XI Reunión. Estado del Arte en
INSUFICIENCIA CARDIACA
PRÁCTICA CLÍNICA Y MODELOS ORGANIZATIVOS
Sede: Hotel Meliá MaríaPita, A Coruña
A CORUÑA 27-28 SEPTIEMBRE 2024

XI Meeting. State of the Art in
HEART FAILURE
CLINICAL PRACTICE AND ORGANIZATIONAL MODELS
Venue: Hotel Meliá MaríaPita, A Coruña
ACoruñaHF2024
A CORUÑA 27-28 SEPTEMBER 2024

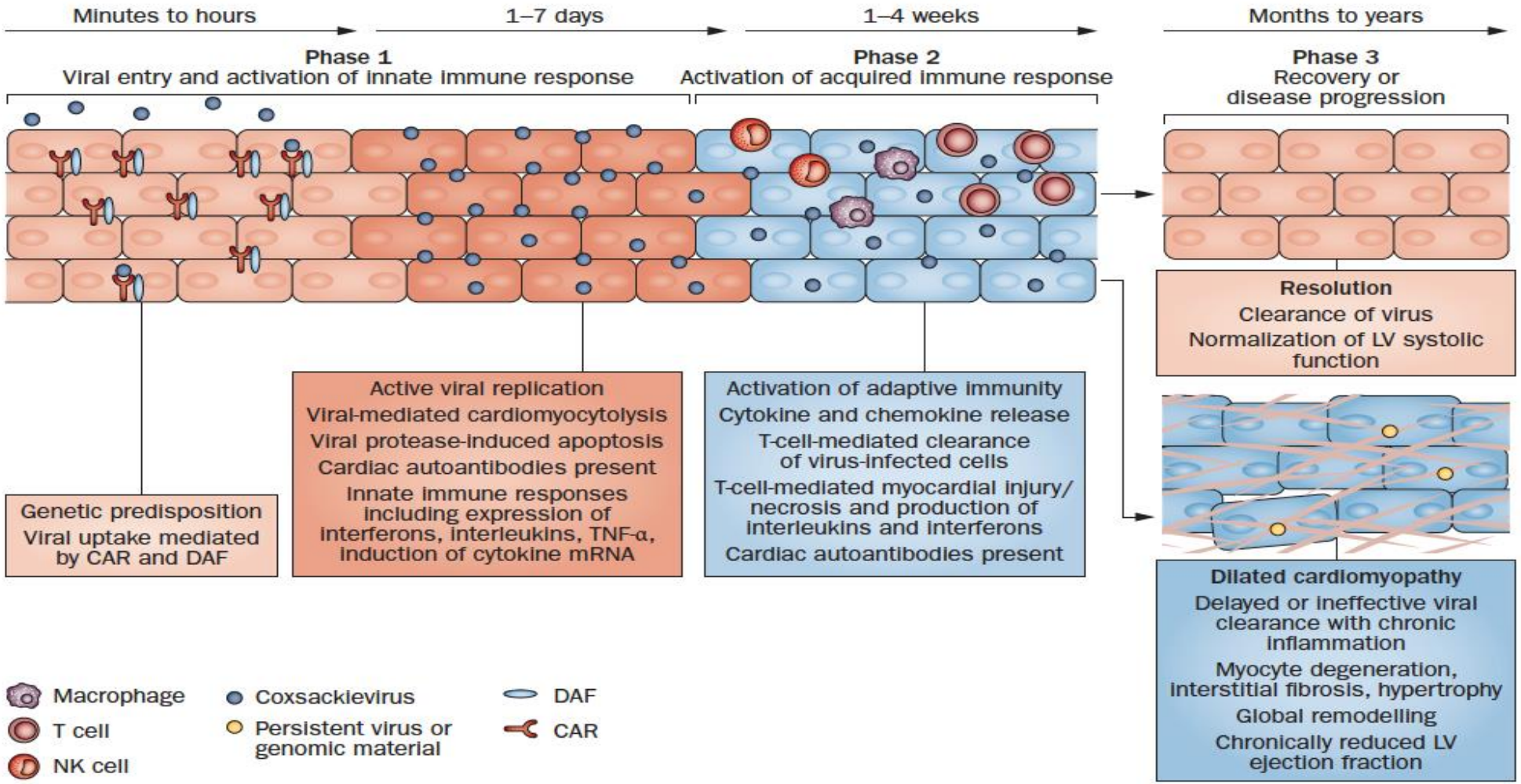
Myocarditis: Challenges in diagnosis, risk stratification and therapy

Antonio Cannata
King's College Hospital and King's College London

Viral myocarditis—diagnosis, treatment options, and current controversies

Ari Pollack, Amy R. Kontorovich, Valentin Fuster and G. William Dec

nature REVIEWS CARDIOLOGY
Nat. Rev. Cardiol. **12**, 670–680 (2015)



A new old story

Myocarditis: Unresolved Issues in Diagnosis and Treatment

S. S. MAZE, M.B., Ch.B., R. J. ADOLPH, M.D., F.A.C.C.

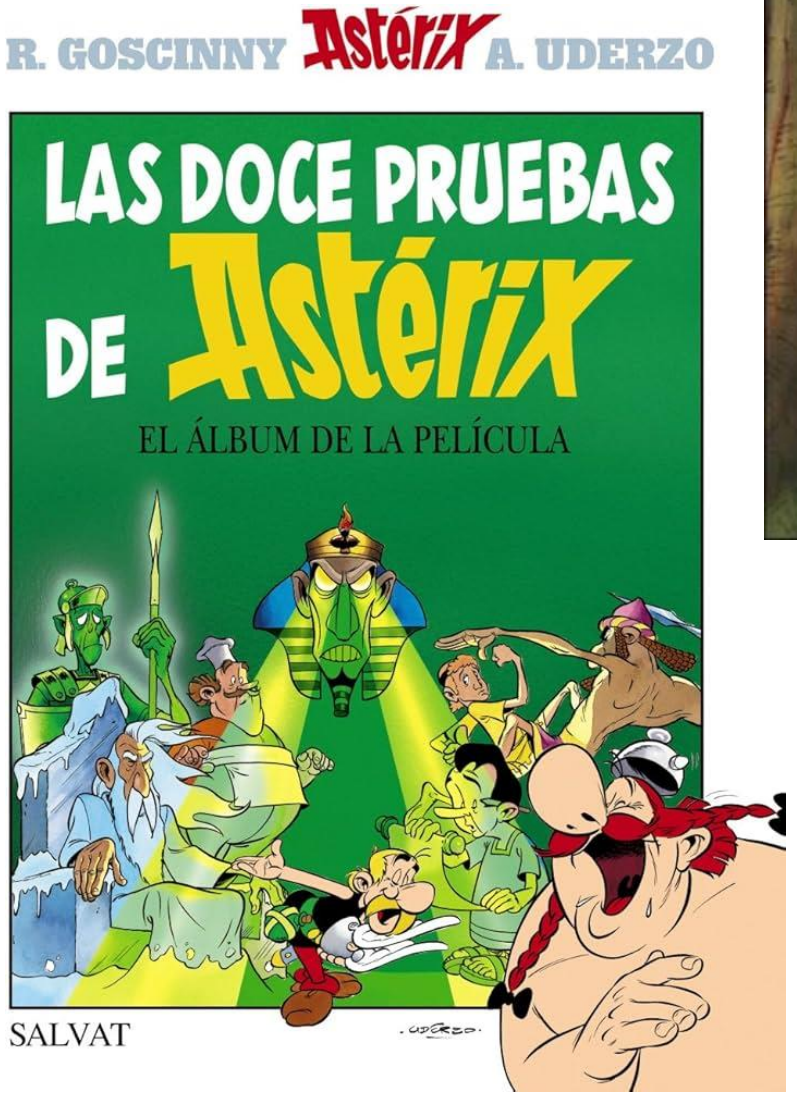
Division of Cardiology, Department of Internal Medicine, University of Cincinnati Medical Center, Cincinnati, Ohio, USA

Clin. Cardiol. Vol. 13, February 1990

my
’90s

A Coruña
Heart Failure
Academy

Outline of the presentation



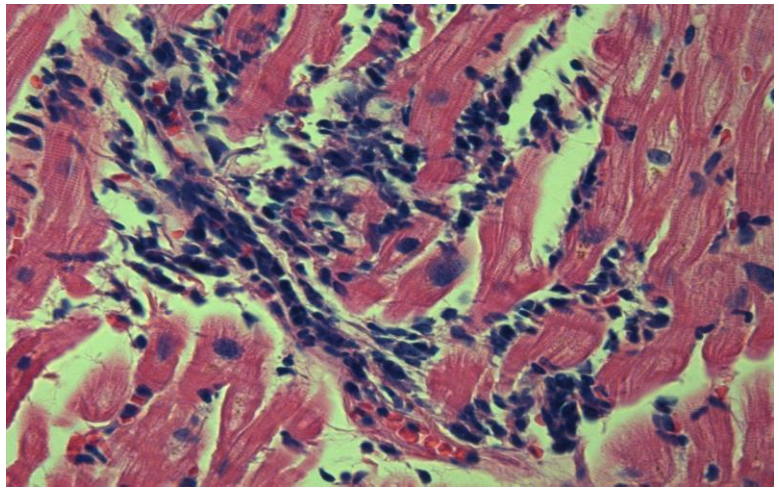
A Coruña Heart Failure Academy

1st challenge: an apparently simple definition

Circulation. 1996 Mar 1;93(5):841-2.

Report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force on the Definition and Classification of cardiomyopathies.

Richardson P, McKenna W, Bristow M, Maisch B, Mautner B, O'Connell J, Olsen E, Thiene G, Goodwin J, Gyarfas I, Martin I, Nordet P.



Myocarditis is an inflammatory disease of the myocardium which involves the myocytes, the interstitium and the vasculature.

