UNIVERSITÀ
DEGLI STUDI
DI PADOVA

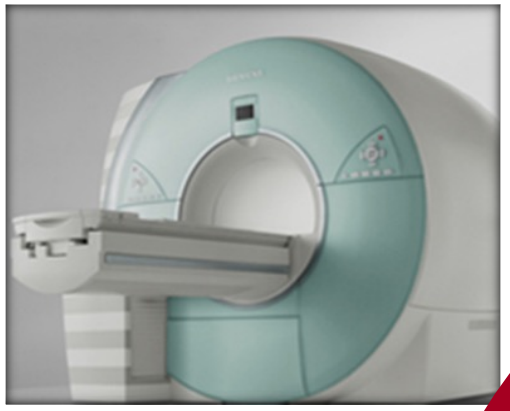
Miocarditi

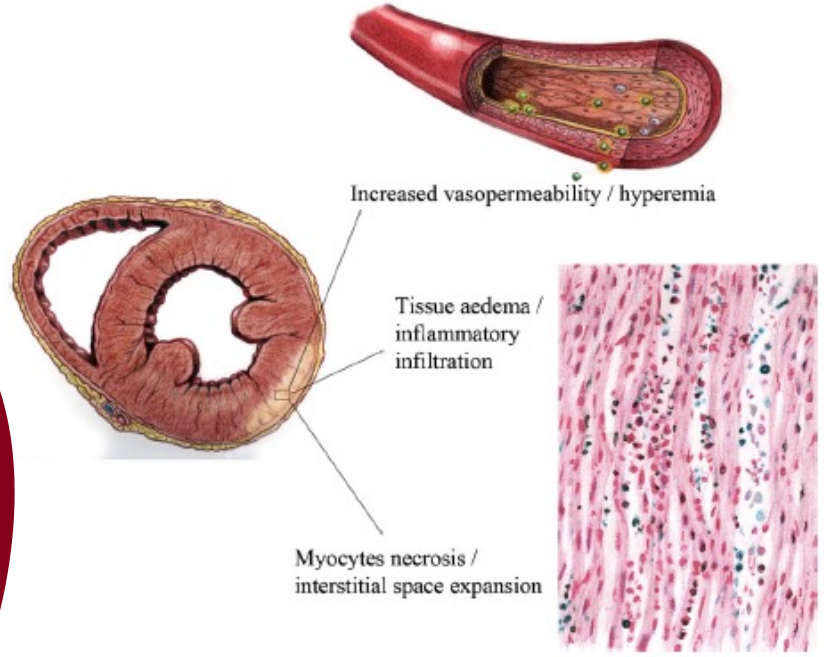
MASTER

Tecniche di acquisizione di risonanza magnetica cardiaca

AA 25_26

«Myocarditis is an inflammatory disease of the heart that may occur as a consequence of infections, exposure to toxic substances, and immune system activation»

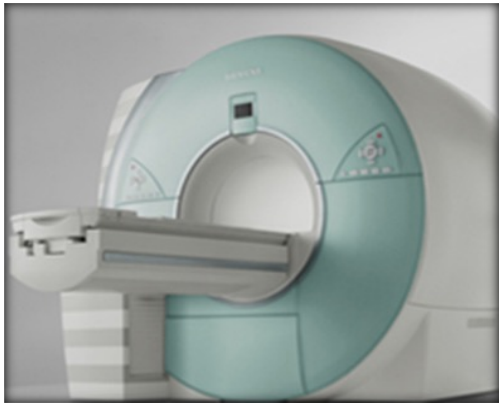




From Pathology to CMR: is it possible?

Definition

From Pathology to Imaging



RATIONALE

Besides providing anatomic and morphological information,

CMR can provide accurate tissue characterization by measuring T1 and T2 relaxation times and spin densities.

«Because active myocarditis is typically associated with myocyte injury, including edema and cellular swelling, assessment of relaxation times provides a sensitive measure for its detection.»

Magnani JW - Circulation 2006;113:876-90

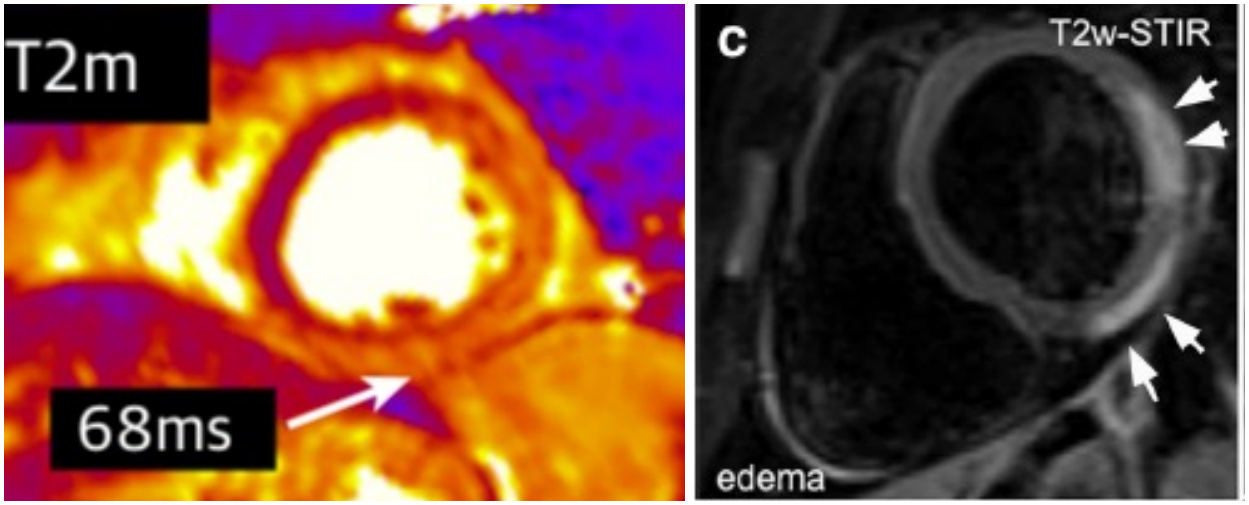
EDEMA

From Pathology to Imaging

- Both intracellular and interstitial in origin and alters signal in both T2- and T1-weighted CMR sequences.
- Even small increases (**~3%**) in cellular water content can prolong T1 and T2 relaxation

The combination of increased cellular water content and increased cellular free water in response to tissue injury therefore significantly increases T2 and T1 relaxation times

T2-based technique (T2-paramegnetic or T2W-spin echo)

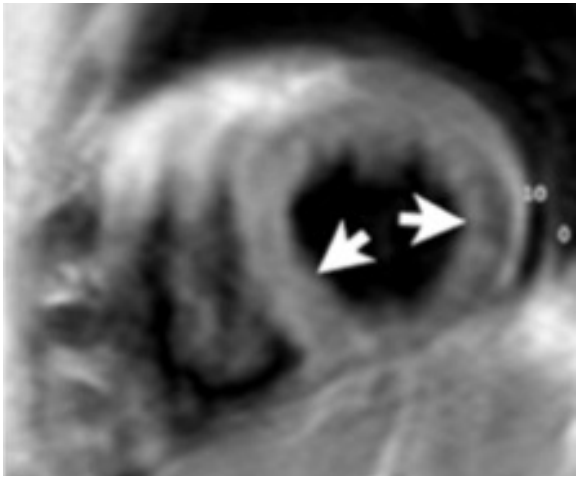


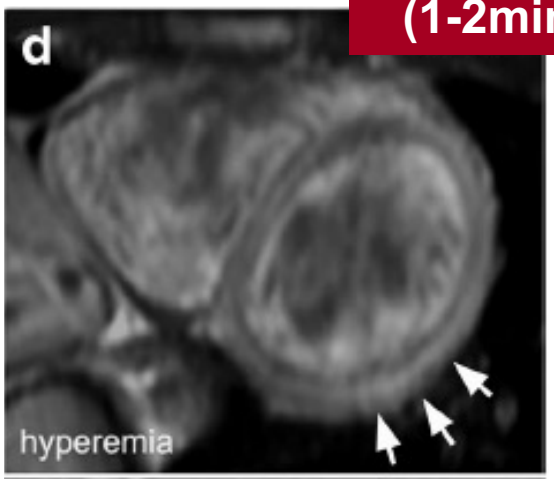
CAPILLARY LEAK

From Pathology to Imaging

- Cardinal feature of inflammation as endothelial permeability is increased by the release of proinflammatory cytokines.
- Leads to myocardial **early gadolinium enhancement**, increased T1 and T2 relaxation times, and expansion of the extracellular volume.

T1-based technique
Sequence T1 IR after late enhancement (1-2min) ("early hyperenhancement")





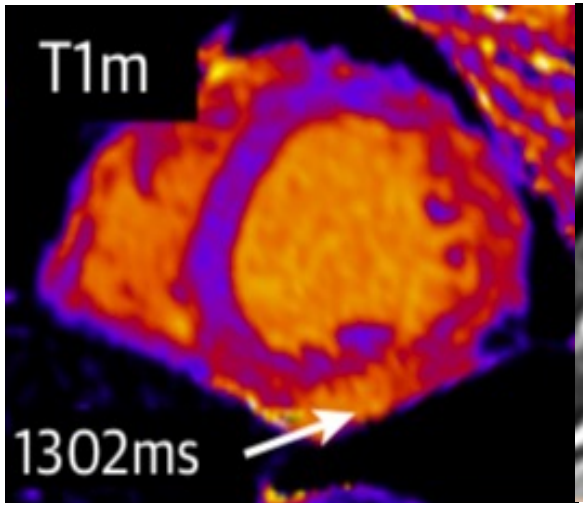
HYPERAEMIA

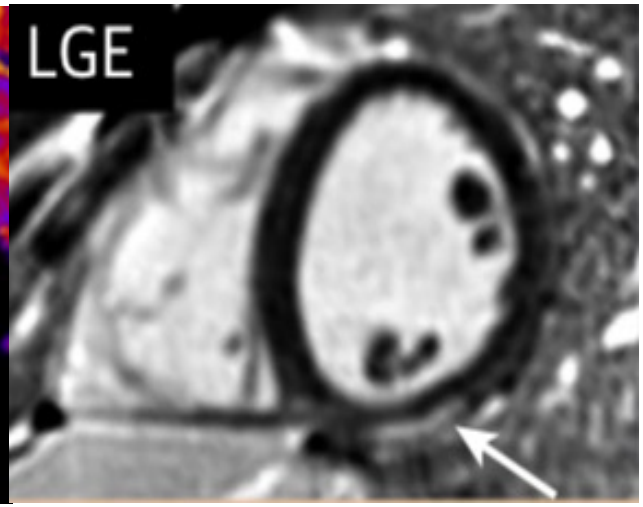
MYOCITE NECROSIS & FIBROSIS

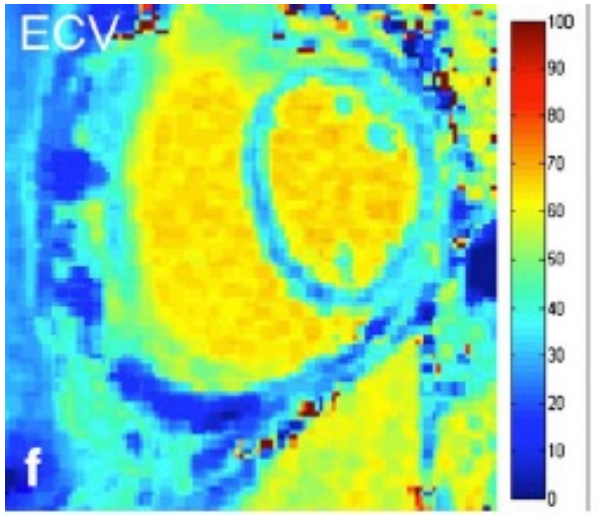
From Pathology to Imaging

- ***Gadolinium agent***: paramagnetic contrast agent that shortens T1 in proportion to its concentration;
- ***LGE technique***: used to accentuate differences in tissue T1 relaxation characteristics. Areas of shortened T1 (areas with increased and prolonged contrast uptake) will appear with a high signal intensity (bright!);
- ***Post-contrast T1 maps*** (@15-20 min after Gd) can be used to confirm ambiguous LGE and to calculate ECV.

T1-based technique
(native T1, LGE or ECV)







The Agenda

- **How to use CMR for myocarditis: Technical Issues**
- **Acute Myocarditis**
  - How to use CMR in different Clinical Settings
  - Diagnostic clues for differential diagnosis
  - Inflammation and systemic diseases
- **Chronic Myocarditis**
  - CMR time-of-course of myocardial inflammation
  - Prognostic significance of CMR

The Agenda

- **How to use CMR for myocarditis: Technical Issues**

- **Acute Myocarditis**
  - How to use CMR in different Clinical Settings
  - Diagnostic clues for differential diagnosis
  - Inflammation and systemic diseases

- **Chronic Myocarditis**
  - CMR time-of-course of myocardial inflammation
  - Prognostic significance of CMR

HOW TO COMBINE THE SEQUENCES

Lake Louise Criteria (2009)

Journal of the American College of Cardiology
© 2009 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 53, No. 17, 2009
ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2009.02.007

JACC White Paper

Cardiovascular Magnetic Resonance in Myocarditis: A JACC White Paper

Matthias G. Friedrich, MD,* Udo Sechtem, MD,† Jeanette Schulz-Menger, MD,‡ Godtfred Holmvang, MD,‖ Pauline Alakija, MD,† Leslie T. Cooper, MD,¶ James A. White, MD,# Hassan Abdel-Aty, MD,§ Matthias Gutberlet, MD,** Sanjay Prasad, MD,†† Anthony Aletras, PHD,‡‡ Jean-Pierre Laissy, MD,§§ Ian Paterson, MD,‖‖ Neil G. Filipchuk, MD,* Andreas Kumar, MD,* Matthias Pauschinger, MD,¶¶ Peter Liu, MD,## for the *International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis*

Cardiovascular magnetic resonance (CMR) has become the primary tool for noninvasive assessment of myocardial inflammation in patients with suspected myocarditis. The International Consensus Group on CMR Diagnosis of Myocarditis was founded in 2006 to achieve consensus among CMR experts and develop recommendations on the current state-of-the-art use of CMR for myocarditis. The recommendations include indications for CMR in patients with suspected myocarditis, CMR protocol standards, terminology for reporting CMR findings, and diagnostic CMR criteria for myocarditis (i.e., "Lake Louise Criteria").

Background: Myocarditis

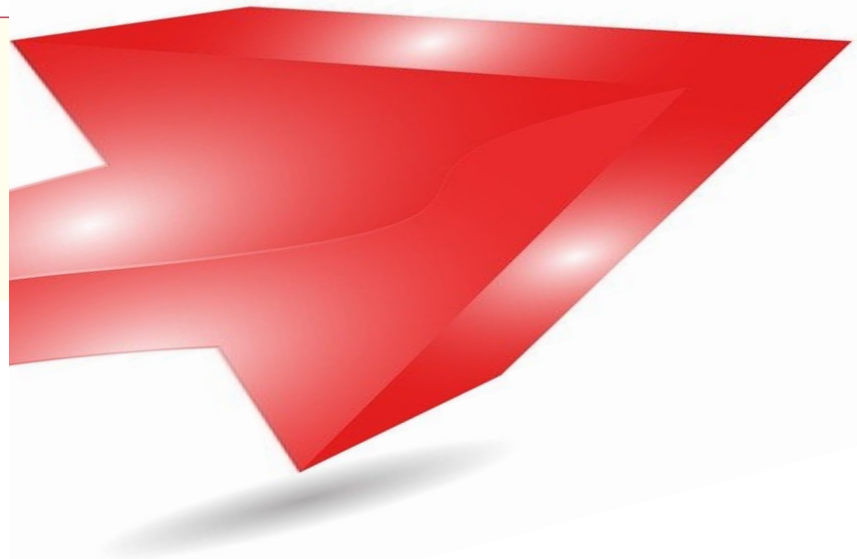
Incidence and Etiology

In this paper, myocarditis is defined as inflammation of myocardial tissue. Myocarditis has been reported in up to 12% of young adults presenting with sudden death (1–4) and is an important underlying etiology of other myocardial diseases such as dilated (5) and arrhythmogenic right ventricular (6) cardiomyopathy. The incidence of nonfatal myocarditis is likely greater than actually diagnosed, mostly as a result of the challenges of establishing the diagnosis in standard clinical settings.

Infectious disease accounts for most cases in previously healthy patients typically either because of a direct viral infection or post-viral immune-mediated reaction. Myocardial inflammation, however, also may be triggered by reversible and/or irreversible toxic, ischemic, or mechanical injury, drug-related inflammation, transplant rejection, or other immune reactions.

From the *Department of Cardiac Sciences and Radiology, Stephenson Cardiovascular MR Centre at the Libin Cardiovascular Institute of Alberta, and the †Department of Pathology, University of Calgary, Calgary, Alberta, Canada; ‡Department of Cardiology, Robert-Bosch-Krankenhaus, Stuttgart, Germany; §Franz-Volhard-Klinik, Charité Universitätsmedizin Berlin, HELIOS-Klinikum Berlin-Buch, Berlin, Germany; ‖Massachusetts General Hospital, Boston, Massachusetts; ¶Mayo Clinic College of Medicine, Rochester, Minnesota; #London Health Sciences Centre, London, Ontario, Canada; **Department of Diagnostic and Interventional Radiology, University Leipzig, Leipzig, Germany; ††Royal Brompton Hospital, London, United Kingdom; ‡‡National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland; §§Department of Radiology, Hôpital Bichat, Paris, France; ‖‖Division of Cardiology, University of Alberta, Edmonton, Alberta, Canada; ¶¶Department of Cardiology, Klinikum Nürnberg Süd, Nürnberg, Germany; and the ##Toronto General Hospital, Max Bell Research Centre, Toronto, Ontario, Canada. Dr. Friedrich is a shareholder and advisor for Circle Cardiovascular Imaging, Inc., Calgary, Alberta, Canada. One of the meetings of the Consensus Group was in part supported by nonrestricted grants from Siemens Medical Solutions Canada and from Berlex Canada Inc. None of the sponsors was involved in the writing process.

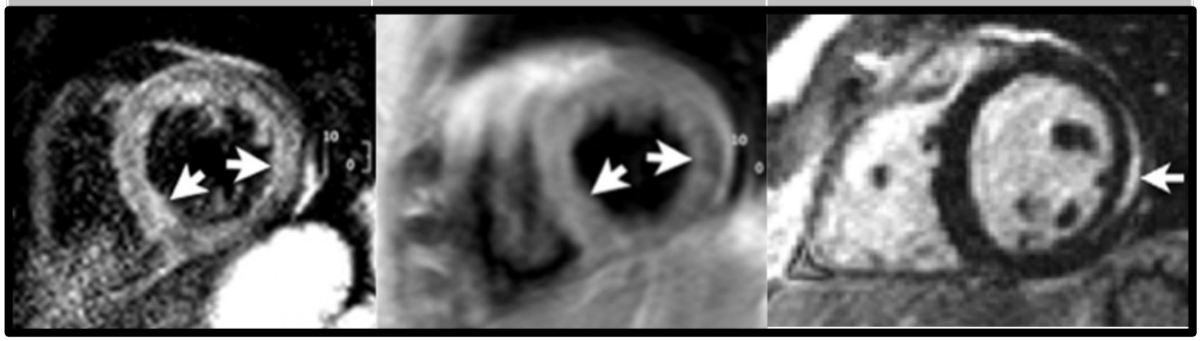
Manuscript received September 3, 2008; revised manuscript received January 31, 2009, accepted February 3, 2009.



The Lake Louise Criteria

For diagnosis: 2 positive out of 3

T2 sequence	Sequence T1 IR after late enhancement (1-2min) ("early hyperenhancement")	Sequence T1 IR after late enhancement (10-15 min) ("late hyperenhancement")
Edema	Iperemia	Necrosis



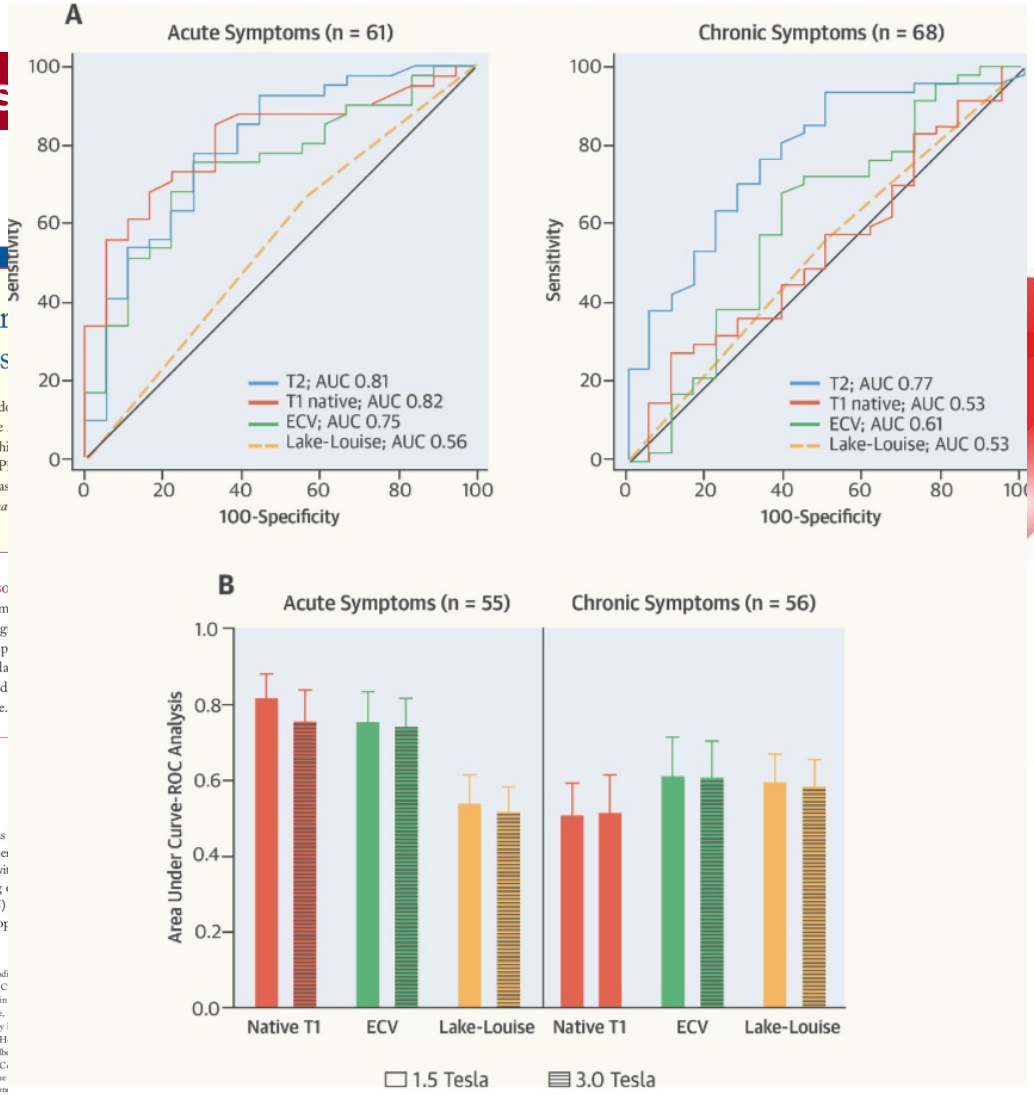
CONS

- **Subjectivity in T2w images interpretation**
- **Many acquisition artifacts in T2w**
- **Lack of validation for Early Enhancement**

COMBINE THE SEQUENCES

Comprehensive Cardiac Magnetic Resonance Imaging in Patients With Suspected Myocarditis

The MyoRacer-Trial



Lurz, P. et al. J Am Coll Cardiol. 2016;67(15):1800-11.

Lake Louis

Journal of the American College of Cardiology
© 2009 by the American College of Cardiology Foundation
Published by Elsevier Inc.

JACC White Paper

Cardiovascular
in Myocarditis

Matthias G. Friedrich, MD,* Ud
Godtfred Holmvang, MD,‖ Pauline
Hassan Abdel-Aty, MD,§ Matthi
Anthony Aletras, PHD,‡‡ Jean-P
Neil G. Filipchuk, MD,* Andreas
Peter Liu, MD,## for the *Interna*
in Myocarditis

Cardiovascular magnetic reso
assessment of myocardial inflamm
Consensus Group on CMR Diag
among CMR experts and develop
for myocarditis. The recommenda
myocarditis, CMR protocol stand
CMR criteria for myocarditis (i.e.

