further development of this evolving field.

Mavrogeni S et al *Int J Cardiol* 2016
CMR FOR TREATMENT IN ARDs
Myocardial inflammation in SSc
Myocardial inflammation in sarcoidosis

First exam

3 months later
Cardiovascular magnetic resonance imaging pattern at the time of diagnosis of treatment naïve patients with connective tissue diseases.

- In 3/5 TA, 3/4 CSS, 4/5 WG, 10/16 SLE, 9/12 RA, 6/8 MCTD, 4/12 AS, 1/3 PMR, 2/8 SSc and 2/5 DM, the T2 ratio was higher compared to normal (2.78±0.25 vs 1.5±0.2, p<0.01).

- Myocarditis was identified in 1 TA, 1 SLE, 1 RA, 1 SSc and 2 DM.

- Diffuse, subendocardial fibrosis in 1 CSS and 1 RA patient, while subendocardial myocardial infarction in 3 SLE, 1 MCTD, 1 PMR, 2 RA.

- CMR re-evaluation after 6 and 12 months of rheumatic and cardiac treatment, available in 28/52 CTDs with increased T2 ratio, showed significant improvement in T2 ratio (p<0.001), non-significant change in LGE extent and normalisation of those with impaired LV function.

Mavrogeni S et al Int J Cardiol 2017)
Tocilizumab increases LVEF and decreases LV mass index in patients with rheumatoid arthritis without cardiac symptoms: assessed using 3.0 tesla CMR.

- TCZ treatment significantly increased LVEF and decreased LVMI associated with disease activity.

Kobayashi H et al. J Rheumatol 2014
Native T1/T2 mapping in lupus myocarditis: Disease recognition and response to treatment

• Native T1 and T2 mapping support recognition of lupus myocarditis and reflect the response to anti-inflammatory treatment.

• Native T1 and T2 mapping may support an effective, noninvasive, radiation- and gadolinium contrast-free screening method for lupus myocarditis.

Hinojar R et al. Int J Cardiol. 2016)
Recognizing and treating myocarditis in recent-onset systemic sclerosis heart disease: potential utility of immunosuppressive therapy in cardiac damage progression.

- **Myocarditis** is a common finding in SSc patients with recent-onset cardiac involvement.

- Its early detection allowed to **timely start immunosuppressive treatment and prevent the cardiac damage progression in most cases.**

*Pieroni M et al. Semin Arthritis Rheum. 2014*
Resolution of abnormal cardiac MRI T2 signal following immune suppression for cardiac sarcoidosis.

- A retrospective study of subjects with cardiac sarcoidosis with abnormal T2 signal on baseline CMR and a follow-up CMR study at least 4 months later was conducted at The Ohio State University from 2011 to 2015.

- Immune suppression treated participants had a significant reduction in peak myocardial T2 value (70.0±5.5 vs 59.2±6.1 ms, pretreatment vs post-treatment; p=0.017), and 83% of immune suppression treated subjects had objective improvement in cardiac arrhythmias.

- Two subjects who had received inadequate immune suppression experienced progression of cardiac sarcoidosis.

Clinical significance of CMR for early initiation of cardiac treatment in ARDs

- ESC guidelines recommend that any cardiac lesion, detected by any technique, should motivate the start of ACE-inhibitors and b-blocker.

- This means that early information by CMR, should motivate early start of cardiac medication in ARDs

Clinical significance of CMR for early initiation of rheumatic treatment in ARDs (1)

• In virus-negative chronic myocarditis or inflammatory cardiomyopathy the beneficial effect of immunosuppressive treatment leading to LVEF improvement was documented. (Escher F et al. Clin Res Cardiol. 2016)

• Immunosuppression for giant cell myocarditis improves long-term survival. (Cooper LT et al. Am J Cardiol 2008)

• We can use the new CMR indices (T2, native, post contrast T1 mapping and ECV), to create a tissue characterisation profile of ARDs patients, irrespective of systolic function.
Clinical significance of CMR for early initiation of rheumatic treatment in ARDs (2)

- We need at least 3 levels of evidence to document the necessity of additive antirheumatic treatment in ARD patients with CMR evidence of myocardial inflammation:
  - Association studies from registries with adequate phenotype, treatment and outcome data.
  - Longitudinal long-term observational studies monitoring ARD patients who have been/have not been treated with additive antirheumatic medication, based on CMR findings
  - Randomized controlled trials of antirheumatic treatment/not treatment, based on CMR findings alone, with long-term outcomes
CARDIO-RHEUMATIC TEAM

- RHEUMATOLOGISTS
  - G. Kitas
  - P. Sfikakis
  - L. Koutsogeorgopoulou
  - M. Tektonidou
  - G. Katsifis
  - E. Stavropoulos
  - K. Boki
  - D. Vassilopoulos
  - M. Matucci-Cerinic
  - L. Guillevin
  - C. Kallenberg

- CARDIOLOGISTS
  - S. Mavrogeni
  - G. Karabela
  - G. Kolovou
  - S. Plastiras
  - E. Gialafos
  - V. Vartela
  - K. Aggeli
  - J. Schwitter
  - A. van Rossum
  - R. Nijveldt
  - J. Lima
  - G. Pohost
Greek College of Clinical Applications in CMR
“CARDIOTOMI”

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