The diagnosis is through histopathological and histochemical criteria

1st challenge: an apparently simple definition

Subacute myocarditis

Virus-triggered myocarditis

Sarcoiditic myocarditis

Virus-induced myocarditis

Viral myocarditis

Immune checkpoint-associated myocarditis

Perimyocarditis

Active myocarditis

Myocarditis with pericardial involvement

Virus-mediated myocarditis

Infarct-like myocarditis

Drug-induced myocarditis

Hypersensitivity myocarditis

Acute myocarditis

Lymphocytic myocarditis

Eosinophilic myocarditis

Chronic myocarditis

Clinically suspected myocarditis

Infective myocarditis

Fulminant myocarditis

Myopericarditis

Probable acute myocarditis

Borderline myocarditis

Healing myocarditis

Chronic inflammatory cardiomyopathy

Complicated acute myocarditis

Giant cell myocarditis

Virus-positive myocarditis

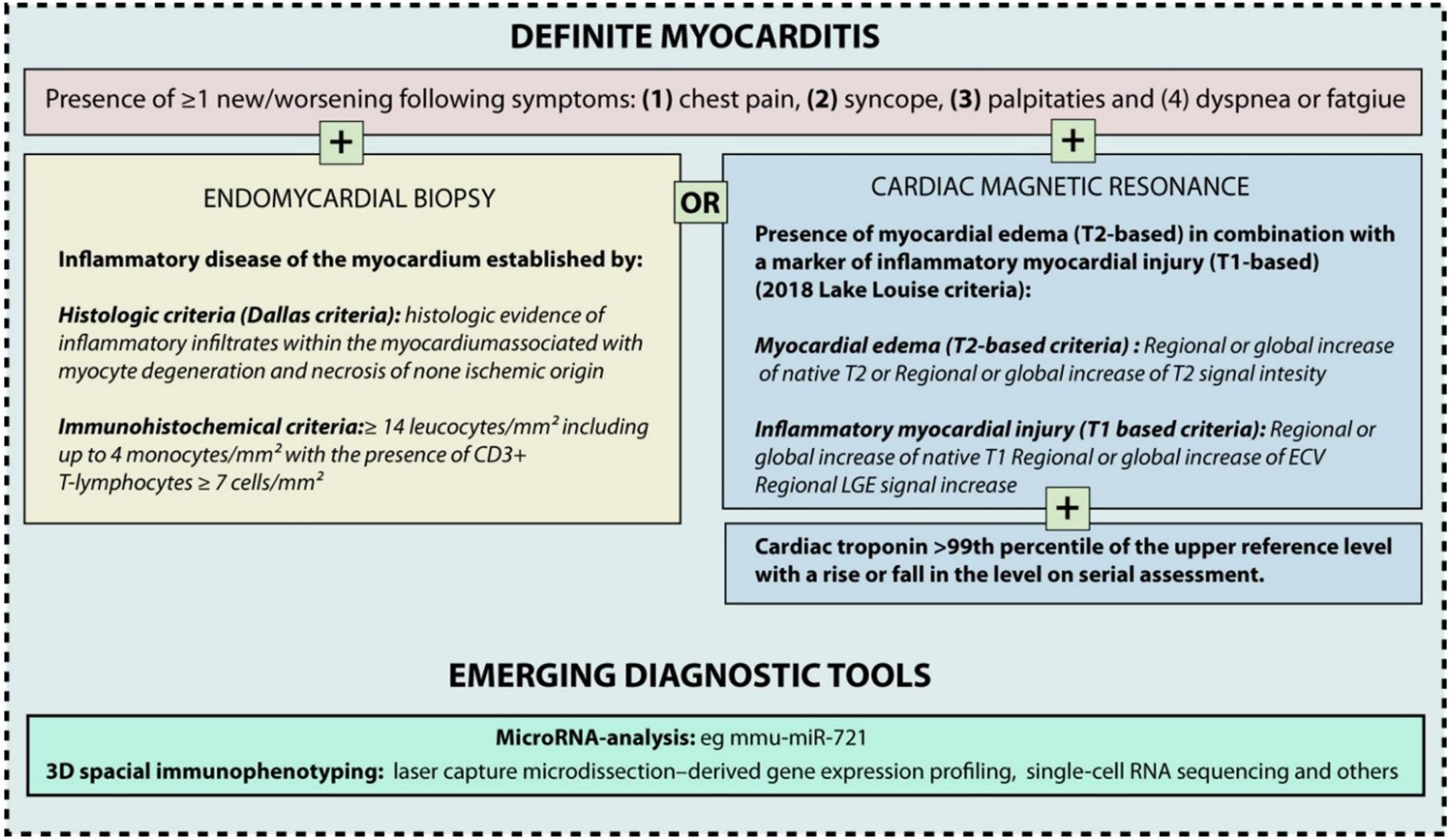
Immune-mediated myocarditis

2nd challenge: an apparently simple classification

According to

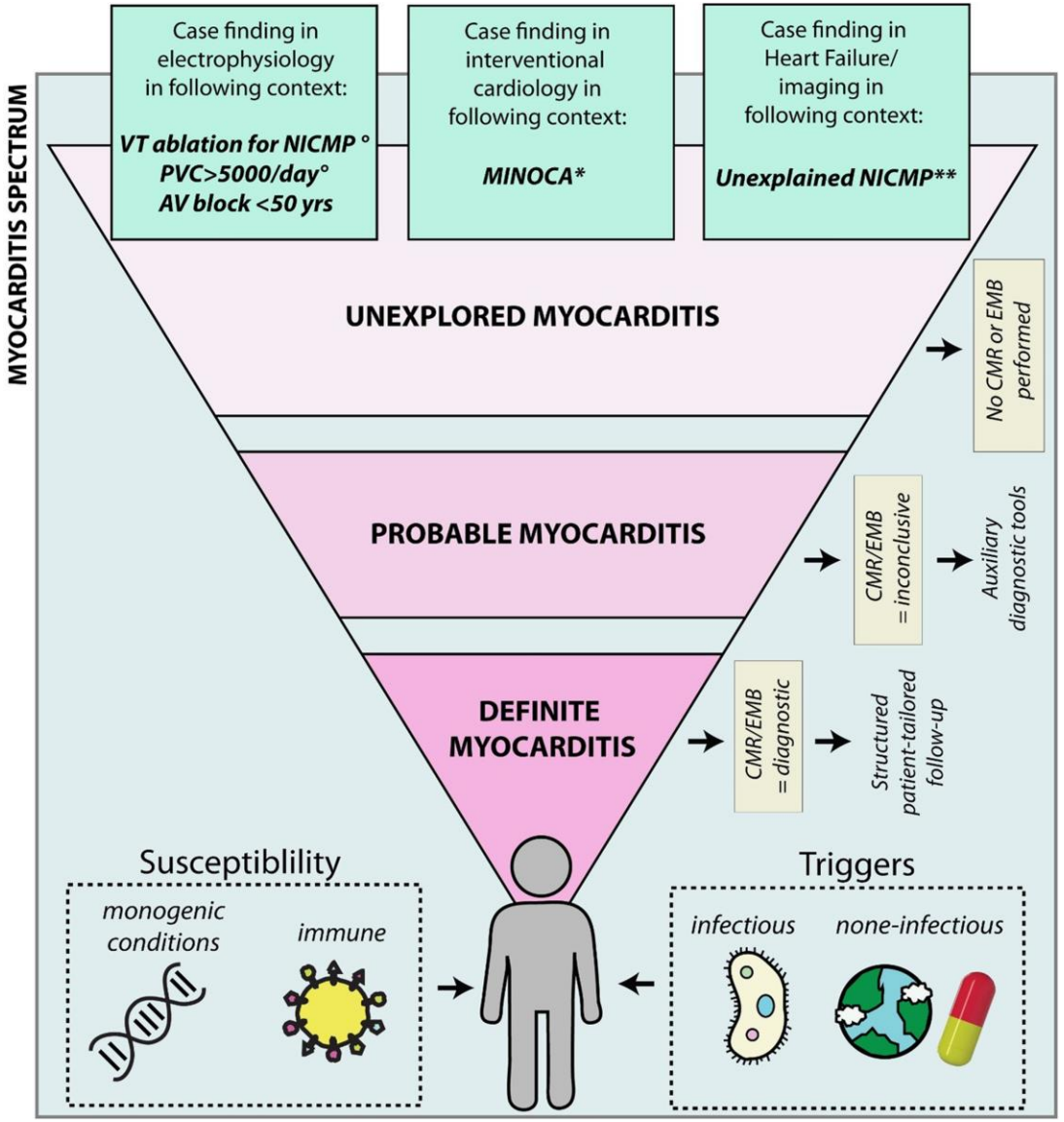
- ***Predominant infiltrate:*** Lymphocytic, eosinophilic, polymorphic, giant cell myocarditis, granulomatous… (but often unknown)
- ***Aetiology:*** Viral myocarditis, autoimmune myocarditis, viral and immune myocarditis, hypersensitivity… (but often unknown)
- ***Clinical presentation:*** Infarct-like, heart failure, arrhythmia (but no evidence for treatment using these criteria)
- ***Clinical course:*** Fulminant, acute, subacute/healing, chronic, complicated/uncomplicated (but no evidence for treatment using these criteria)
- **Risk of adverse events**: low-risk, intermediate, high-risk (but no evidence for treatment using these criteria)

3rd challenge: an apparently simple diagnosis



Martens P et al. J Am Heart Assoc. 2023;12:e031454.

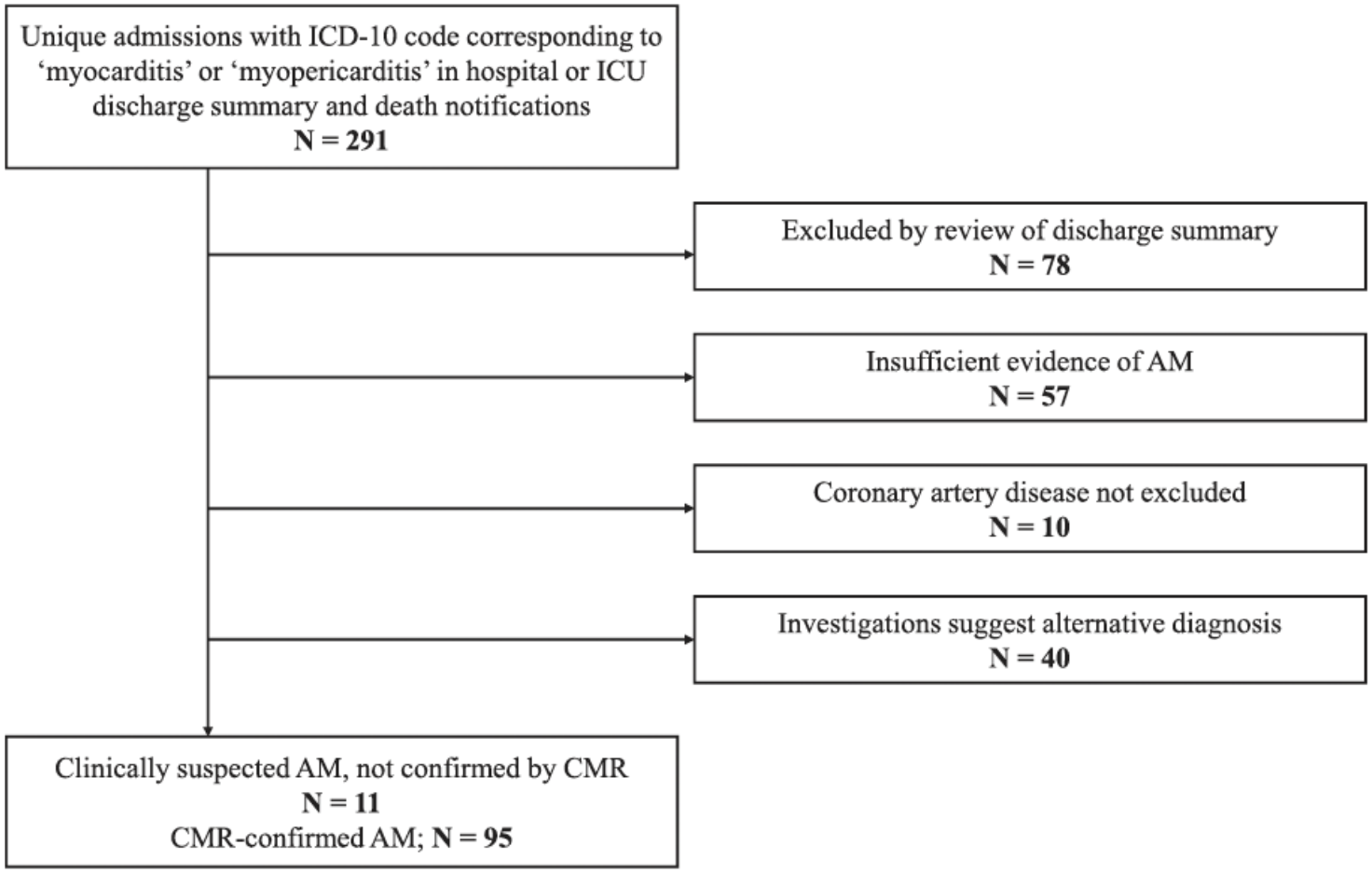
3rd challenge: an apparently simple diagnosis