Background: Myocarditis

Incidence and Etiology

In this paper, myocarditis is defined as
myocardial tissue. Myocarditis has beer
to 12% of young adults presenting wi
(1–4) and is an important underlying
myocardial diseases such as dilated (5)
genic right ventricular (6) cardiomyo

From the *Department of Cardiac Sciences and Radi
†Department of Pathology, University of Calgary, C
§Franz-Volhard-Klinik, Charité Universitätsmedizin
Massachusetts; ¶Mayo Clinic College of Medicine,
Diagnostic and Interventional Radiology, University
Lung and Blood Institute, National Institutes of H
Cardiology, University of Alberta, Edmonton, Alb
##Toronto General Hospital, Max Bell Research C
Imaging, Inc., Calgary, Alberta, Canada. One of the
Solutions Canada and from Berlex Canada Inc. Nors
Manuscript received September 3, 2008; revised m

HOW TO COMBINE THE SEQUENCES

Lake Louise Criteria (2009)

Journal of the American College of Cardiology
© 2009 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 53, No. 17, 2009
ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2009.02.007

JACC White Paper

Cardiovascular Magnetic Resonance in Myocarditis: A JACC White Paper

Matthias G. Friedrich, MD,* Udo Sechtem, MD,† Jeanette Schulz-Menger, MD,§ Godtfred Holmvang, MD,‖ Pauline Alakija, MD,† Leslie T. Cooper, MD,¶ James A. White, MD,# Hassan Abdel-Aty, MD,§ Matthias Gutberlet, MD,** Sanjay Prasad, MD,†† Anthony Aletras, PHD,‡‡ Jean-Pierre Laissy, MD,§§ Ian Paterson, MD,‖‖ Neil G. Filipchuk, MD,* Andreas Kumar, MD,* Matthias Pauschinger, MD,¶¶ Peter Liu, MD,## for the *International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis*

Cardiovascular magnetic resonance (CMR) has become the primary tool for noninvasive assessment of myocardial inflammation in patients with suspected myocarditis. The International Consensus Group on CMR Diagnosis of Myocarditis was founded in 2006 to achieve consensus among CMR experts and develop recommendations on the current state-of-the-art use of CMR for myocarditis. The recommendations include indications for CMR in patients with suspected myocarditis, CMR protocol standards, terminology for reporting CMR findings, and diagnostic CMR criteria for myocarditis (i.e., "Lake Louise Criteria").

Background: Myocarditis

Incidence and Etiology

In this paper, myocarditis is defined as inflammation of myocardial tissue. Myocarditis has been reported in up to 12% of young adults presenting with sudden death (1–4) and is an important underlying etiology of other myocardial diseases such as dilated (5) and arrhythmogenic right ventricular (6) cardiomyopathy. The incidence of nonfatal myocarditis is likely greater than actually diagnosed, mostly as a result of the challenges of establishing the diagnosis in standard clinical settings.

Infectious disease accounts for most cases in previously healthy patients typically either because of a direct viral infection or post-viral immune-mediated reaction. Myocardial inflammation, however, also may be triggered by reversible and/or irreversible toxic, ischemic, or mechanical injury, drug-related inflammation, transplant rejection, or other immune reactions.

From the *Department of Cardiac Sciences and Radiology, Stephenson Cardiovascular MR Centre at the Libin Cardiovascular Institute of Alberta, and the †Department of Pathology, University of Calgary, Calgary, Alberta, Canada; ‡Department of Cardiology, Robert-Bosch-Krankenhaus, Stuttgart, Germany; §Franz-Volhard-Klinik, Charité Universitätsmedizin Berlin, HELIOS-Klinikum Berlin-Buch, Berlin, Germany; ‖Massachusetts General Hospital, Boston, Massachusetts; ¶Mayo Clinic College of Medicine, Rochester, Minnesota; #London Health Sciences Centre, London, Ontario, Canada; **Department of Diagnostic and Interventional Radiology, University Leipzig, Leipzig, Germany; ††Royal Brompton Hospital, London, United Kingdom; ‡‡National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland; §§Department of Radiology, Hôpital Bichat, Paris, France; ‖‖Division of Cardiology, University of Alberta, Edmonton, Alberta, Canada; ¶¶Department of Cardiology, Klinikum Nürnberg Süd, Nürnberg, Germany; and the ##Toronto General Hospital, Max Bell Research Centre, Toronto, Ontario, Canada. Dr. Friedrich is a shareholder and advisor for Circle Cardiovascular Imaging, Inc., Calgary, Alberta, Canada. One of the meetings of the Consensus Group was in part supported by nonrestricted grants from Siemens Medical Solutions Canada and from Berlex Canada Inc. None of the sponsors was involved in the writing process.

Manuscript received September 3, 2008; revised manuscript received January 31, 2009, accepted February 3, 2009.

Revised Lake Louise Criteria (2018)

AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation

EBAC CME MOC ACCREDITED

Expert Recommendations

Vanessa M. Ferreira, MD, DPHIL,[a] Jeanette Schulz-Menger, MD,[b] Godtfred Holmvang, MD,[c] Christopher M. Kramer, MD,[d] Iacopo Carbone, MD,[e] Udo Sechtem, MD,[f] Ingrid Kindermann, MD,[g] Matthias Gutberlet, MD,[h] Leslie T. Cooper, MD,[i] Peter Liu, MD,[j] Matthias G. Friedrich, MD[k,l,m]

JACC JOURNAL CME/MOC/ECME

This article has been selected as the month's *JACC* CME/MOC/ECME activity, available online at http://www.acc.org/jacc-journals-cme by selecting the *JACC* Journals CME/MOC/ECME tab.

Accreditation and Designation Statement

The American College of Cardiology Foundation (ACCF) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The ACCF designates this Journal-based CME activity for a maximum of 1 *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1 Medical Knowledge MOC point in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations will be accredited by the European Board for Accreditation in Cardiology (EBAC) for 1 hour of External CME credits. Each participant should claim only those hours of credit that have actually been spent in the educational activity. The Accreditation Council for Continuing Medical Education (ACCME) and the European Board for Accreditation in Cardiology (EBAC) have recognized each other's accreditation systems as substantially equivalent. Apply for credit through the post-course evaluation. While offering the credits noted above, this program is not intended to provide extensive training or certification in the field.

Method of Participation and Receipt of CME/MOC/ECME Certificate

To obtain credit for *JACC* CME/MOC/ECME, you must:

1. Be an ACC member or *JACC* subscriber.
2. Carefully read the CME/MOC/ECME-designated article available online and in this issue of the *Journal*.
3. Answer the post-test questions. A passing score of at least 70% must be achieved to obtain credit.
4. Complete a brief evaluation.
5. Claim your CME/MOC/ECME credit and receive your certificate electronically by following the instructions given at the conclusion of the activity.

CME/MOC/ECME Objective for This Article: Upon completion of this activity, the learner should be able to: 1) identify patients with an appropriate indication for a CMR assessment for nonischemic myocardial inflammation; 2) describe the diagnostic targets used by cardiovascular magnetic resonance (CMR) to identify active myocardial inflammation; 3) discuss the Consensus Recommendations for CMR in nonischemic myocardial inflammation (2018 Update of the Lake Louise Criteria) in comparison with the original Lake Louise Criteria; 4) compare the diagnostic utility of CMR with that of other imaging modalities; 5) estimate the diagnostic accuracy of a CMR in patients with suspected myocardial inflammation; and 6) list the CMR techniques that are recommended in the 2018 Lake Louise Criteria.

CME/MOC/ECME Editor Disclosure: *JACC* CME/MOC/ECME Editor Ragavendra R. Baliga, MD, FACC, has reported that he has no financial relationships or interests to disclose.

Author Disclosures: Dr. Ferreira acknowledges support from the National Institute of Health Research Biomedical Research Centre, Oxford, and the British Heart Foundation Centre of Research Excellence, Oxford. Dr. Friedrich is a board member, adviser, and shareholder of Circle Cardiovascular Imaging. Dr. Kramer is a consultant for Bayer Healthcare; and has received a research grant from Biotelemetry. Dr. Schulz-Menger is a consultant for Bayer Healthcare and Siemens Healthineers. Dr. Gutberlet has received moderate speaker honoraria from Bayer, Bracco, Siemens, and Philips. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Medium of Participation: Print (article only); online (article and quiz).

CME/MOC/ECME Term of Approval

Issue Date: December 18, 2018
Expiration Date: December 17, 2019

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

From the [a]University of Oxford Centre for Clinical Magnetic Resonance Research, John Radcliffe Hospital, Oxford, United Kingdom; [b]Charité-Universitätsmedizin, Department of Cardiology and Helios-Klinikum, DZHK-Partnersite-Berlin, Germany; [c]Division of Cardiology and Department of Radiology, Massachusetts General Hospital, Boston, Massachusetts; [d]Departments of Medicine (Cardiology) and Radiology, University of Virginia Health System, Charlottesville, Virginia; [e]Department of Radiological,

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2018.09.072

HOW TO COMBINE THE SEQUENCES

Revised Lake Louise Criteria (2018)
- **Sensitivity: 87.5%**
- **Specificity: 96.2%**


JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2018 PUBLISHED BY ELSEVIER ON BEHALF OF THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
VOL. 72, NO. 24, 2018

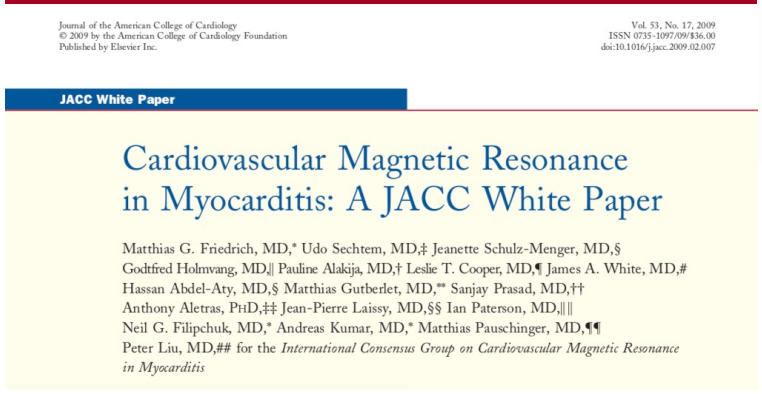
THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation

Expert Recommendations

Lake Louise Criteria (2009)
- **Sensitivity: 74%**
- **Specificity: 86%**


Journal of the American College of Cardiology
© 2009 by the American College of Cardiology Foundation
Published by Elsevier Inc.
Vol. 53, No. 17, 2009
ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2009.02.007

JACC White Paper

Cardiovascular Magnetic Resonance in Myocarditis: A JACC White Paper

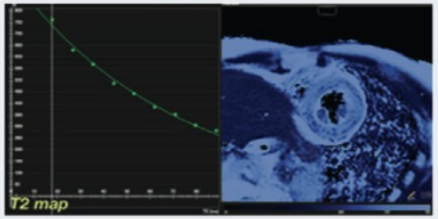
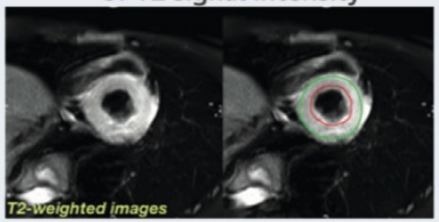
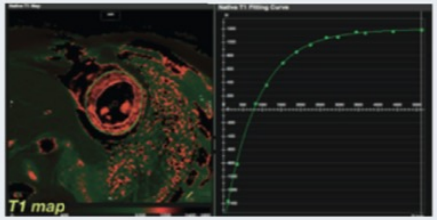
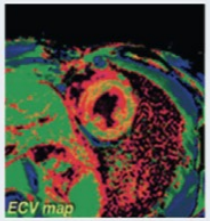
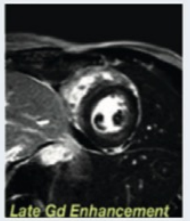
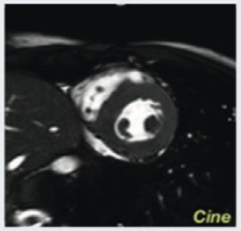
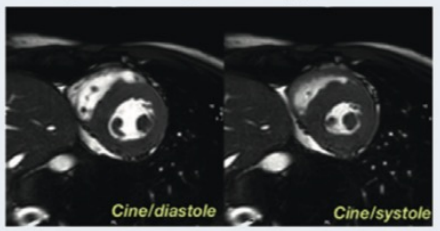
Matthias G. Friedrich, MD,* Udo Sechtem, MD,‡ Jeanette Schulz-Menger, MD,§ Godtfred Holmvang, MD,‖ Pauline Alakija, MD,† Leslie T. Cooper, MD,¶ James A. White, MD,# Hassan Abdel-Aty, MD,§ Matthias Gutberlet, MD,** Sanjay Prasad, MD,†† Anthony Aletras, PHD,‡‡ Jean-Pierre Laissy, MD,§§ Ian Paterson, MD,‖‖ Neil G. Filipchuk, MD,* Andreas Kumar, MD,* Matthias Pauschinger, MD,¶¶ Peter Liu, MD,## for the *International Consensus Group on Cardiovascular Magnetic Resonance in Myocarditis*

JACC STATE-OF-THE-ART REVIEW

Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation

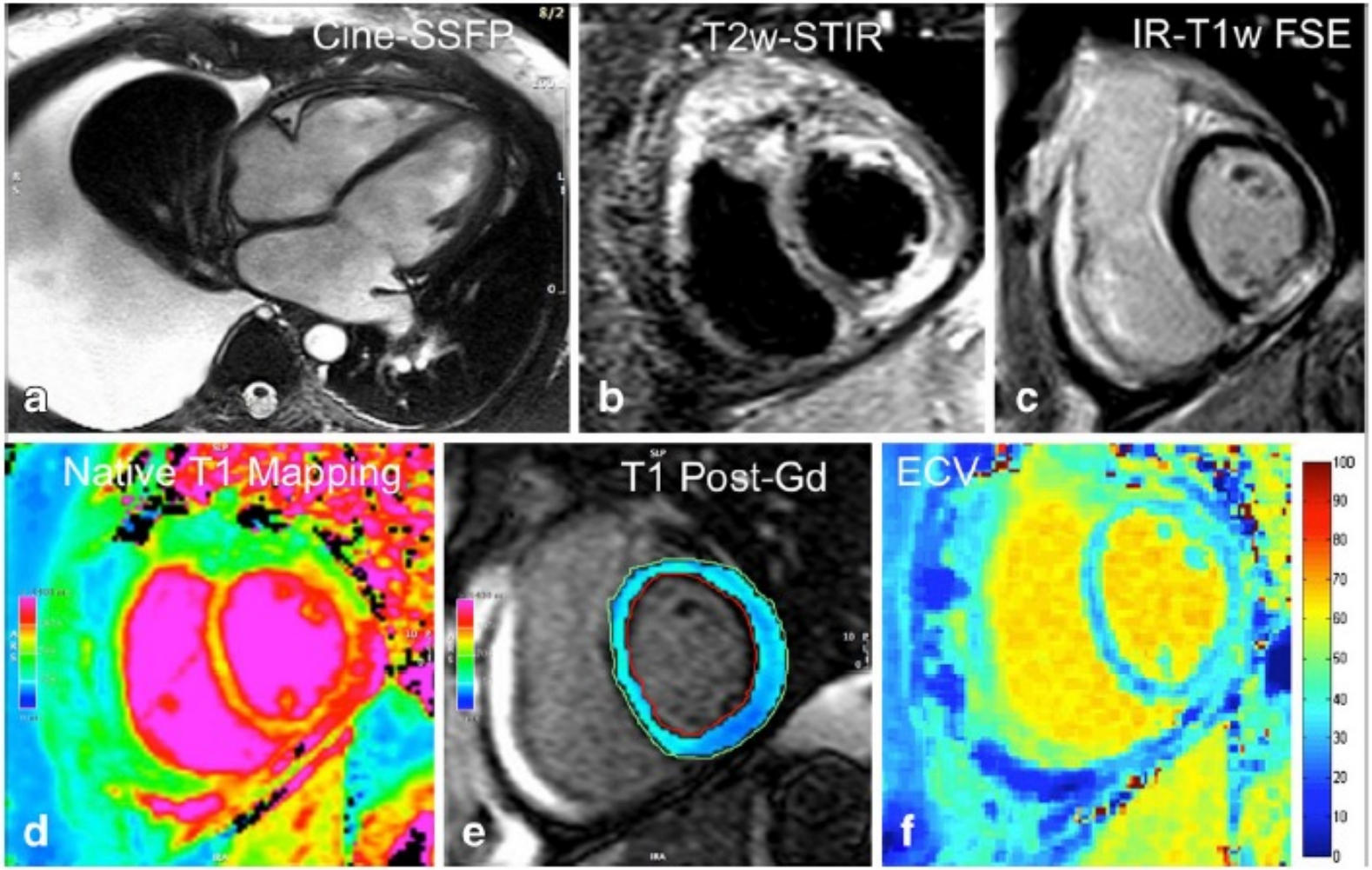
Expert Recommendations

EBAC

	2018 Lake Louise Criteria	CMR Image Examples
Main Criteria	**Myocardial Edema** (T2-mapping or T2W images)	Regional or global increase of native T2  or Regional or global increase of T2 signal intensity 
	Non-ischemic Myocardial Injury (Abnormal T1, ECV, or LGE)	Regional or global increase of native T1  or Regional or global increase of ECV  or Regional LGE signal increase 
Supportive Criteria	**Pericarditis** (Effusion in cine images or abnormal LGE, T2, or T1)	Pericardial effusion 
	Systolic LV Dysfunction (Regional or global wall motion abnormality)	Regional or global hypokinesis 

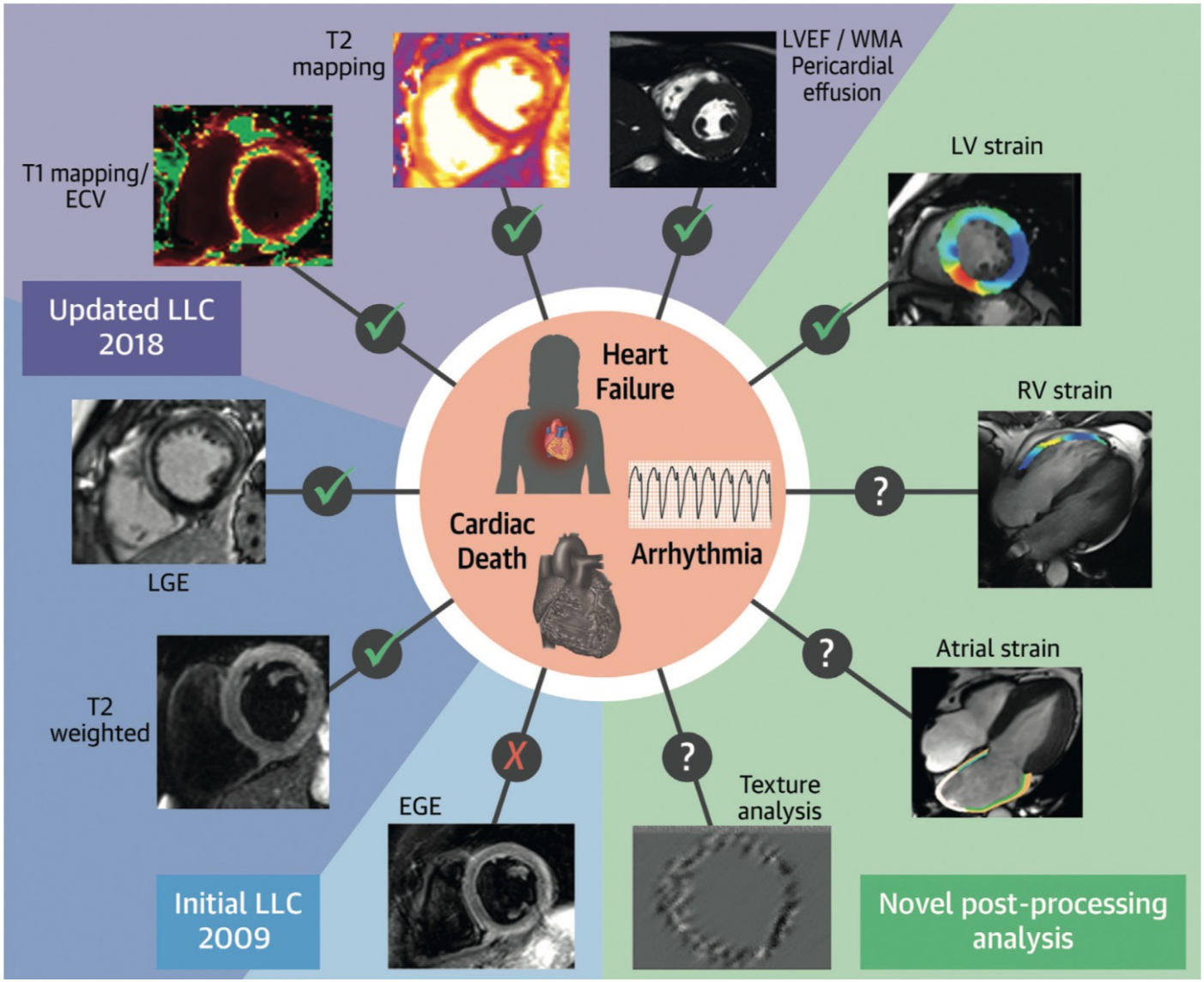
Ferreira V. et al. JACC 2018

HOW TO COMBINE THE SEQUENCES



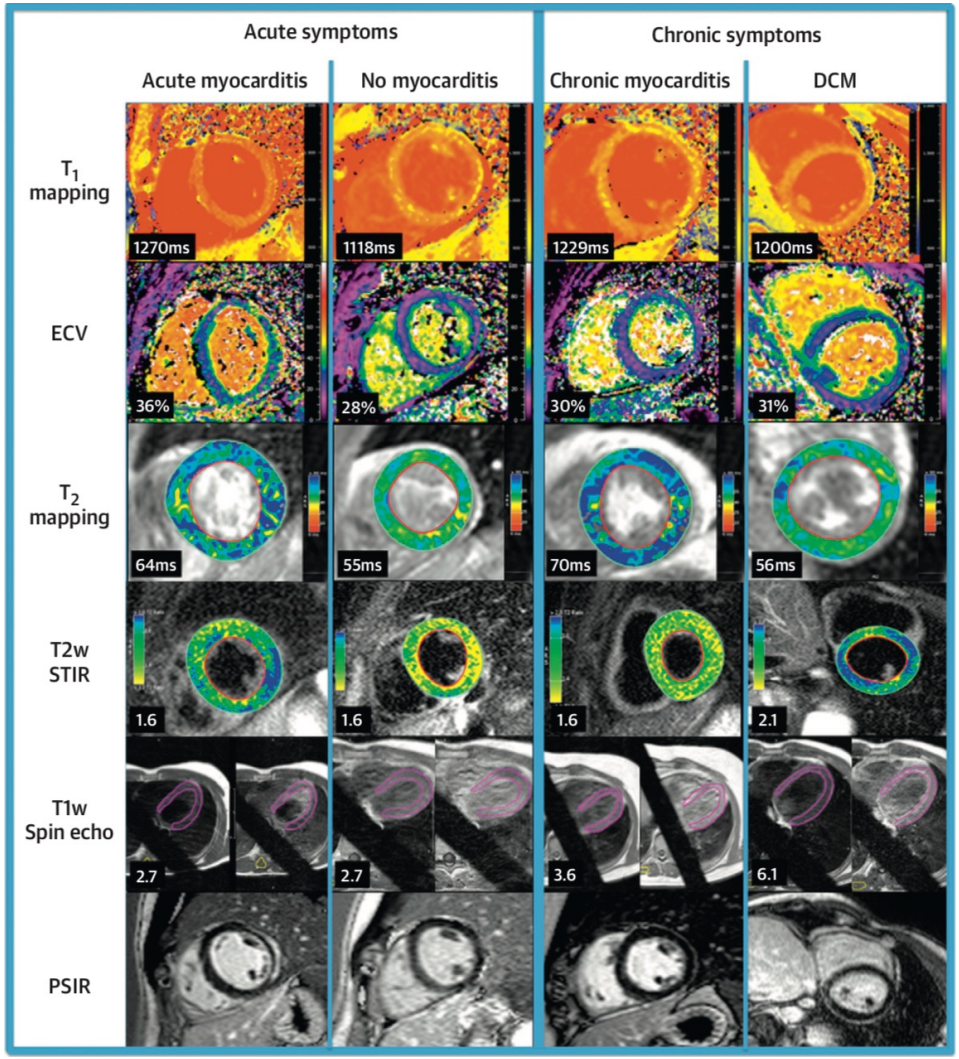
Esposito Insights Imaging 2015

HOW TO COMBINE THE SEQUENCES



Eichhorn C et al. J Am Coll Cardiol Img 2021

HOW TO COMBINE THE SEQUENCES



J Am Coll Cardiol 2016;67:1800–11

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation

Expert Recommendations

A single positive criterion can support diagnosis of myocardial inflammation if clinical suspicion is strong

CMR cannot identify specific cause of myocardial inflammation, and the histological subtypes, although regional distribution of inflammatory changes in the tissue provide diagnostic clues

