The challenge of myocarditis: An update

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MYOCARDITIS

- "Inflammation of myocardium"
- Clinical presentation ranges from nonspecific systemic symptoms to fulminant collapse and sudden death
- Sudden death at rates 8.6%-12%
- Cause of cardiomyopathy in 9% of cases
- Active: Inflammatory cellular infiltrate with myocardial necrosis
- Borderline: Inflammatory cellular infiltrate without myocyte injury

CLINICAL PRESENTATION

- Asymptomatic ECG abnormalities
- Cardiogenic shock
- Fulminant heart failure presenting as a new-onset cardiomyopathy
- Prodrome viral symptoms in 10-80% of cases
- Fulminant: Severe hemodynamic compromise requiring vasopressor or mechanical support
- Masquerading acute coronary syndrome

  (ST elevation 54%, T-inversion 27%, ST-depression 18%, pathologic Q 18-27%, VT in <5%)

DIAGNOSTIC EVALUATION: MYOCARDIAL IMAGING

- Echocardiography (LV dysfunction 69%, RV dysfunction 23%, reversible LV hypertrophy 15%)
- Ultrasonic tissue characterization could not accurately differentiate DCM vs Myocarditis
- Indium111-labeled monoclonal antibody fragments (bind to cardiac myocytes that lost their integrity) sens 83%, spec 53%, NPV 92%
- CMR :Lake Louise Criteria
- Increase T2: sens 84%, spec 74%, accur 79%
- Early T1: sens 80%, spec 68%, accur 74.5%
- LGE: sens 44%, spec 95.5%, accur 71%
- Combined any two: sens 76%, spec 95.5%, accur 85%

CMR in Nonischemic Myocardial Inflammation: Expert Recommendations

CMR provides strong evidence for myocardial inflammation, with increasing specificity, if

- It demonstrates the combination of edema with other CMR markers of inflammation (at least one T2-based criterion , with at least one T1-based criterion

- While having both a positive T2-based and a T1-based marker will increase specificity for acute myocardial inflammation,
- having only one (i.e., T2-based OR T1-based) marker may still support a diagnosis of acute myocardial inflammation in an appropriate clinical scenario, but with less specificity.

Ferreira VM et al JACC 2018

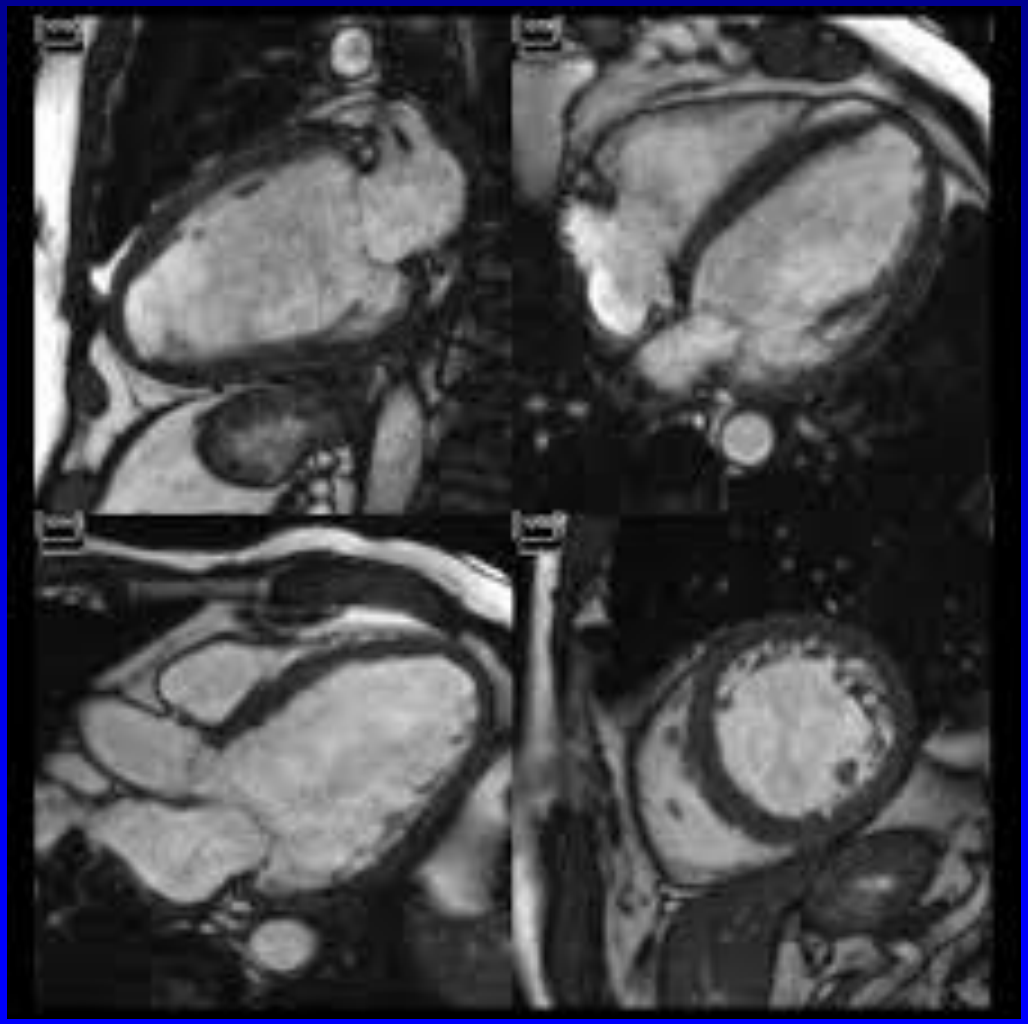
2025 ESC Guidelines for the management of myocarditis/ pericarditis.

- Upgrade the role of CMR in:
- myocarditis diagnosis/follow up

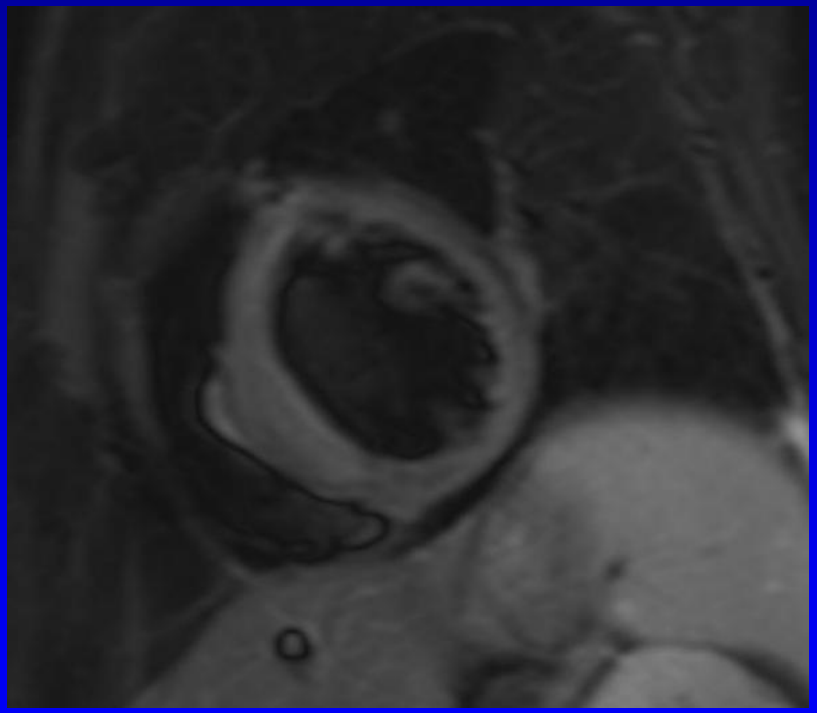
- pericarditis diagnosis, coexisting myocardiadis, treatment follow up

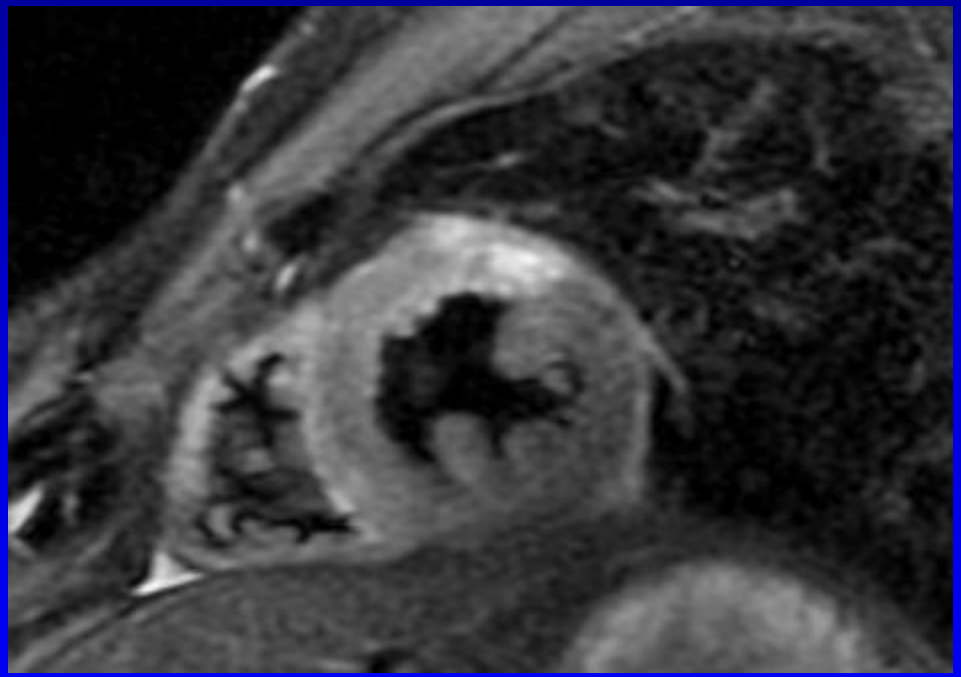
- EMB only in:
- High-risk myocarditis and
- To reconsider treatment

Function evaluation

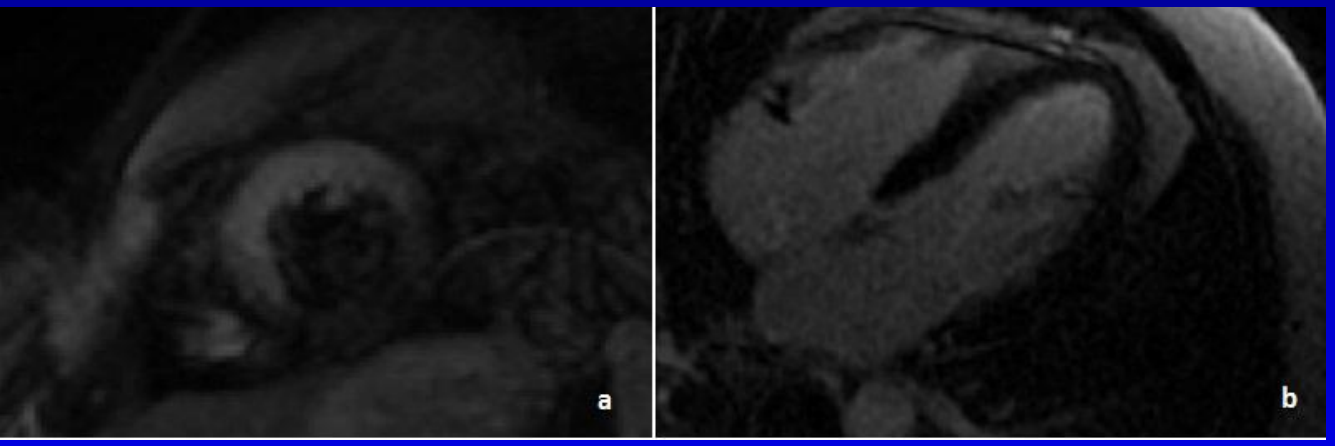


Oedema Imaging in ARDs.
T2-W Imaging





FULMINANT MYOCARDITIS (FM): CAN CMR PREDICT EVOLUTION TO HEART FAILURE?

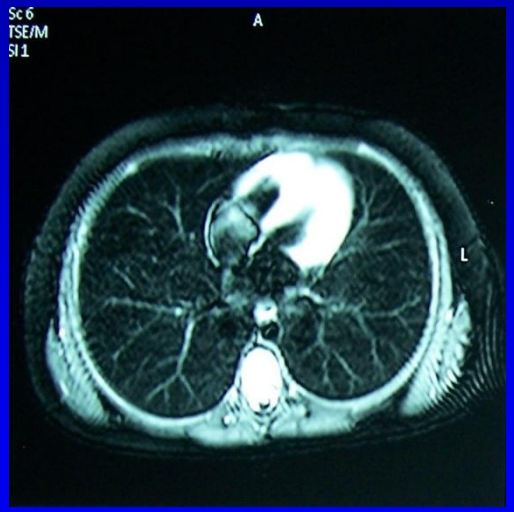


- The only abnormal CMR finding in fulminant myocarditis was the oedema detection in T2W images.
- The application of a standard CMR in fulminant myocarditis can clarify pathophysiology and also predict the evolution to HF.