Martens P et al. J AHA. 2023;12:e031454.

4th challenge: an apparently accurate diagnosis

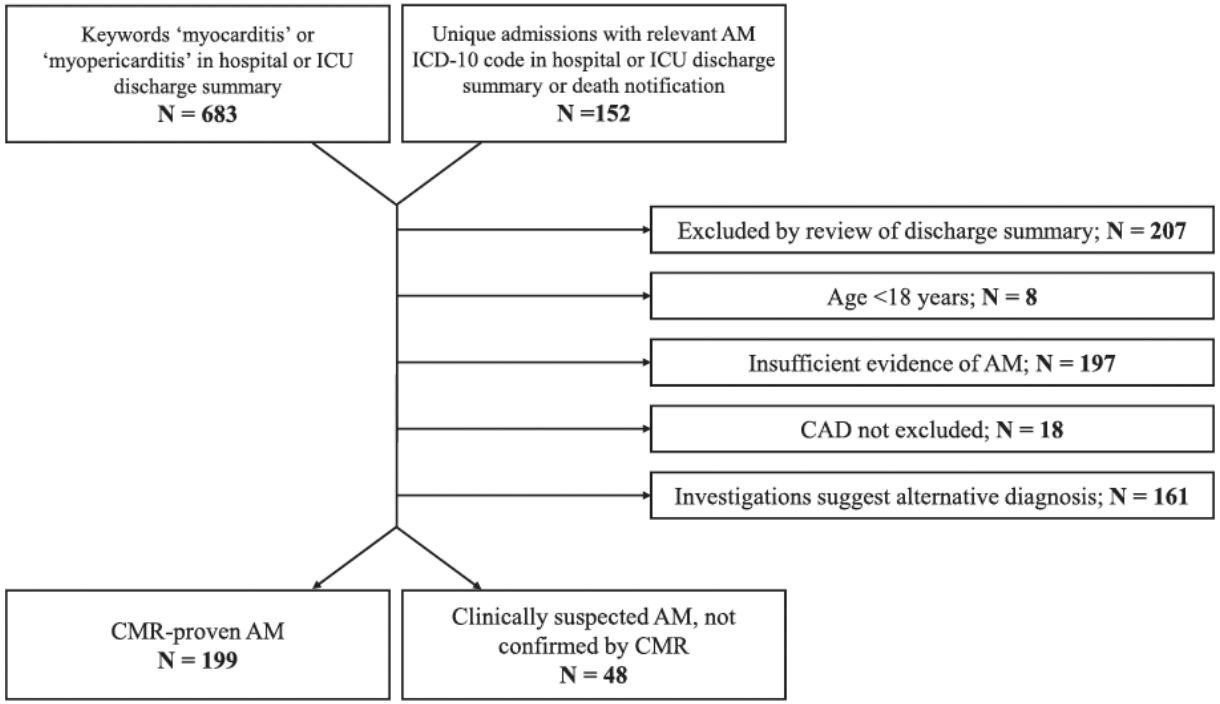
33%

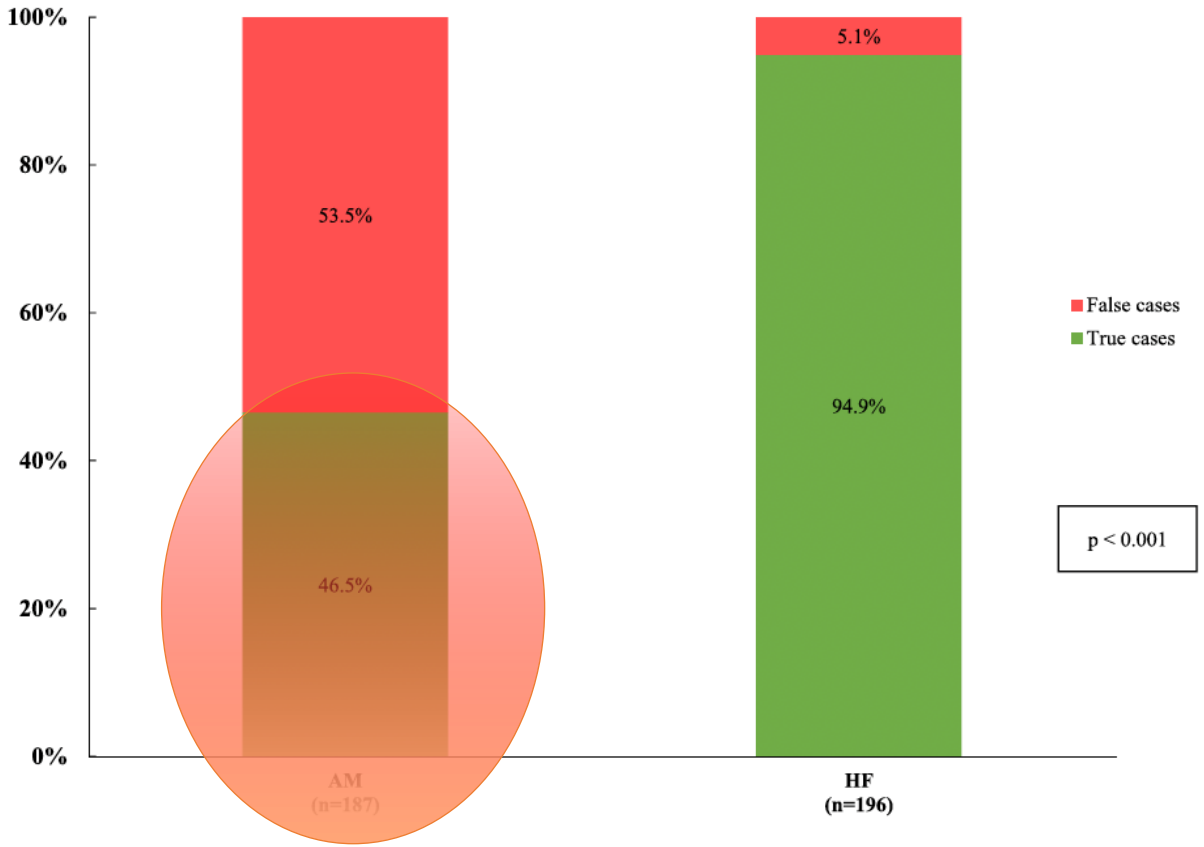


67%

Roy R, Cannata A, Bromage D. EHJ: QCCO 2023

4th challenge: an apparently accurate diagnosis





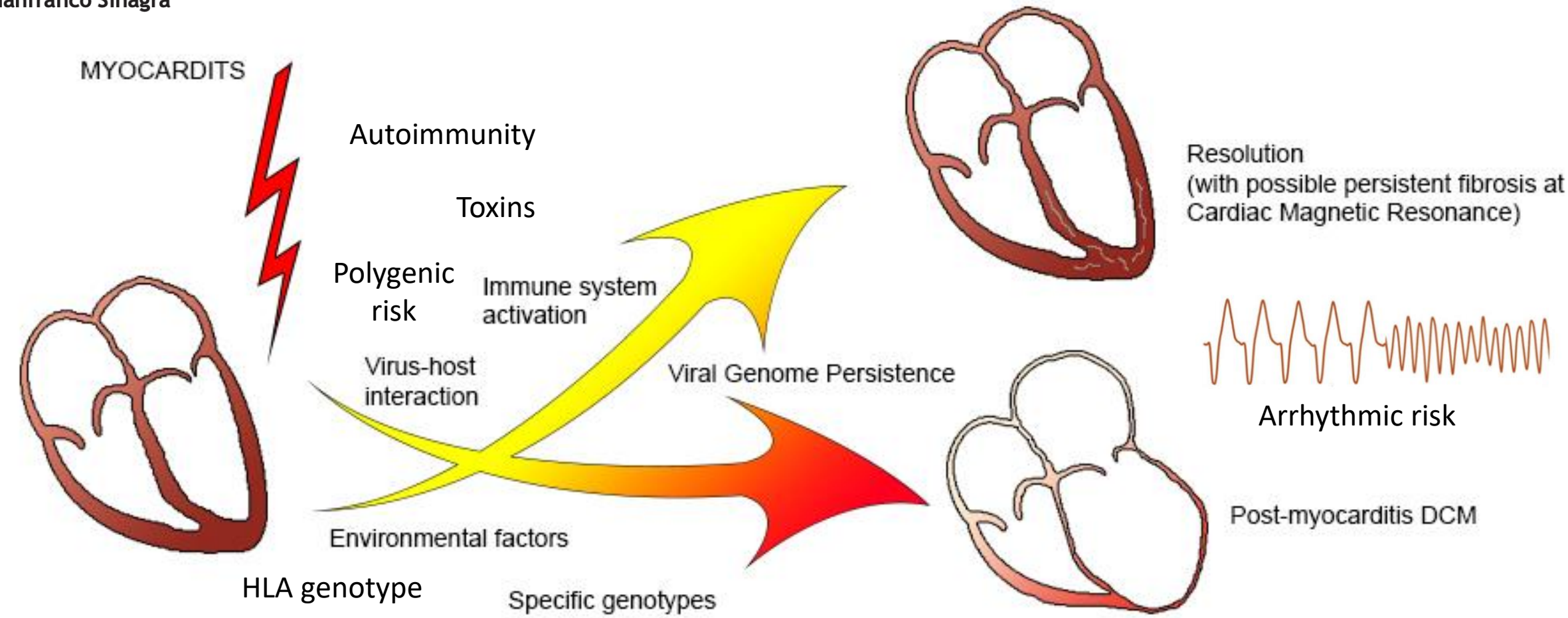
Roy R, Cannata A, Bromage D. EHJ: QCCO 2023