HOW TO COMBINE THE SEQUENCES

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

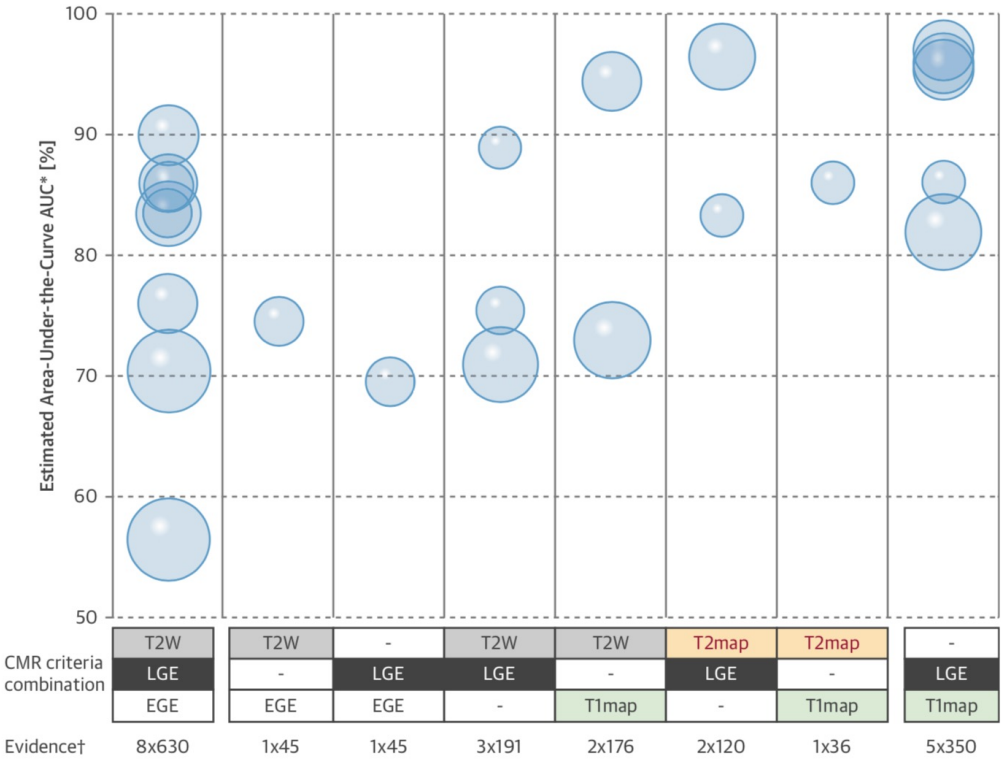
Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation

EBAC

Expert Recommendations

Ferreira V. et al. JACC 2018

FIGURE 1 Overview of the Current Evidence Comparing the Diagnostic Performance of Various CMR Criteria Combinations in Detecting Acute Myocarditis

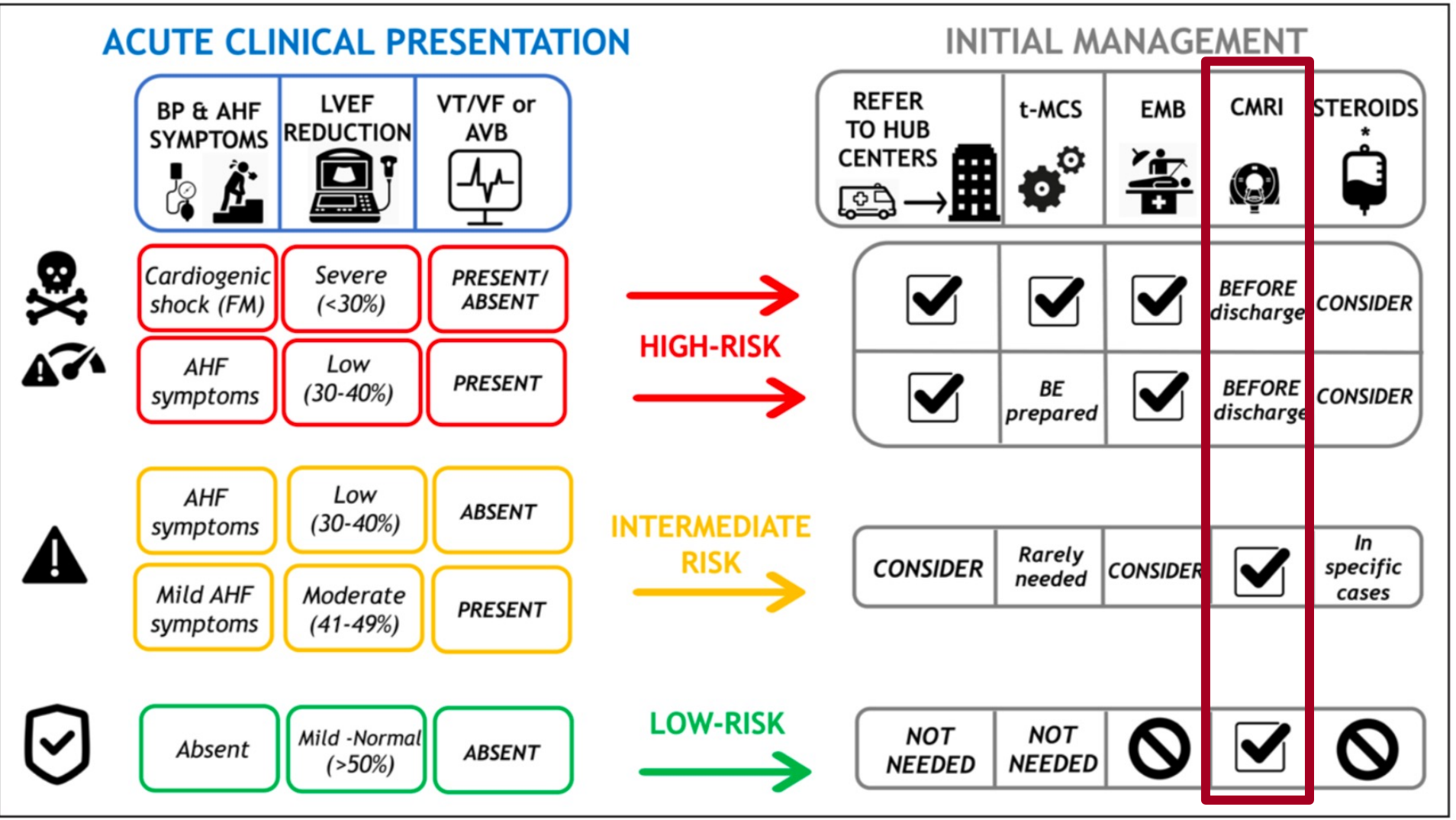


The Agenda

- How to use CMR for myocarditis: Technical Issues
- **Acute Myocarditis**
  - How to use CMR in different Clinical Settings
  - Diagnostic clues for differential diagnosis
  - Inflammation and systemic diseases
- **Chronic Myocarditis**
  - CMR time-of-course of myocardial inflammation
  - Prognostic significance of CMR

Management of Acute Myocarditis and Chronic Inflammatory Cardiomyopathy

An Expert Consensus Document



Circ Heart Fail. 2020;13:e007405.

MYOCARDITIS & IMAGING >>> MRI

Clinical presentations[a]

- Acute chest pain, pericarditic, or pseudo-ischaemic
- New-onset (days up to 3 months) or worsening of: dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs
- Subacute/chronic (>3 months) or worsening of: dyspnoea at rest or exercise, and/or fatigue, with or without left and/or right heart failure signs
- Palpitation, and/or unexplained arrhythmia symptoms and/or syncope, and/or aborted sudden cardiac death
- Unexplained cardiogenic shock

Diagnostic criteria

I. ECG/Holter/stress test features

- Newly abnormal 12 lead ECG and/or Holter and/or stress testing, any of the following: I to III degree atrioventricular block, or bundle branch block, ST/T wave change (ST elevation or non ST elevation, T wave inversion), sinus arrest, ventricular tachycardia or fibrillation and asystole, atrial fibrillation, reduced R wave height, intraventricular conduction delay (widened QRS complex), abnormal Q waves, low voltage, frequent premature beats, supraventricular tachycardia

II. Myocardiocytolysis markers

- Elevated TnT/TnI

III. Functional and structural abnormalities on cardiac imaging (echo/angio/CMR)

- New, otherwise unexplained LV and/or RV structure and function abnormality (including incidental finding in apparently asymptomatic subjects): regional wall motion or global systolic or diastolic function abnormality, with or without ventricular dilatation, with or without increased wall thickness, with or without pericardial effusion, with or without endocavitary thrombi

IV. Tissue characterization by CMR

- Oedema and/or LGE of classical myocarditic pattern (see text)

Clinically suspected myocarditis if ≥1 clinical presentation and ≥1 diagnostic criteria from different categories, in the absence of: (1) angiographically detectable coronary artery disease (coronary stenosis ≥ 50%); (2) known pre-existing cardiovascular disease or extra-cardiac causes that could explain the syndrome (e.g. valve disease, congenital heart disease, hyperthyroidism, etc.) (see text). Suspicion is higher with higher number of fulfilled criteria.

[a]If the patient is asymptomatic ≥2 diagnostic criteria should be met.

European Heart Journal (2013) 34, 2636–2648

UNIVERSITÀ DEGLI STUDI DI PADOVA

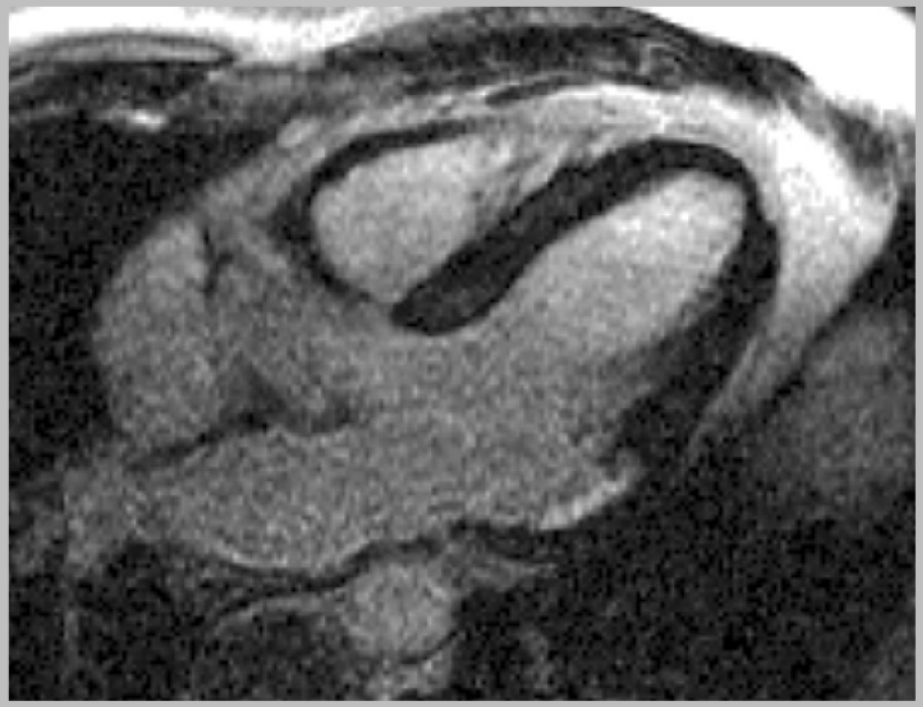
EUROPEAN SOCIETY OF CARDIOLOGY

European Heart Journal (2017) **38**, 143–153
doi:10.1093/eurheartj/ehw149

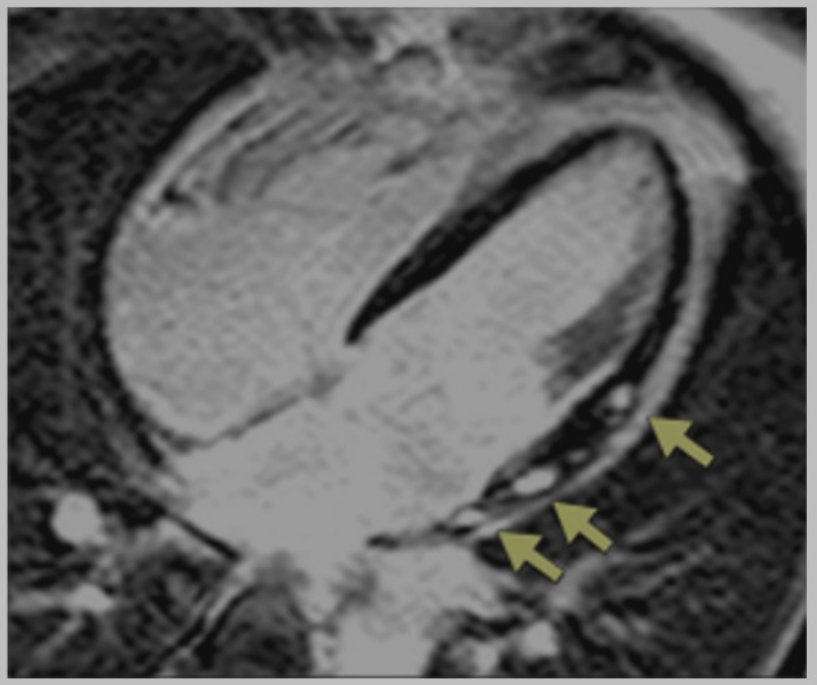
CURRENT OPINION

ESC working group position paper on myocardial infarction with non-obstructive coronary arteries

MINOCA



Myocarditis



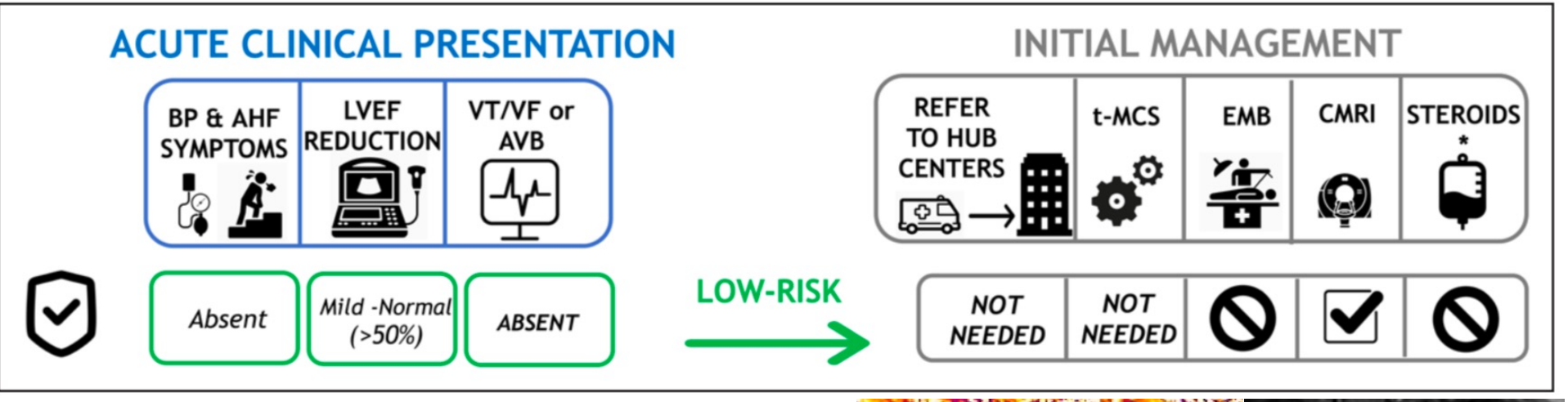
Plaque disruption
Dissection
Takotsubo
Epicardial or microvascular spasm
Coronary thromboembolism

Cardiac MRI
- LGE (myocarditis****)
- AMI

TEE
- Cardioembolism

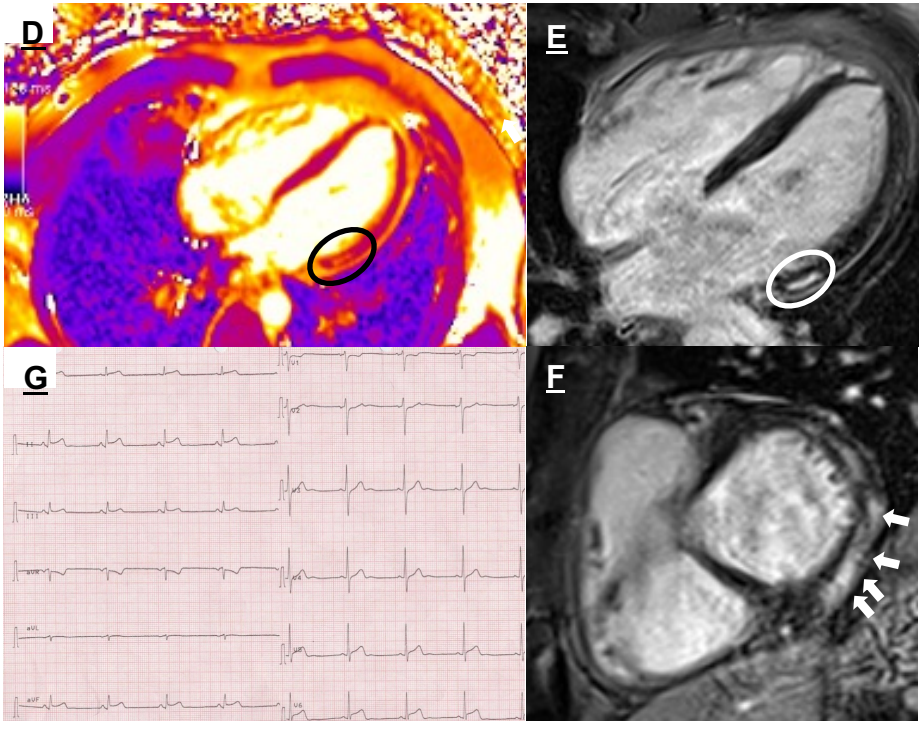
ACUTE CLINICAL SCENARIOS

Infarct-like presentation



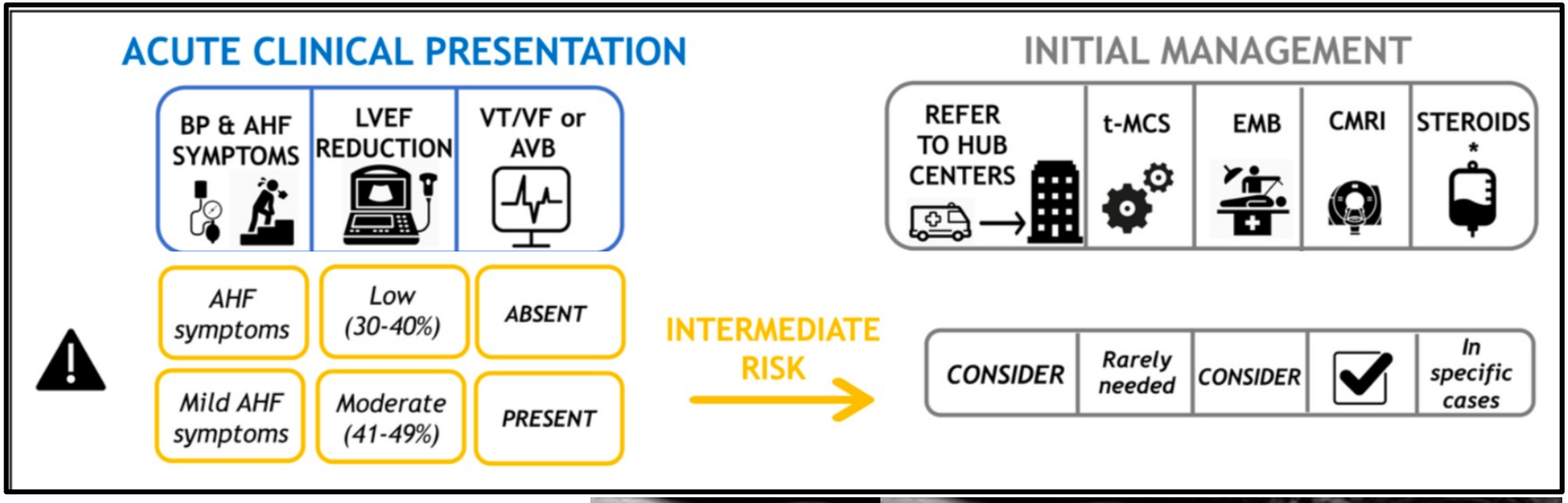
Circ Heart Fail. 2020;13:e007405.

A 18-yrs boy referred for chest pain and gastroenteritis with traditional and mapping CMR findings suggesting an acute myocarditis



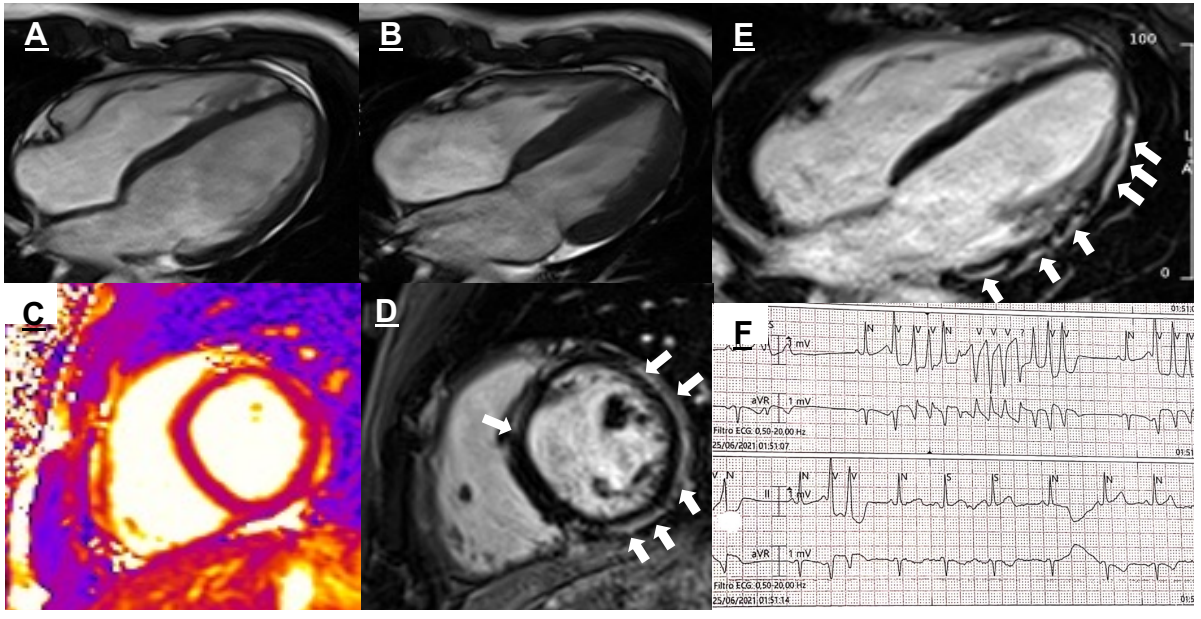
ACUTE CLINICAL SCENARIOS

Refractory arrhythmias clinical presentation and preserved EF



Circ Heart Fail. 2020;13:e007405.