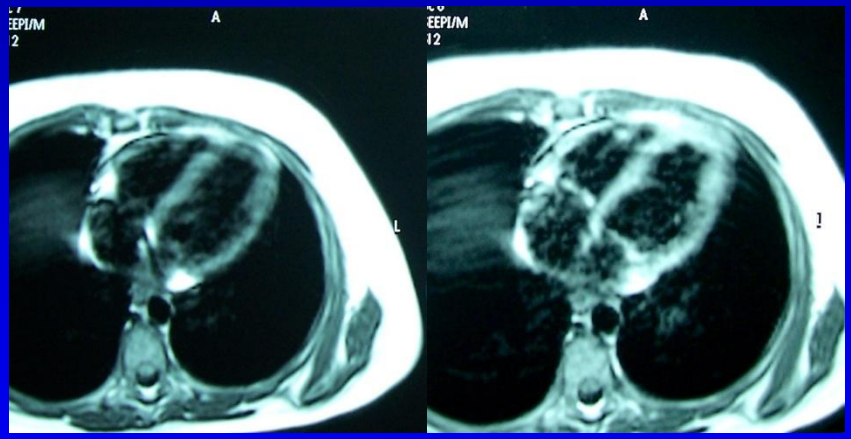
Mavrogeni S et al. Int J Cardiol 2012

CMR for inflammation (Lake Louise Criteria)

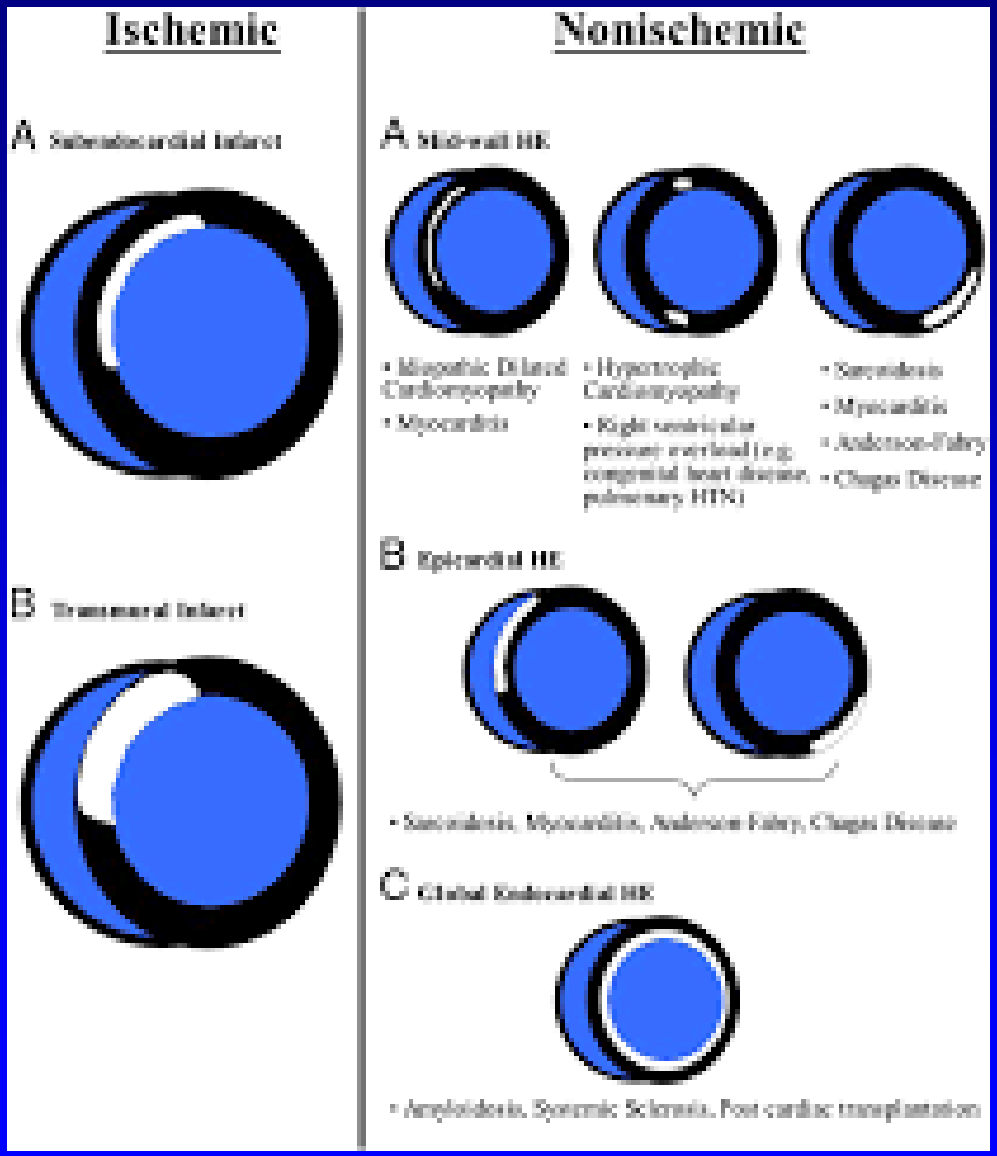
- STIRT2>2



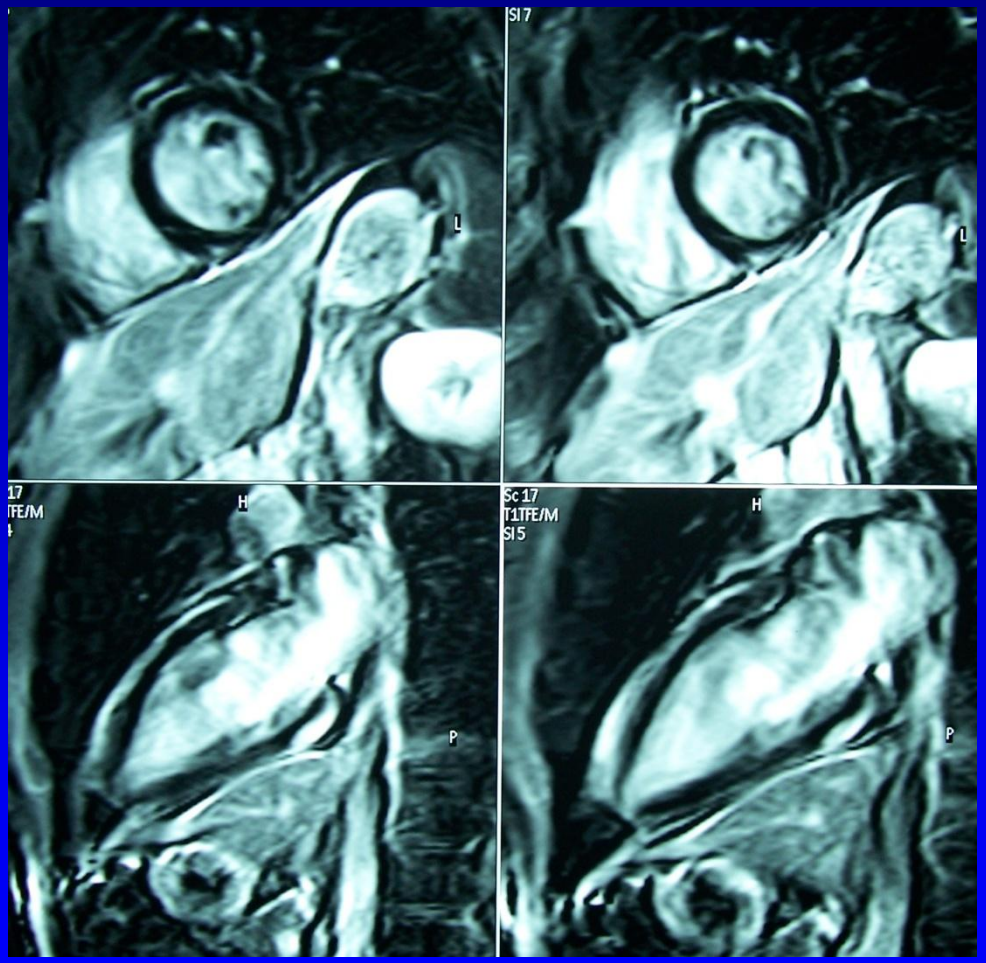
- T1-W before and after Gd to assess EGE>4



Fibrosis assessment

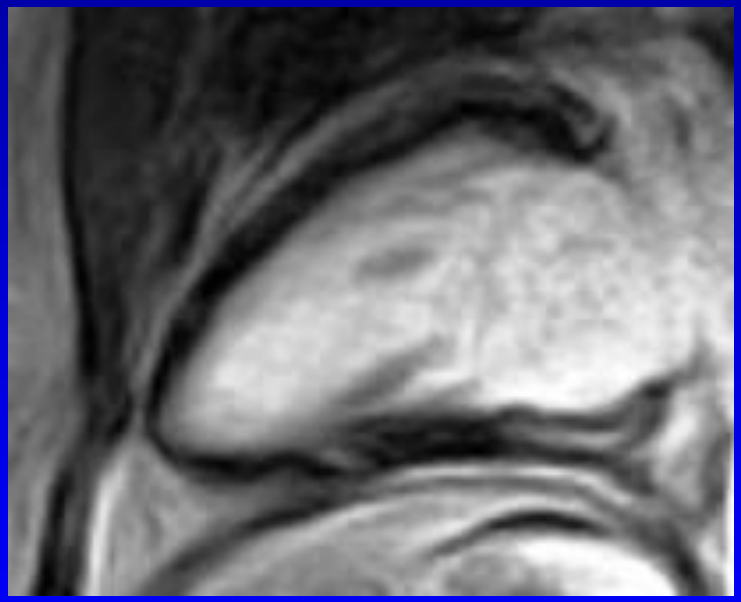


Inversion recovery sequence for LGE



Mavrogeni S et al. Eur J Heart Fail 2011

CMR assessment of myocarditis in patients with cardiac symptoms during H1N1 viral infection.

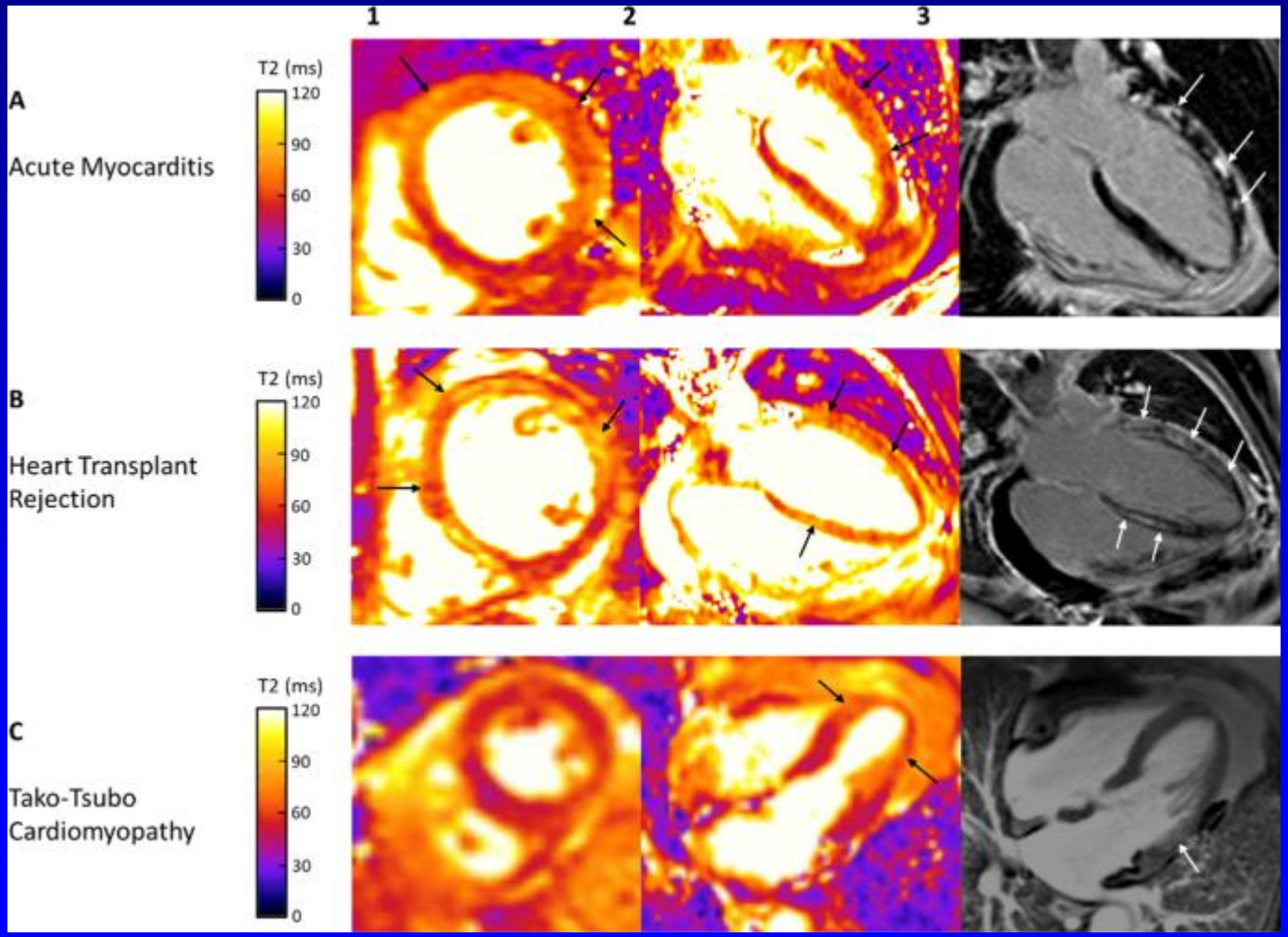


- Mild cardiac symptoms were detected in a considerable number of patients with H1N1 influenza.
- However, we also documented the presence of pericarditis and myocarditis in a minority of them.

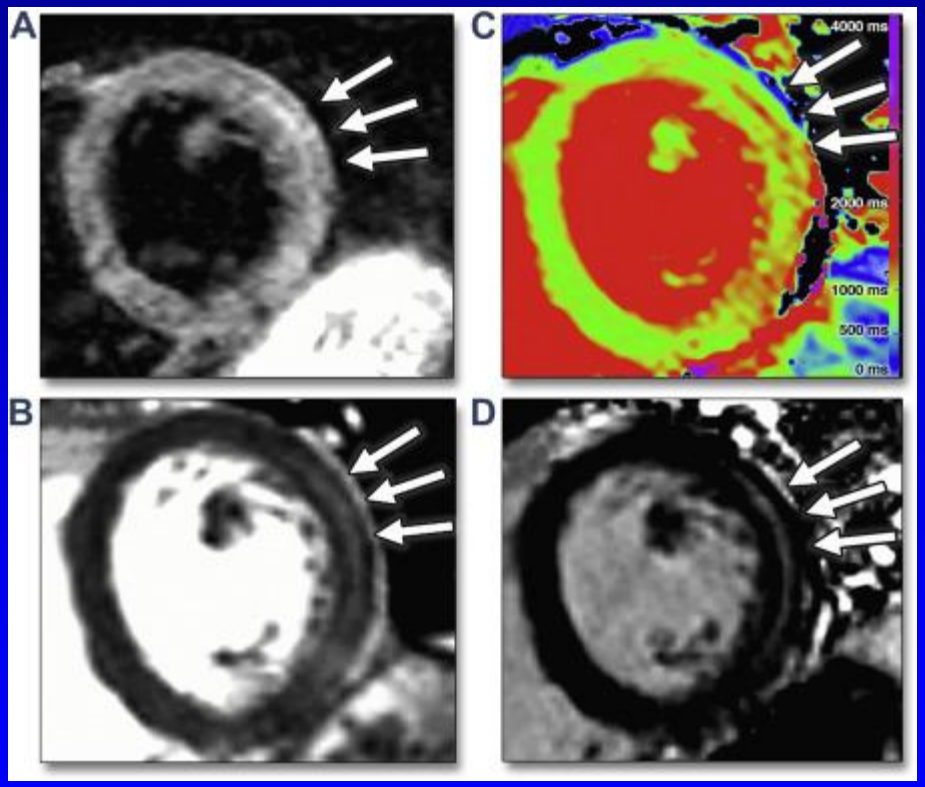
- These findings should aware the clinicians about possible pericardial/myocardial involvement during H1N1 infection and support the application of CMR as a tool for cardiac assessment in these patients, especially if the echocardiographic evaluation is negative.

