WHAT’S NEW IN CMR?

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TISSUE CHARACTERIZATION

- Oedema (T2STIR)
- Cellular proliferation (EGE)
- Fibrosis (LGE)
- Iron (T2STAR)
- Function (SSFP)
- Fat (T1, fat suppression)
- Microfibrosis (T1 mapping)
MUSCULAR DISEASES
DUCHEENNE MYOPATHY

Mavrogeni S et al. Chest 2004
CMR in Becker Muscular Dystrophy

- CMR is sensitive in detecting abnormal findings in BMD patients, missed by conventional echo.
- Myocardial damage is predominantly subepicardial and can be detected in both BMD patients and carriers.
- CMR, due its ability to perform tissue characterization noninvasively can early detect silent myocardial involvement in both BMD asymptomatic patients and carriers.

Mavrogeni et al. Neuromuscular Disorders 2010
Silent myocarditis in myasthenia gravis. Role of cardiovascular magnetic resonance imaging.

• Silent myocarditis can be detected during MG with concurrent myositis

• CMR is of great value to establish diagnosis in oligo-asymptomatic patients

• However, further studies are needed to fully understand the clinical implications of these findings.

Mavrogeni s et al Intern J Cardiol 2016
THALASSEMIA AND OTHER IRON OVERLOADED DISEASES
INDICES FOR IRON EVALUATION

- Serum ferritin
  - estimates total body iron stores
  - limited by many common clinical conditions (inflammation, fever, liver disease)
  - it does not reflect myocardial iron overload
- liver biopsy (invasive, information only for liver)
- ECG (late)
- Echocardiography (late)
HOW DOES CMR WORK IN IRON OVERLOAD?

- Ability of intracellular iron to enhance magn susceptibility
- Both ferritin, hemosiderin super-paramagnetic
- Their common direction fluctuates rapidly, and only the average magnetization can be observed (each ferritin molecule has its own susceptibility>>large field gradients).
- Moderate decrease in T1 (paramagnetic enhancement or alterations of hydrated tissue proteins). **No correlation with iron overload.**
- Substantial decrease in T2 (dephasing of water protons as they diffuse through field inhomogeneities created by magnetic bodies). **Good correlation with iron overload.**
MRI STUDY OF IRON DEPOSITION IN b-THALASSEMIA

• Liver is affected earlier and more severely, compared to heart.

• Heart iron deposition is a late event in b-thalassemia


Myocardial iron deposition in β-Thalassemia studied by magnetic resonance imaging

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Abstract

Myocardial iron deposition is a common finding in β-thalassemia. The iron content of the myocardium was assessed using the T2 relaxation time of the heart. The T2 relaxation time of the liver and skeletal muscle was also assessed in order to study the relation of iron deposition between heart, liver and skeletal muscle. ECG gated spin echo images were obtained from thirty-eight consecutive adult thalassemic patients examined in an outpatient clinic, aged (x±SD) 25±6 years, using a 0.5 T system. Patients were divided into groups A and B, according to their average serum ferritin levels of the preceding five years (> or < 2000 ng/ml). Results were compared with nine controls, aged 24±7 years. Heart T2 relaxation time in the control group (x±SD)(48.3±5.5 msec) was higher compared to group A (38.4±6.7 msecs, p<0.001) but not to group B (43.4±7.4 msecs). The T2 relaxation time of the heart correlated positively with the T2 relaxation time of the liver (r=0.68, p<0.001) and negatively with ferritin levels (r=-0.67, p<0.001). There was no correlation with the T2 relaxation time of skeletal muscle. This study indicates that regularly transfused β-thalassemia patients may present with a broad variation of heart iron deposition which, however, is related to serum ferritin levels.
T2* MEASUREMENT

Anderson et al. Eur Heart J 2001
MRI vs. BIOPSY in b-THALASSEMAIA

Heart T2 is in agreement with cardiac biopsy, both in high and low iron.