5th challenge: a communicable disease

Myocarditis evolving in cardiomyopathy: when genetics and offending causes work together

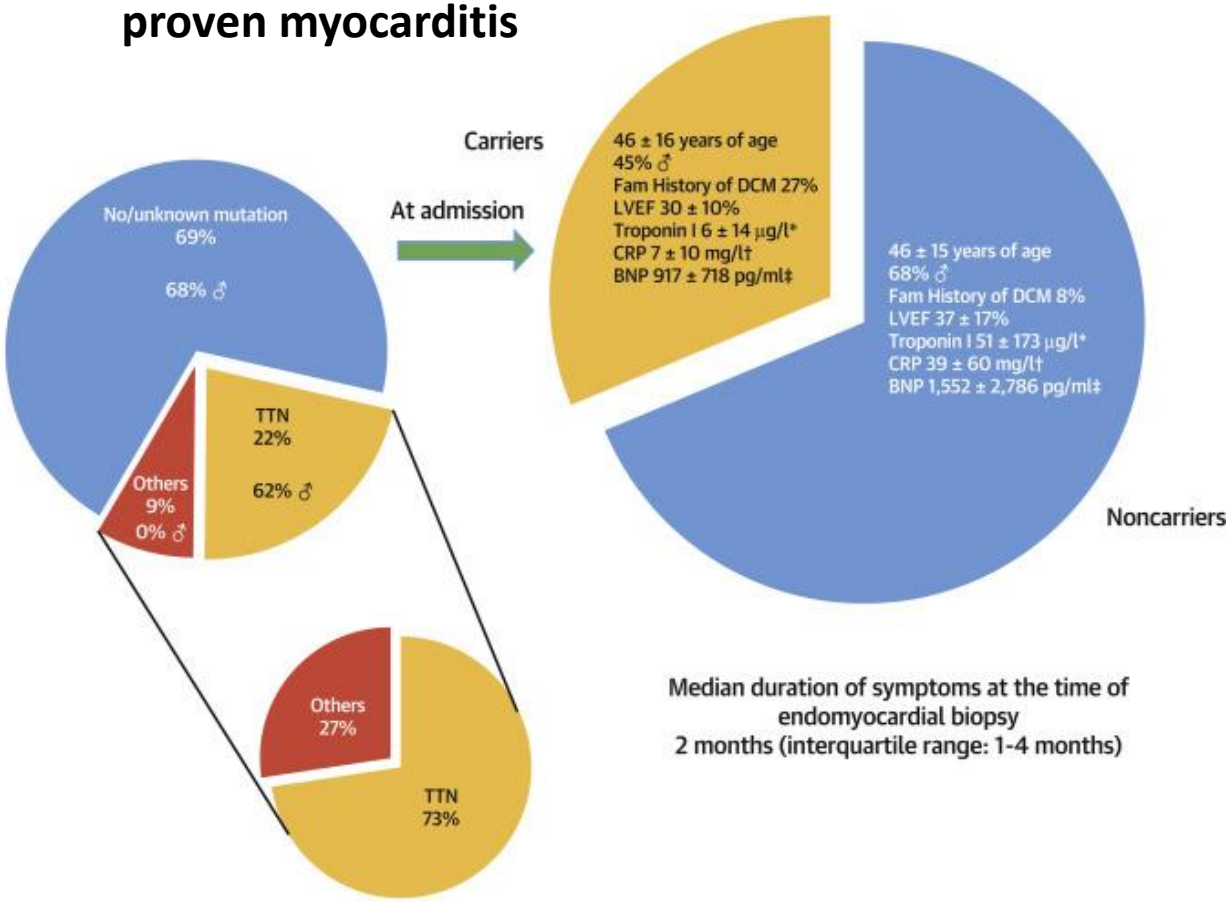
Antonio Cannata', Jessica Artico, Piero Gentile, Marco Merlo, and Gianfranco Sinagra

European Heart Journal Supplements 2019;21:B90–B95

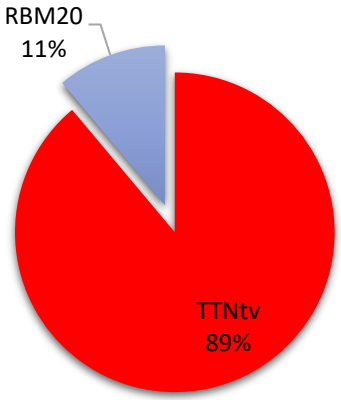


5th challenge: a communicable disease

36 Patients with **biopsy-proven myocarditis**

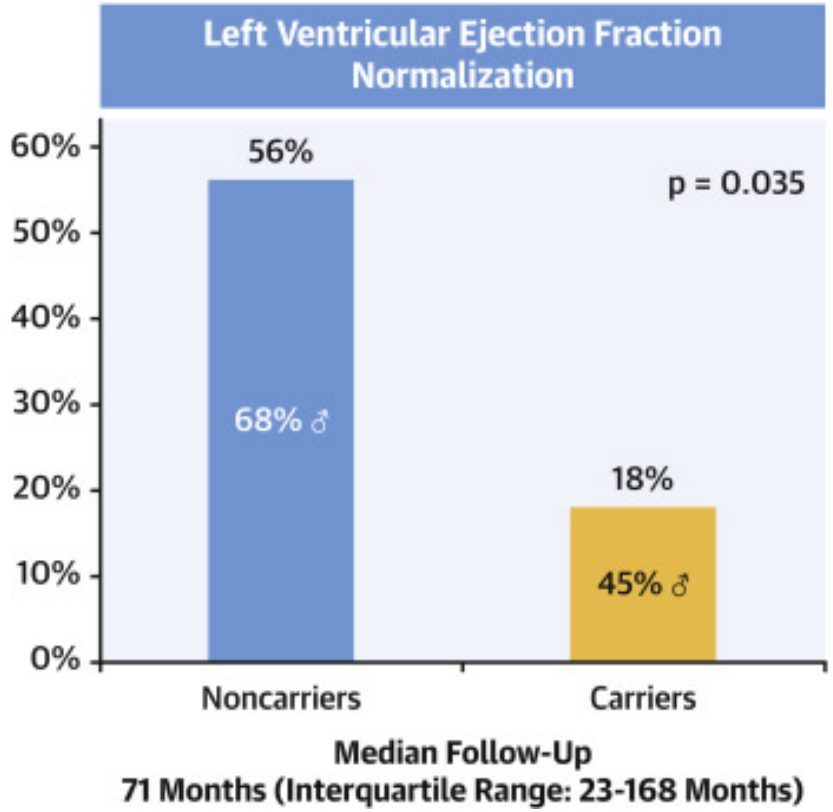


Median duration of symptoms at the time of endomyocardial biopsy
2 months (interquartile range: 1-4 months)



Lymphocytic Myocarditis

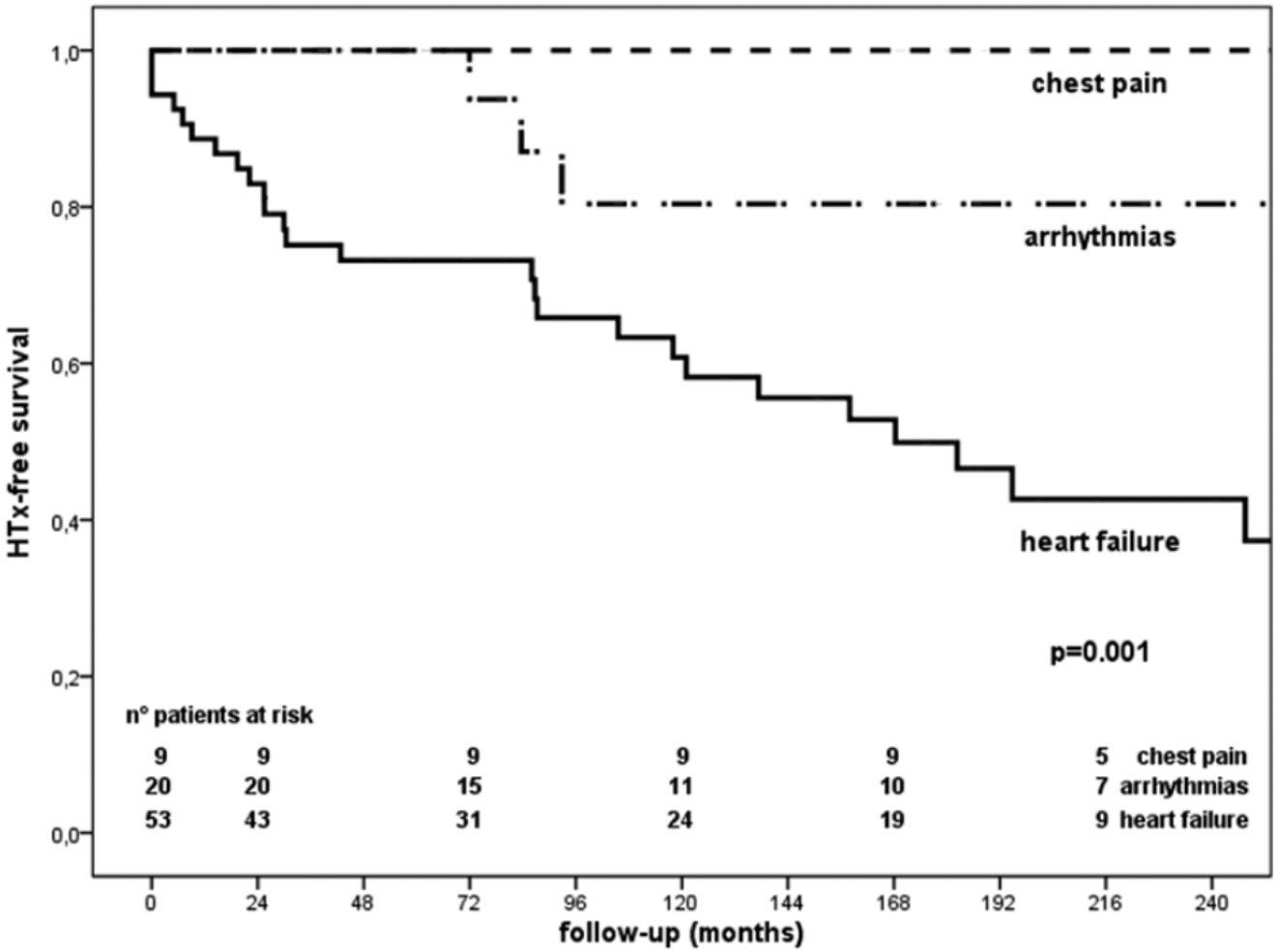
A Genetically Predisposed Disease?