Mavrogeni S et al JACC Cardiovasc Imag 2011

T2 MAPPING IMAGES



Native T1 mapping in acute myocarditis



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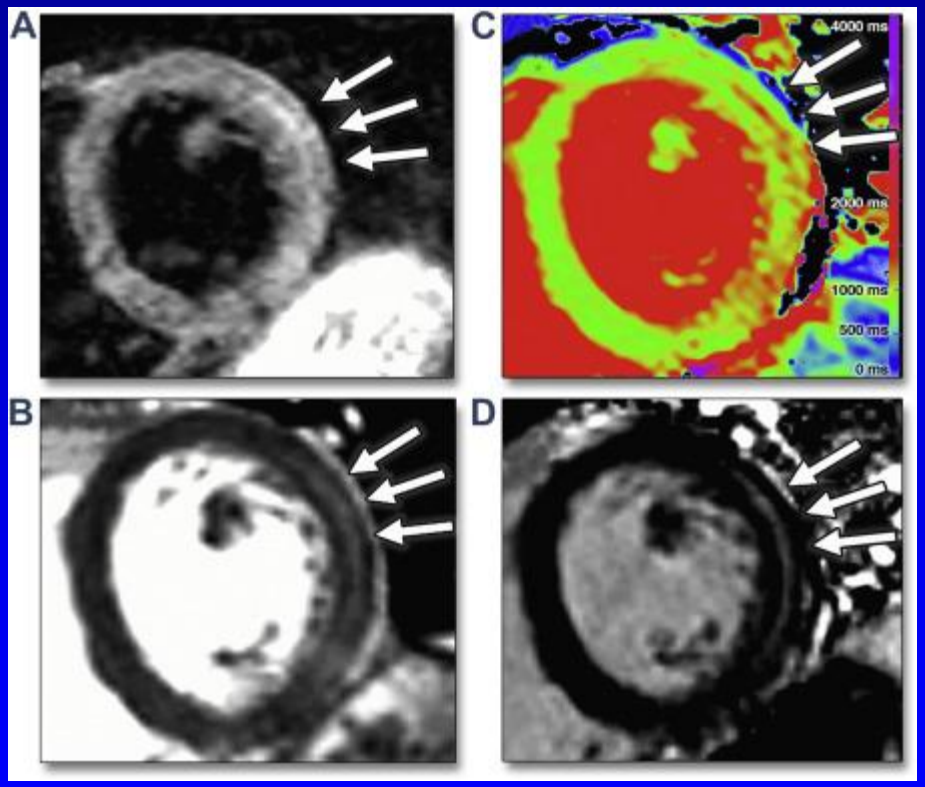

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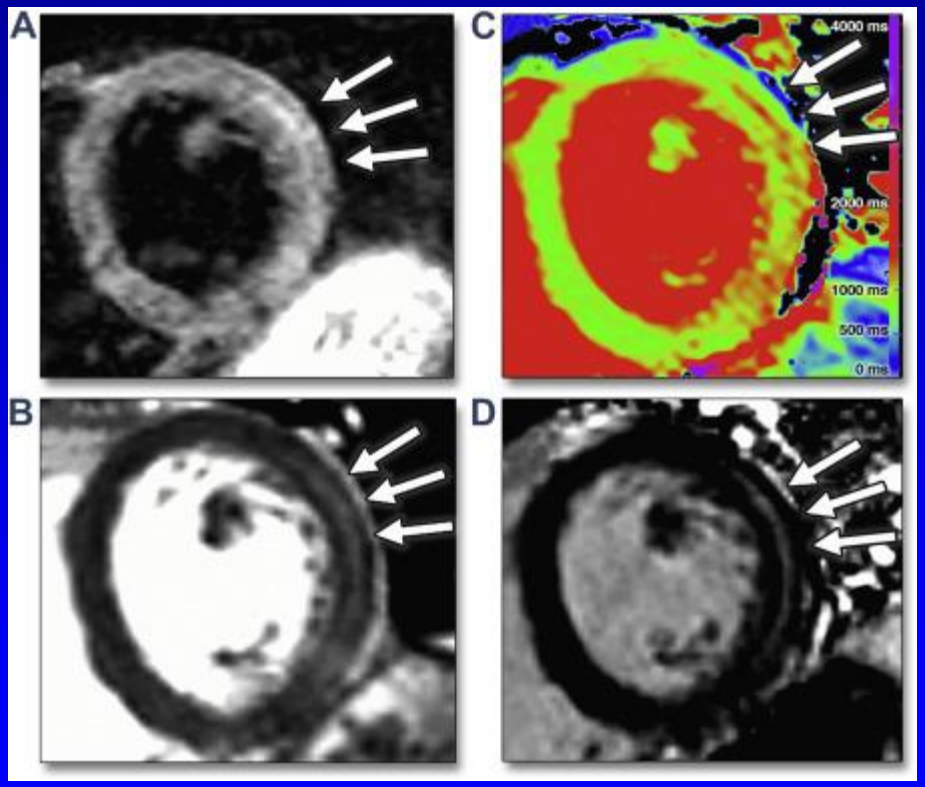

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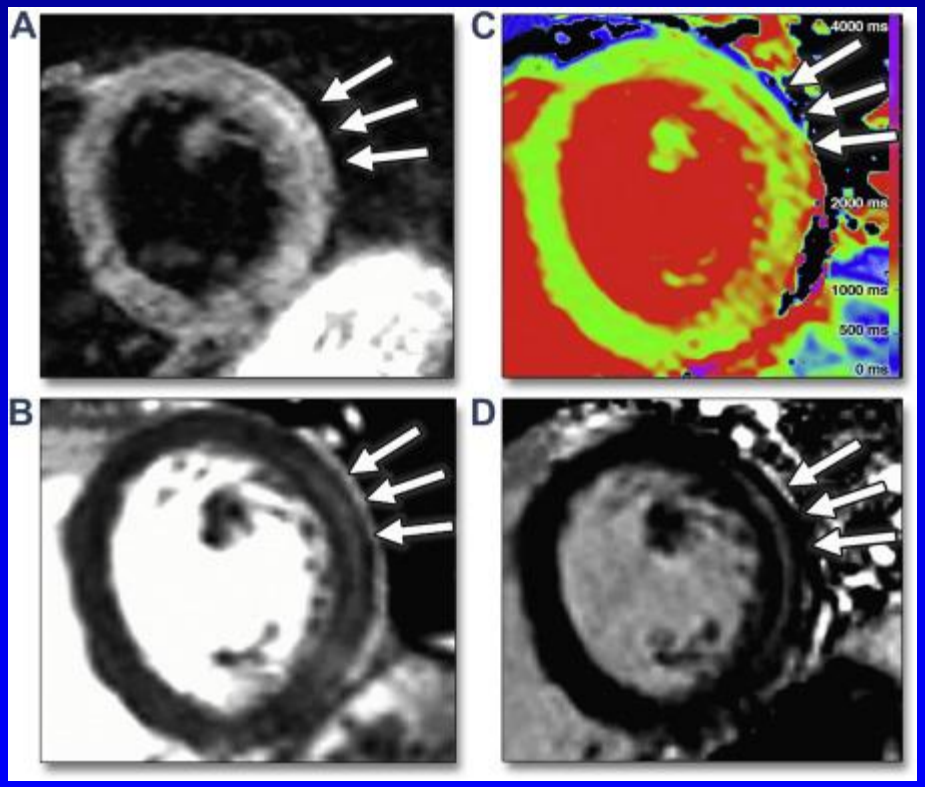
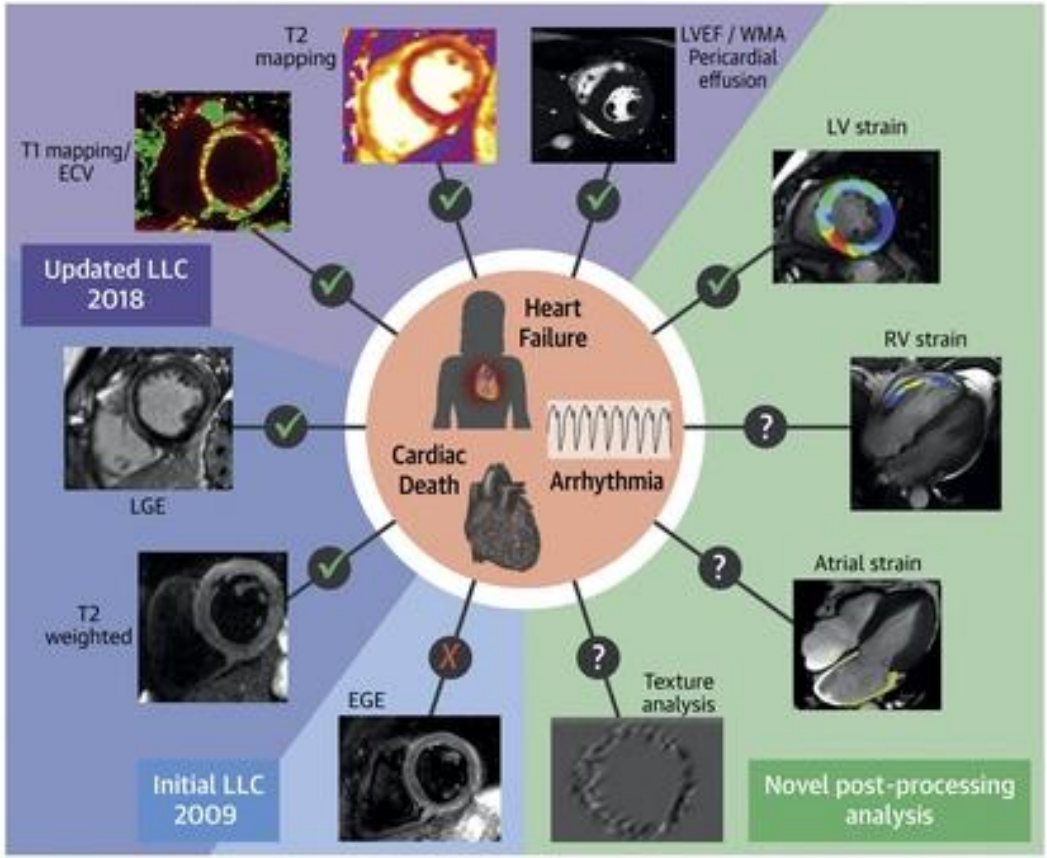


CMR IN MYOCARDITIS

CENTRAL ILLUSTRATION: Association of CMR Parameters With Outcome in Patients With Clinically Suspected Myocarditis



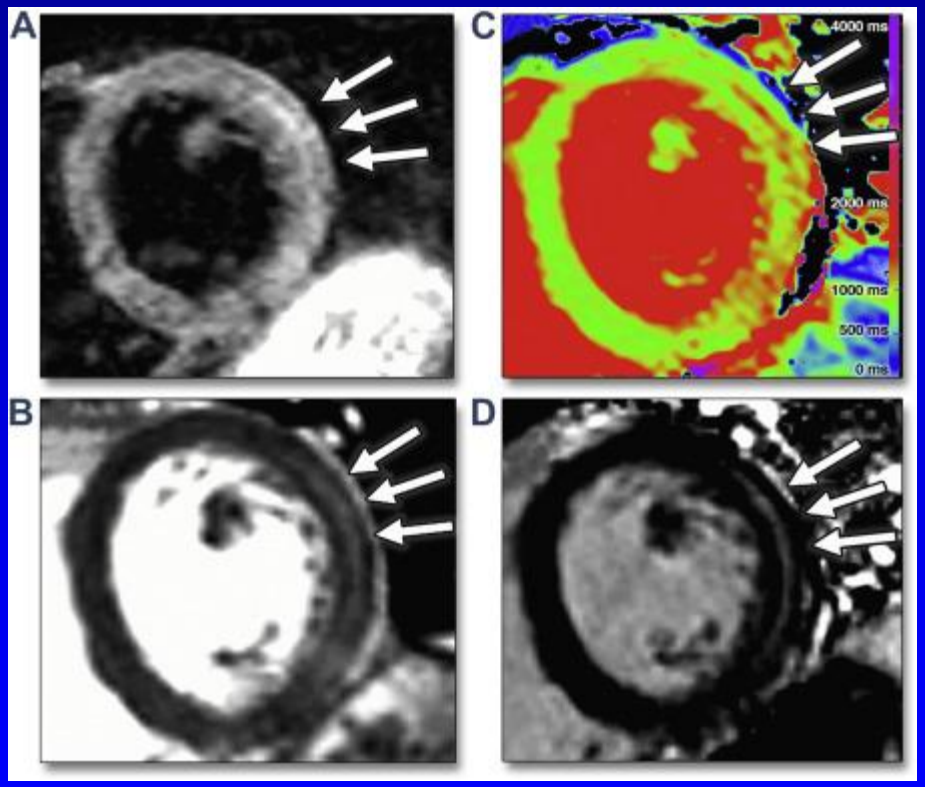
Eichhorn C, et al. J Am Coll Cardiol Img. 2022;15(7):1325-1338.