• 50% of the ex-thalassemic patients had detectable residual hepatic iron overload, although iron depletion therapy was applied and ferritin levels were considerably low.
Effect of iron overload on exercise capacity in thalassemic patients with heart failure

HF thalassemic patients have reduced exercise indexes compared to non HF. Myocardial iron overload, expressed as T2*, has a direct influence on exercise capacity, independent of LV ejection fraction and functional class.

MRI Evaluation of Liver and Myocardial Iron in Thalassemia Intermedia and b-Thalassemia Major

- In **TM** iron $T2^*$ plays a crucial role in the evolution of the disease.

- In **TI** the high output cardiac state seems to be the most prominent finding.

Mavrogeni S et al. *Int J Cardiovasc Imaging* 2008
FOLLOW UP USING T2*

- Oral deferiprone is more effective than the conventional desferrioxamine in removal of myocardial iron (Anderson et al Lancet 2002).

- Standardized T2* maps used to correct T2* segmental artefacts in normals and patients with thalassemia intermedia and thalassemia major with myocardial iron overload and fibrosis (Ramazzotti et al Hemoglobin. 2008).
CMR IN RHEUMATOLOGY
Why CMR in Rheumatic Diseases (RD)?

- RD usually have a silent or oligo-symptomatic cardiac presentation
- **Myocardial inflammation**, assessed by pathology studies in RD, can not be detected by echo, before serious deterioration of cardiac function occurs.
- **Diffuse, subendocardial vasculitis** (primary or secondary in RD) can not be detected by echo, nuclear, CT
- **Small epicardial, intramyocardial, subendocardial fibrosis**, due to myocardial infarction or inflammation can not be detected by echo, nuclear, CT
- **Acuity** of heart involvement can not be detected by echo, nuclear, CT
- **Great vessels angiography** with assessment of wall inflammation can not be assessed by echo, nuclear
- **Tissue characterization** can not be performed by echo, nuclear, CT
- CMR is operator independent, reproducible, nonradiating= ideal for serial evaluation
- Most patients are female unable to exercise, due to arthritis or muscular weakness; pharmacologic stress CMR, offering a nonradiative option, without the limitations of acoustic window and/or breast artifacts, may be ideal for CAD and microvascular disease assessment
Myopericarditis, as the first sign of rheumatoid arthritis relapse, evaluated by CMR

- Myopericarditis with atypical presentation, diagnosed by CMR in RA under remission and may precede the development of RA relapse.

- In 1-year follow-up RA patients with history of myocarditis have a higher frequency of disease relapse and may develop HF.

Mavrogeni S et al. Inflamm Allergy DT 2013
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
Pathophysiology of Q waves in II, III, avF in SLE. Evaluation using CMR

• Q in II, III, avF in SLE may indicate:
  • myocardial infarction
  • acute or past inflammation
  • be a positional finding
  • The lack of Q does not exclude the possibility of infarction or inflammation

• CMR is the best tool to reveal the pathophysiology of Q waves in SLE and guide treatment

Mavrogeni et al. Lupus 2012
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
Frequent Detection Of Myocardial Inflammation In Autoimmune Diseases

- Autoimmune diseases with myocarditis: SLE, RA, Takayasu’s art, SSC, thyroid disease.

- Assess by T2-w, EGE, LGE.

- Positive histology and PCR in agreement with 50% and 87.5% of positive CMR.

- Herpes virus, Adeno, Coxsackie B6, Echo, Parvo-B19, CMV, Chlamydia trachomatis or coexistence

- CMR can early diagnose myocardial inflammation

Mavrogeni S et al. Inflam Allergy and DT 2009
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.

Mavrogeri et al Arthr Rheum 2009
Cardiac involvement in ANCA (+) and ANCA (-) Churg-Strauss syndrome evaluated by CMR

- Cardiac involvement either as DSF or myocarditis, can be detected in both ANCA (+) and ANCA (-) CSS, although more clinically overt in ANCA (-).

- DSF carries an ominous prognosis for LV function.

