EMB in Myocarditis: who needed?

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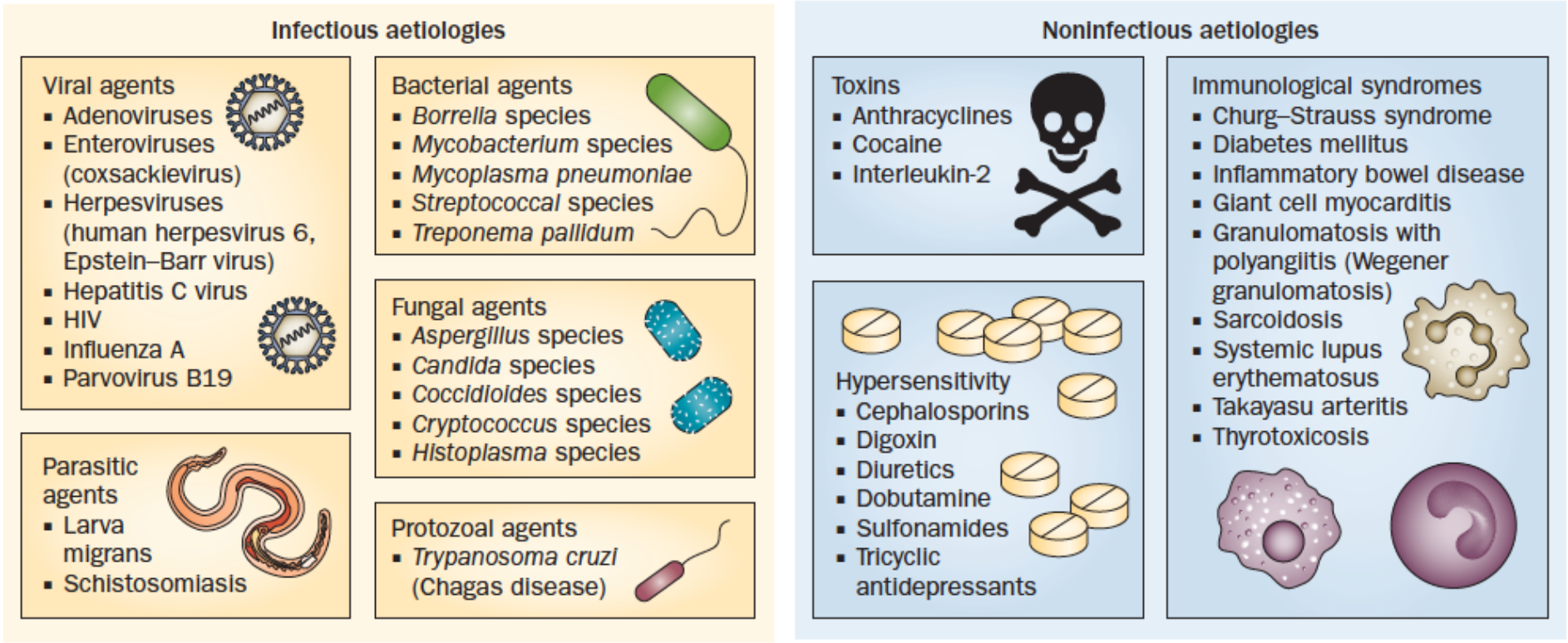
nature REVIEWS CARDIOLOGY

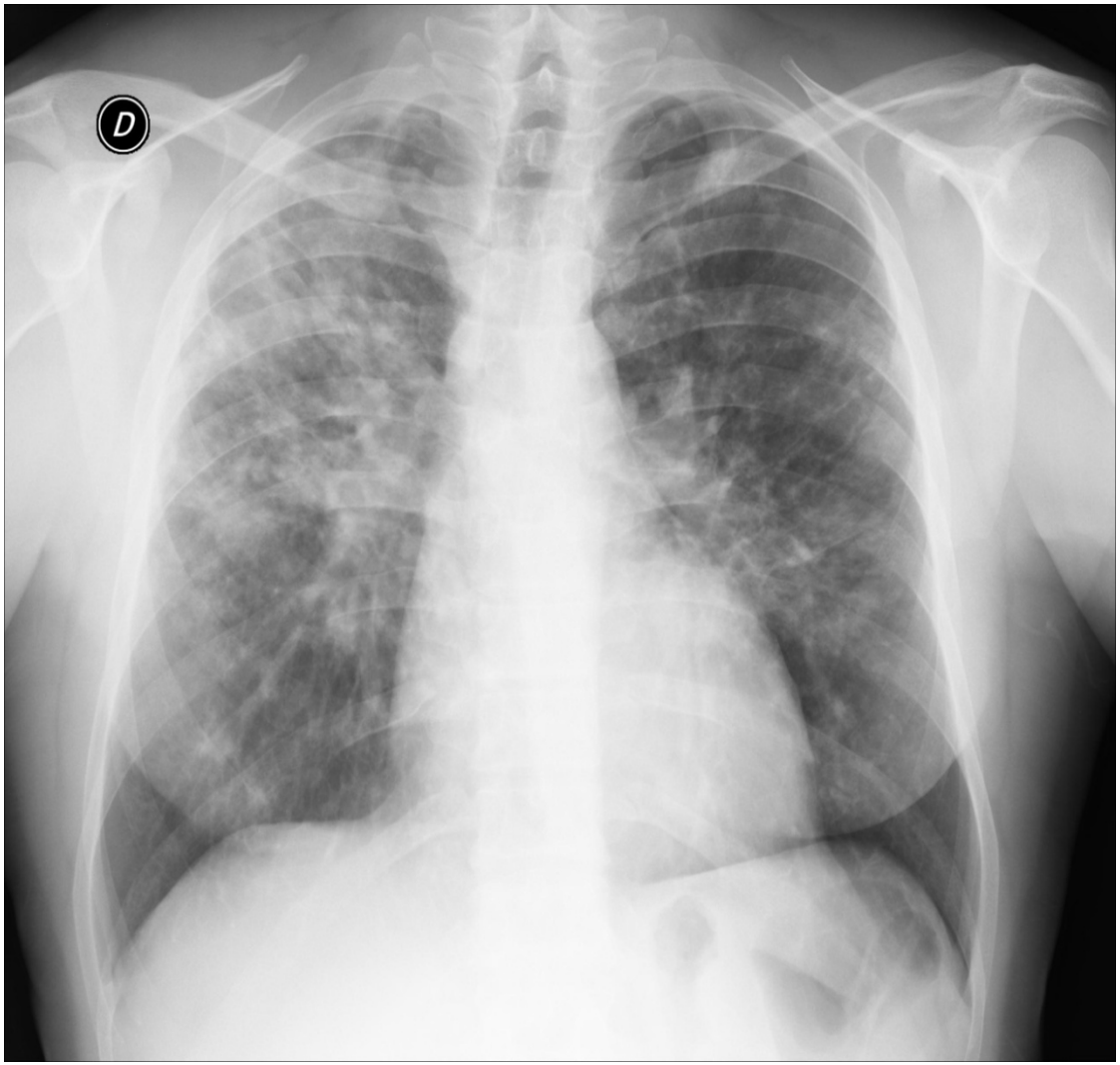