Prognostic Value of Repeating CMR in Patients With Acute Myocarditis

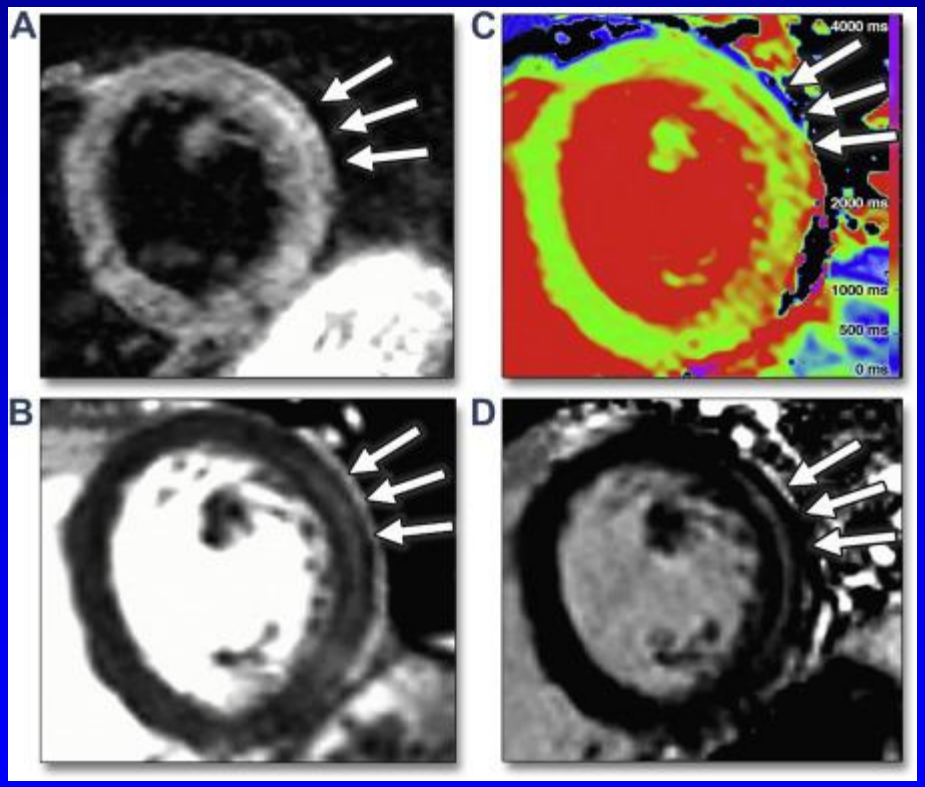
- In the acute setting, LGE does not mean definite fibrosis, and it may disappear at 6 months.
- LGE without edema at 6-month CMR is associated with worse prognosis, particularly when distributed with a midwall septal pattern.
- LGE without edema could represent definite fibrosis whereas the presence of edema suggests a residual chance of recovery.

Donato Aquaro G et al JACC 2019

Native T1 mapping in acute myocarditis



Native T1 mapping in acute myocarditis



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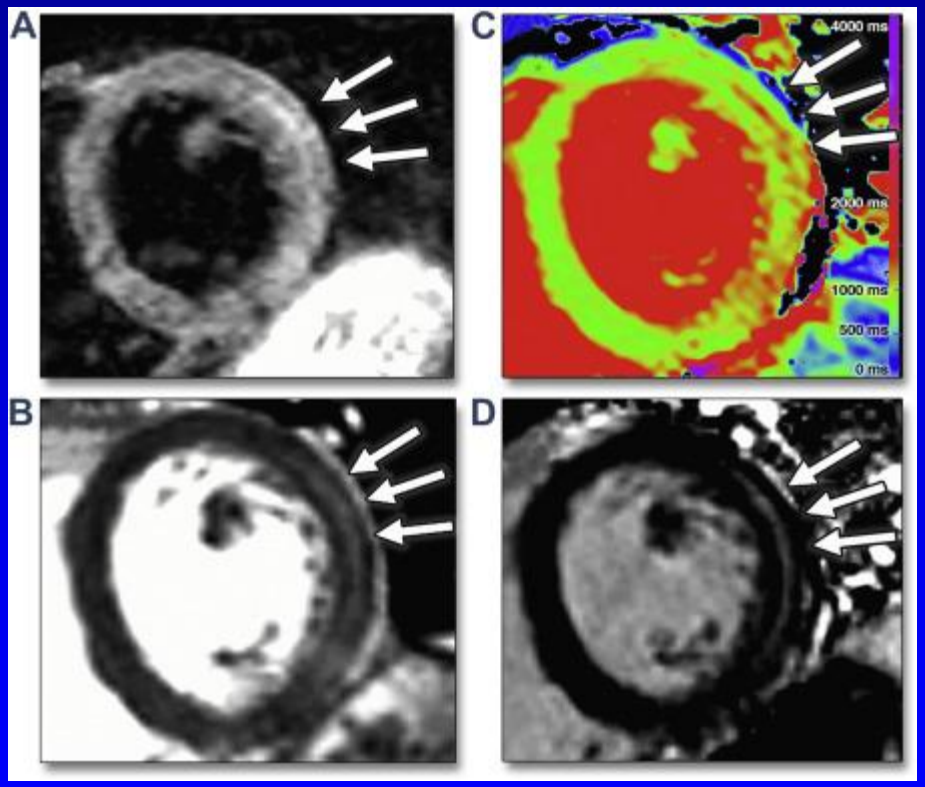

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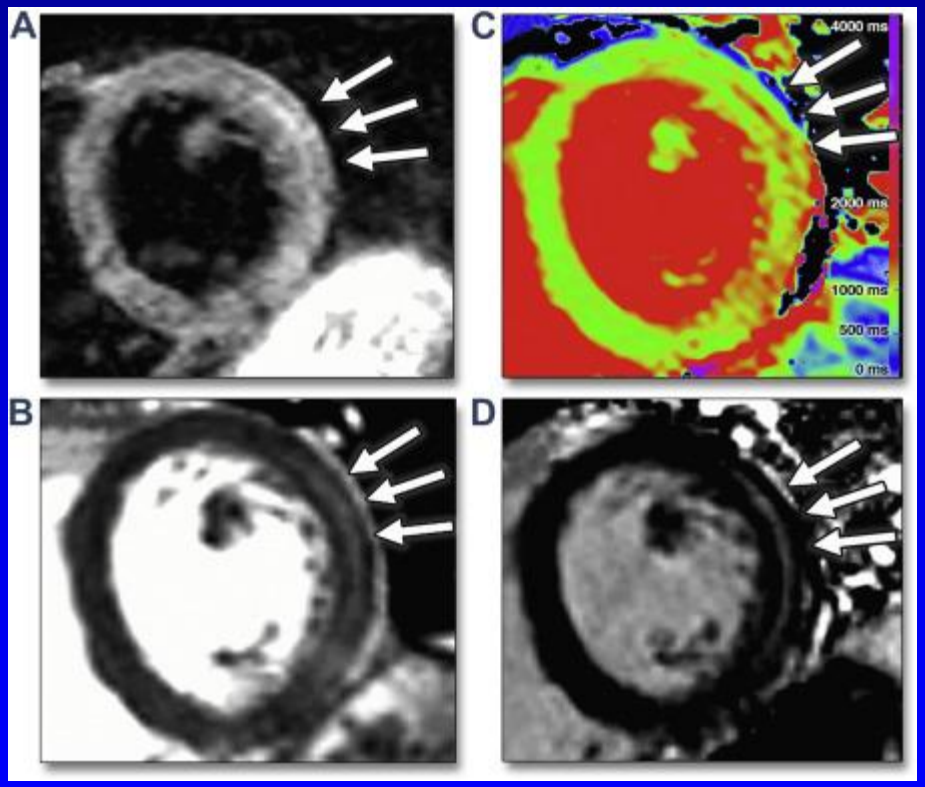

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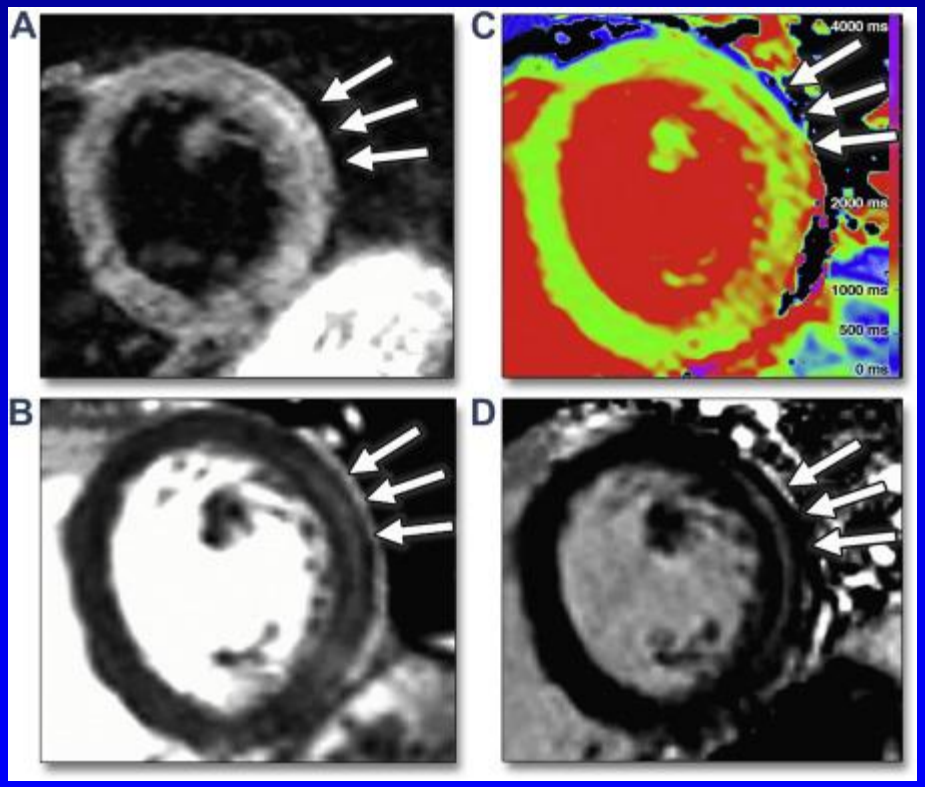

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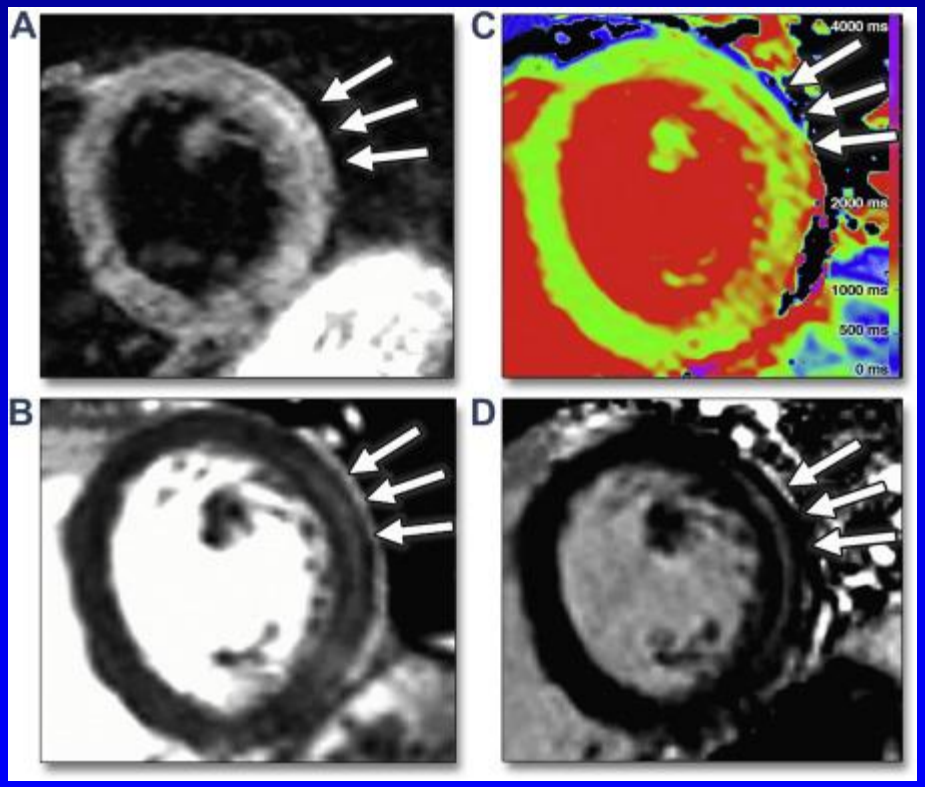
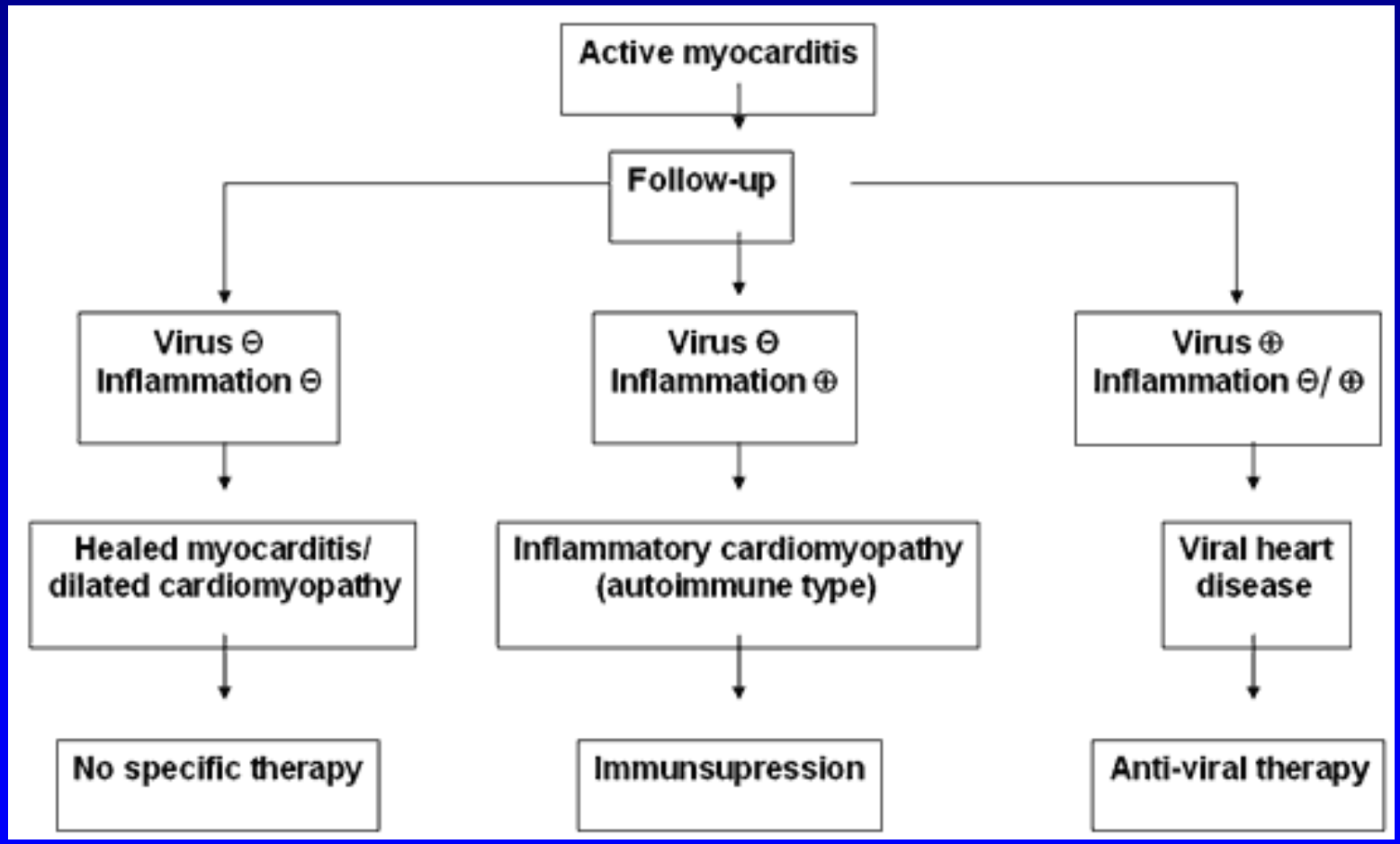