- CMR, due to its capability to detect disease severity, before cardiac dysfunction takes place, is an excellent tool for CSS risk stratification and treatment individualization.

Mavrogeni et al. Inflam Allergy DT 2013
Diffuse, subendocardial vasculitis. A new entity identified by CMR and its clinical implications.

- Diffuse, subendocardial vasculitis (DSV) can be identified by CMR both in acute and chronic autoimmune diseases.

- Acute DSV has the potential to be reversed by autoimmune and cardiac treatment modification.

Mavrogeni S et al. Int J Cardiol 2013
Myocarditis and subclavian stenosis in Takayasu arteritis

- CMR in TA can be used as a non-invasive, non-radiating technique for the evaluation of
  - subclavian stenosis
  - myocardial inflammation

INFLAMMATORY MYOPATHIES

- CMR unveils silent myocardial involvement in PM/DM.
- To establish the utility of CMR as a routine diagnostic approach in PM/DM, further studies are mandatory, including CMR at early and late time of PM/DM and correlation with clinical/laboratory data.

Mavrogeni et al. JACC Imag 2011
Myocarditis during acute inflammatory myopathies. Evaluation using clinical criteria and CMR

- CMR unveils:
  - Clinically silent myocarditis during acute IM
  - CMR may remain positive, although IM is considered under remission, after steroids treatment.
  - The clinical implications of CMR in the diagnostic algorithm of IM need further evaluation.

Mavrogeni S et al. Int J Cardiol 2013
Myocardial perfusion-fibrosis pattern in systemic sclerosis assessed by cardiac magnetic resonance

Mavrogeni et al. Int J Cardiol 2012
Cardiovascular Magnetic Resonance Imaging clarifies cardiac pathophysiology in early, asymptomatic diffuse systemic sclerosis

- CMR reveals severe cardiac involvement (CI) in early, asymptomatic diffuse SSc with normal routine cardiac evaluation.

- CI presents either as myocardial inflammation or as severe reduction of MPRI and diffuse fibrosis with further deterioration in the longterm follow up.

Mavrogeni S et al. Inflam Allergy and DT 2016
AMYLOIDOSIS

Maceira A et al, Circulation 2005
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
Myocardial stress perfusion-fibrosis imaging pattern in sarcoidosis, assessed by CMR.

• Results:
  • CMR was performed in 43/45 patients (2 were excluded due to technical reasons); In 34/43 SRC with T2 ratio<2 (Group A), a stress perfusion-fibrosis CMR revealed a significant reduction in myocardial perfusion reserve index (MPRI), compared to 34 age-sex matched controls (0.95±0.3 vs 3.5±0.8, p<0.001). Although clear evidence of late gadolinium enhancement was not identified, the quantitative analysis revealed diffuse fibrosis in all patients with an extent of 4.5±3.4% LV (range 2-15).

  • Available CMR after 1 year in 18/34 patients, documented LVEF<50% in 3 patients. Notably, in 6/9 SRC patients with T2 ratio>2 (Group B), the myocarditis protocol was positive and steroids treatment was promptly given. Six months later, their CMR was normal. No correlation between CMR, SRC duration and / or other organs involvement was identified.

• Conclusions:
  • In sarcoidosis without cardiac symptoms and normal routine assessment, CMR can detect early cardiac involvement that may in some cases necessitate immediate treatment.

Cardiac tissue characterization and the diagnostic value of CMR in systemic connective tissue diseases

- **Background-Aim.**
- Accurate diagnosis of CV involvement in CTDs remains challenging.
- Hypothesis: CMR reveals cardiac lesions in symptomatic CTDs with normal echo.

- **Patients-Methods.**
- CMR from 246 CTDs with typical (TCS) (n=146, group A) or atypical (ATCS) (n=100, group B) cardiac symptoms were retrospectively evaluated.
- Group A included 9 IM, 35 SRC, 30 SSc, 14 SLE, 10 RA and 48 small vessel vasculitis.
- Group B included 25 RA, 20 SLE, 20 SRC, 15 SSc, 10 IM and 10 small vessel vasculitis.