A 42-yrs old woman presenting with syncope and presence of non-sustained ventricular tachycardia on monitoring in intensive care unit; coronary disease was excluded by angiography.
EMB: lymphocytic myocarditis

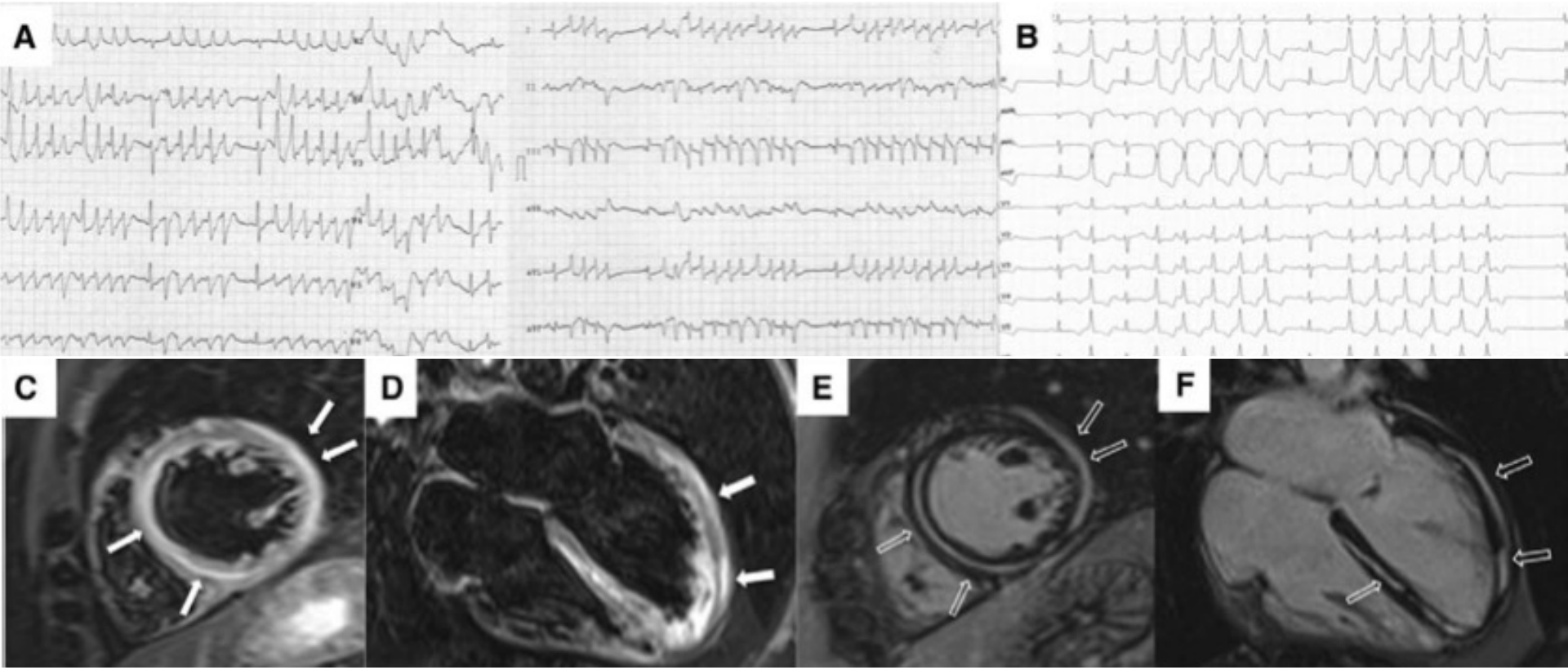


ACUTE CLINICAL SCENARIOS

Refractory arrhythmias clinical presentation and preserved EF

Nonamyloidotic Light Chain Cardiomyopathy

The Arrhythmogenic Magnetic Resonance Pattern



De Lazzari M et al Circulation. 2016;133:1421-1423.

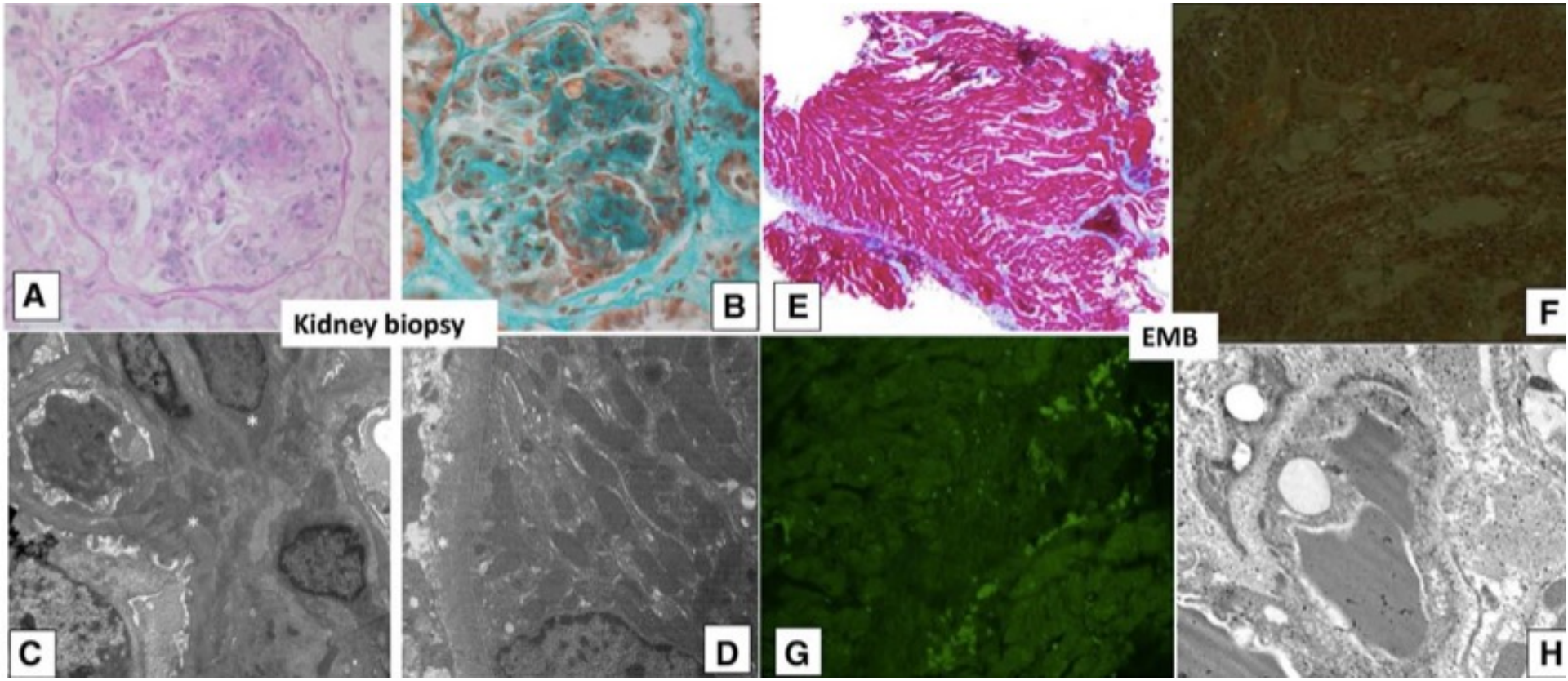
ACUTE CLINICAL SCENARIOS

Refractory arrhythmias clinical presentation and preserved EF

Nonamyloidotic Light Chain Cardiomyopathy

The Arrhythmogenic Magnetic Resonance Pattern

Kidney & Cardiac κ-light chain deposition



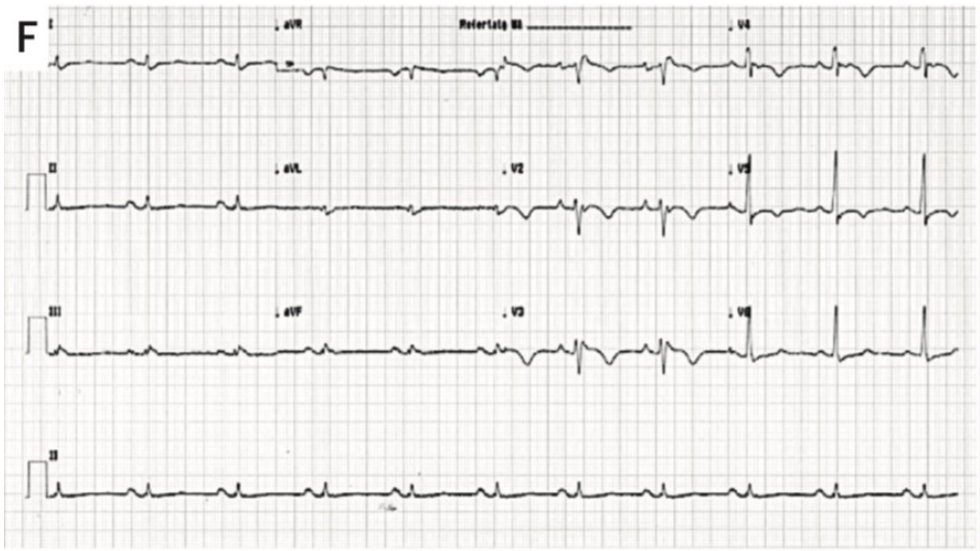
De Lazzari M et al Circulation. 2016;133:1421-1423.

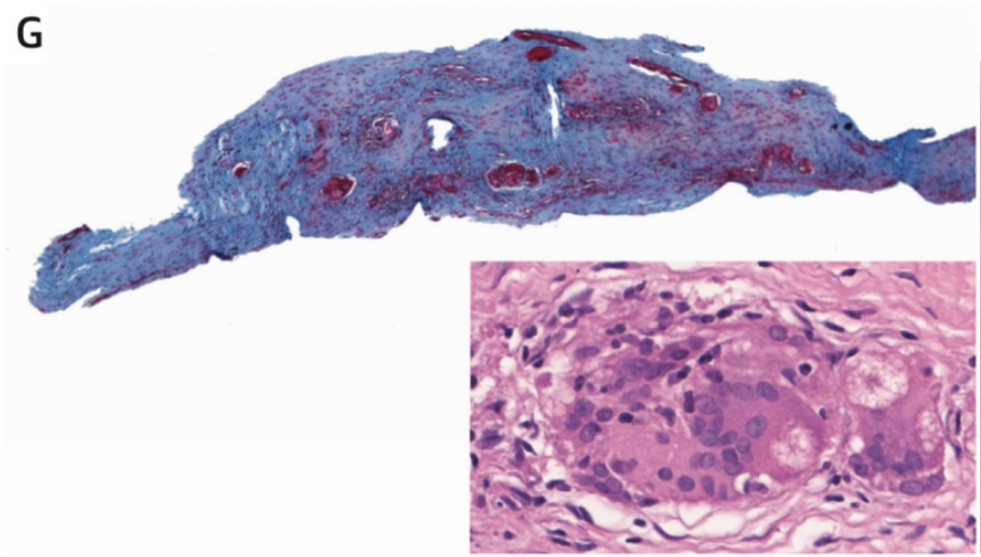
The Agenda

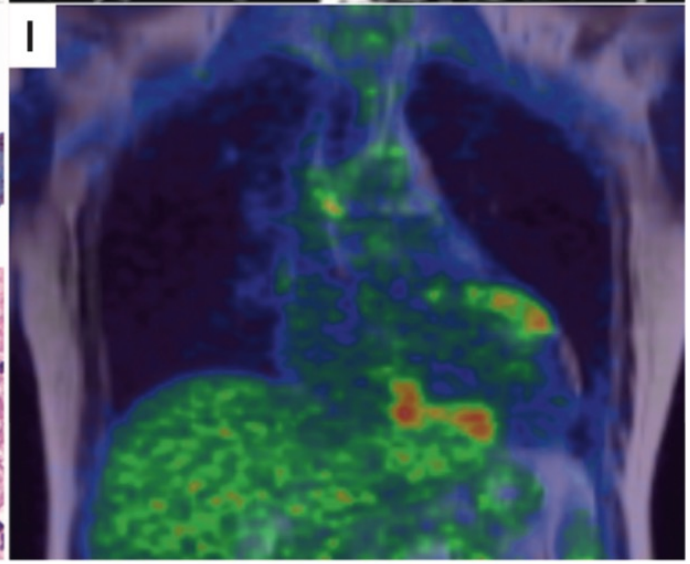
- How to use CMR for myocarditis: Technical Issues
- **Acute Myocarditis**
  - How to use CMR in different Clinical Settings
  - Diagnostic clues for differential diagnosis
  - Inflammation and systemic diseases
- **Chronic Myocarditis**
  - CMR time-of-course of myocardial inflammation
  - Prognostic significance of CMR

Diagnostic clues for differential diagnosis

Cardiac Sarcoidosis



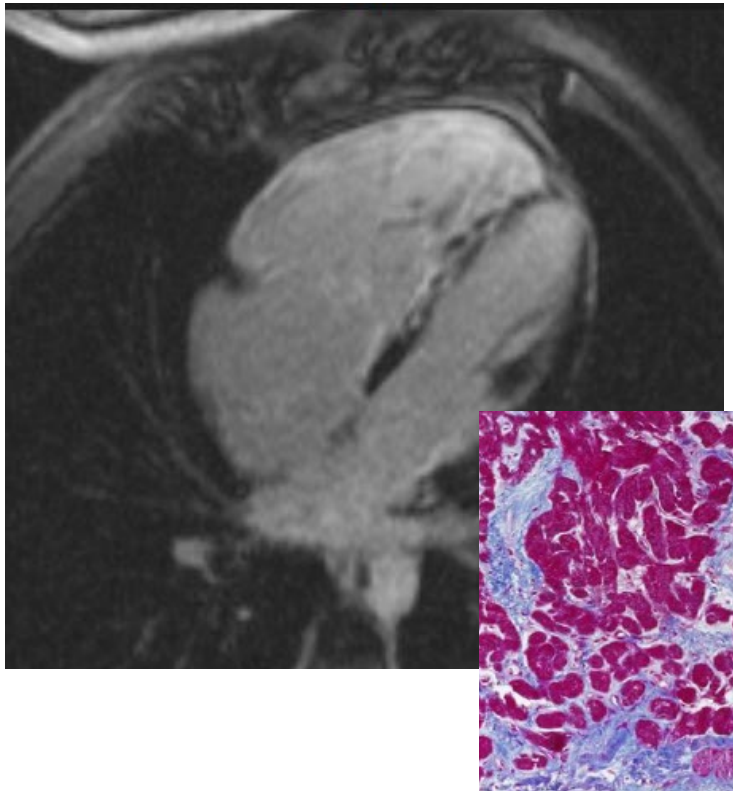




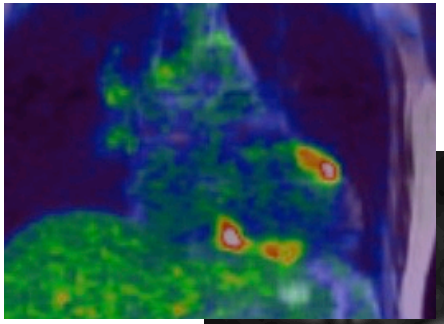
Martina Perazzolo Marra, JACC Img 2021

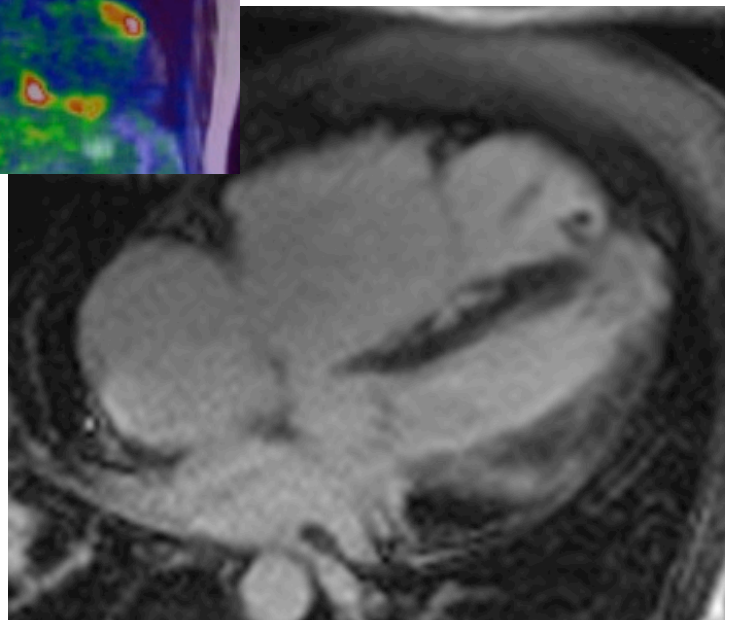
Myocardial Tissue Characterization in Arrhythmogenic Cardiomyopathy. Comparison Between Endomyocardial Biopsy and Cardiac Magnetic Resonance

AC



SARCOIDOSIS





➽ need for an histologic exclusion!!!

Tips & Tricks
LGE in Cardiac Sarcoidosis

Basal Inferoseptal **Triangular** Late Gadolinium

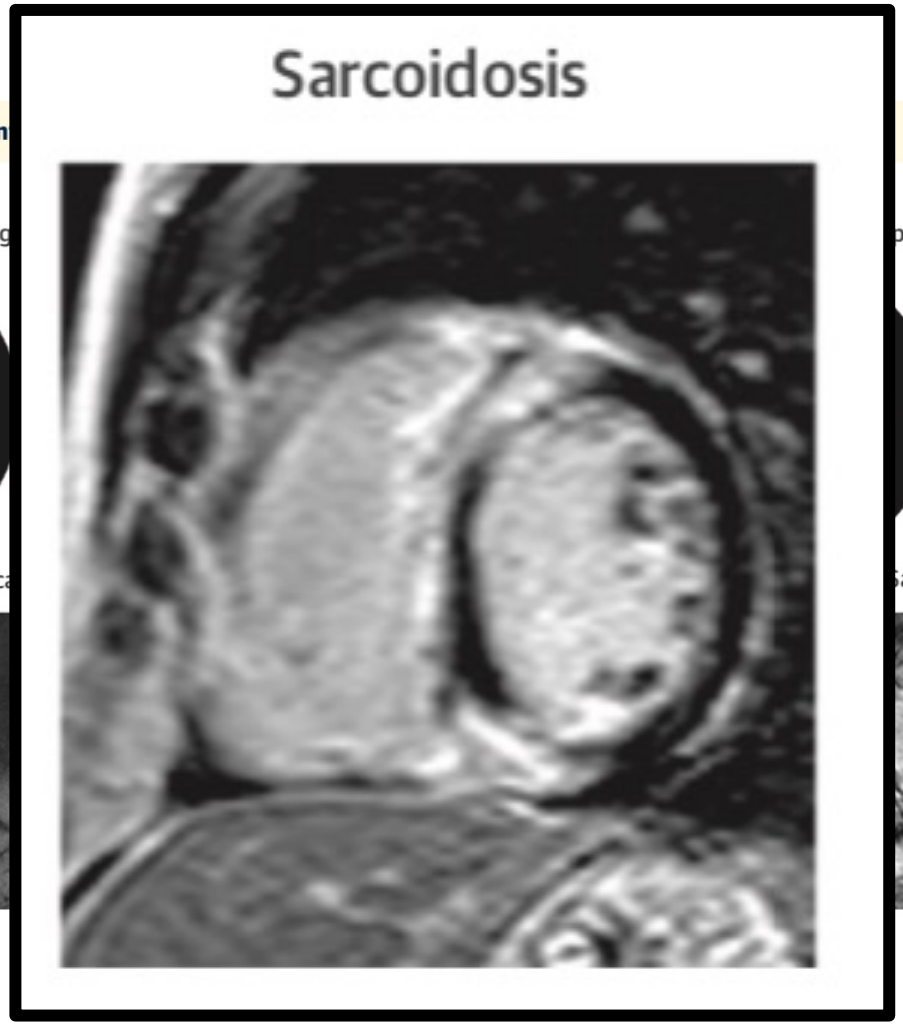


FIGURE 1 Illustration of Septal and In

A Pattern A: Basal inferoseptal triang

otal LGE

Pattern C: Mid-Septal LGE

Sarcoidosis

Lamin A ca

Sarcoidosis

Idiopathic

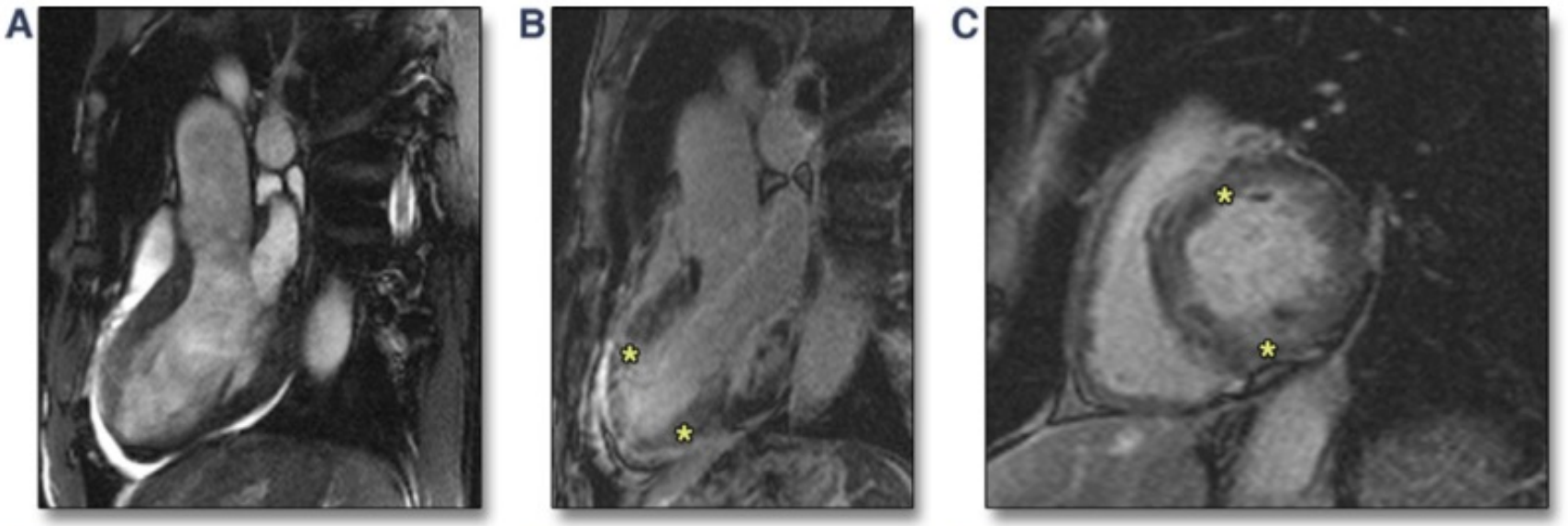
Kuo L. et al. JACC: CARDIOVASCULAR IMAGING, VOL. 12, NO. 12, 2019

Diagnostic clues for differential diagnosis

Endocardial disease

Cardiac Magnetic Resonance Features of Biopsy-Proven Endomyocardial Diseases

JACC: CARDIOVASCULAR IMAGING, VOL. 7, NO. 3, 2014

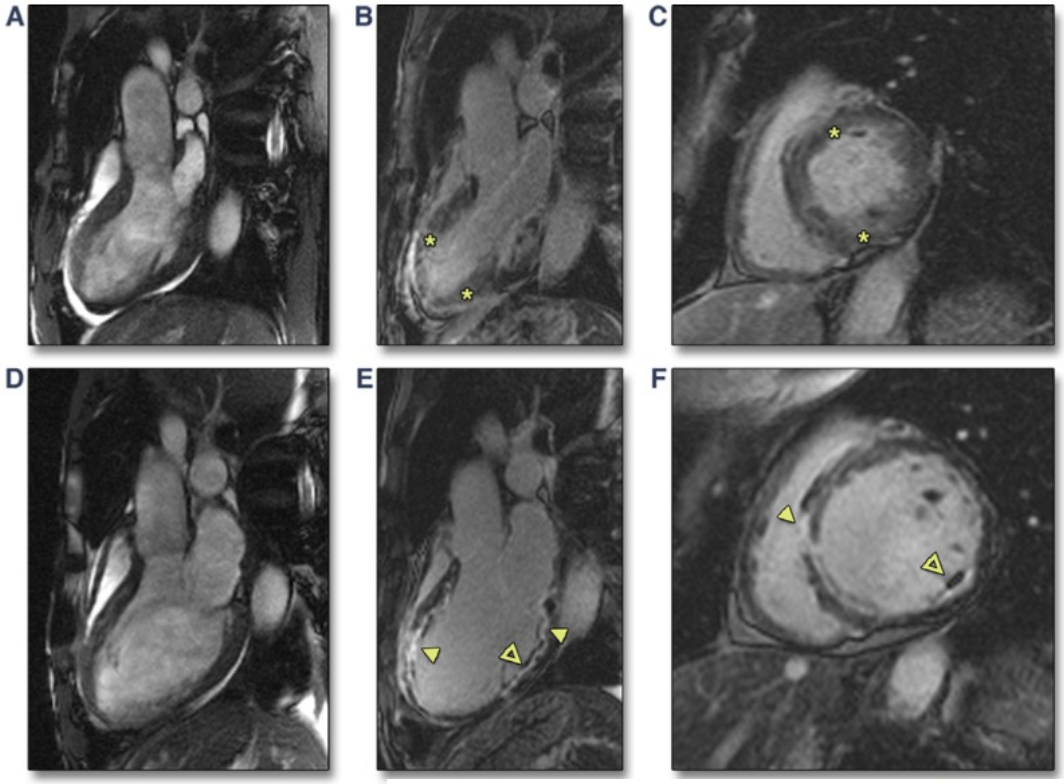


Great amount of edema (also increased LV mass) **+** ***Diffuse endocardial thrombosis***

…think to eosinophilic myocarditis!!!!