MYOCARDITIS ALGORITHM



TREATMENT

- **Supportive care** (vasopressors, positive inotropic agents, diuretics, vasodilators, assist devices)
- After stabilization: ACE-inhibitors, b-blockers and aldosterone antagonist in NYHA III-IV, defibrillator deferred for several months
- **Immunosuppression** benefits giant cell and autoimmune myocarditis
- Intravenous immune globulin in acute phase
- **Azathioprine and prednisone** if PCR (-) for virus
- **Interferon-a and –b** if PCR (+) for virus

Prognostic Value of Reparative Cardiac Magnetic Resonance in Patients With Acute Myocarditis

Immunosuppressive therapy for active lymphocytic myocarditis: virological and immunologic profile of responders versus nonresponders.

- In patients with active lymphocytic myocarditis, those with circulating **cardiac autoantibodies and no viral genome** in the myocardium are the most likely to **benefit** from immunosuppression.

- The beneficial effect of **immunosuppression in hepatitis C virus myocarditis** suggests a relevant immunomediated component of damage.

Frustaci A. et al Circulation 2003

Myocarditis in autoimmune diseases

Multimodality imaging and the emerging role of CMR in autoimmune myocarditis.

- Autoimmune myocarditis is an inflammatory reaction of the heart during the course of autoimmune disorders, with most cases seen in SLE.
- Early diagnosis is of great significance because of the likelihood of progression to severe and potentially fatal complications such as arrhythmias, heart block, and HF.
- The clinical presentation of the disease is silent leading to delayed diagnosis when dilated cardiomyopathy or HF has already advanced.
- CMR has emerged as an important technique in the evaluation of myocarditis using three types of images:
- T2-weighted (T2-W),
- early T1-weighted (EGE) images taken after 1 min, and
- delayed enhanced images (LGE) taken 15 min after the injection of contrast agent.
- If 2/3 of the imaging sequences are positive, myocardial inflammation can be predicted or ruled out with a diagnostic accuracy of 78%.

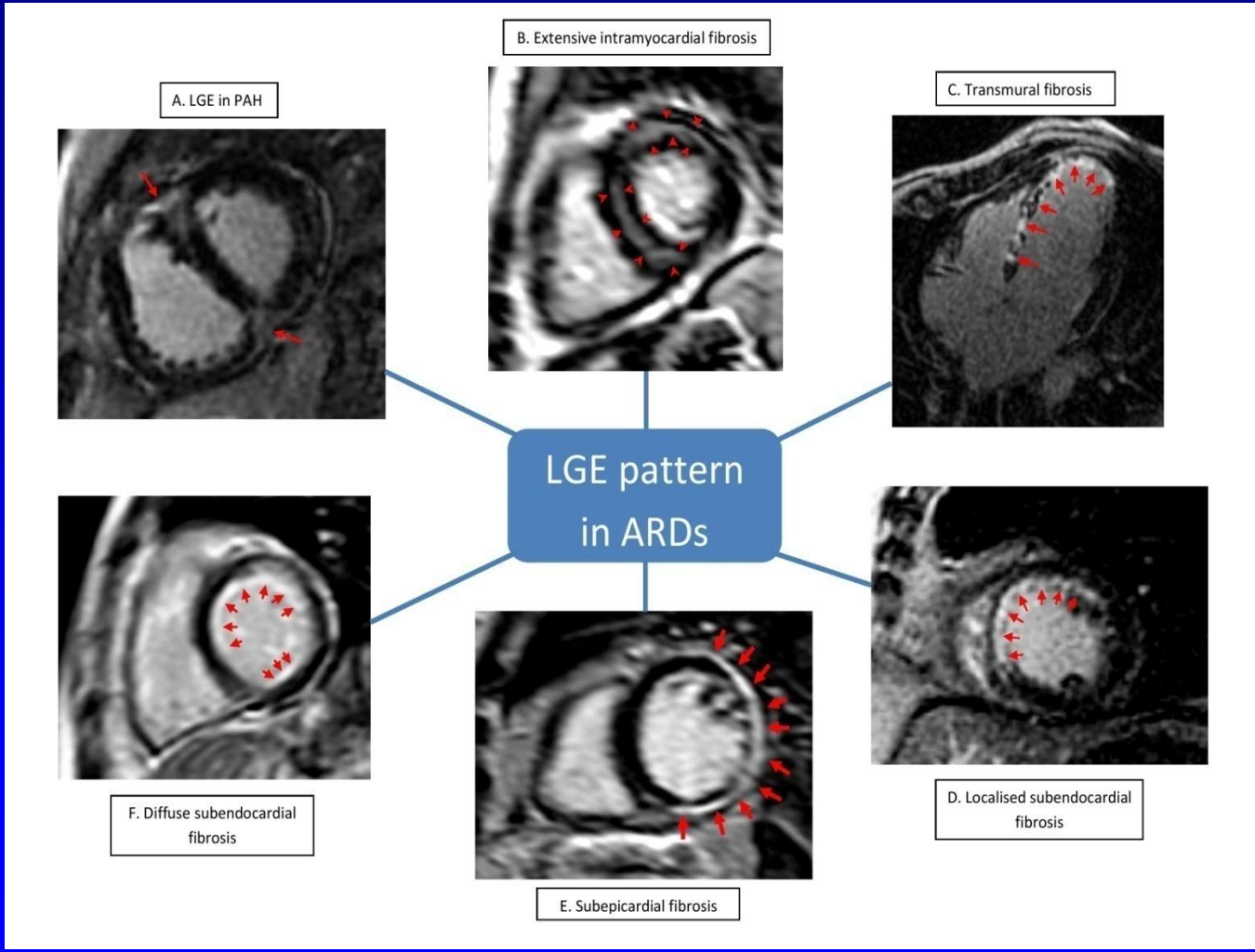
Mavrogeni S et al. Autoimmune Rev 2012

The diagnostic role of CMR in detecting myocardial inflammation in SLE. Differentiation from viral myocarditis.

- CMR-positive IM patients were more symptomatic than active SLE.
- >50%of CMR-positive patients also had positive EMB.
- PCR was positive in almost all IM, but unusual in SLE.
- Due to the subclinical presentation of SLE myocarditis and the limitations of EMB, CMR presents the best alternative for the diagnosis of SLE myocarditis.

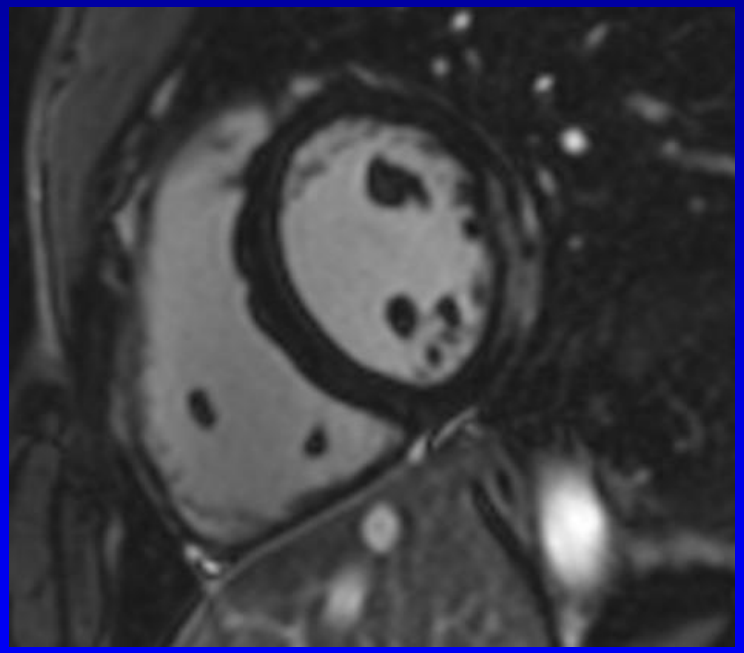
Mavrogeni S et al. Lupus 2013

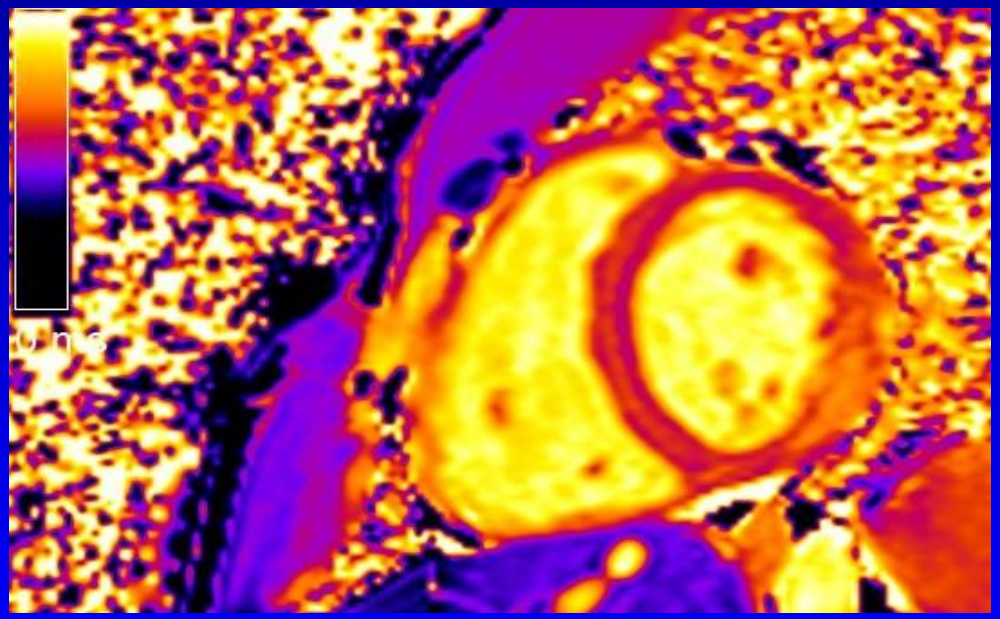
Fibrosis Imaging in ARDs. T1 Imaging



Mavrogeni et al. JACC CVI 2017

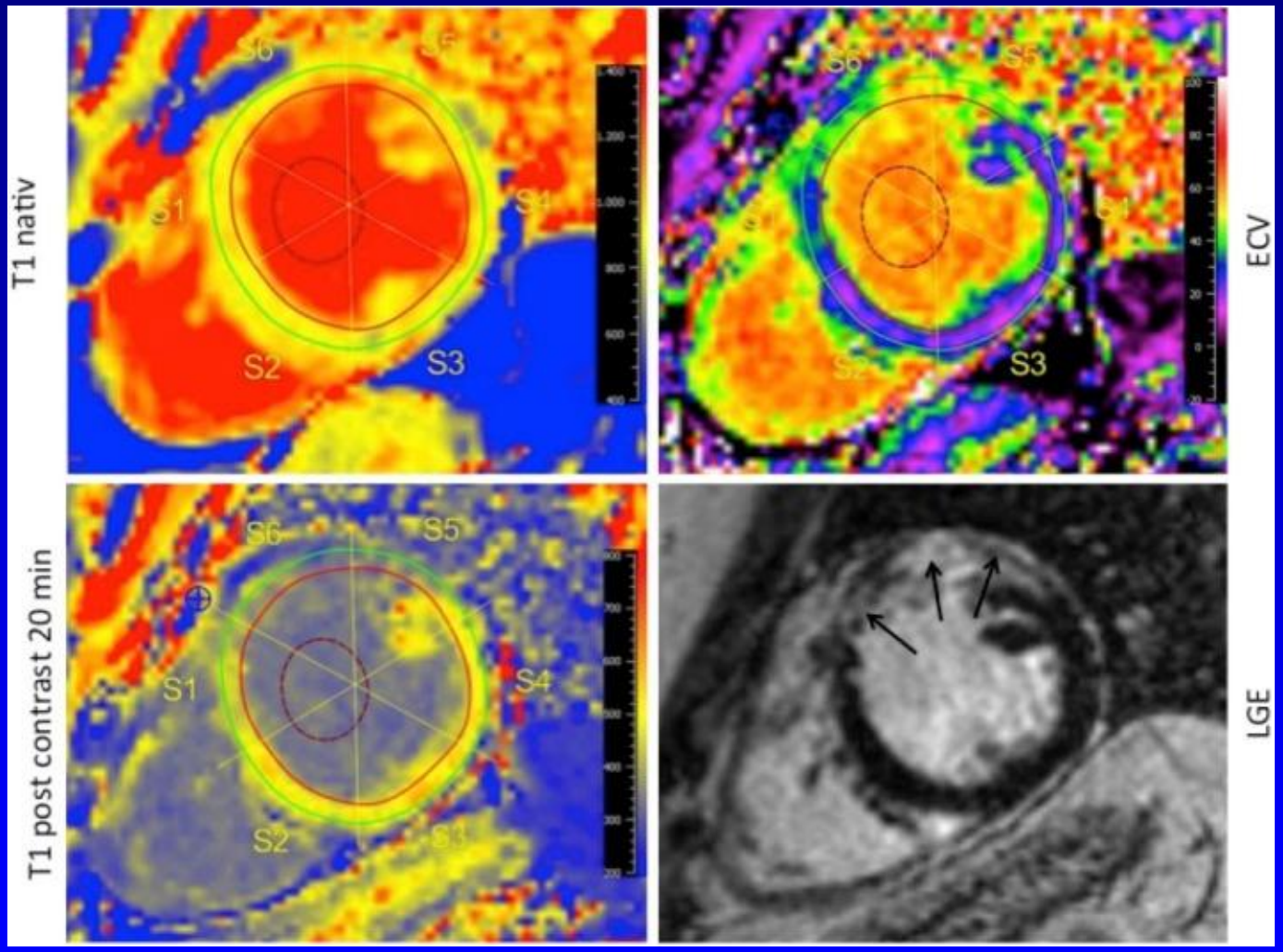
CMR detects Inflammatory Cardiomyopathy in Symptomatic Patients with Inflammatory Joint Diseases and a Normal Routine Workup