- **Results.**
- Abnormal CMR in 32 % (chronic 27%) and 15 % (chronic12%) of TCS and ATCS.
- Lesions due to vasculitis, myocarditis and myocardial infarction in 27.4%, 62.6% and 9.6% of CTDs.
- Stress studies in CTDs with negative CMR revealed CAD in 20%.

- **Conclusions.**
- CMR in symptomatic CTDs can assess disease acuity and vasculitis, myocarditis and myocardial infarction; therefore, it can be part of CTDs diagnostic algorithm.

Mavrogeni et al. Arthr Care Research 2014
CMR in asymptomatic patients with connective tissue disease and recent onset LBBB

- **Background-Aim.**
  Diagnostic evaluation of recent onset left bundle branch block (LBBB) in connective tissue disease (CTD) patients is a challenge, due to high incidence of underlying pathology and limitations of imaging tests.

- **Patients-Methods.**
  Twenty-six CTDs, aged 27± 6 yrs (19F/7M) and 26 non CTDs, aged 60±4 yrs (10F/16 M) with recent asymptomatic LBBB and normal echo study were evaluated by CMR. The CTD population included 6 sarcoidosis (SRC), 4 systemic sclerosis (SSc), 6 lupus erythematosus (SLE), 6 rheumatoid arthritis (RA), 4 inflammatory myopathies (IM).

- **Results.**
  11/26 CTDs (42%) had abnormal CMR, including DCM in 3, diffuse subendocardial fibrosis in 3, silent myocardial infarction in 2 and acute myocarditis in 3.
  In non CTDs, abnormal CMR was found in 8/26 (30.7%), including DCM in 5, myocardial infarction in 2 and myocarditis in 1.

- **Conclusions.**
  In recent LBBB, CMR documented high incidence of acute and chronic cardiac pathology, with preponderance of myocarditis, in CTDs compared to non CTDs. Therefore, CMR should be considered as a valuable adjunct to conventional work up of asymptomatic CTDs with recent onset of LBBB and normal echo.

Imaging patterns of cardiovascular involvement in mixed connective tissue disease evaluated by CMR

- CMR can reveal myocardial lesions in MCTD patients with cardiac symptoms including
  - myocardial infarction,
  - inflammation,
  - diffuse subendocardial fibrosis and
  - diffuse perfusion defects, necessitating further cardiac investigation and/or treatment.

Mavrogeni S et al. Inflam Allergy and DT 2016
CARDIO-RHEUMATIC TEAM

• Rheumatologists
  • George Kitas
  • Petros Sfikakis
  • Theodoros Dimitroulas
  • Efthymios Stavropoulos
  • George Spiliotis
  • Gikas Katsifis
  • Loukia Koutsogeorgopoulou
  • Maria Tektonidou

• Cardiologists
  • Sophie Mavrogeni
  • Konstantinos Bratis
  • Eliza Sfendouraki
  • Georgia Karabela
  • Elias Gialafos
  • Sotiris Plastiras
  • Genovefa Kolovou
Interventional CMR

- CMR, as an innovating imaging technique, can
- a) provide reliable information about the pattern of stress myocardial perfusion-fibrosis in both ischemic and nonischemic heart disease and
- b) guide the traditional interventional procedures.

- iCMR, by using excellent tissue imaging, can create a surrogate for direct visualization and offer multiplanar views and real-time functional imaging without ionizing radiation. These images can facilitate the usual interventional procedures and promote the innovation of new interventional approaches.