Median Follow-Up
71 Months (Interquartile Range: 23-168 Months)

Artico J et al. JACC 2020;75:3098–3099

6th challenge: an apparently dire prognosis



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association.

Long-Term Evolution and Prognostic Stratification of Biopsy-Proven Active Myocarditis

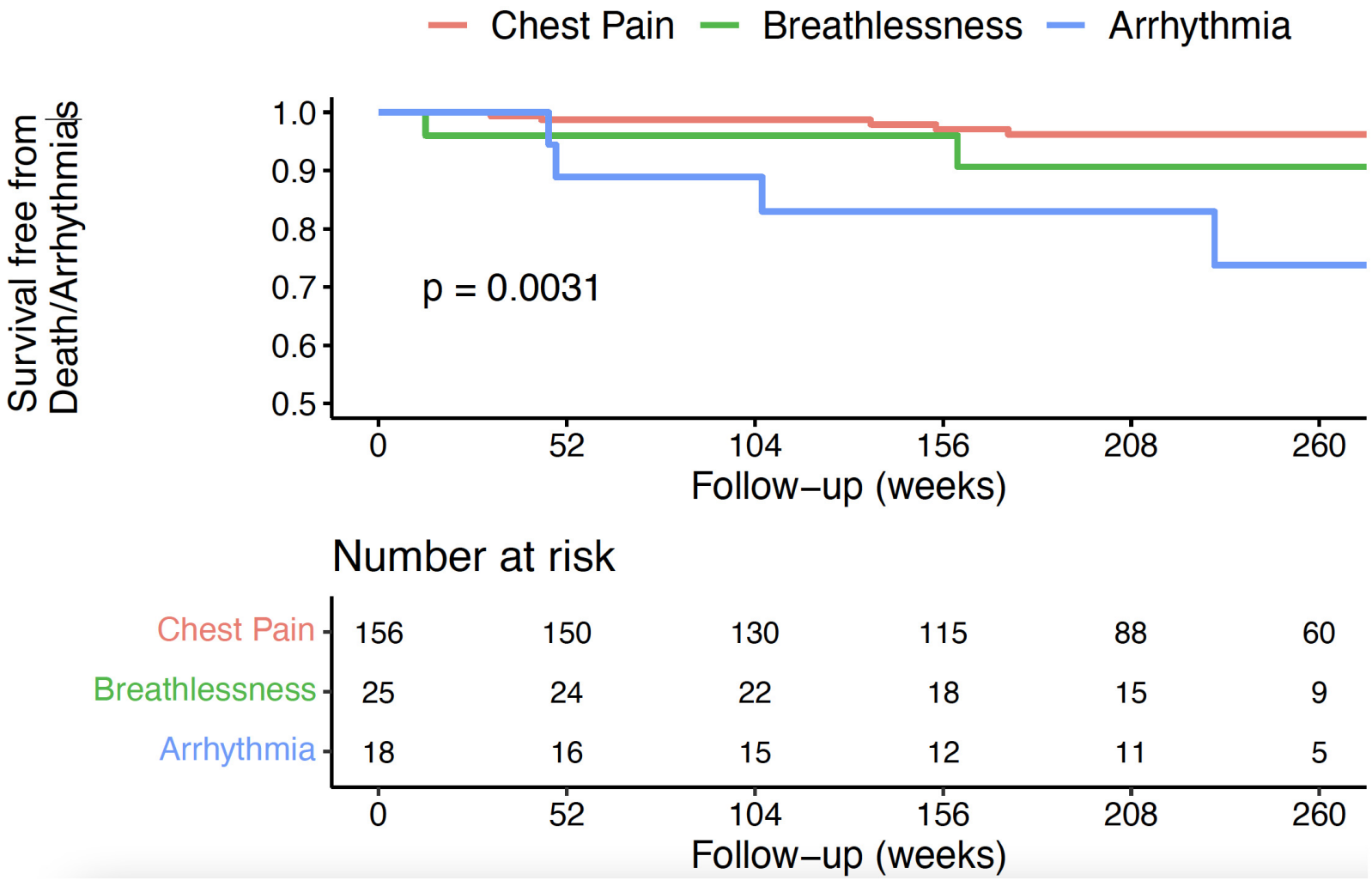
Marco Anzini, Marco Merlo, Gastone Sabbadini, Giulia Barbati, Gherardo Finocchiaro, Bruno Pinamonti, Alessandro Salvi, Andrea Perkan, Andrea Di Lenarda, Rossana Bussani, Jozef Bartunek and Gianfranco Sinagra

Circulation. 2013;128:2384-2394; originally published online October 1, 2013;
doi: 10.1161/CIRCULATIONAHA.113.003092

82 pts; Fup 147 mo;
53% 6 mo impr/norm LVEF

Biopsy proven myocarditis

7th challenge: a "*benign*" contemporary prognosis



Prognostic relevance of demographic factors in cardiac magnetic resonance-proven acute myocarditis: A cohort study

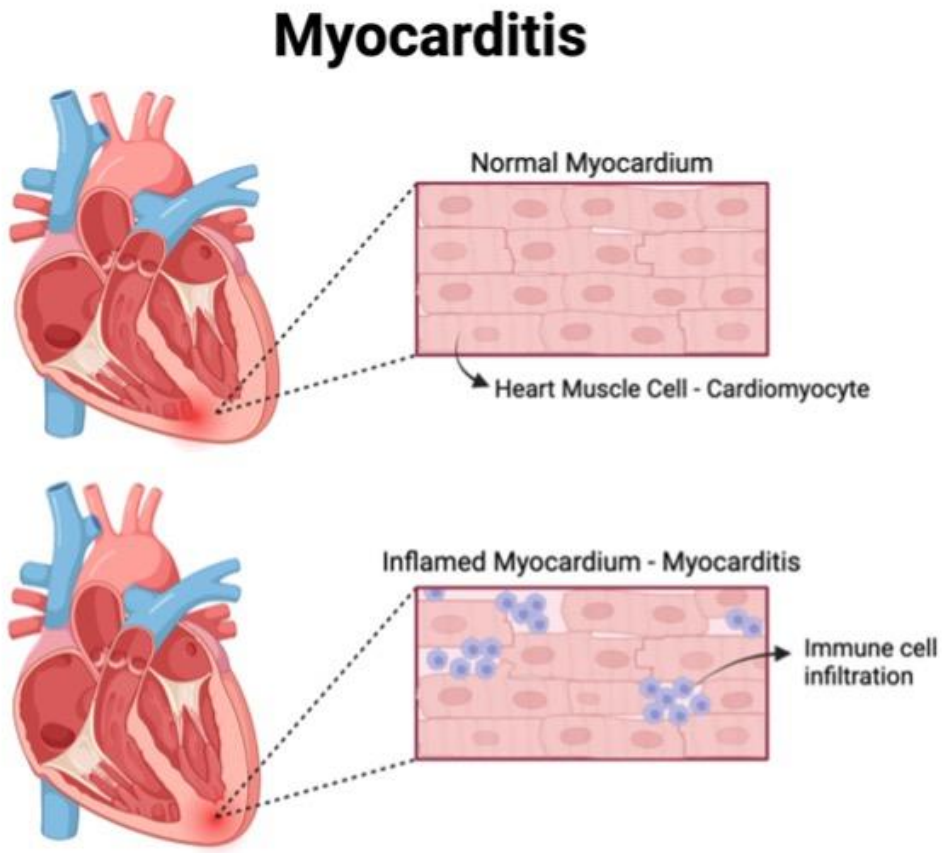
199 patients with CMR-proven myocarditis