Markousis-Mavrogenis G et al JCM 2022

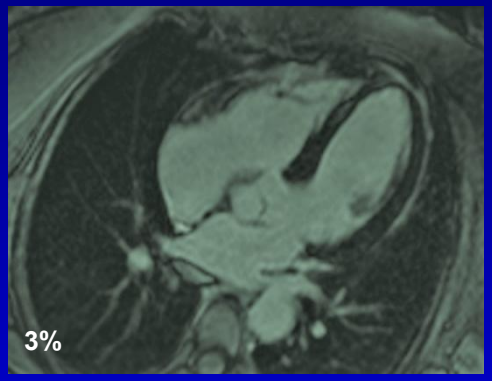
Parametric Imaging in Cardiac Sarcoidosis

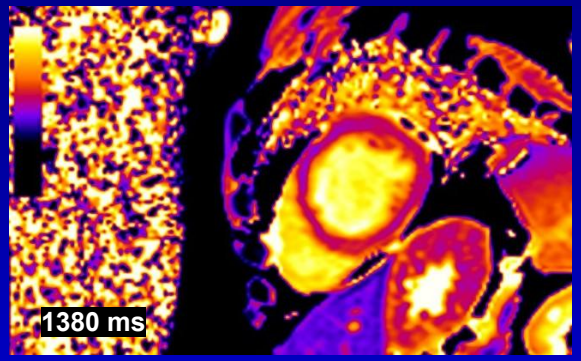


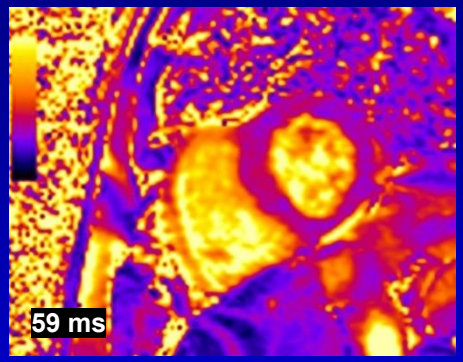
Smedema JP et al . Progress in CVD 2020

CMR in Systemic Sclerosis

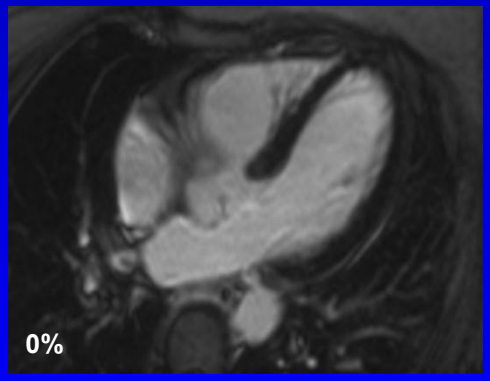
At diagnosis

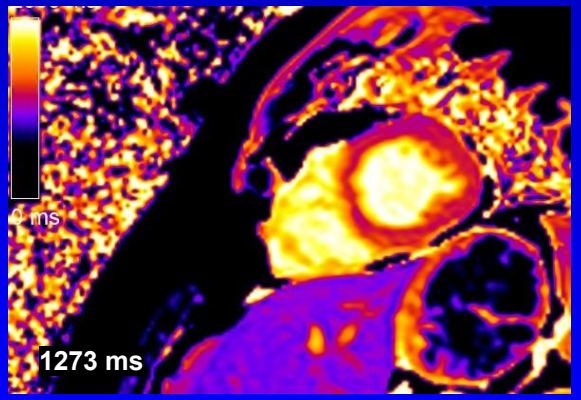


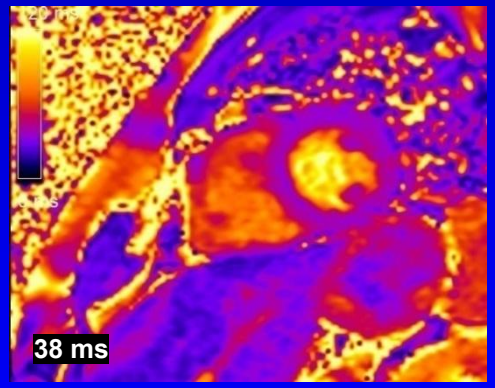




After treatment with cyclo-phosphamide







LGE

Nat T1 map

T2 map

Panopoulos S et al. Rheumatology 2022

Myocardial infarction with normal coronaries in systemic sclerosis

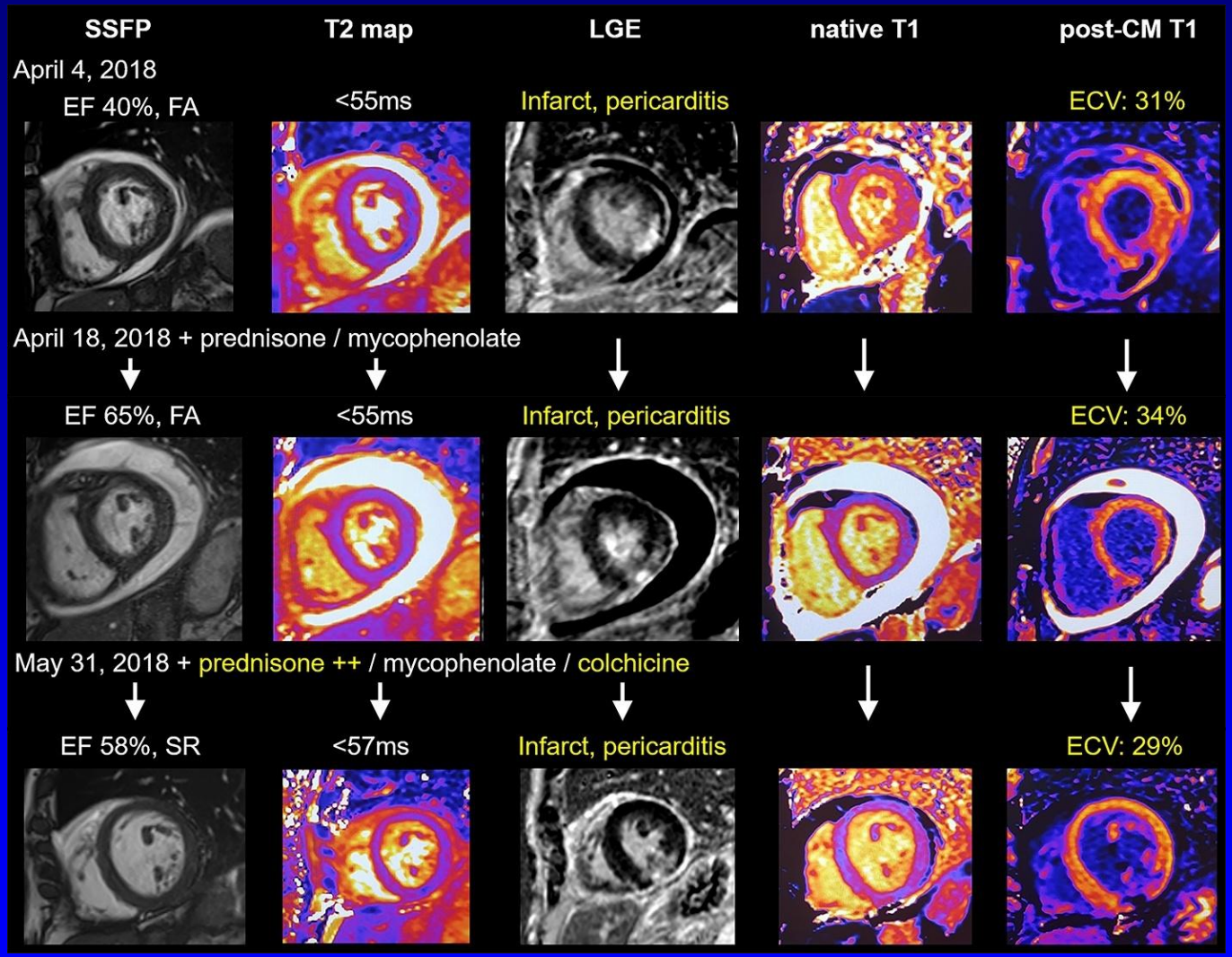


Image provided by Prof. Juerg Schwitter, University Hospital Lausanne, Switzerland

CMR in Churg-Strauss Vasculitis

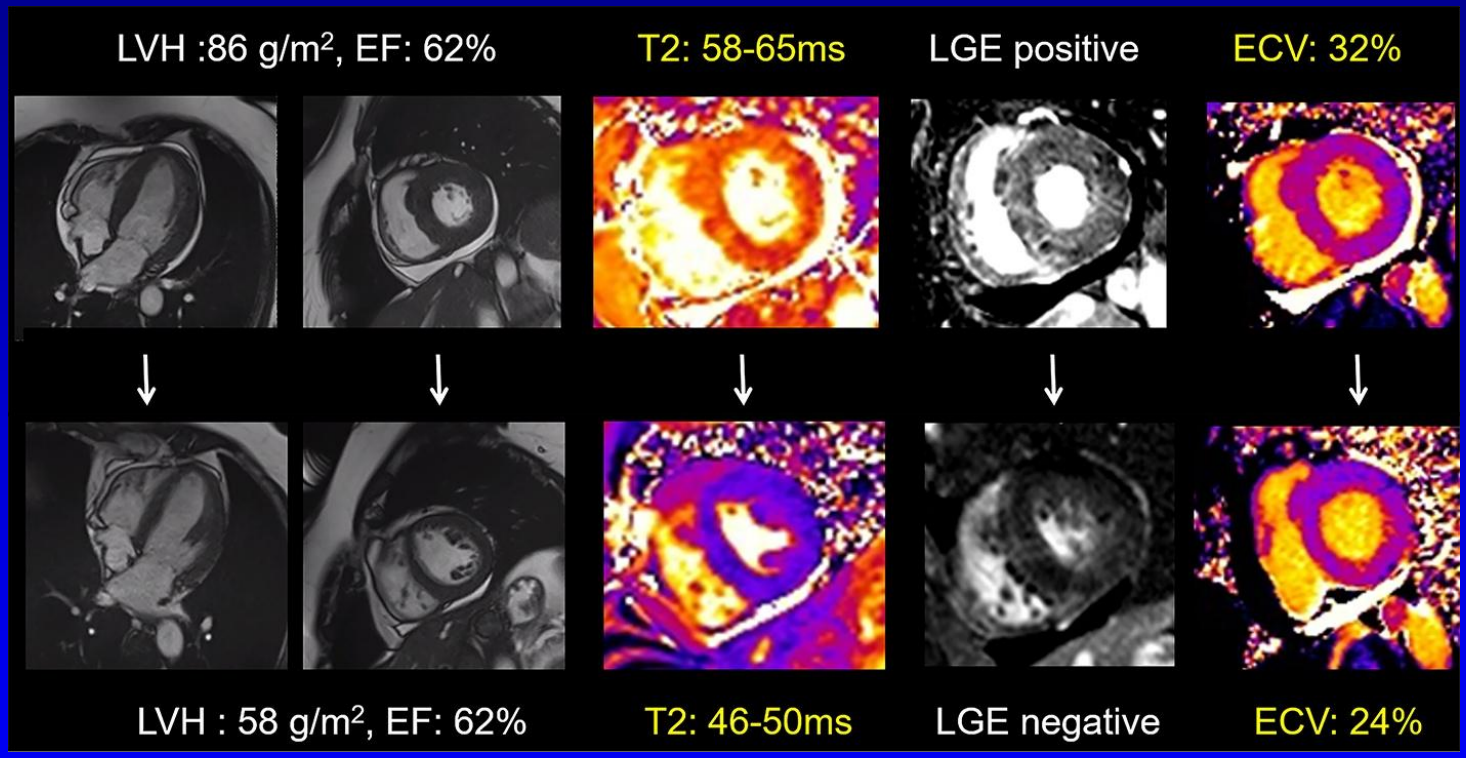
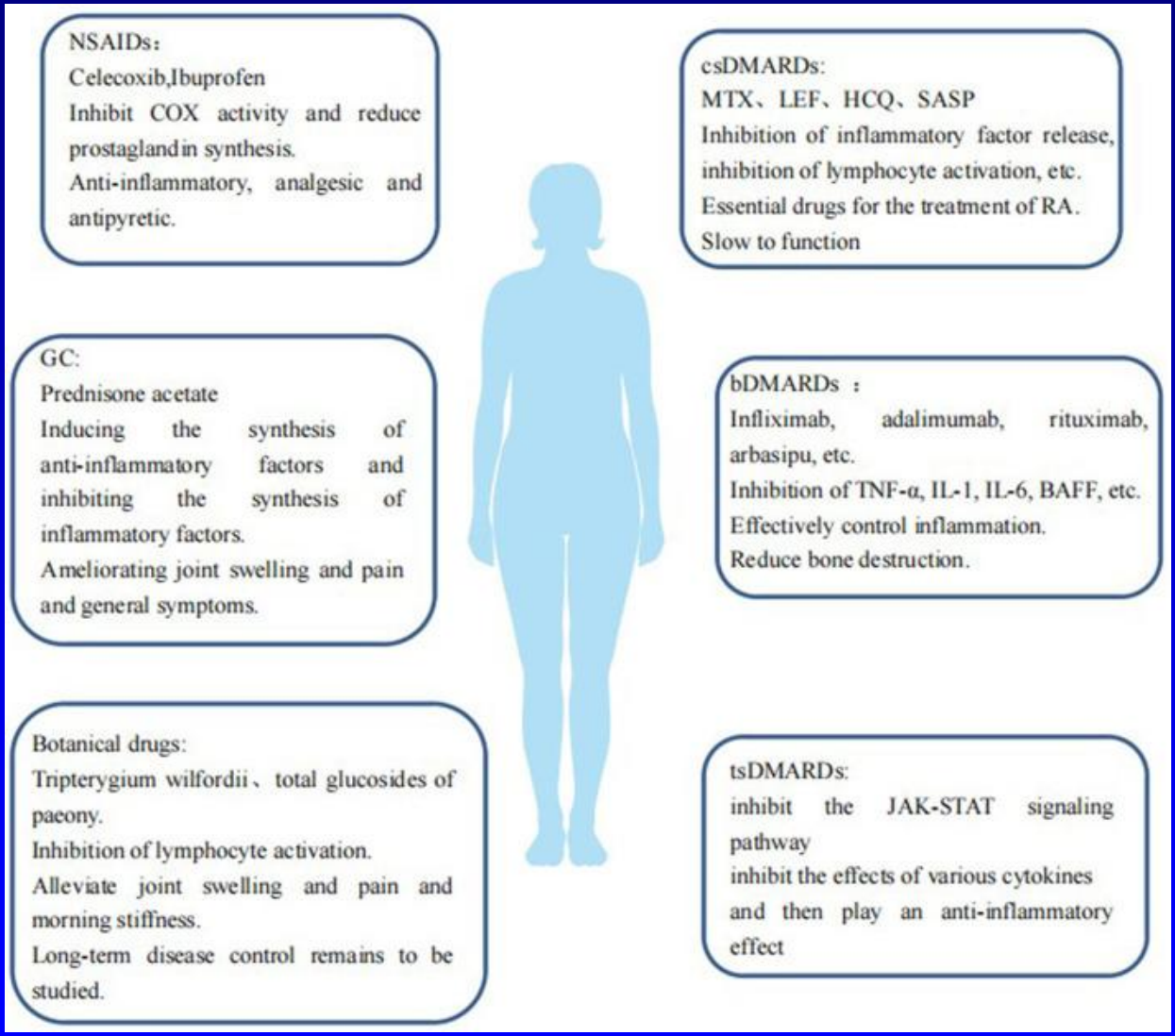