Viral myocarditis—diagnosis, treatment options, and current controversies

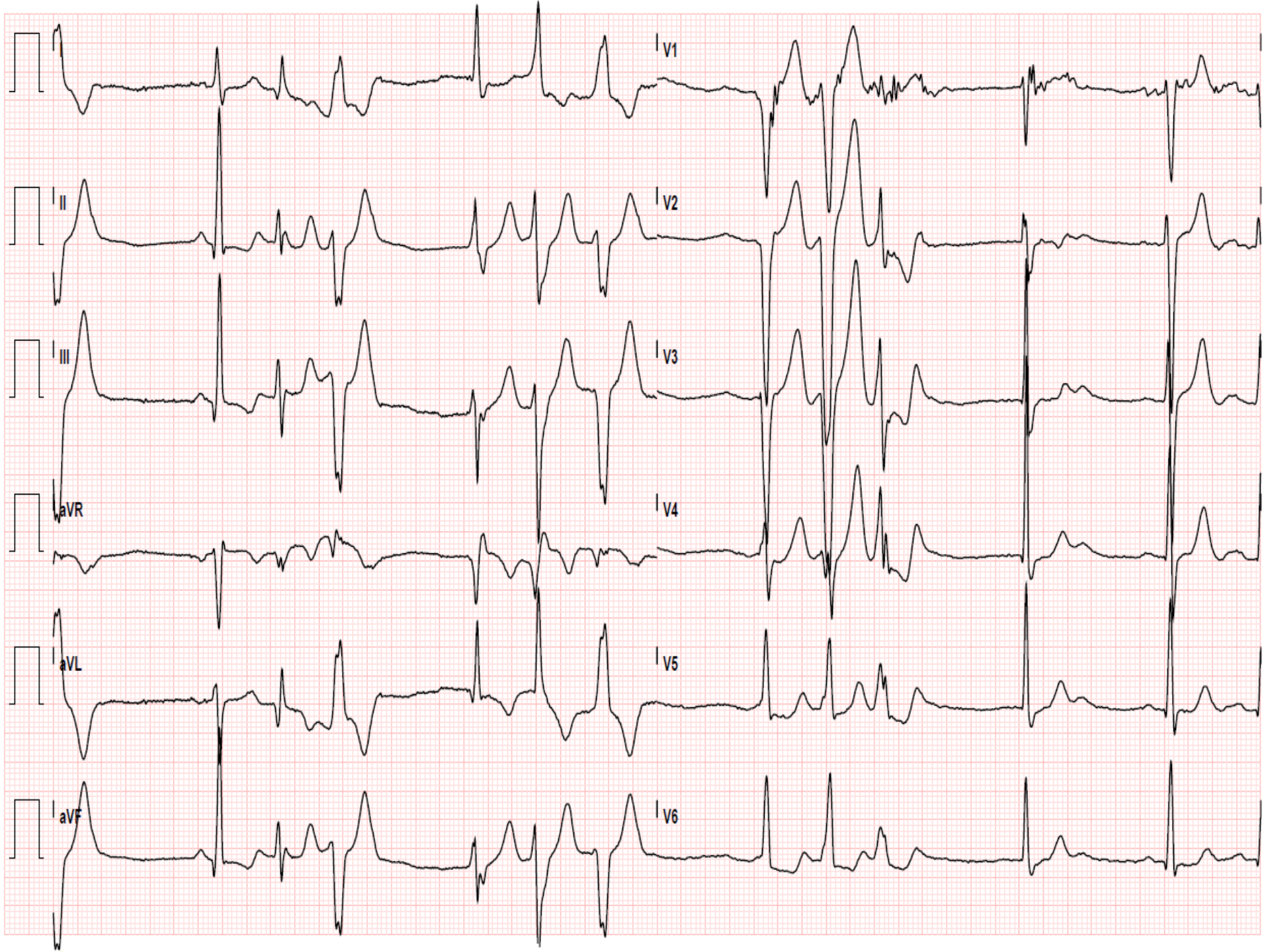
Ari Pollack, Amy R. Kontorovich, Valentin Fuster and G. William Dec



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