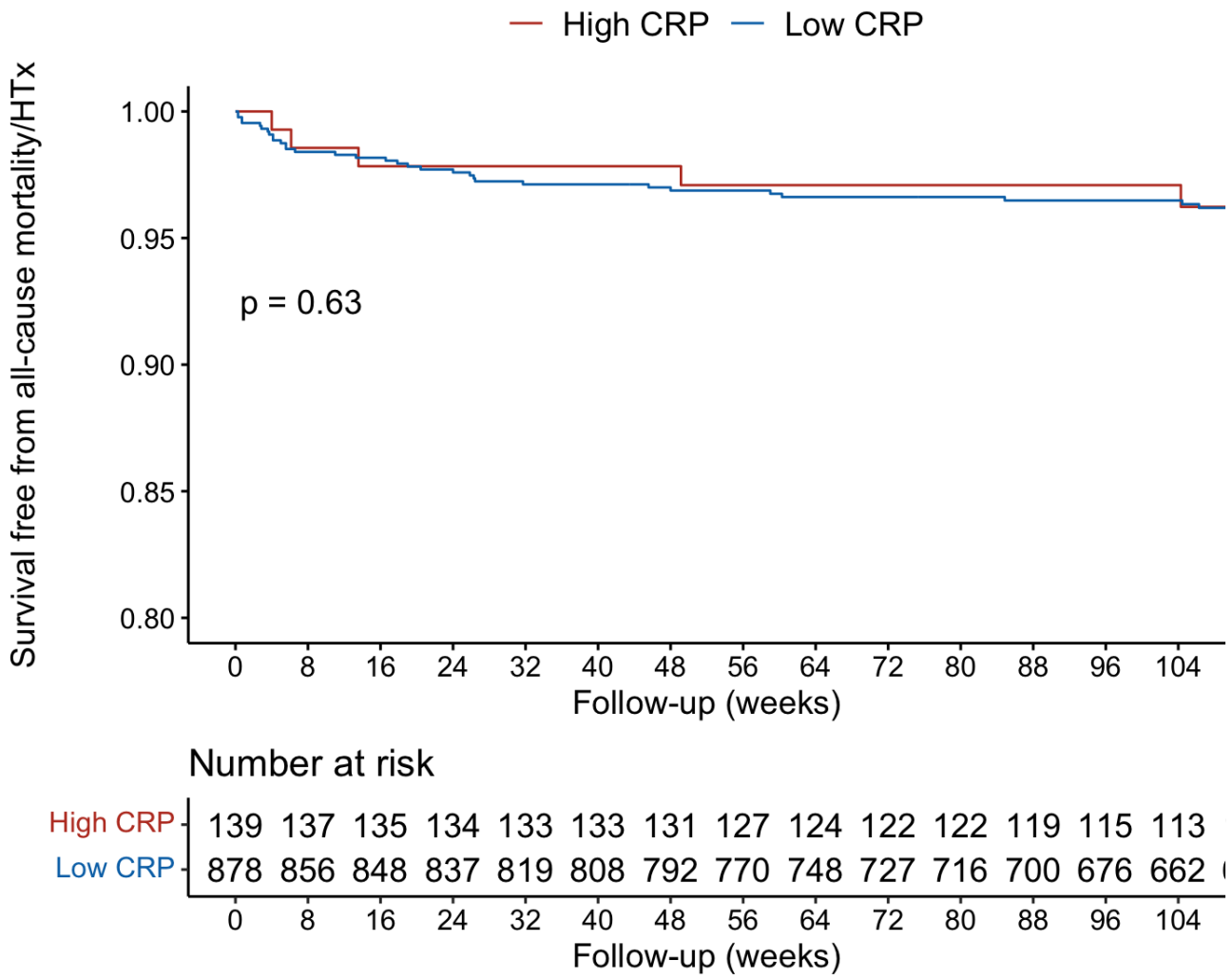
3-year event free survival 96%

- 98% chest pain
- 96% breathlessness
- 89% arrhythmia

Cannata, Bromage. *Front. Cardiovasc. Med. 2022. 9:1037837*

8th challenge: quantify the risk of inflammation





Cannata, Bromage. Under review

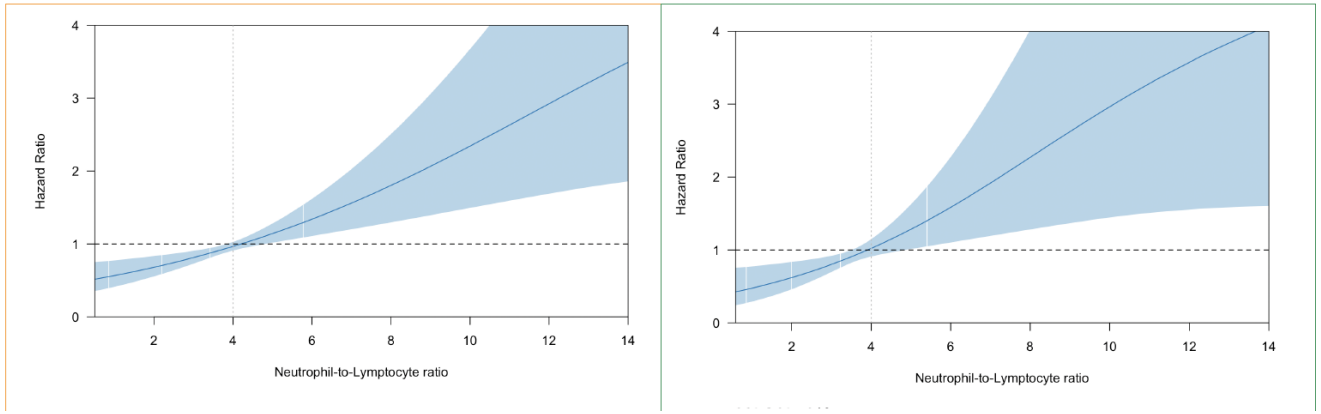
8th challenge: quantify the risk of inflammation

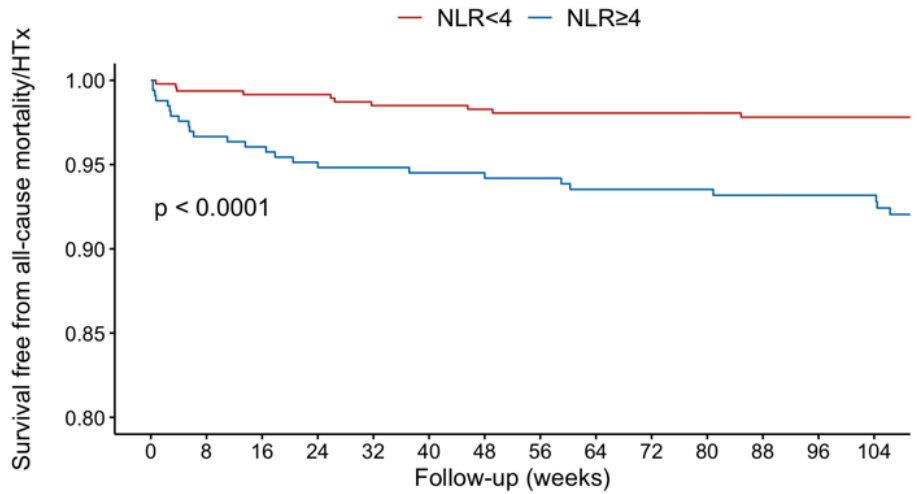
Neutrophil-to-lymphocyte Ratio (NLR): a marker of inflammation

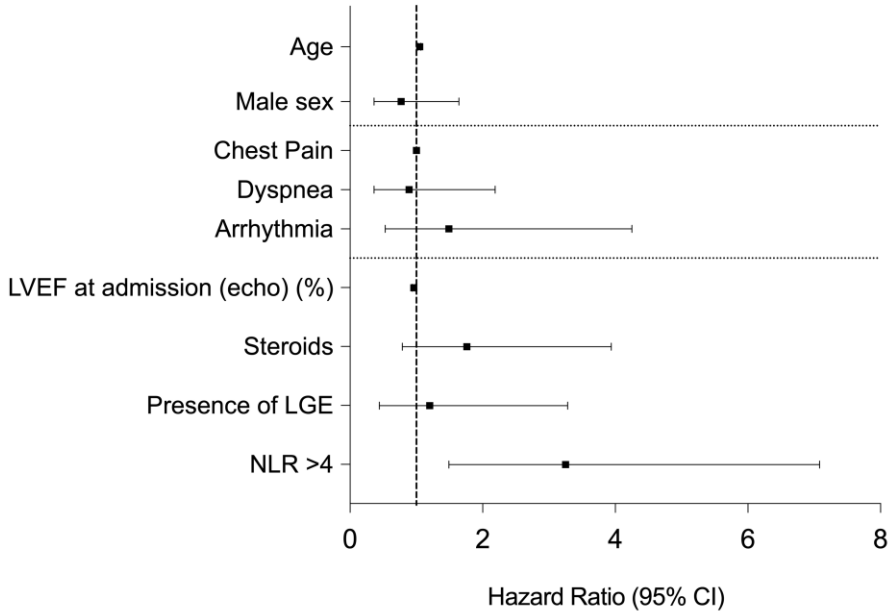
Final cohort 1150 patients

Randomly split into training and testing sets (70:30 ratio)