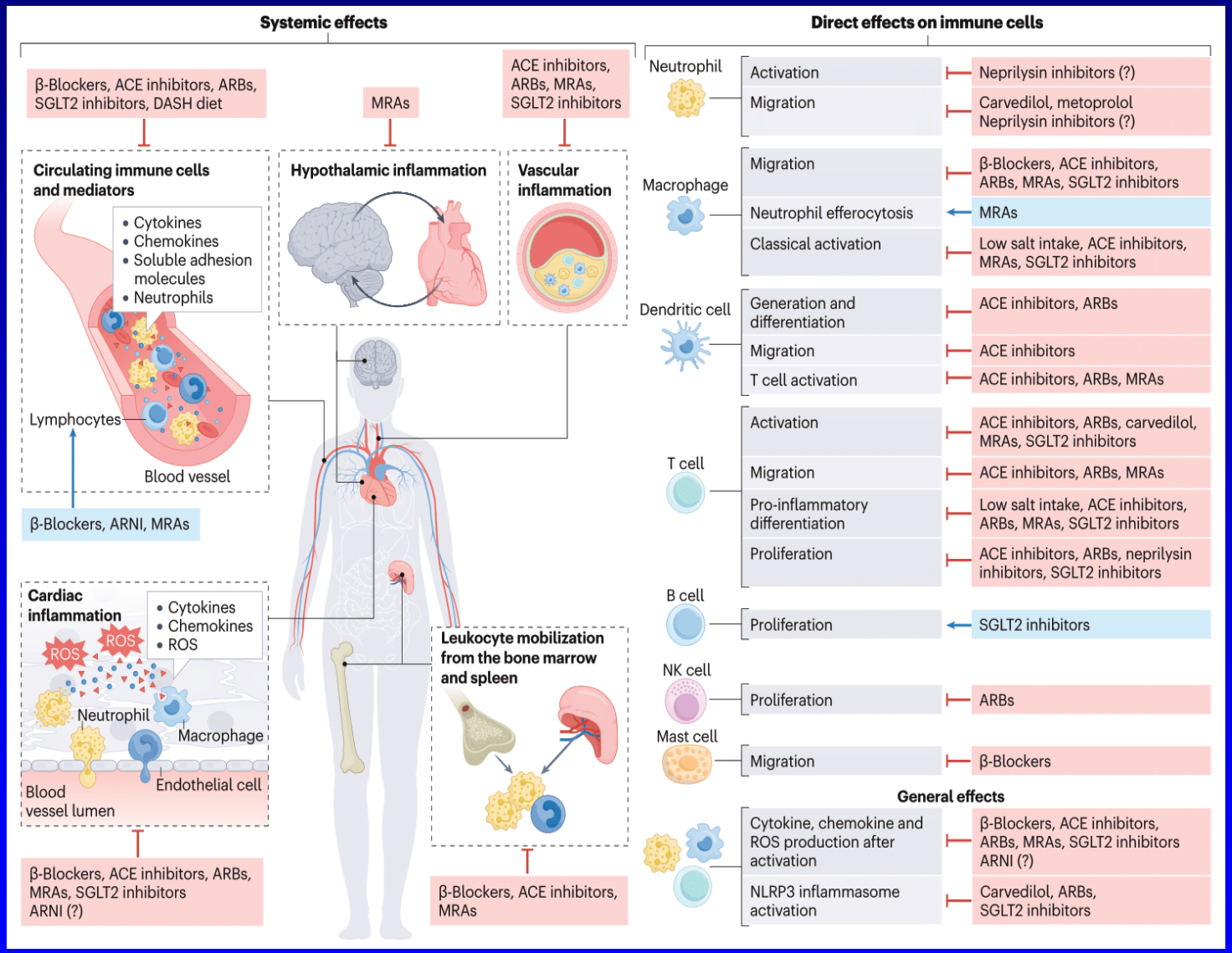
Image provided by Prof. Juerg Schwitter,
University Hospital Lausanne, Switzerland

CV effect of anti-rheumatic medication



Baogi Y et al. Frontiers in CV Medicine 2021

Immunomodulatory effects of cardiac medication



Markousis-Mavrogenis G et al. Nature Reviews Cardiol 2023

JOURNAL ARTICLE

European Heart Journal
Cardiovascular Imaging

Cardiovascular magnetic resonance in autoimmune rheumatic diseases: a clinical consensus document by the European Association of Cardiovascular Imaging

FREE

S Mavrogeni ✉, A Pepe, R Nijveldt, N Ntusi, L M Sierra-Galan, K Bratis, J Wei, M Mukherjee, G Markousis-Mavrogenis, L Gargani, L E Sade, N Ajmone-Marsan, P Seferovic, E Donal, M Nurmohamed, M Matucci Cerinic, P Sfikakis, G Kitas, J Schwitter, J A C Lima

Author Notes

European Heart Journal - Cardiovascular Imaging, Volume 23, Issue 9, September 2022, Pages e308–e322, https://doi.org/10.1093/ehjci/jeac134

- CMR enables timely decision-making and facilitates the tailoring of treatment to individual patients.
- We present a consensus-based decision algorithm for when a CMR study could be considered in ARDs, together with a standardized study protocol.
- We discuss the clinical implications of CMR findings

Novel Imaging Approaches to Cardiac Manifestations of Systemic Inflammatory Diseases: JACC Scientific Statement.

Weber BN, Paik JJ, Aghayev A, Klein AL, Mavrogeni SI, Yu PB, Mukherjee M.

J Am Coll Cardiol. 2023 Nov 28; 82(22):2128-2151.

ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ
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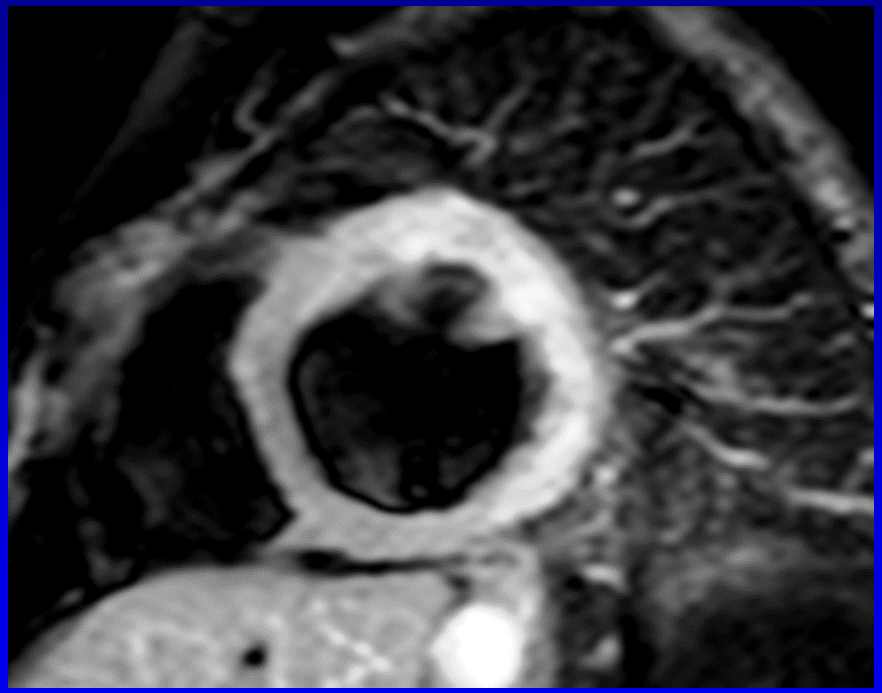
Myocarditis in Neuromuscular Diseases

Myocardial inflammation in Duchenne Muscular Dystrophy as a precipitating factor for heart failure: a prospective study.



Mavrogeni S et al. BMC Cardiology 2010

Heart Failure Post-SARS-CoV-2 Infection in Children with Duchenne Muscular Dystrophy: The Additive Value of CMR

- Despite the mild clinical presentation, this case series demonstrates the diagnostic strength of CMR in the diagnosis and evaluation of post-COVID-19 myocarditis and serves to increase awareness of this potential complication amongst treating physicians.

Markousis –Mavrogenis G et al Children (Basel) 2023

Myocarditis in other clinical entities

Myocardial and Systemic Inflammation in Acute Stress-Induced (Takotsubo) Cardiomyopathy

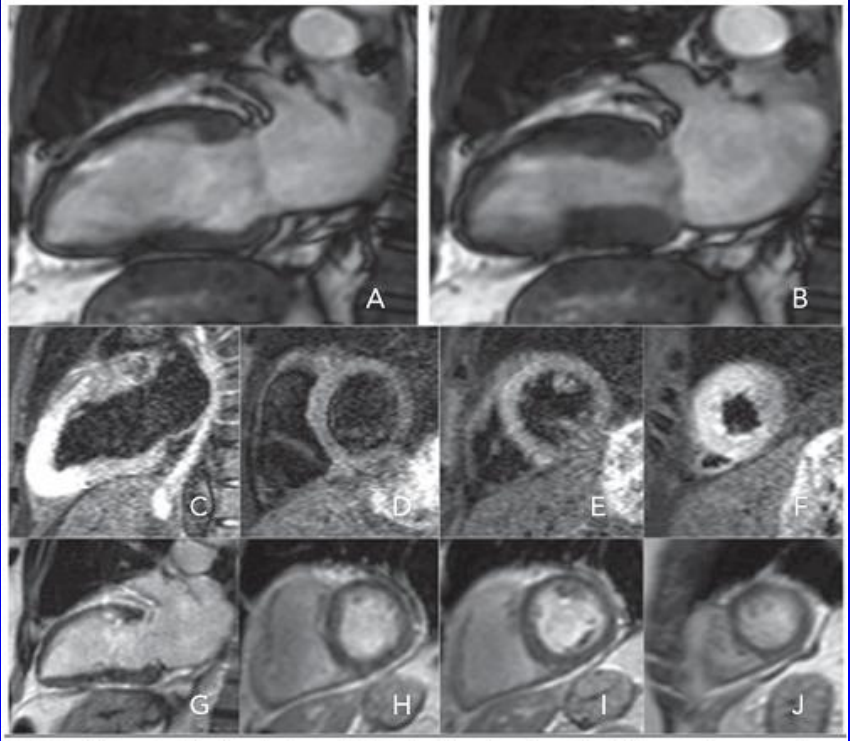
- **Takotsubo cardiomyopathy is characterized by a myocardial macrophage inflammatory infiltrate, changes in the distribution of monocyte subsets, and an increase in systemic proinflammatory cytokines.**

- **These changes persist for at least 5 months, suggesting a low-grade chronic inflammation**