Mavrogeni S et al (in press)
Stress perfusion fibrosis
From: Interventional Cardiovascular Magnetic Resonance Imaging: A New Opportunity for Image-Guided Interventions


CMR-Guided Transapical Aortic Valve Replacement  (A) Bioprosthesis mounted on a platinum iridium stent with a stainless-steel marker welded on the side of the stent between the commissures. (B) The marker is visible as a dark signal in the cardiovascular magnetic resonance (CMR) and indicates the orientation of the prosthesis. Short-axis view and long-axis view of the implanted prosthesis in a pig under real-time CMR are shown in C and D, respectively. Blue dots are digital markers indicating the coronary ostia whereas the yellow dot shows aortic annulus location. (E) Three-dimensional rendering snapshots show multiple image planes displayed at their relative 3-dimensional position. Images courtesy of Ming Li, PhD, and Keith A. Horvath, MD, Cardiothoracic Surgery Research Program, National Heart, Lung, and Blood Institute.
Electrophysiological Cardiac Mapping Under Real-Time CMR Guidance  
(Top) Roadmap-based real-time 3-dimensional visualization of the catheter position during recording (red dot) on the magnetic resonance-electrophysiological workstation. The yellow dots in the 3-dimensional rendering of the heart indicate previous mapping positions. (Bottom) In-bore electrophysiological recordings at 2 selected positions showing an atrial signal (left) and a ventricular signal (right). Graphic courtesy of Steffen Weiss, PhD, Philips Healthcare.

• The 2 first-in-man MR-guided interventions were performed in a child and an adult, both with PVS.

• Catheter manipulations were monitored with real-time MRI. Temporal resolution was 11 to 12 frames/s. Catheterization procedure times were 110 and 80 minutes, respectively.

• Both patients had successful relief of the valvar stenosis and no procedural complications.

Tzifa A et al. Circ Cardiovasc Interv 2010
ΕΜΠΕΙΡΙΑ ΩΚΚ

• >150 ΔΗΜΟΣΙΕΥΣΕΙΣ ΣΕ ΔΙΕΘΝΗ ΠΕΡΙΟΔΙΚΑ (70/150 CMR in Rheumatology)

• 4 ΔΗΜΟΣΙΕΥΣΕΙΣ ΤΟΥ ΩΚΚ ΣΥΜΠΕΡΙΛΗΦΘΗΚΑΝ ΣΤΑ REFERENCE PAPERS ΤΟΥ CIRCULATION 2008 ΓΙΑ ΤΙΣ ΕΝΔΕΙΞΕΙΣ ΜΑΓΝΗΤΙΚΗΣ ΣΤΕΦΑΝΙΟΓΡΑΦΙΑΣ ΚΑΙ 1 ΓΙΑ ΤΙΣ ΕΝΔΕΙΞΕΙΣ ΒΙΟΨΙΑΣ ΜΥΟΚΑΡΔΙΟΥ

• ΣΥΜΜΕΤΟΧΗ ΣΤΟ ΔΙΕΘΝΕΣ REGISTRY ΜΥΟΚΑΡΔΙΤΙΔΑΣ ΚΑΙ ΣΤΟ ΕΥΡΩΠΑΪΚΟ REGISTRY ΚΑΡΔ. ΑΝΕΠΑΡΚΕΙΑΣ ΚΑΙ ΜΥΟΚΑΡΔΙΟΠΑΘΕΙΩΝ ΜΕ CMR

• ΟΡΓΑΝΩΣΗ ΑΝΕΠΑΡΚΕΙΑΣ REGISTRY ΓΙΑ ΤΑ ΚΑΡΔΙΑΚΑ ΝΟΣΗΜΑΤΑ ΣΤΙΣ ΣΥΣΤΗΜΑΤΙΚΕΣ ΠΑΘΗΣΕΙΣ ΜΕ CMR

• ΟΡΓΑΝΩΣΗ ΑΝΕΠΑΡΚΕΙΑΣ ΟΜΑΔΑΣ ΜΕΛΕΤΗΣ ΚΑΡΔΙΑΚΩΝ ΝΟΣΗΜΑΤΩΝ ΓΥΝΑΙΚΩΝ ΜΕ CMR

• Euros/SCMR level 1 in Athens, 1-3 October 2016 endorsed by EACVI and SCMR and accredited by EBAC
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