43 aa; M; palpitazioni; sincope; FEVsin 43%; asinergie++ SIV e postero-basali

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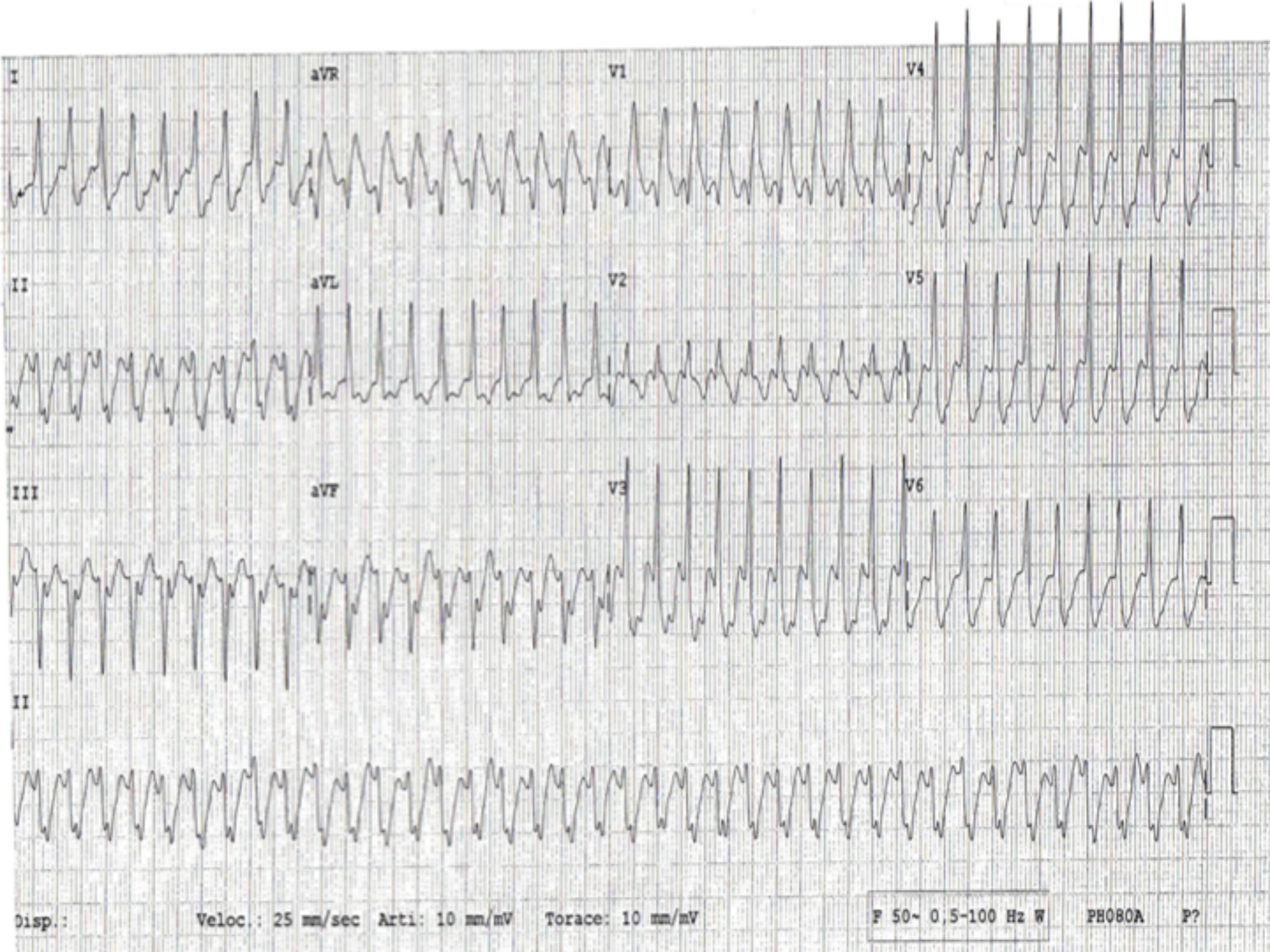
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F 50~ 0,5-100 Hz W