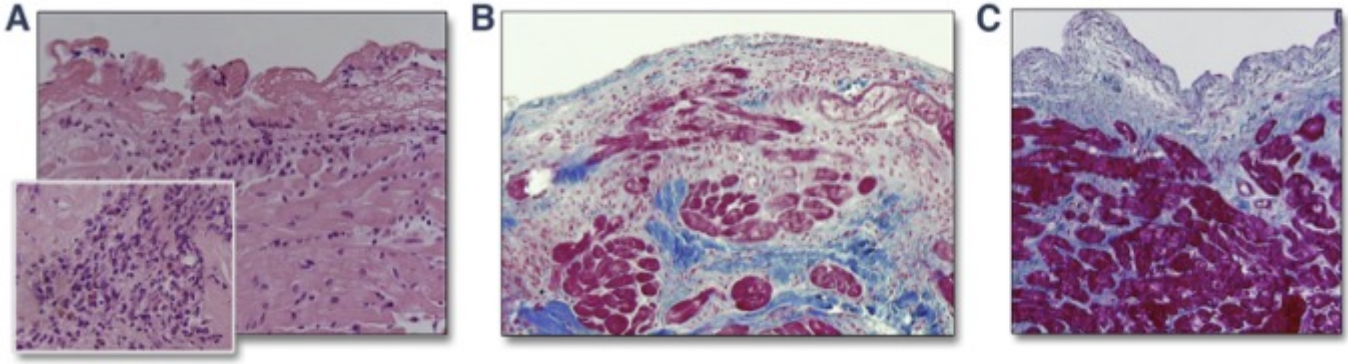
Cardiac Magnetic Resonance Features of Biopsy-Proven Endomyocardial Diseases

JACC: CARDIOVASCULAR IMAGING, VOL. 7, NO. 3, 2014



Acute Phase

Chronic Phase



The Agenda

- How to use CMR for myocarditis: Technical Issues
- **Acute Myocarditis**
  - How to use CMR in different Clinical Settings
  - Diagnostic clues for differential diagnosis
  - Inflammation and systemic diseases
- **Chronic Myocarditis**
  - CMR time-of-course of myocardial inflammation
  - Prognostic significance of CMR

ESC European Society of Cardiology

European Heart Journal - Cardiovascular Imaging (2022) **00**, 1–15
https://doi.org/10.1093/ehjci/jeac021

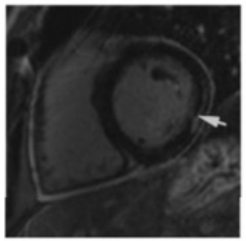
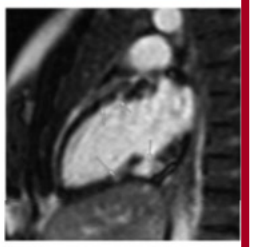
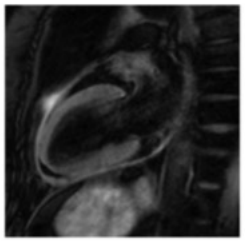
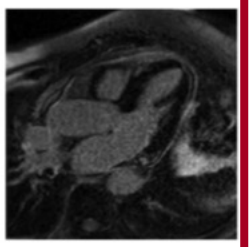
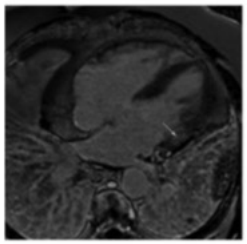
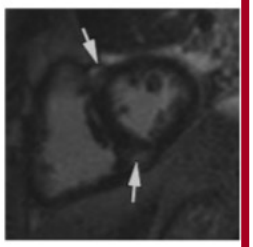
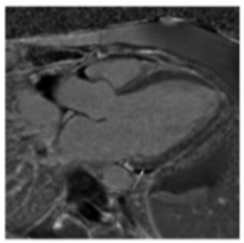
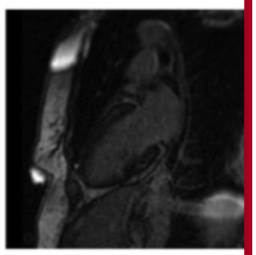
REVIEW

The role of cardiovascular magnetic resonance in the evaluation of acute myocarditis and inflammatory cardiomyopathies in clinical practice — a comprehensive review

Myocardial Inflammation and systemic diseases

Inflammatory cardiomyopathy

Non-infectious, autoimmune, connective tissue disease

	Disease	Imaging findings			
A	Systemic lupus erythematosus	LGE		LGE	
B	Rheumatoid arthritis	T2w-spin echo		LGE	
C	Systemic sclerosis/scleroderma	LGE		LGE	
D	Polymyositis	LGE		LGE	

European Heart Journal - Cardiovascular Imaging (2022) 00, 1–15

The Agenda

- How to use CMR for myocarditis: Technical Issues
- Acute Myocarditis
  - How to use CMR in different Clinical Settings
  - Diagnostic clues for differential diagnosis
  - Inflammation and systemic diseases
- **Chronic Myocarditis**
  - CMR time-of-course of myocardial inflammation
  - Prognostic significance of CMR

CHRONIC PHASE

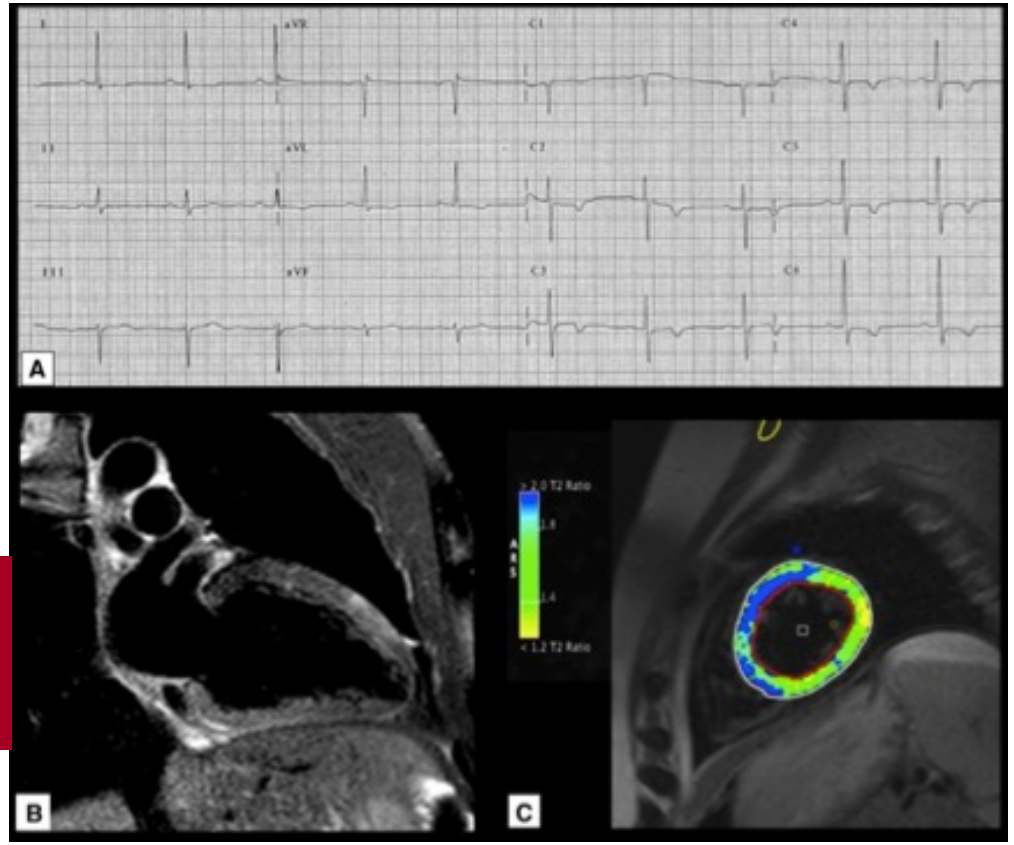
The time-course of EDEMA

M. De Lazzari et al. / Journal of Electrocardiology 49 (2016) 587–595

Relationship between T-wave inversion and transmural myocardial edema as evidenced by cardiac magnetic resonance in patients with clinically suspected acute myocarditis: clinical and prognostic implications

To rule in or rule out myocardial inflammation reliably, CMRI should be performed within 2 to 3 weeks from the onset of symptoms, although accuracy may be lower during the first days.

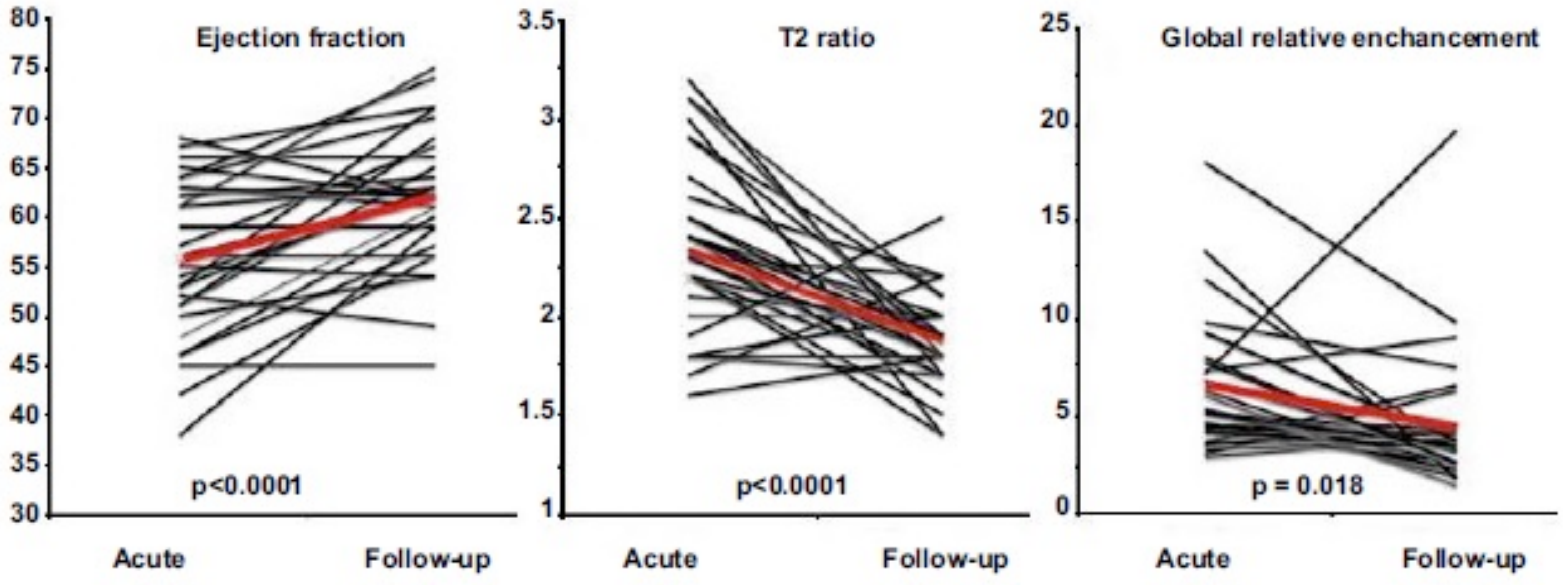
Unless recurrent flares occur, edema tends to decline 4 weeks after disease onset



CHRONIC PHASE

The time-course of EDEMA

Cardiac Magnetic Resonance Monitors Reversible and Irreversible Myocardial Injury in Myocarditis



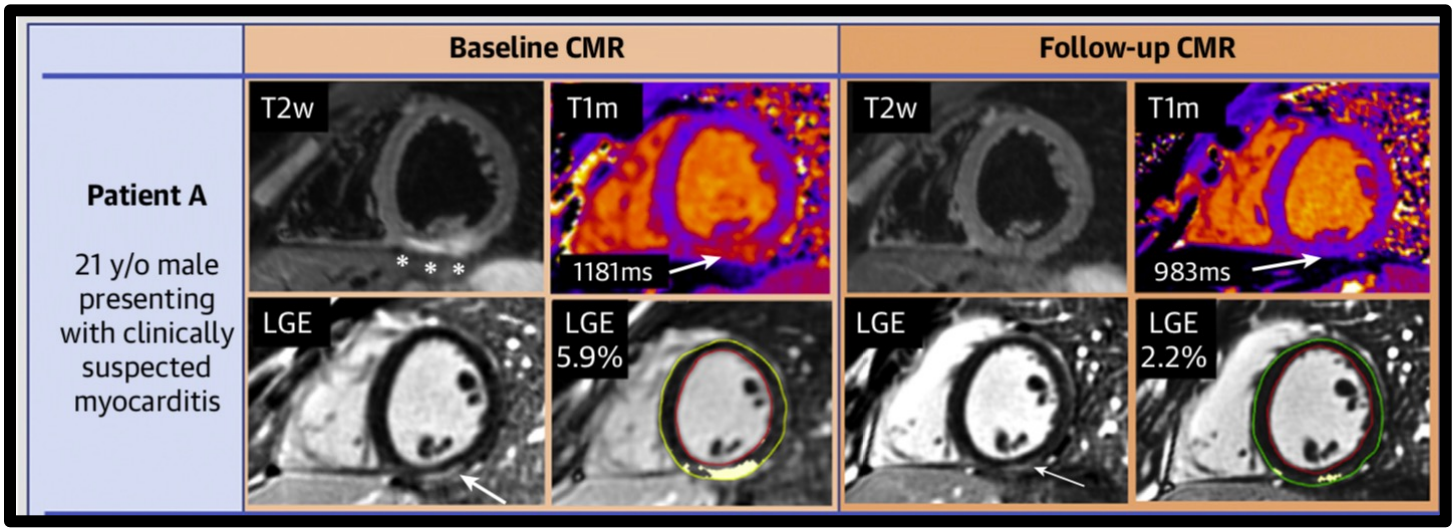
JACC Img 2009;2:131–8

CHRONIC PHASE

The time course of EDEMA

EDEMA: disappearance of edema is frequent @FU

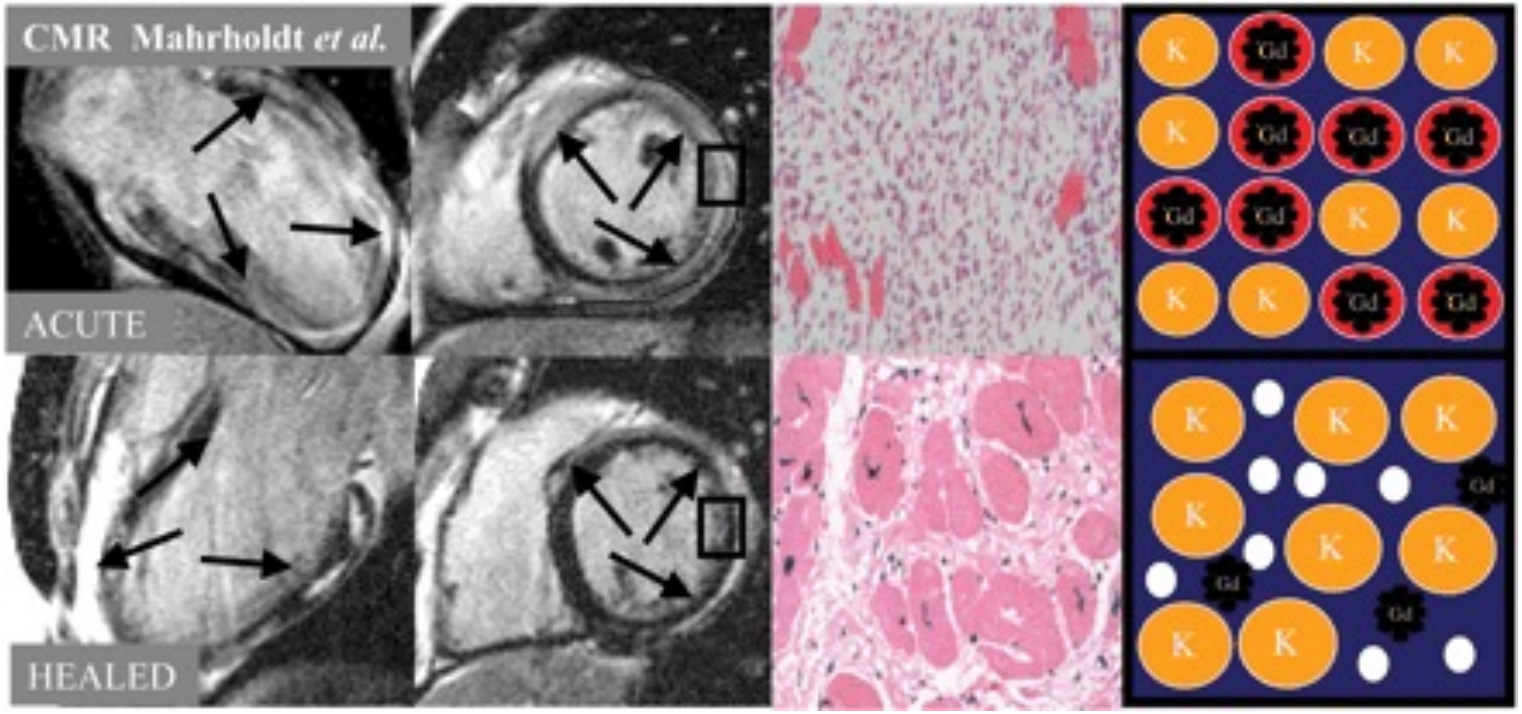
@FU: negative T2-based technique up to 84%



Eichhorn C et al. J Am Coll Cardiol Img 2021

CHRONIC PHASE

The time course of LGE

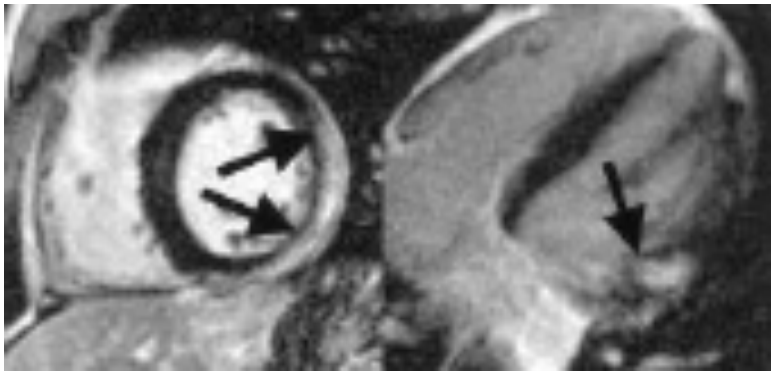


Eur Heart J. 2005;26(15):1461-1474.

CHRONIC PHASE

The time course of LGE

CMR in the acute phase



CMR at follow-up (3 months later)

During follow-up: a reduction of LE area from 9±11% to 3±4% of LV mass, and the EF improved from 47±19% to 60±10%.

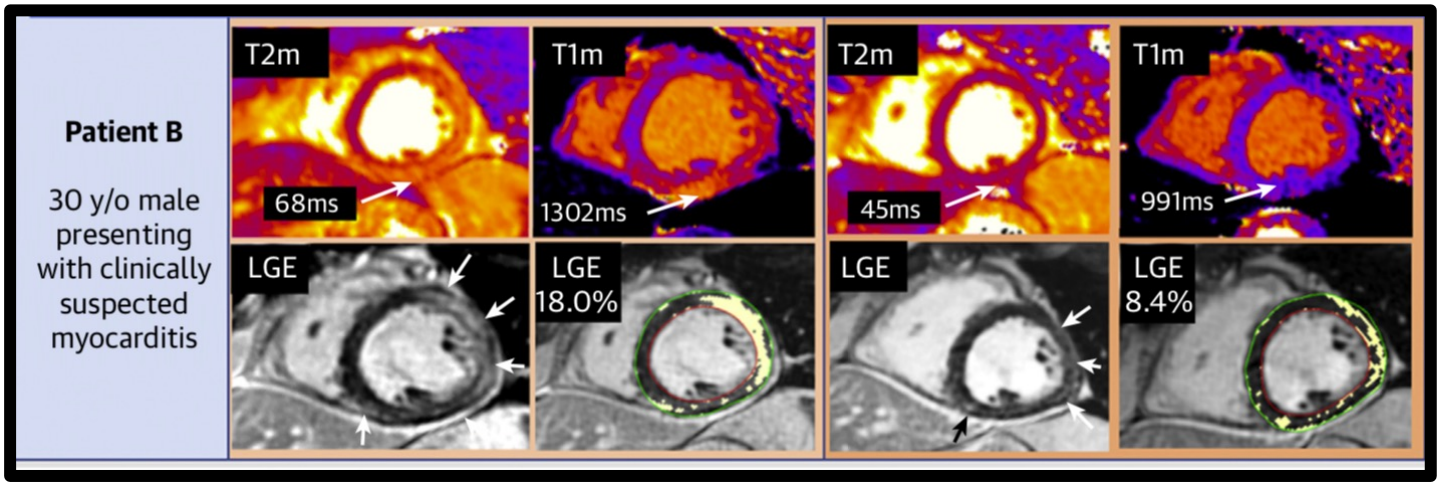
Mahrholdt, MD et al. - Circulation. 2004;109:1250-1258

CHRONIC PHASE

The time course of LGE

LGE: disappearance of LGE is not complete @FU and generally persists, although reduced

@FU: positive T1-based technique up to 89%



…LGE in myocarditis is a dynamic process!!!!

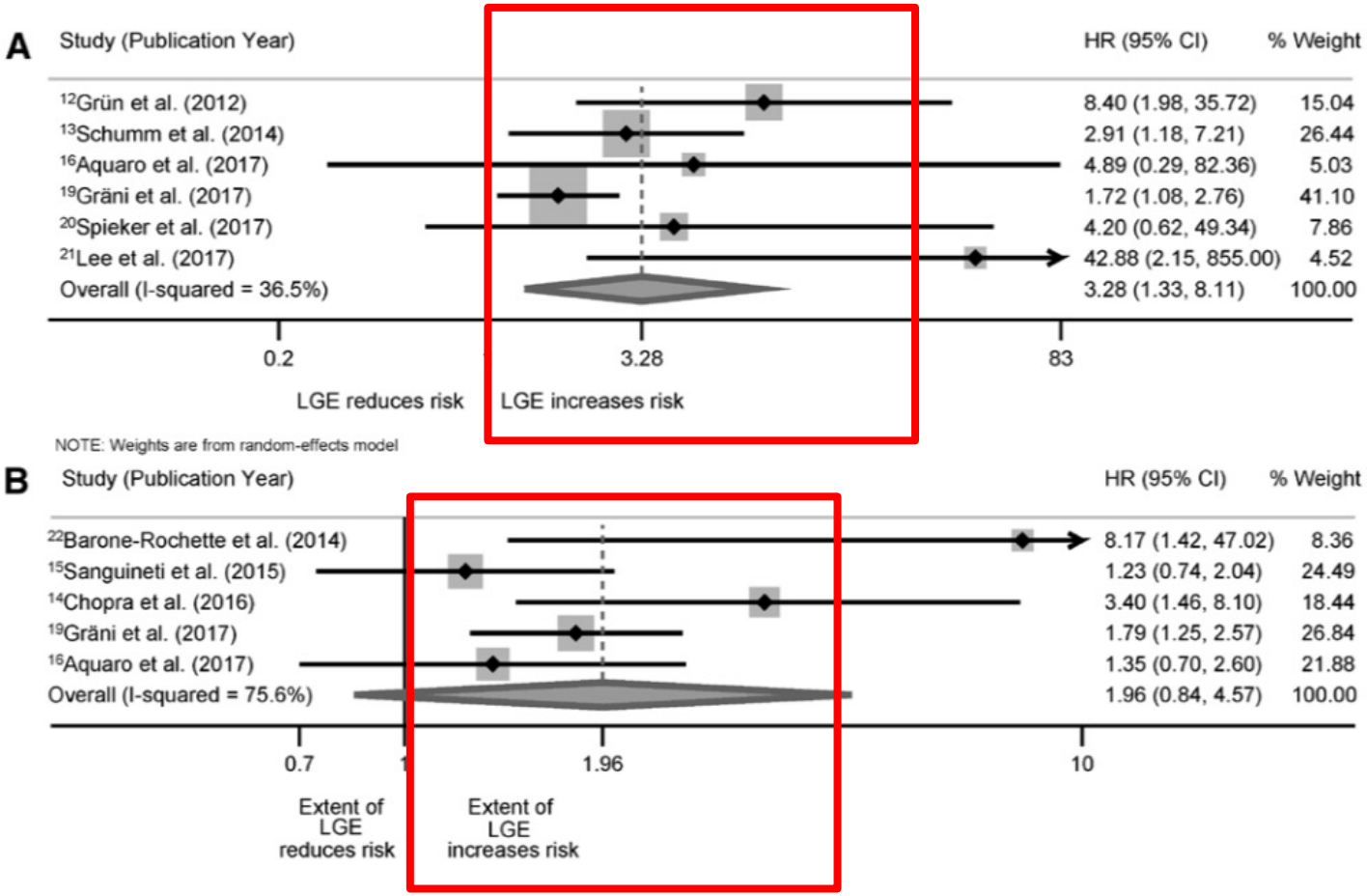
Eichhorn C et al. J Am Coll Cardiol Img 2021

The Agenda

- How to use CMR for myocarditis: Technical Issues
- Acute Myocarditis
  - How to use CMR in different Clinical Settings
  - Diagnostic clues for differential diagnosis
  - Inflammation and systemic diseases
- **Chronic Myocarditis**
  - CMR time-of-course of myocardial inflammation
  - Prognostic significance of CMR