Scally C et al Circulation 2019

CMR in Takotsubo

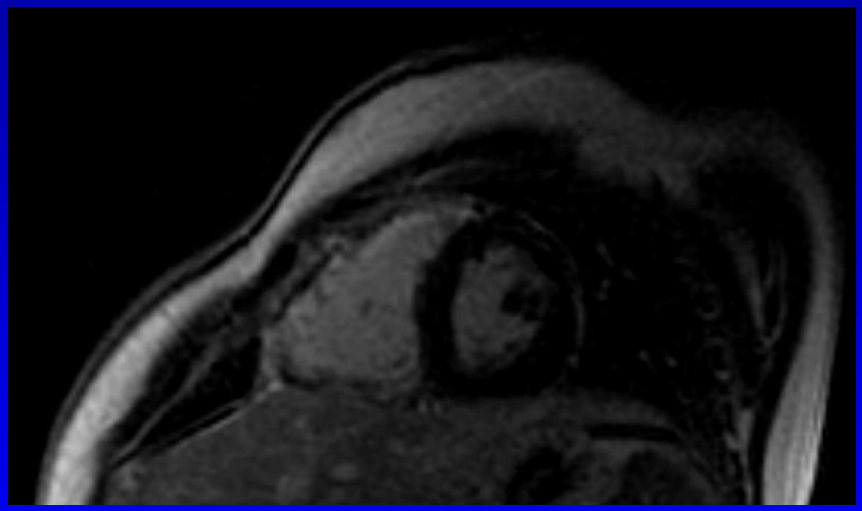
Figure 1: Cardiac Magnetic Resonance Exam of a 70-year-old Female Patient with Takotsubo Cardiomyopathy

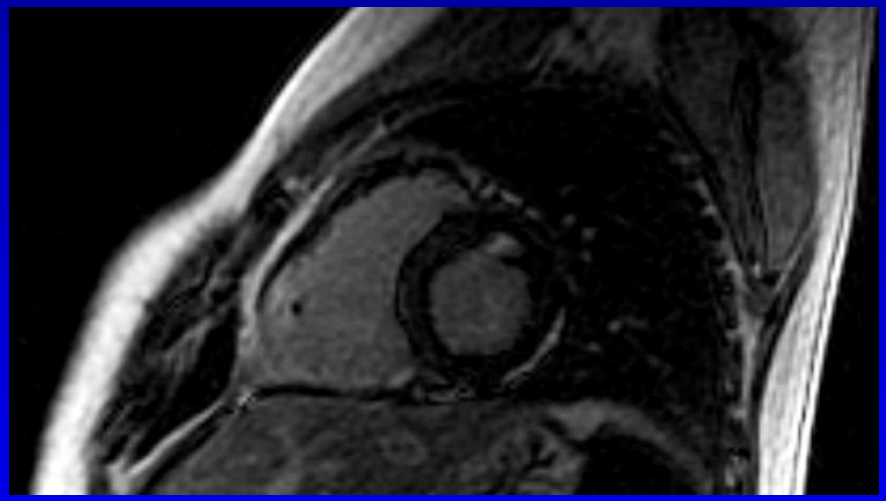


Typical mid-to-apical ballooning in end-diastolic (A) and end-systolic (B) images (upper row). Associated transmural increased signal on T2-weighted two-chamber (C) and basal (D), mid-ventricular (E) and apical (F) images, representing myocardial oedema (middle row). Absence of myocardial necrosis is noted in the matched late gadolinium enhancement images (G, H, I and J, respectively).

Bratis C ECR 2017

Naxos disease evolution mimicking acute myocarditis: the role of CMR





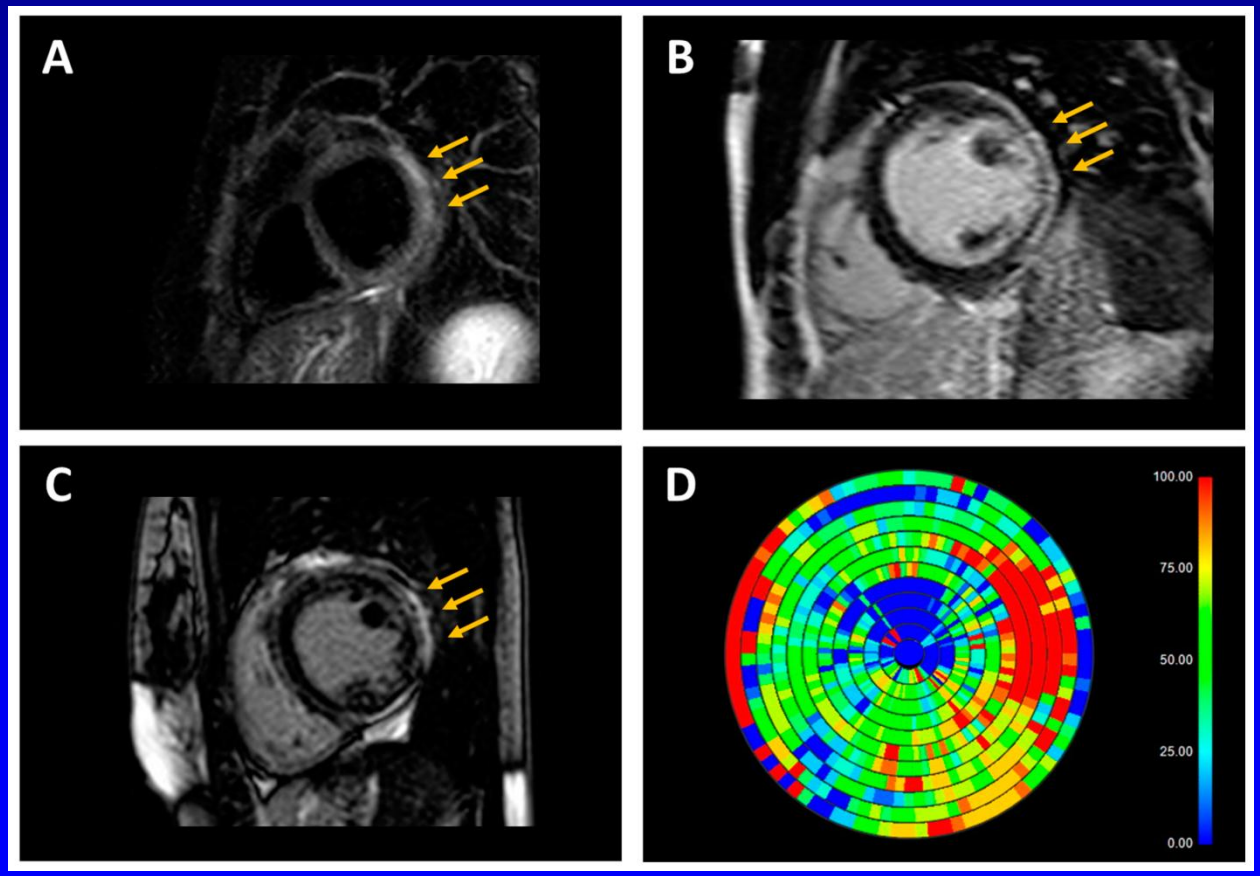
Mavrogeni S et al Int J Cardiol 2013

Myocardial inflammation detected by CMR in Arrhythmogenic Right Ventricular Cardiomyopathy: A paediatric case series

- ARVC can present as recurrent myocarditis-like episodes with CMR evidence of myocarditis despite absent infectious trigger in children.
- We believe they represent an active hot phase of the disease and may lead to disease progression.

Martins D et al Int J Cardiol 2018

Myocardial Inflammation as a Manifestation of Genetic Cardiomyopathies: From Bedside to Bench



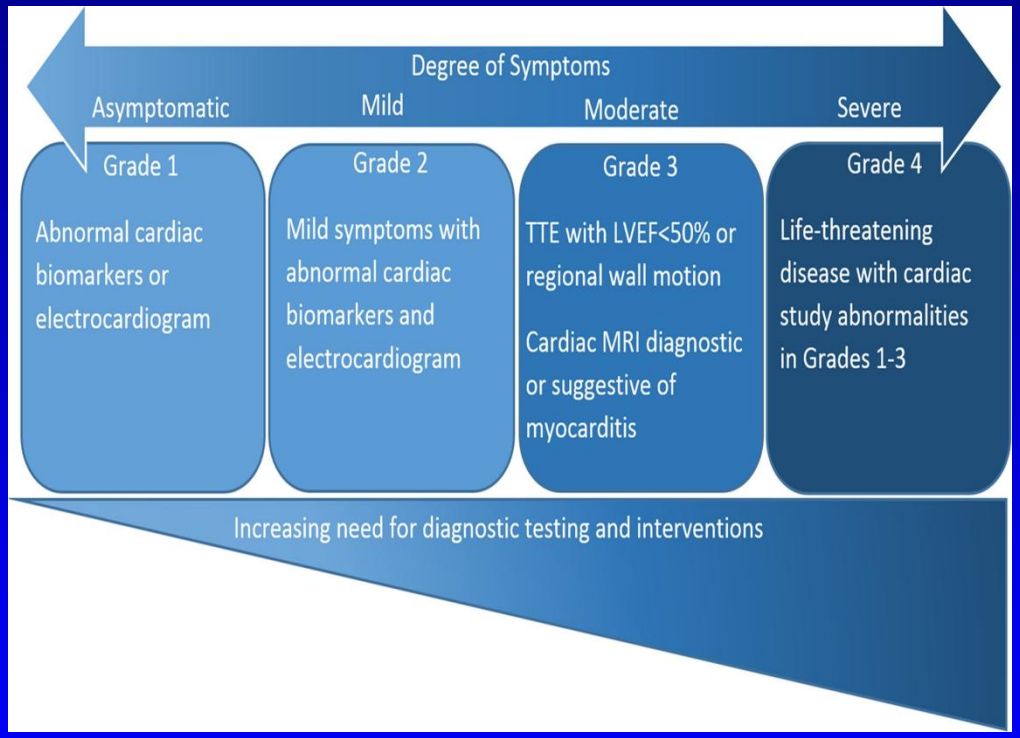
Peretto G et Biomolecules 2023

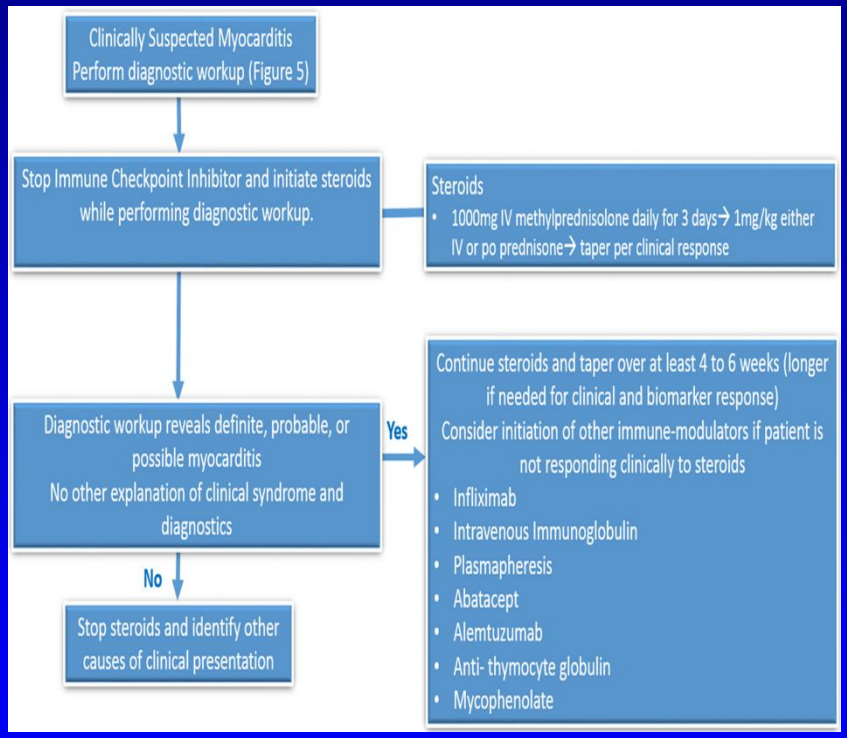
Myocardial edema measured by T2 mapping is an independent predictor of ventricular arrhythmias in hypertrophic cardiomyopathy

- **Elevated T2 is an independent predictor of VA** and adverse outcome in HMC patients. These results suggest the impact of myocardial edema in myocardial disease activity in HCM.

Kiershenboim ZK t al Eur Heart Journal 2023

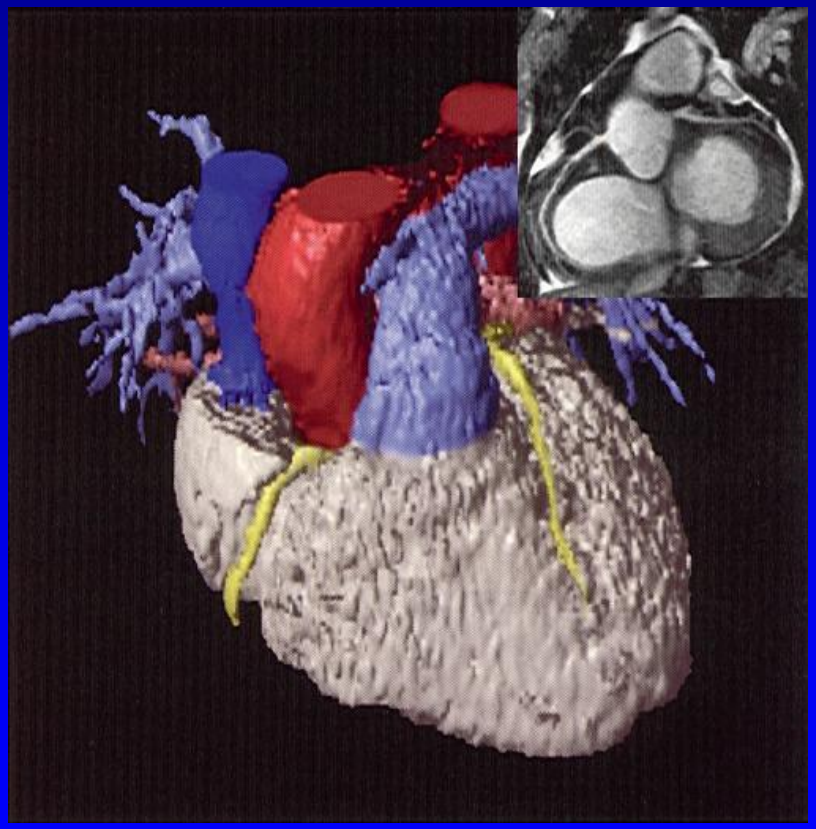
Immune Checkpoint Inhibitor Myocarditis





Palaskas N et al JAHA 2020

WHAT CMR CAN OFFER TO THE CLINICIAN?



- Assessment of myocardial oedema
- Detection of inflammation
- Detailed evaluation of LV-RV function
- "Noninvasive myocardial biopsy"
- Detection of very small pericardial effusion
- "Noninvasive follow-up"

ATHENSCMR level 1-2
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