Training set n = 805 | **Testing set n = 345**





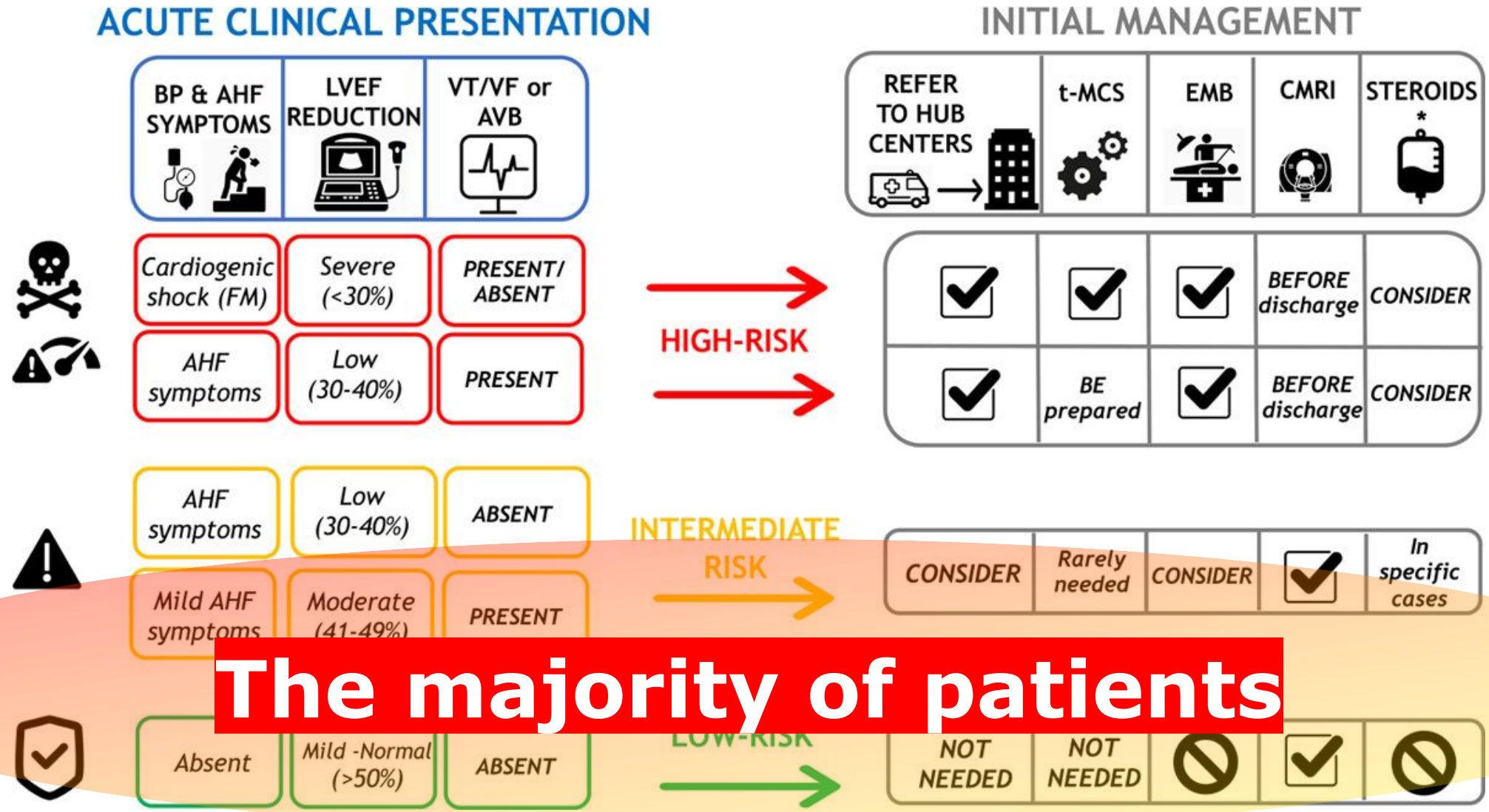


10 International Centres

2 UK; 5 Italy; 1 Germany; 1 Israel; 1 Sweden; 1 Switzerland

Cannata, Bromage. Under review

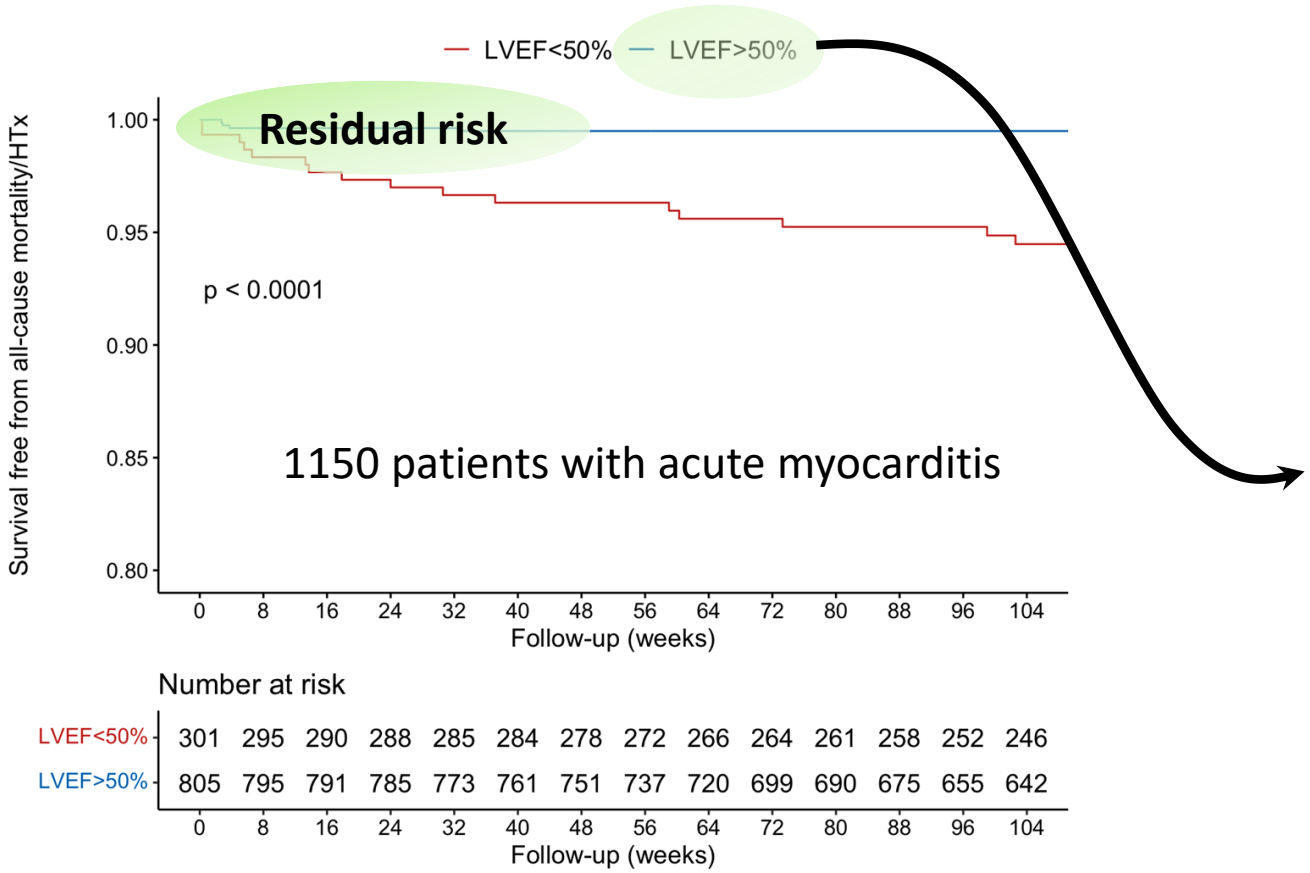
9th challenge: Risk stratification

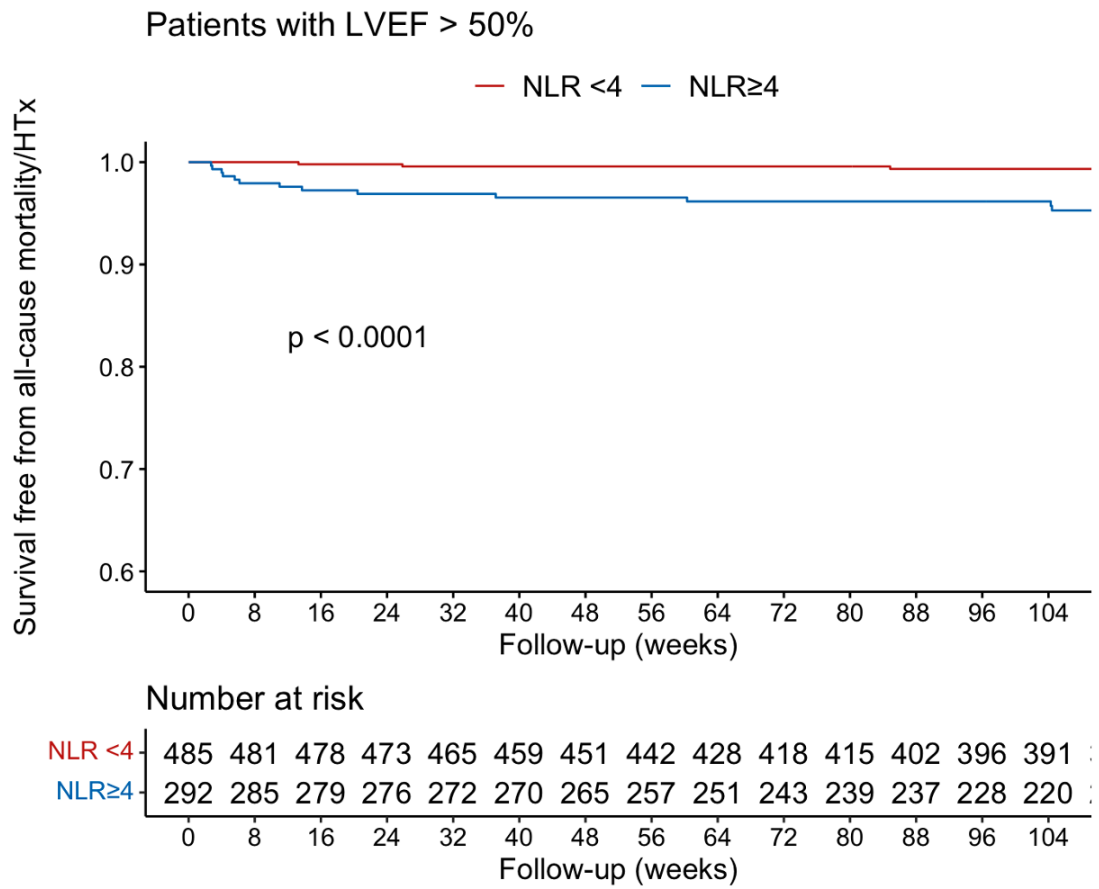


The majority of patients

Ammirati et al. Circ Heart Fail. 2020;13:e007405.

9th challenge: risk stratification in "low-risk" patients





Cannata, Bromage. Under review

10th challenge: specific therapy and immunosuppression

Suggested conventio

Chest pain
- No treatment if normal LVEF and no arrhtyhmias
- Associated peric
- Excercise restric

Arrhythmias
- Bradyarrhythmia
  - temporary
- Non sustained V
  - HF treatme
  - Case by ca
- Life threatening a
  - Antiarrhyth
  - ICD evalua

Heart failure
- Guideline guided
- Oxygen/ventilato
- Inotropic support
- Immunosuppress
- Mechanical assisted devices for refractory heart failu

Study or Subgroup	Cortic Events
Aziz 2010	1
Latham 1989	1
Maisch 1995	
Mason 1995	2
Wojnicz 1999	1
Total (95% CI)	
Total events:	7
Heterogeneity: Tau² = 0.00; Ch	
Test for overall effect: Z = 0.37	
Test for subgroup differences:	

MYTHS TRIAL
MYocarditis THerapy with Steroids

Study duration: **3 years** Study Start: **Oct. 2021** Follow up: **6 months**

Single blind, randomized controlled, multicenter, international, phase III trial – **Coordinating center: Niguarda hospital, Milan, ITALY**
PI: Dr. Enrico Ammirati

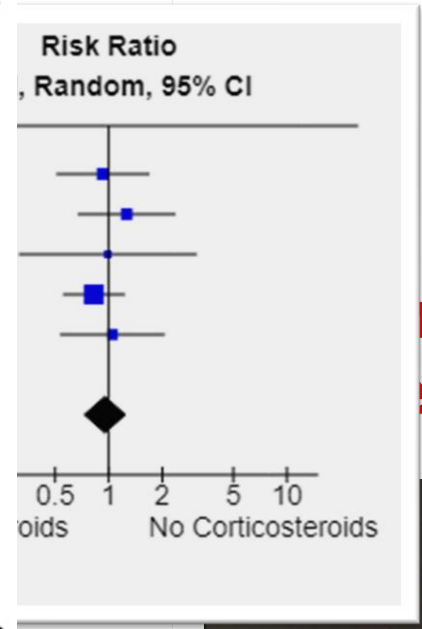
Suspected AM complicated by acute HF/cardiogenic shock (LVEF<41% & LVEDD <56 mm on echo)

Control arm (n=144) (placebo)

Intervention arm (n=144) (i.v. methylprednisolone 1g x 3d)

Primary endpoint:
To demonstrate a reduction in the rate of all-cause death, HTx, LVAD implant, need for upgrading t-MCS, VA treated with DC shock, hospitalization due to HF, VA, AVB