Prognostic Impact of Late Gadolinium Enhancement by Cardiovascular Magnetic Resonance in Myocarditis

A Systematic Review and Meta-Analysis



Presence of LGE

Extent of LGE

CMR Predictors for MACE in Myocarditis

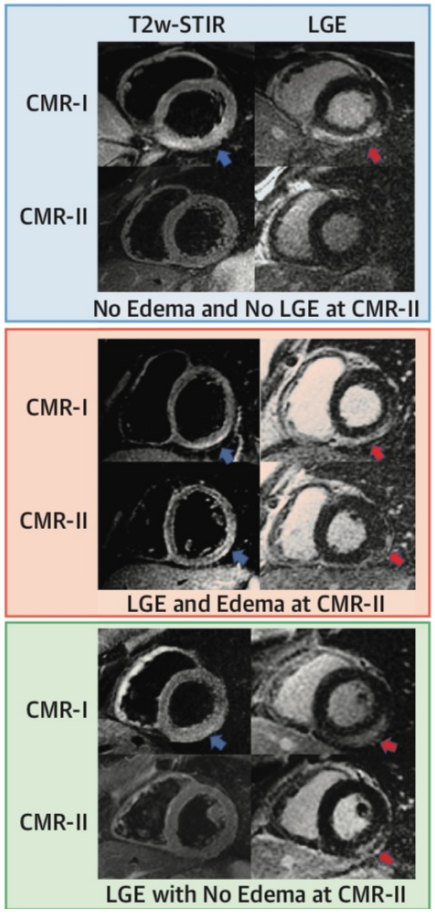
- Presence of LGE
- Extent of LGE
- Pattern of LGE (septal)
- ECV>35%
- Persistence of edema

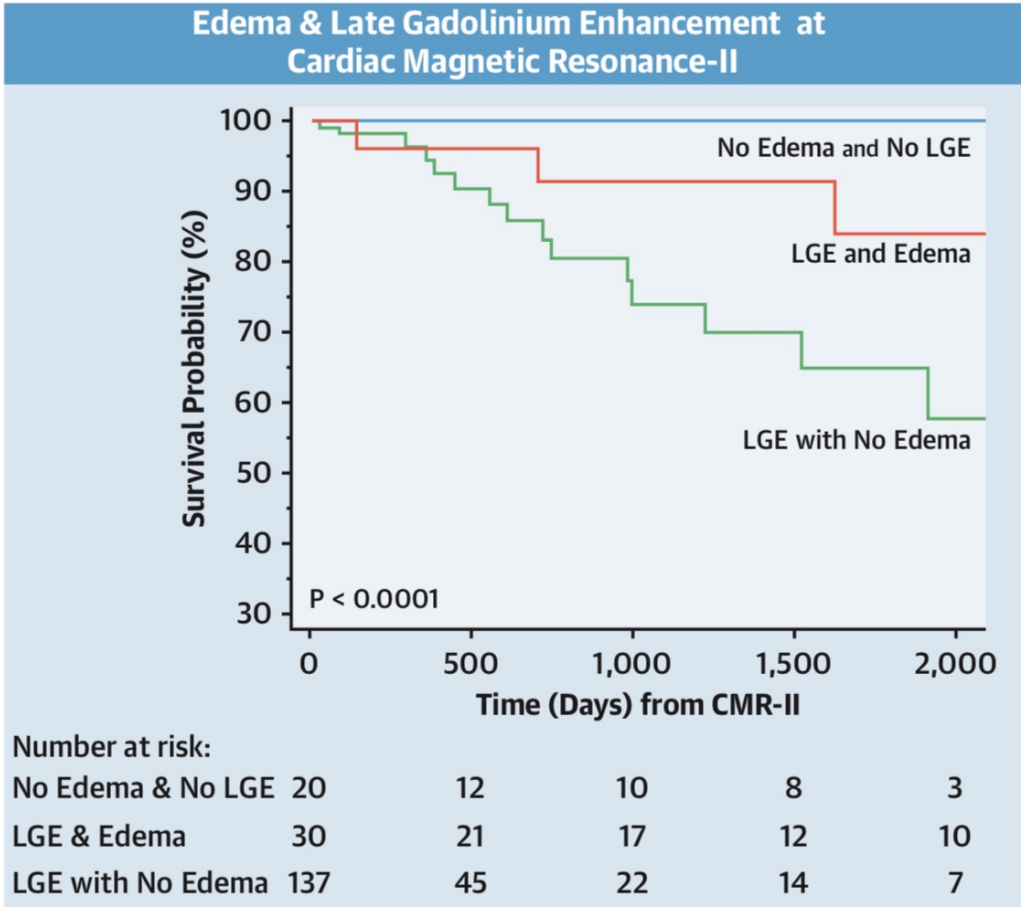
CMR Predictors for MACE in Myocarditis

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

Giovanni Donato Aquaro, MD,[a] Yacob Ghebru Habtemicael, MD,[a] Giovanni Camastra, MD,[b] Lorenzo Monti, MD,[c] Santo Dellegrottaglie, MD,[d,e] Claudio Moro,[f] Chiara Lanzillo, MD,[g] Alessandra Scatteia, MD,[h] Mauro Di Roma, MD,[i] Gianluca Pontone, MD,[j] Martina Perazzolo Marra,[k] Andrea Barison, MD,[a] Gianluca Di Bella,[l] on behalf of the "Cardiac Magnetic Resonance" Working Group of the Italian Society of Cardiology

J Am Coll Cardiol 2019;74:2439–48





CMR Predictors for MACE in Myocarditis

- Presence of LGE
- Extent of LGE
- Pattern of LGE (septal)
- ECV>35%
- Persistence of edema

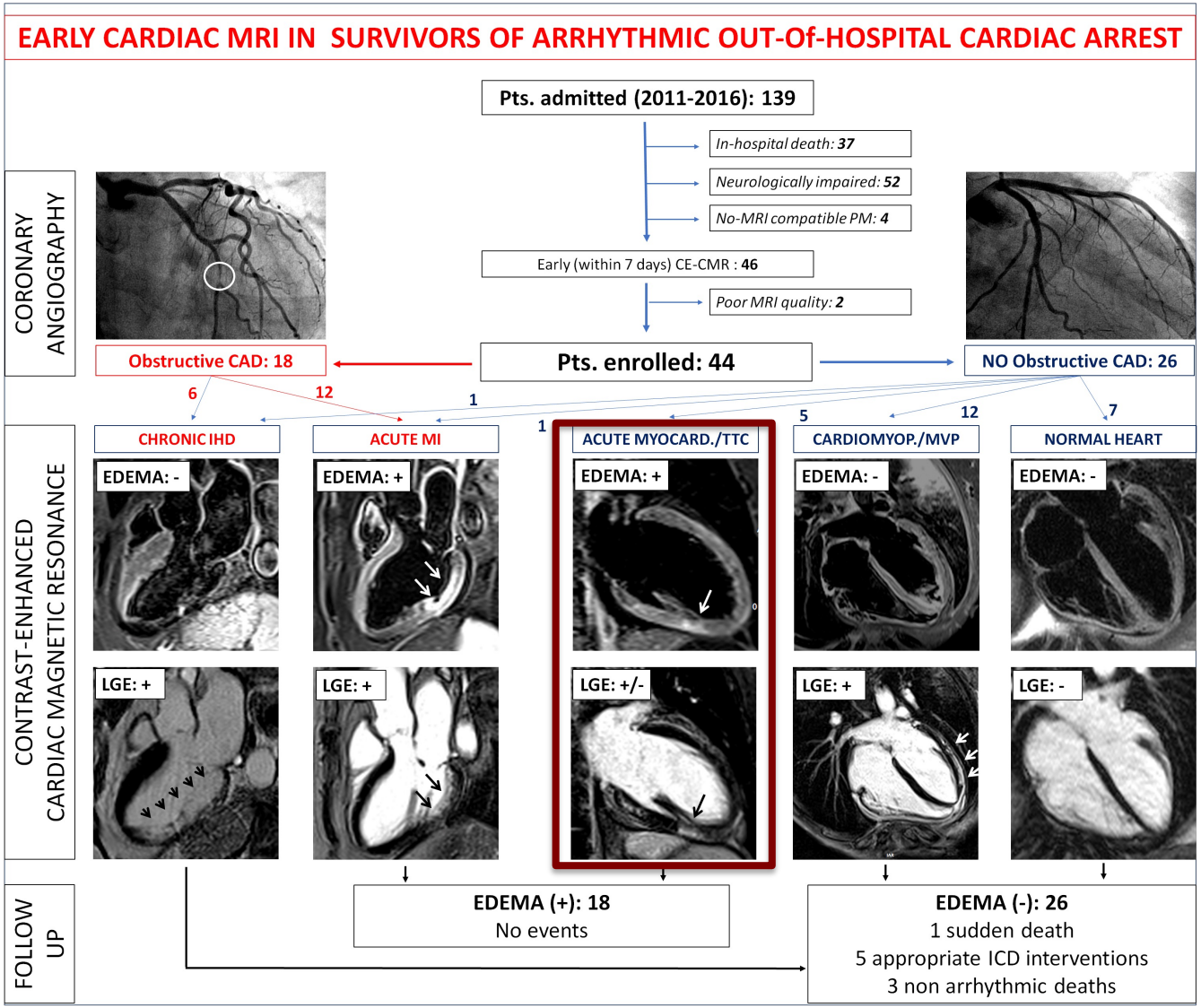
Knownledge Gaps:

- When perform the FU CMR?

Generally after 3 to 12 months (no consensus!)

- Clinical persistence of edema:
  - Still residual change of recovery!
  - Which role for monitoring therapy?
  - **Which role for arrhythmogenesis?**

Diagnostic value and prognostic implications of early cardiac magnetic resonance in survivors of out of hospital cardiac arrest

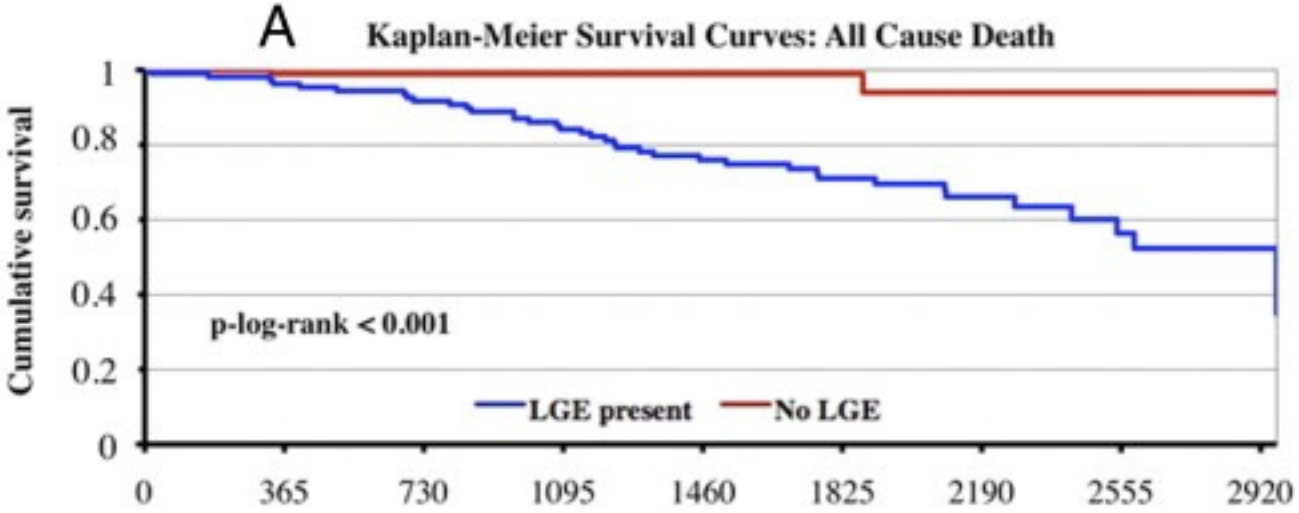


Zorzi A,…Perazzolo Marra. Heart Rhythm 2017

CMR Predictors for MACE in Myocarditis

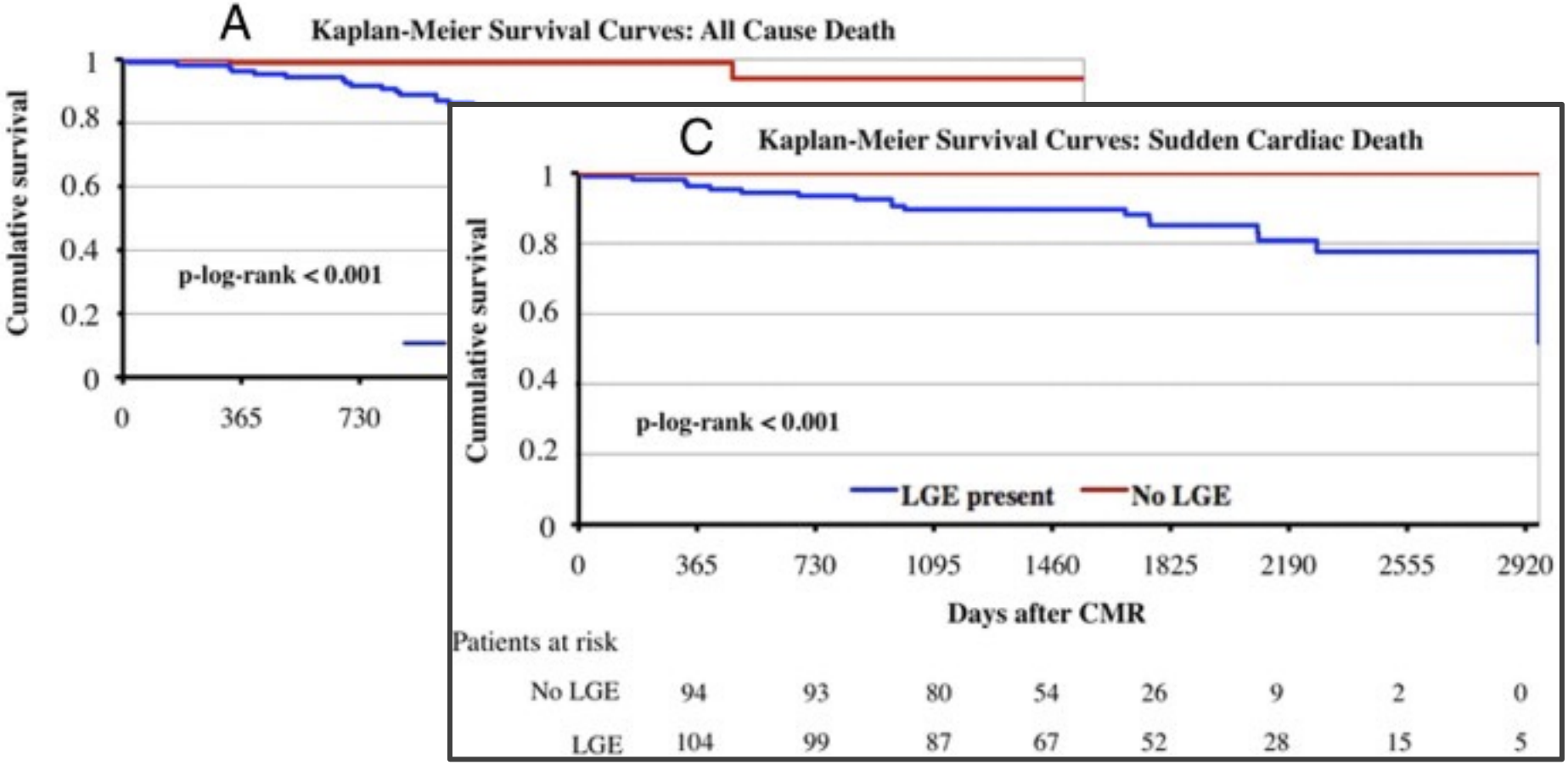
Underlying LGE & myocarditis: something else?

Long-Term Follow-Up of Biopsy-Proven Viral Myocarditis : Predictors of Mortality and Incomplete Recovery



J Am Coll Cardiol. 2012;59:1604-15

Long-Term Follow-Up of Biopsy-Proven Viral Myocarditis : Predictors of Mortality and Incomplete Recovery



J Am Coll Cardiol. 2012;59:1604-15

Al di là dei numeri guardiamo le immagini

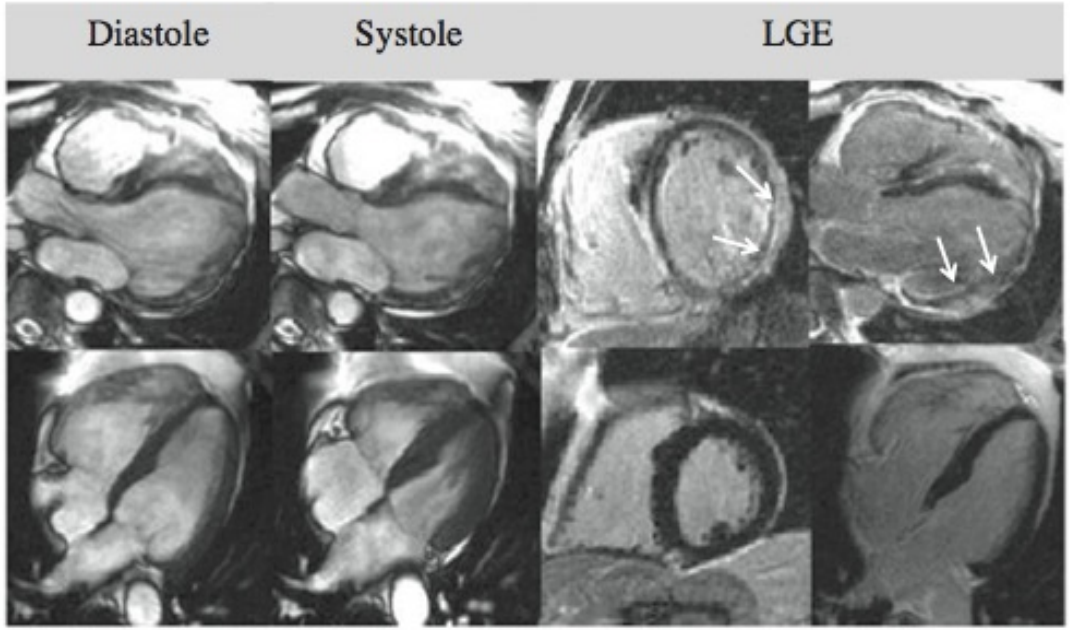
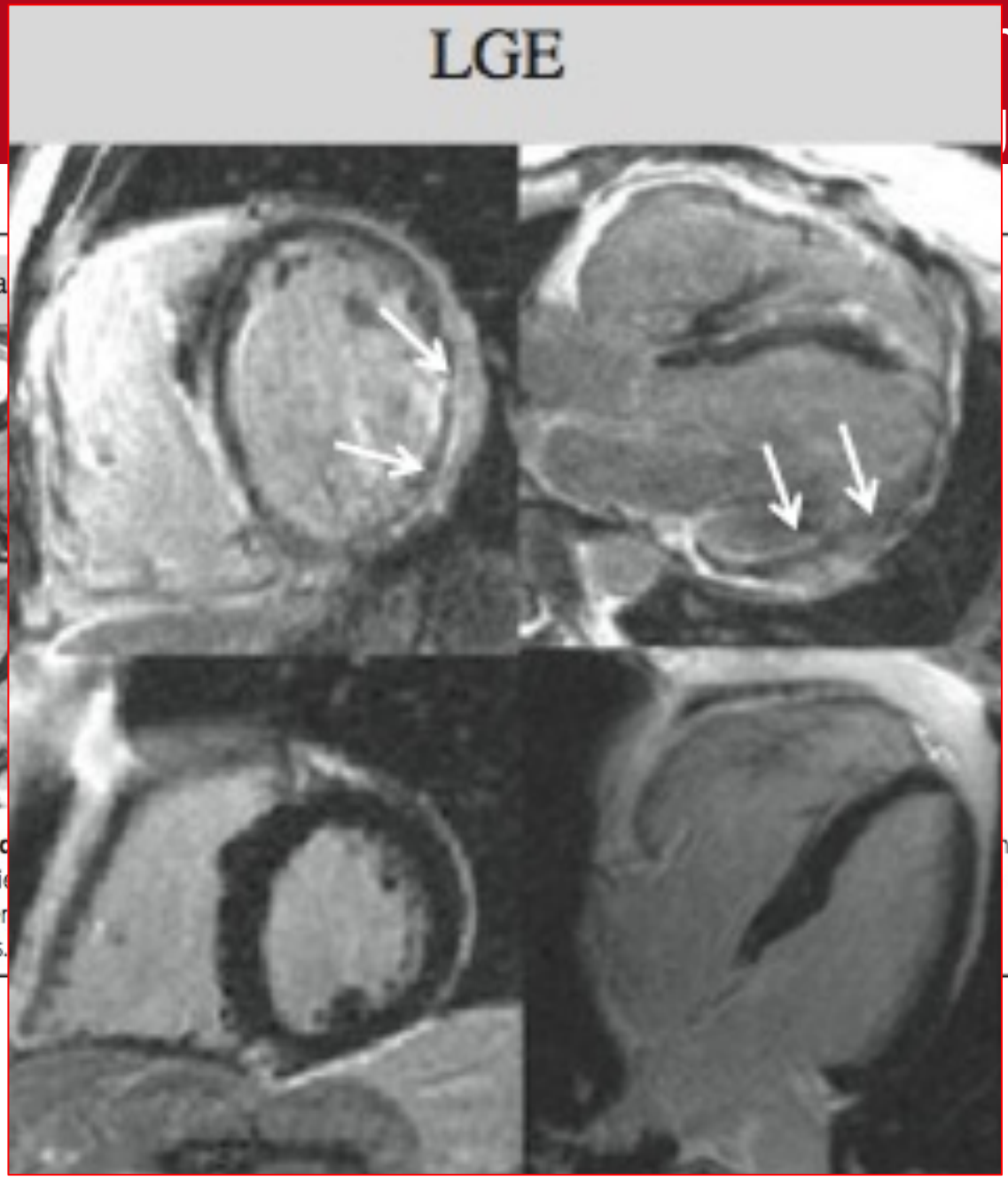


Figure 2 Patients with similar symptoms, but different CMR results and outcomes. Patient 250 presented with dyspnea and chest pain, the same symptoms as **patient 161**. While in patient 250 CMR revealed an EF of 22% and epicardial LGE of the posterolateral wall typical for myocarditis (EMB: viral HHV6 myocarditis, no other pathology (e.g. no sarcoid)), patient 161 had a normal CMR. **Patient 250** died from SCD during follow-up while patient 161 had no events.

Schumm et al. Journal of Cardiovascular Magnetic Resonance 2014, 16:14



Patient 250

Patient 161

Figure 2 Patients with similar symptoms, but d
the same symptoms as **patient 161**. While in pati
myocarditis (EMB: viral HHV6 myocarditis, no other
during follow-up while patient 161 had no events.

Schumm et al. Journal of Cardiovascular Magnetic Resonance 2014, 16:14

«Hot Phase» of ARVC

Letter to the Editor

Arrhythmogenic right ventricular cardiomyopathy/dysplasia and troponin release. Myocarditis or the "hot phase" of the disease?

International Journal of Cardiology 157 (2012) e26–e28

Myocardial inflammation detected by cardiac MRI in Arrhythmogenic right ventricular cardiomyopathy: A paediatric case series

International Journal of Cardiology 271 (2018) 81–86

High Prevalence of Myocarditis Mimicking Arrhythmogenic Right Ventricular Cardiomyopathy

Differential Diagnosis by
Electroanatomic Mapping-Guided Endomyocardial Biopsy

J Am Coll Cardiol 2009;53:681–9

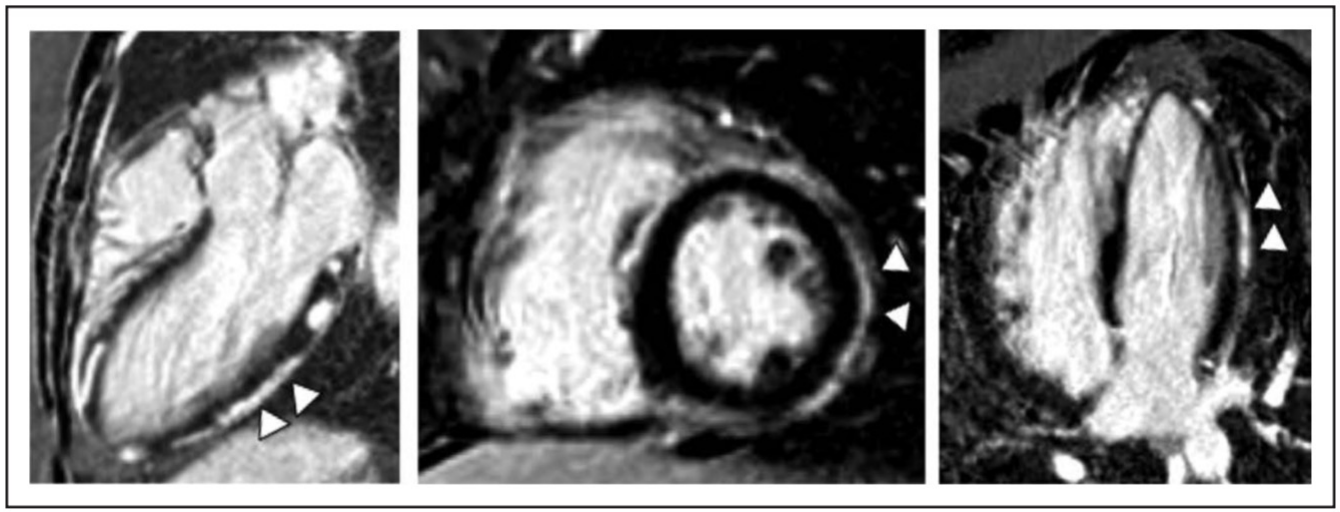
ORIGINAL RESEARCH ARTICLE

Desmoplakin Cardiomyopathy, a Fibrotic and Inflammatory Form of Cardiomyopathy Distinct From Typical Dilated or Arrhythmogenic Right Ventricular Cardiomyopathy

107 DSPC + PKP2 gene positive

***DSP* cardiomyopathy** is a distinct form of arrhythmogenic cardiomyopathy characterized by

- ***episodic myocardial injury***
- LV fibrosis that precedes systolic dysfunction
- high incidence of ventricular arrhythmias.



Smith ED et al. Circulation. 2020

UNIVERSITÀ DEGLI STUDI DI PADOVA

ESC European Society of Cardiology
Europace (2021) **23**, 907–917
doi:10.1093/europace/euaa343

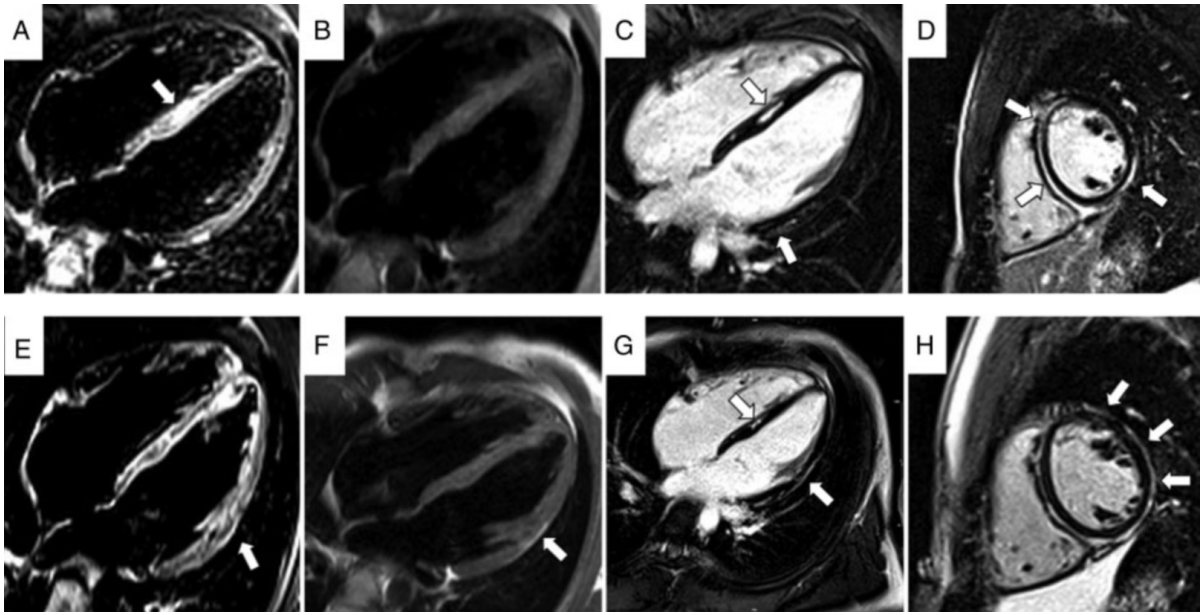
CLINICAL RESEARCH
Channelopathies and cardiomyopathies

'Hot phase' clinical presentation in arrhythmogenic cardiomyopathy

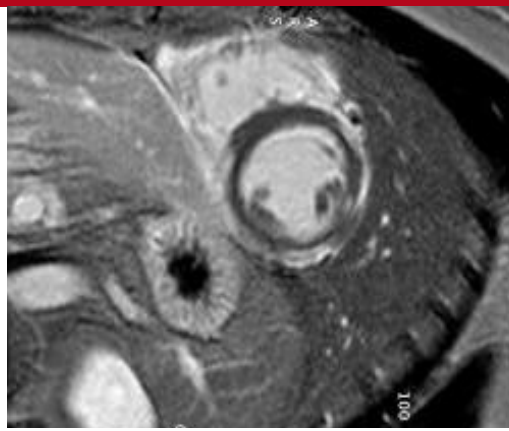
Bariani R et al. Europace 2021

23 ARVC pts with «hot phase» presentation *(out of 506 AC probands and family members)*

- A myocarditis-like picture is a rather uncommon clinical presentation of AC, with a 5% prevalence
- 39% carried a rare putative pathogenic variant in DSP
- LGE was present in all patients (100%), with biventricular distribution in seven (77%) and LV in two (22%).



Clinical Case



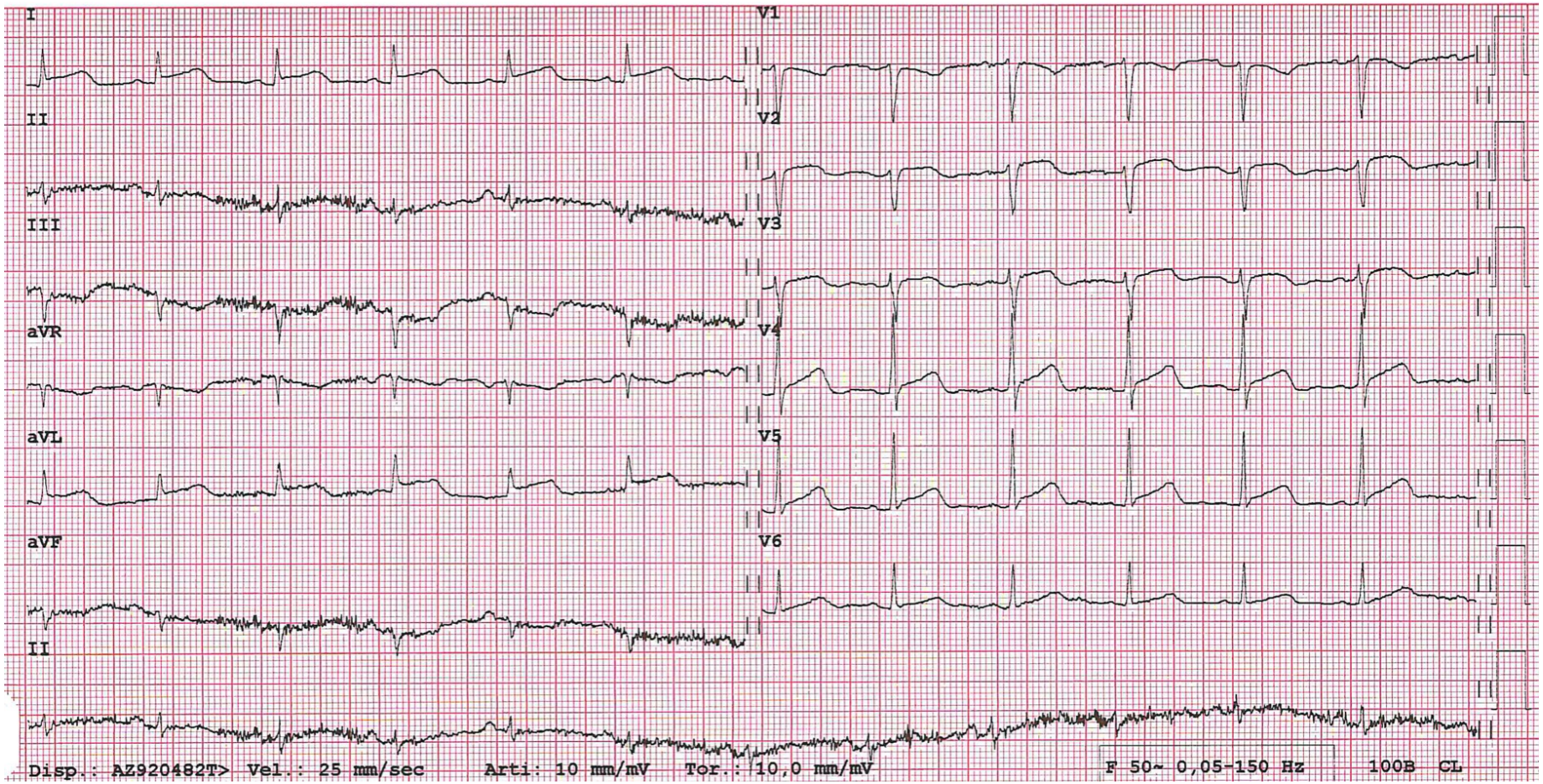
M.A. male, 39-yrs old.

Referred to Emergency Departmente for chest pain.
Vital signs: BP170/115 mmHg, HR 75 bpm, SatO2 100% without oxygen supplementation; no fever.

Past medical History: Previous TBC at 14-yrs old.

CV risk factors: positive family history for ischemic heart disease (mother and grandfather), smoker, hyperomocisteinemia.

Clinical Case



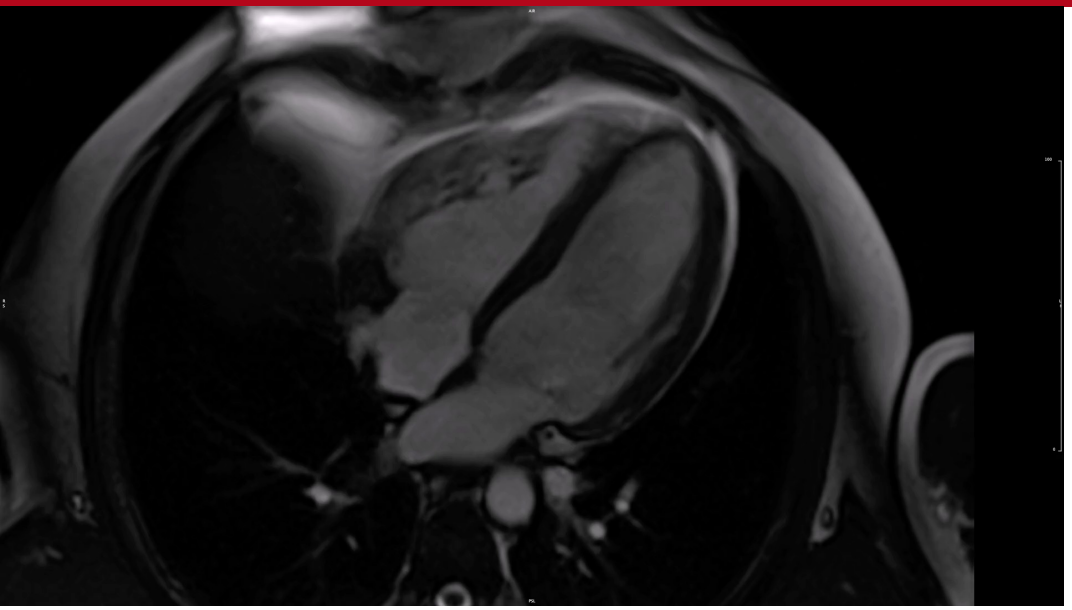
Clinical Case

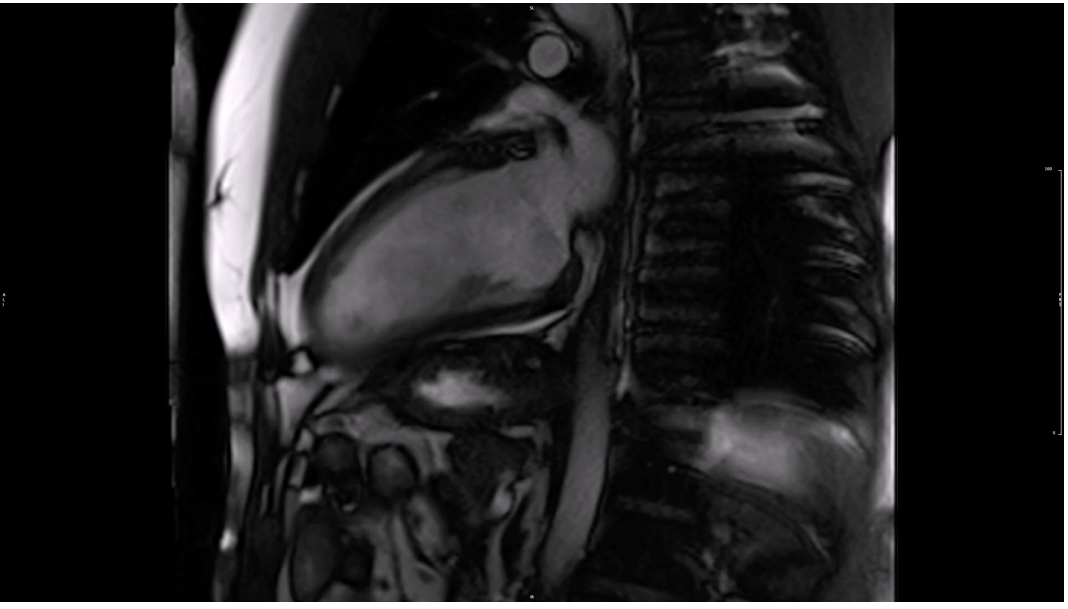
Coronary angiography: no coronary lesions.

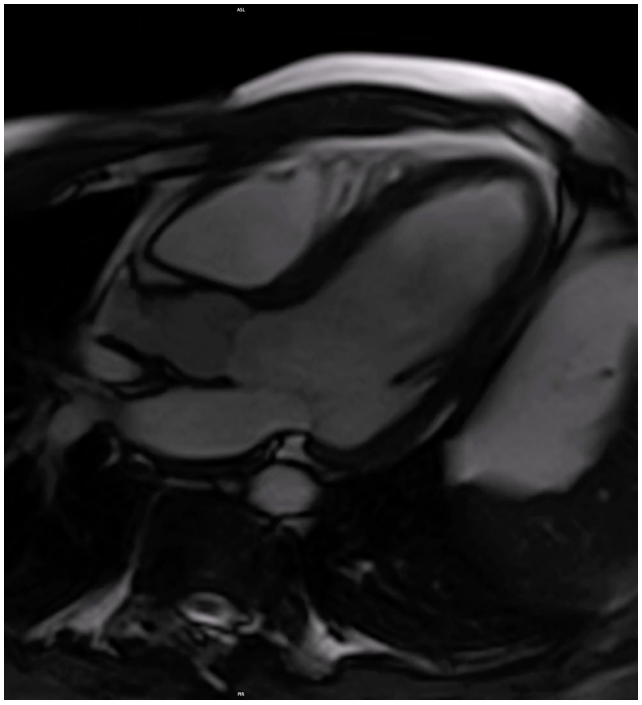
Echocardiogram: Left ventricle with normal dimensione and systolic function, whitout cine abnormalities (EDV 70 ml/m2; EVS 24 ml/m2). Right ventricle with mild dilatation and preserved systolic function, subtricuspid ipokinesia (TDA 14,87 cm2/m2, TSA 9,64 cm2/m2). No valvular diseases. No pulmonary hypertension. No pleural effusion.

Peak of Troponin I: 177600 ng/l (v.n. 0-34 ng/l)

Cine CMR

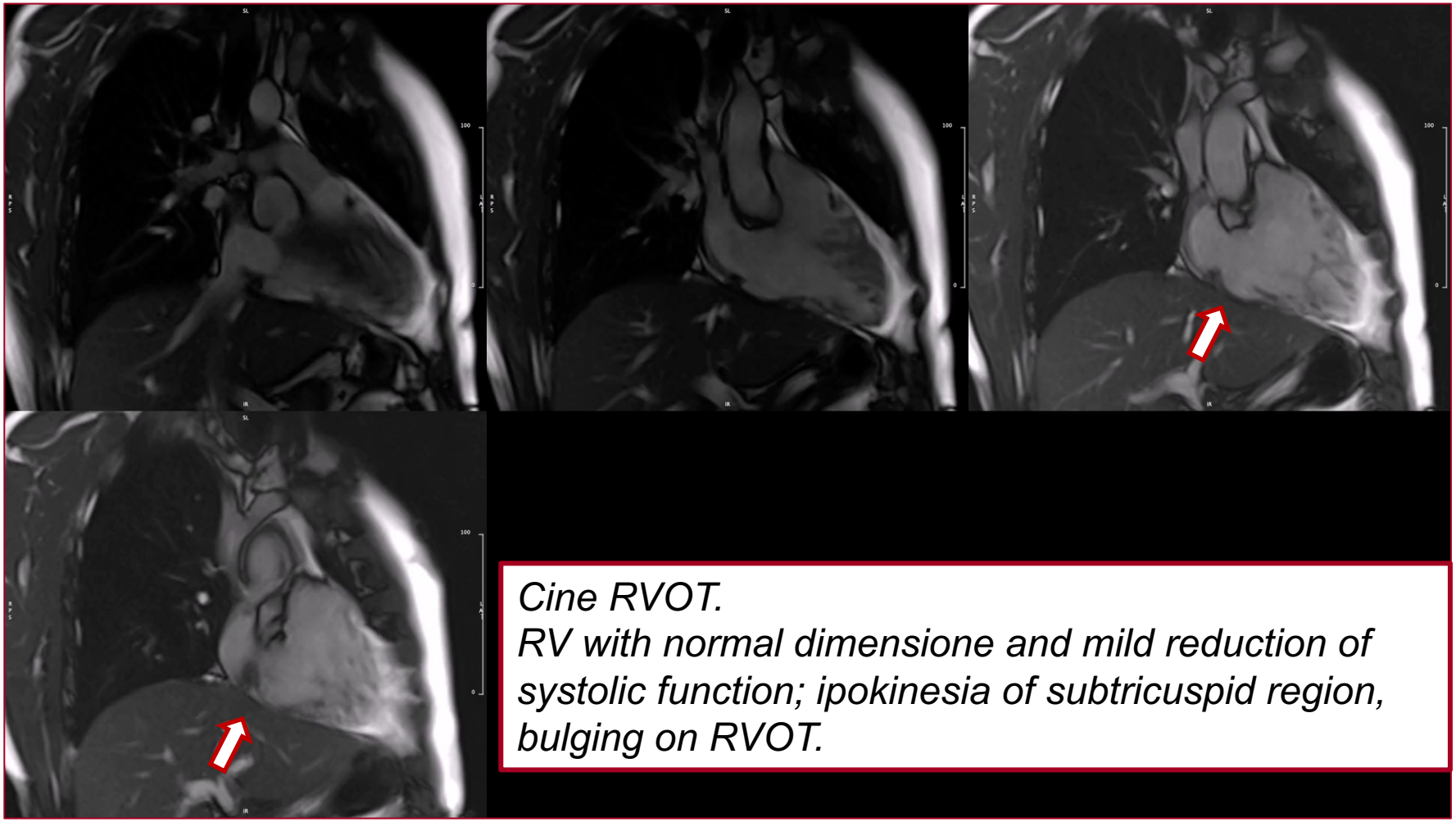






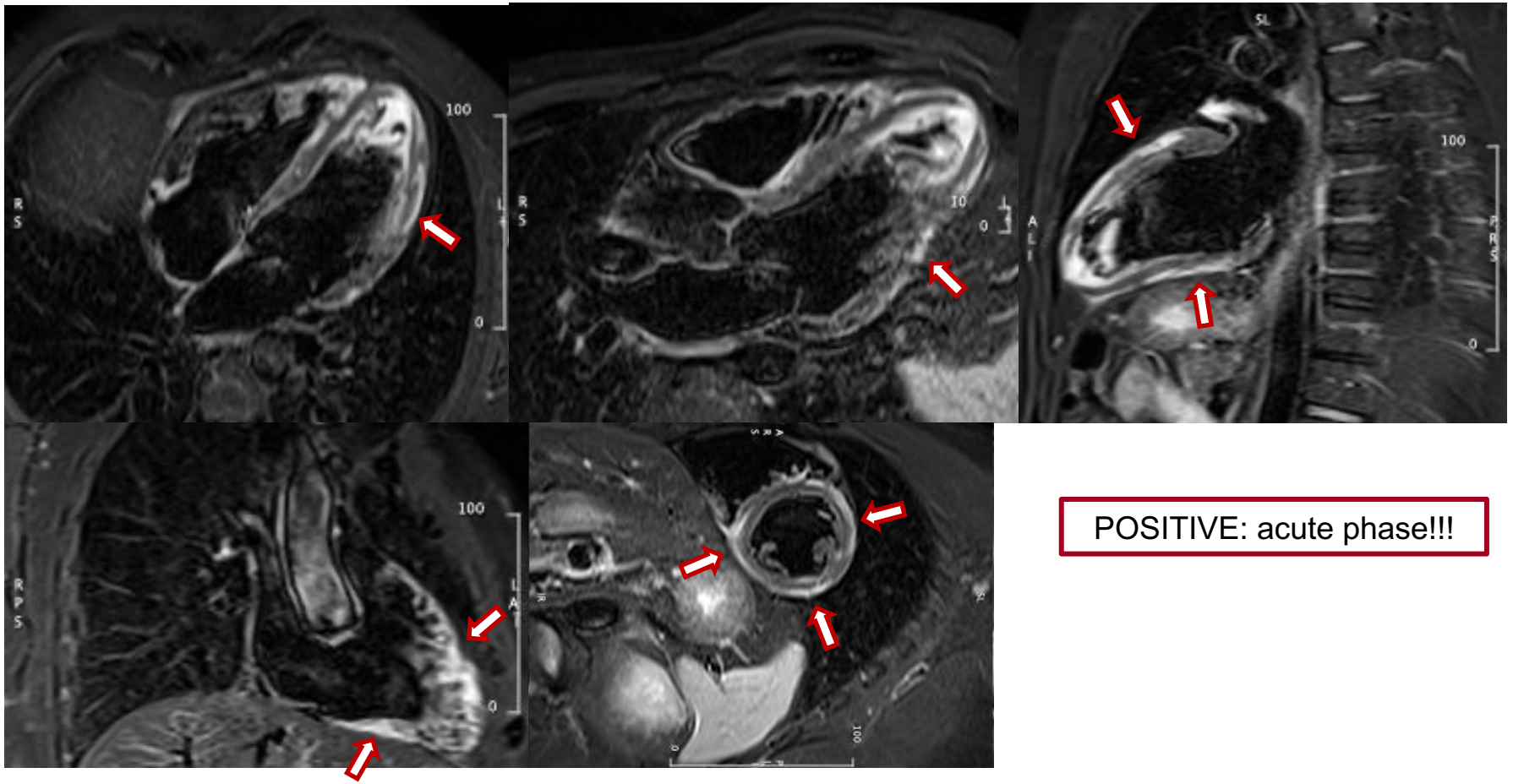
VSX with systolic function at lower limit.
Focal ipokinesia of LV mid lateral wall

Cine CMR



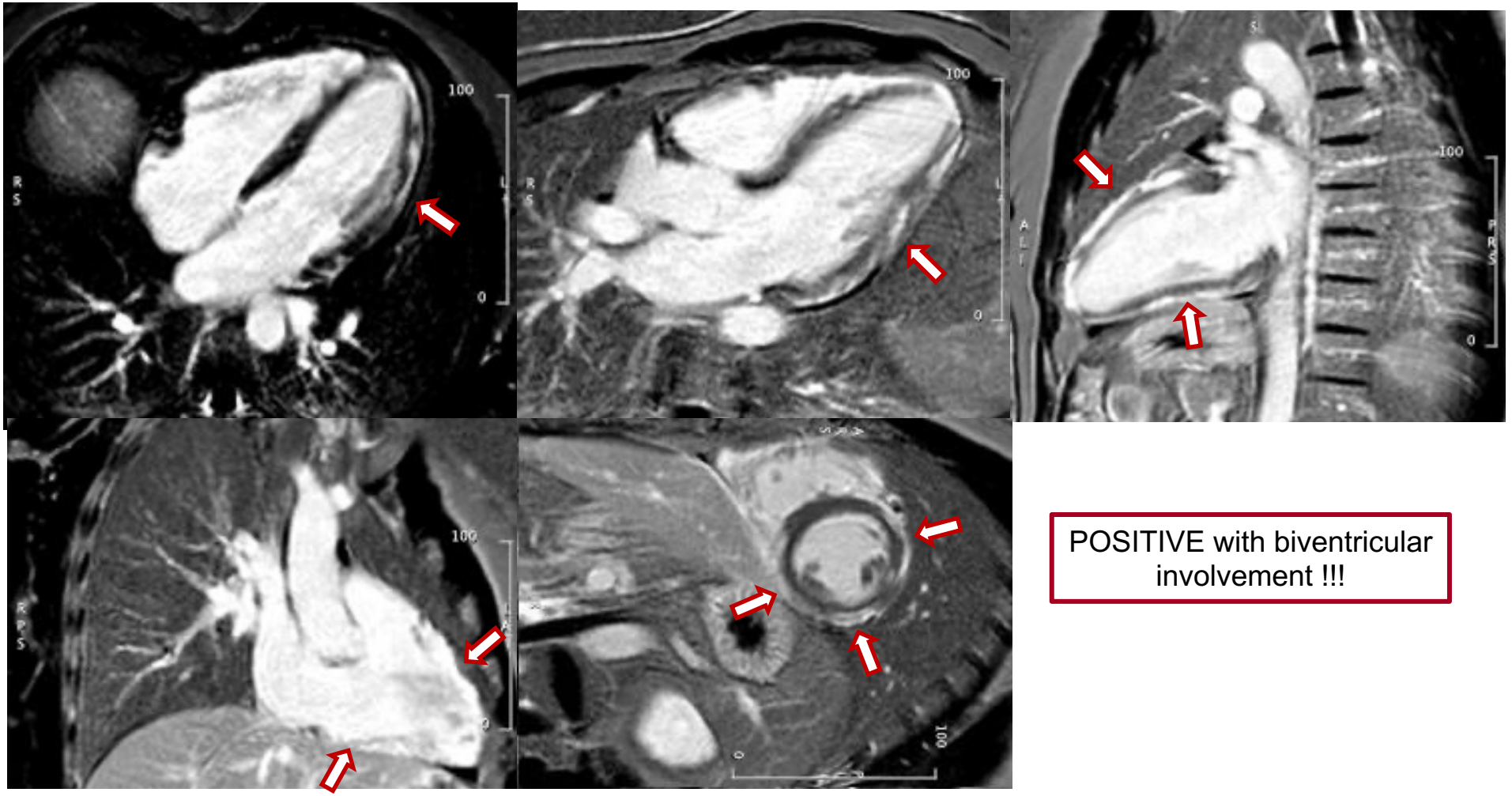
Cine RVOT.
RV with normal dimensione and mild reduction of systolic function; ipokinesia of subtricuspid region, bulging on RVOT.