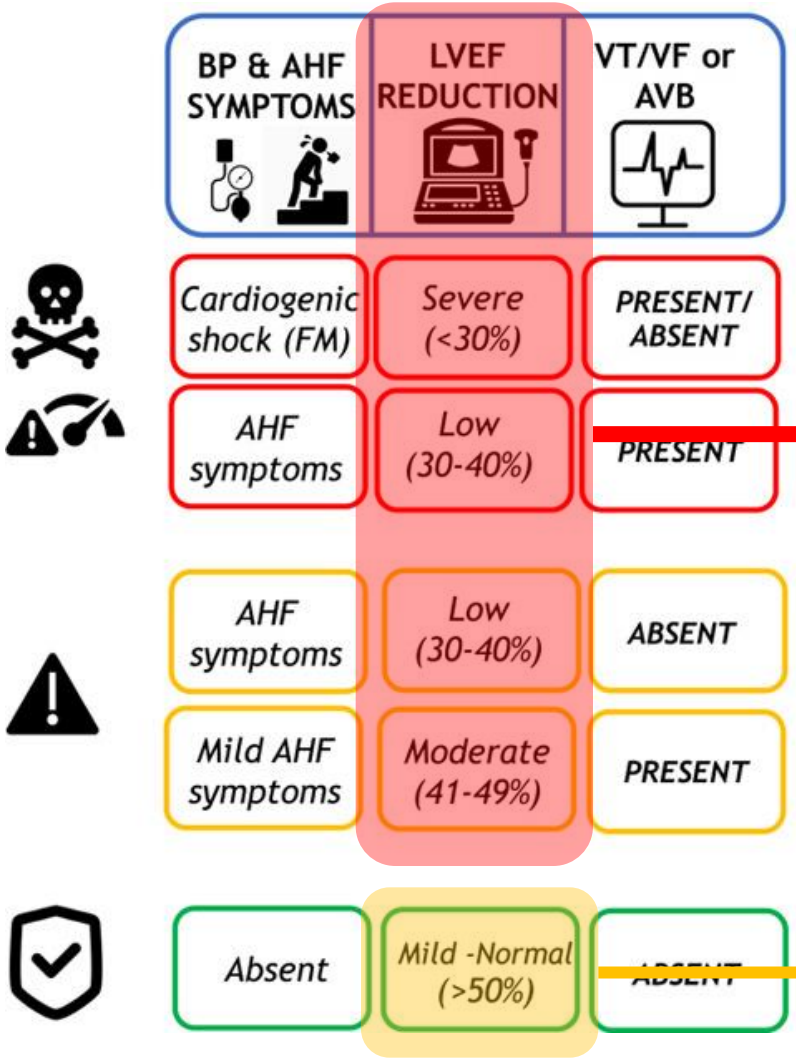
Clinicaltrials.gov: NCT05150704
Funded by the Italian Ministry of Health (GR-2019-12368506)



npiric
eroids?

Ferone E, Bromage D, Cannata A. J Cardiovasc Pharmacol. 2024; 83(5):364-376.
Chen et al. Cochrane Database Syst Rev.2013(10):CD004471

11th challenge: conventional treatment



Recommendations	Class	Level
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.	I	A

?

McDonagh T et al. Eur Heart J. 2021 Sep 21;42(36):3599-3726

Ammirati et al. Circ Heart Fail. 2020;13:e007405.

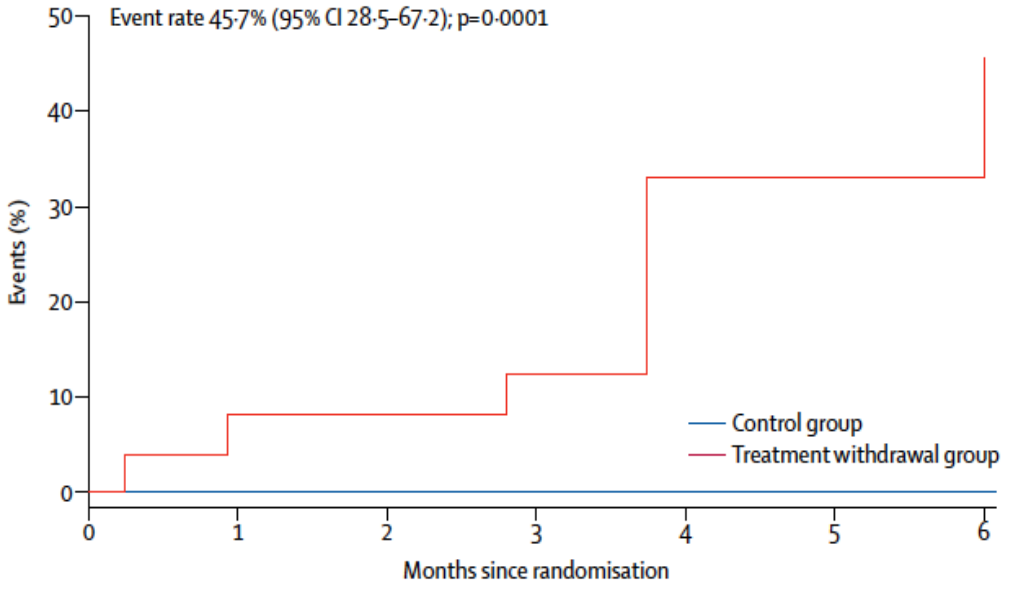
12th challenge: withdrawing treatment

As myocarditis may have a reversible precipitant, is it safe to withdraw (heart failure) treatment?

In heart failure, some evidence comes from the pilot TRED-HF

- Withdrew medical treatment in patients with non-ischaemic DCM with partial to complete recovery of LVEF
- Relapse within 6 months observed in 44% of patients
- Only ***one (… 1 …)*** patient had previous myocarditis

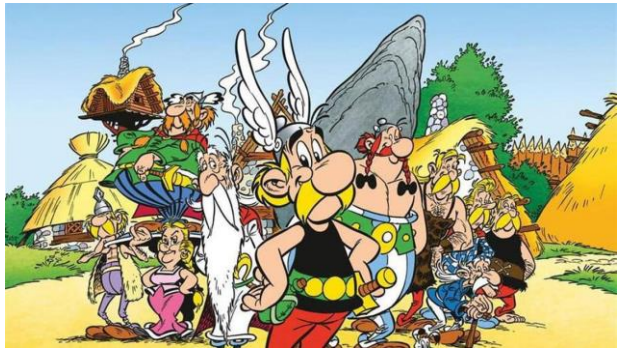
Need more evidence…

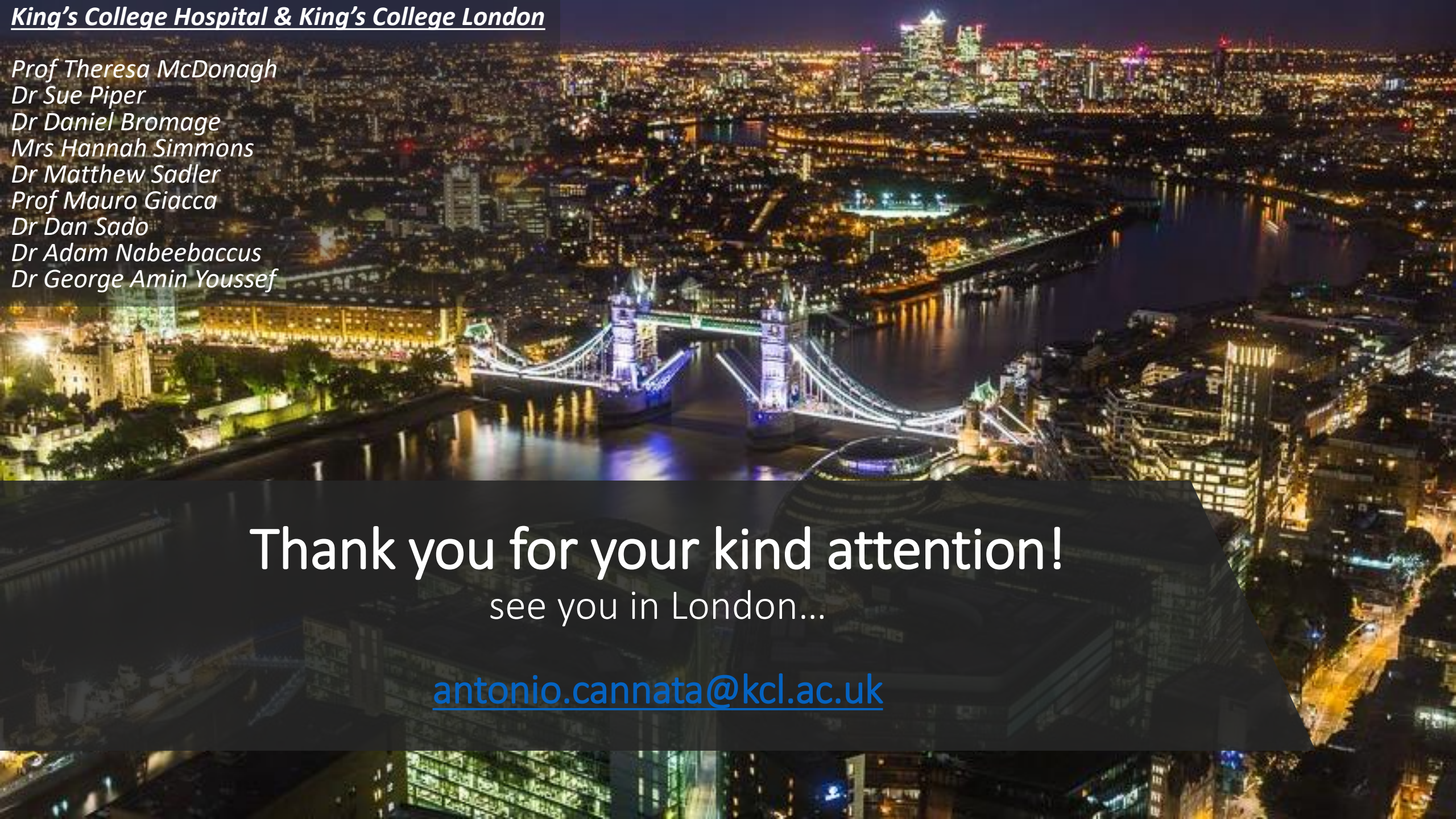


Halliday. Lancet 2018;393:61-73

Conclusions

- Myocarditis is a ***heterogeneous*** disease with an overall favourable prognosis
- Two-thirds of patients with AM present with ACS-like symptoms, and this is associated with a ***benign prognosis***
- ***Lots of unknowns***, largely related to difficulty conducting trials in this area
- Specific forms of myocarditis may require ***targeted therapies***
- ***Risk stratification*** is important, and new (and old) biomarkers are required to better characterise patients
- Don't forget the ***gene-environment*** interaction (!)
- Don't forget the ***long-term implications*** of our actions (!)





King's College Hospital & King's College London

Prof Theresa McDonagh
Dr Sue Piper
Dr Daniel Bromage
Mrs Hannah Simmons
Dr Matthew Sadler
Prof Mauro Giacca
Dr Dan Sado
Dr Adam Nabeebaccus
Dr George Amin Youssef

Thank you for your kind attention!

see you in London…

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