Edema T2w



POSITIVE: acute phase!!!

Post Contrast LGE



POSITIVE with biventricular involvement !!!

Caso Clinico

Final Report: «…CMR suggestive for acute myocarditis»….But!!!!!

Some days later the patients referred to physicians that a mother's aunt died suddenly at 50-yrs old.

In his past medical history the patients was referred to a Cardiologist for palpitations and on 24-hrs ECG Holter monitoring ventricular premature beats with LBBB were founded!

Caso Clinico

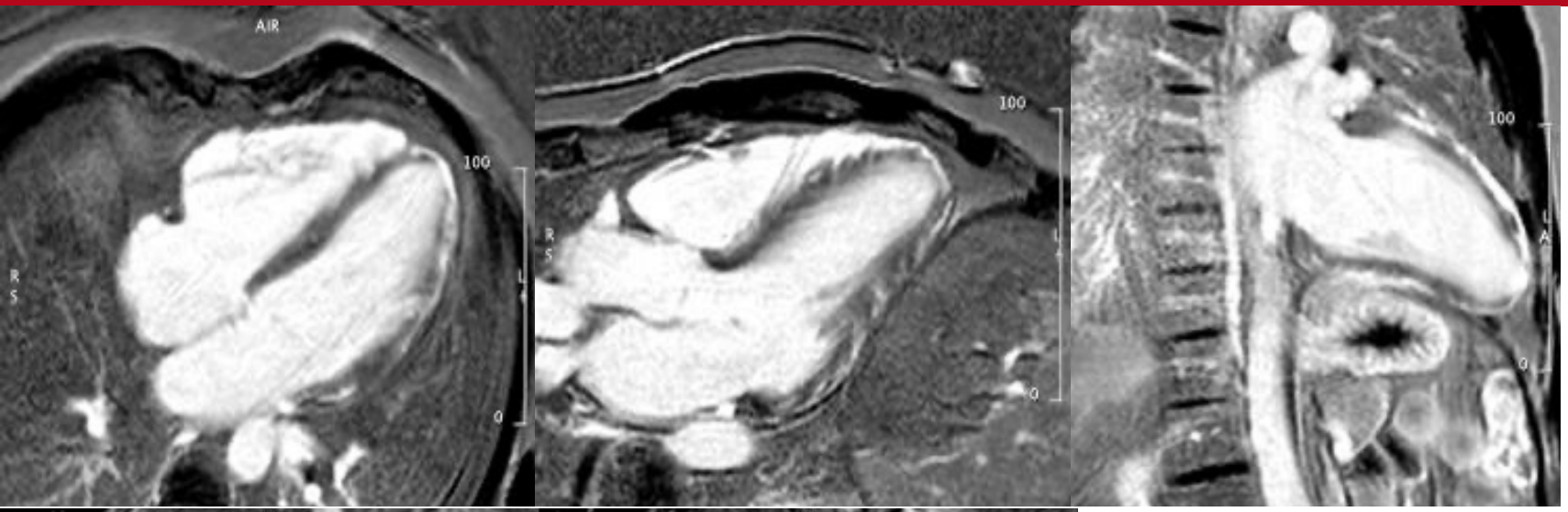
EMB: suggestive for active myocites. Negative virus

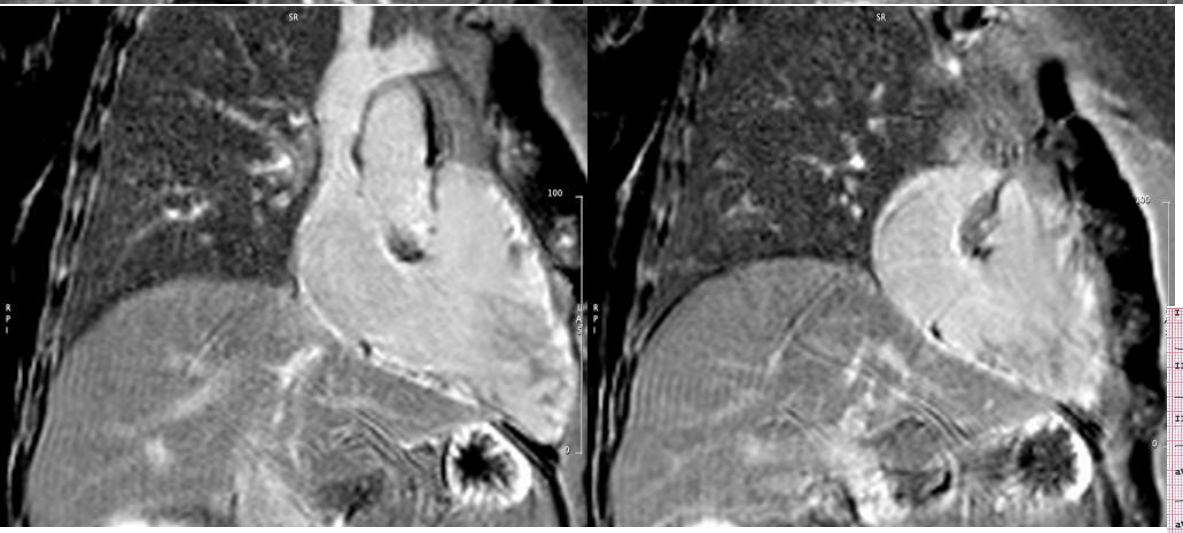
CMR + EMB
Clinical Conclusion: **possible hot-phase of an arrhythmogenic cardiomiopathy**

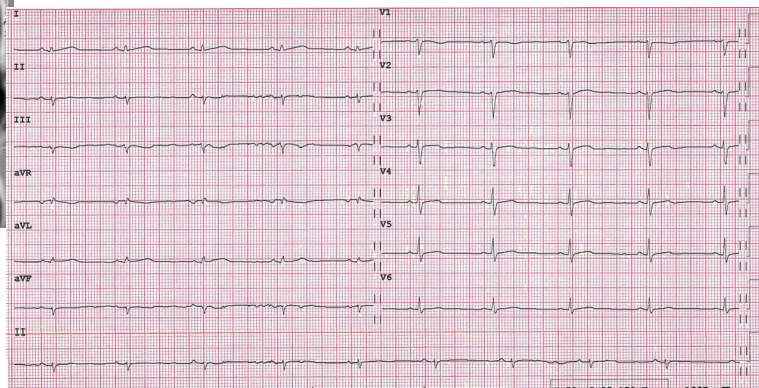
Indication for FU CMR after 6 months and genetic test.

Genetic analysis
A rare variant c.c. 1652-1G>T introne 11 of the Gene DSC2 (desmocollin).

CMR: follow-up after 6 months





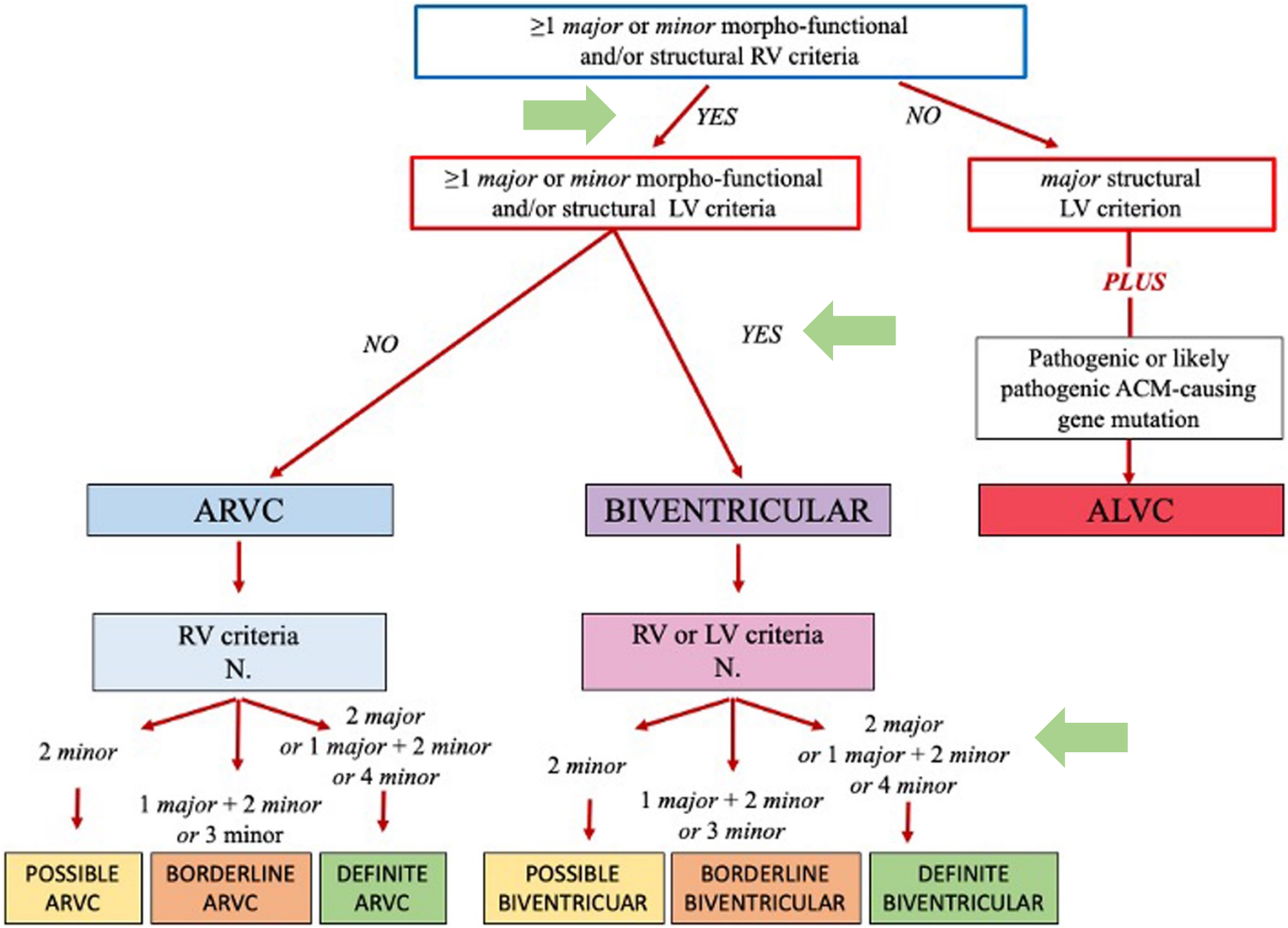


The 2020 International Criteria for Diagnosis of ALVC

Category	Diagnostic criteria
I. Morpho-functional ventricular abnormalities	*Minor* • Global LV systolic dysfunction* (depression of LV EF or reduction of echocardiographic global longitudinal strain), with or without LV dilatation (increase of LV EDV according to the imaging test specific nomograms for age, sex, and BSA) *Minor* • Regional LV hypokinesia or akinesia of LV free wall, septum, or both
II. Structural myocardial abnormalities	*Major* • LV LGE (stria pattern) of ≥1 Bull's Eye segment(s) (in 2 orthogonal views) of the free wall (subepicardial or midmyocardial), septum, or both (excluding septal junctional LGE)
III. Repolarization abnormalities	*Minor* • Inverted T waves in left precordial leads (V_4–V_6) (in the absence of complete LBBB)
IV. Depolarization abnormalities	*Minor* • Low QRS voltages (<0.5 mV peak to peak) in limb leads (in the absence of obesity, emphysema, or pericardial effusion)
V. Ventricular arrhythmias	*Minor* • Frequent ventricular extrasystoles (>500 per 24 h), nonsustained or sustained ventricular tachycardia with a RBBB morphology (excluding the "fascicular pattern")
VI. Family history/genetics	*Major* • ACM confirmed in a first-degree relative who meets diagnostic criteria • ACM confirmed pathologically at autopsy or surgery in a first-degree relative • Identification of a pathogenic or likely pathogenetic ACM mutation in the patient under evaluation *Minor* • History of ACM in a first-degree relative in whom it is not possible or practical to determine whether the family member meets diagnostic criteria • Premature sudden death (<35 y of age) because of suspected ACM in a first-degree relative • ACM confirmed pathologically or by diagnostic criteria in second-degree relative

Corrado D, et al., J Am Heart Assoc. 2021 Sep

Work-up diagnostico



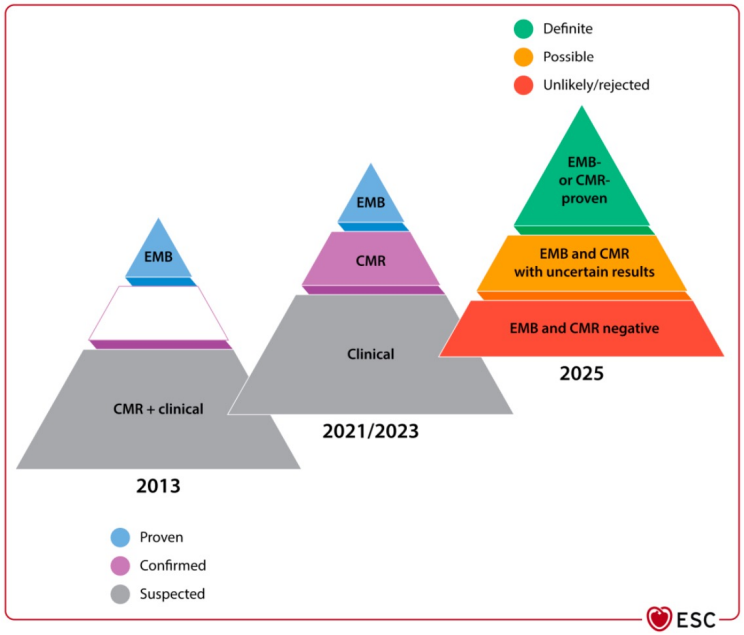
Corrado D, et al., J Am Heart Assoc. 2021 Sep

ESC European Society of Cardiology
European Heart Journal (2025) **00**, 1–90
https://doi.org/10.1093/eurheartj/ehaf192

2025 ESC Guidelines for the management of myocarditis and pericarditis

Figure 2

Paradigm change in the clinical diagnosis of myocarditis



ESC European Society of Cardiology
European Heart Journal (2025) **00**, 1–90
https://doi.org/10.1093/eurheartj/ehaf192

2025 ESC Guidelines for the management of myocarditis and pericarditis

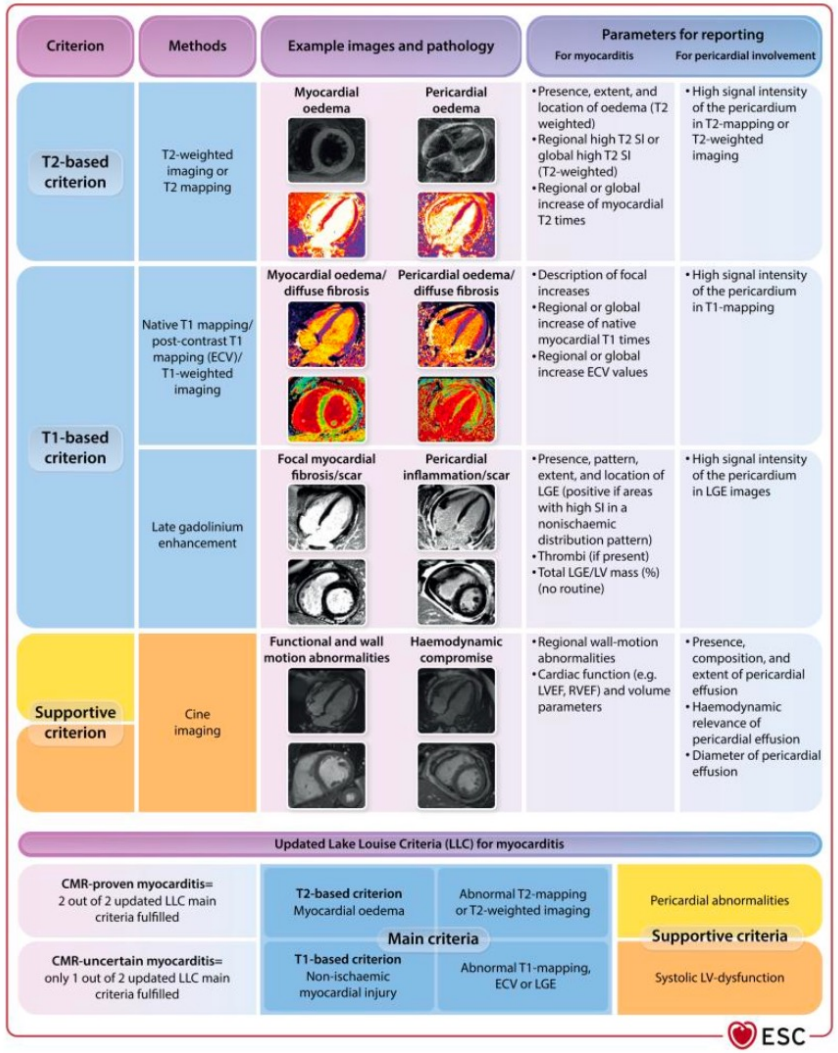
Table S5 Capabilities of multimodality imaging in inflammatory myopericardial syndrome

Modality		Echocardiography			CMR					^{18}F-FDG-PET	CT
technique		2D/3D	Strain	Doppler	Cine	LGE	T1 mapping	T2 mapping/ T2 weighted	Overview images (coverage thorax)	^{18}F-FDG-PET	
Myocardium	**Morphology/function**										
	LV function (global/segmental)	+++/+++	+++/++	++/++	+++/+++					+/+	+/+
	RV function (global/segmental)	+++/+++	++/++	+/+	+++/+++						+/-
	Tissue characteristics										
	Scar		+	+	+	+++	++			+++	++
	Oedema	+			+	+	++	+++			
	Inflammatory reaction					+	+++	+++		+++	
Pericardium	Inflammation					+++	++	+++		+	
	Calcification	+			+	+	+	+	+		+++
	Effusion	+++			+++	+++	++	++	+		++
	Diastolic dynamics	++		+++	++						
	Thickness/adhesions	+/++			+++/+++	+++	+	+	+/–		+++/+
	Masses	+++			+++	+++	+	+	+	+	++
Extracardiac findings		+			+	+	+	+	+++	+++	+++

2D, two-dimensional; 3D, three-dimensional; CMR, cardiovascular magnetic resonance; CT, computed tomography; [18F]-fluorodeoxyglucose positron emission tomography; LGE, late gadolinium enhancement; LV, left ventricle; RV, right ventricle; +++=excellent; ++=good; +=sufficient.

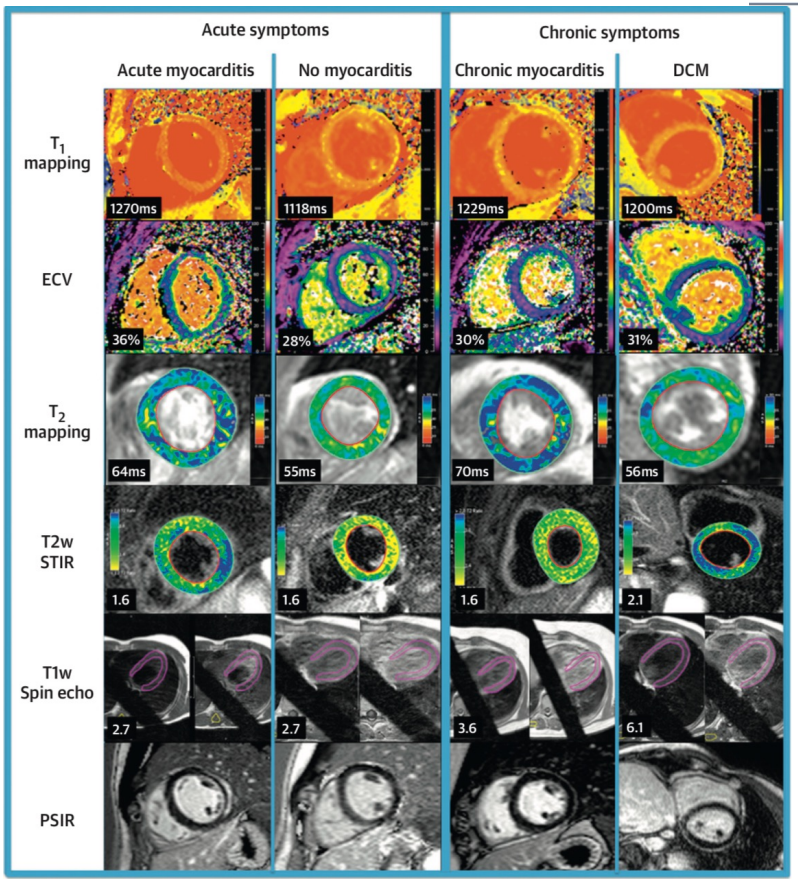
ESC European Society of Cardiology
European Heart Journal (2025) **00**, 1–90
https://doi.org/10.1093/eurheartj/ehaf192

2025 ESC Guidelines for the management of myocarditis and pericarditis



European Heart Journal (2025) 00, 1–90

CMR: DIAGNOSTIC CRITERIA



THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation

Expert Recommendations

A single positive criterion can support diagnosis of myocardial inflammation if clinical suspicion is strong

CMR cannot identify specific cause of myocardial inflammation, and the histological subtypes, although regional distribution of inflammatory changes in the tissue provide diagnostic clues

CONCLUSIONS

- Tra le metodiche di Imaging
  - l'ecocardiogramma è il first step >> diagnosi differenziale
  - La CMR riveste un ruolo centrale
  - La TC al momento per rule out coronaropatia
- La CMR è
  - clinicamente fondamentale e la sua applicabilità dipende dal contesto clinico
  - Non fornisce diagnosi di certezza utile alla terapia specifica
  - Complementare alla BEM in molti casi
- Applicabilità nuove linee guida: revisione modello esecuzione-refertazione CMR

CONCLUSIONS

- CMR is the preferred diagnostic tool for acute myocarditis without complications on presentation (preserved/mildly reduce LVEF and no ventricular arrhythmias).
- The application of T2-based and T1-based techniques including mapping increase the accuracy
- The definition of aetiology is not possible by CMR, however its complementary role with EMB is crucial for diagnosis & treatment
- CMR is suggested at 3–6 months of follow-up to demonstrate resolution of edema (to modulate immunosuppression if any or to resume intense physical activities) and define the final LGE extent.
- A single episode of myocarditis can be the first manifestation of a cardiomyopathy (LGE@FU: expression of post-inflammatory scar or cardiomyopathic-scar?)