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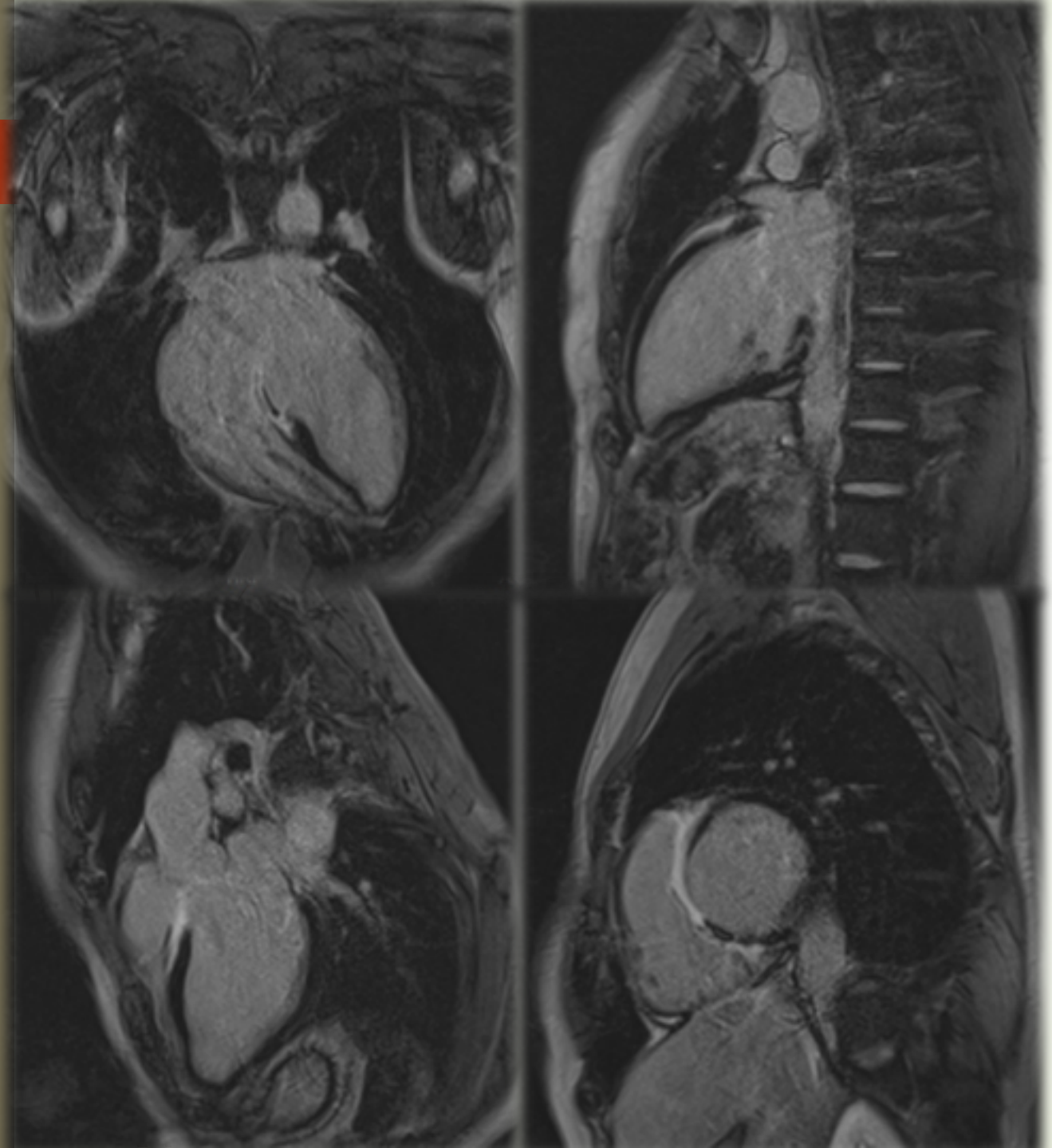
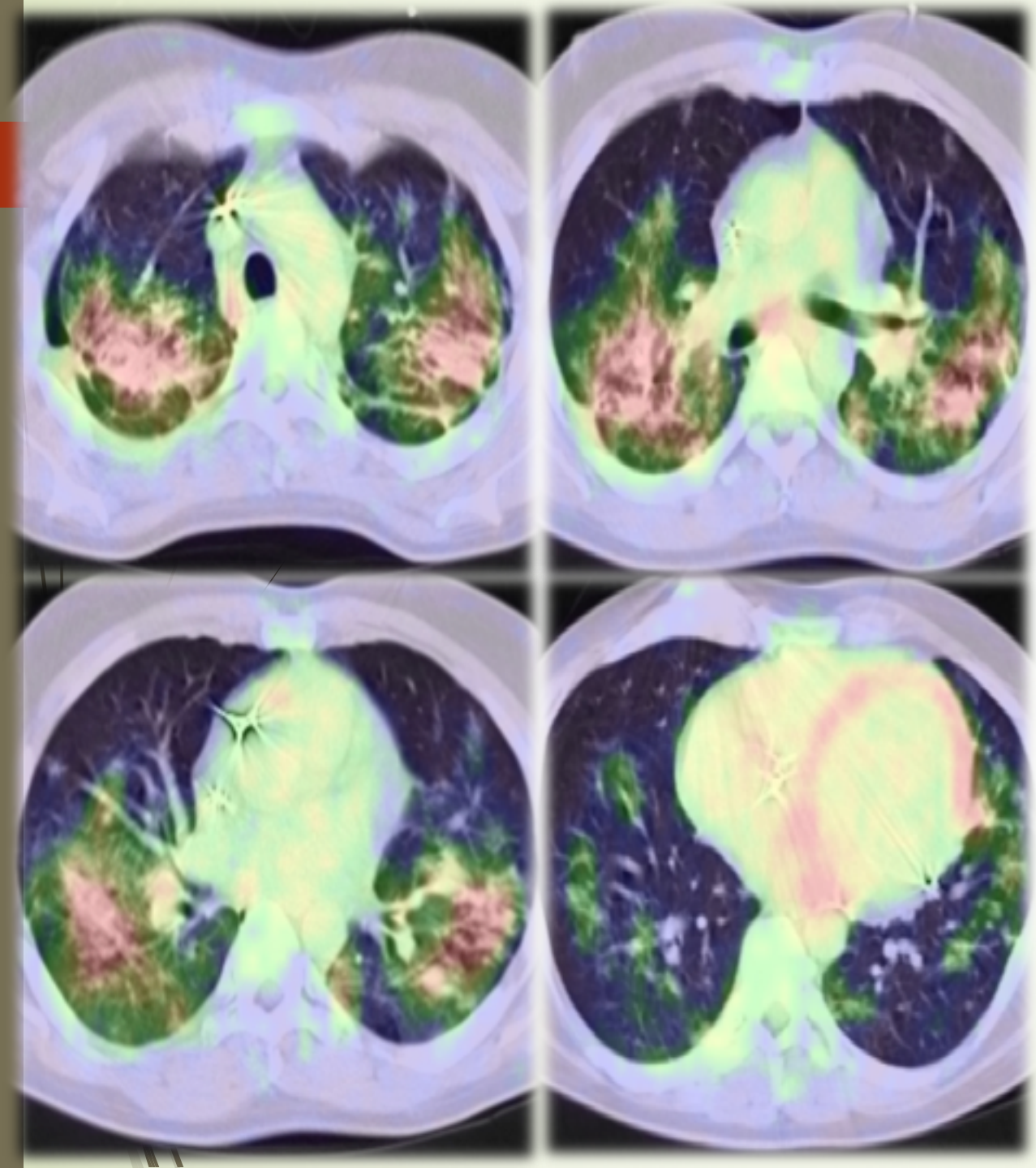
P?





Myocarditis with Immune Checkpoint Blockade

Cardiovascular Adverse Events Reported in Phase 3 Trials of Immune Checkpoint Inhibitors

Study and Year	Tumor Type	Drug	Exposed Patients	Reported Cases of Cardiovascular Toxicity
			no.	*no. (%)*
All studies			5347	10 (0.19)
Hodi et al., 2010	Melanoma	Ipilimumab	511	0
Robert et al., 2011	Melanoma	Ipilimumab	247	0
Weber et al., 2015	Melanoma	Nivolumab	268	0
Robert et al., 2015	Melanoma	Nivolumab	206	1 case of hypotension (0.49)
Robert et al., 2015	Melanoma	Pembrolizumab or ipilimumab	811	1 cardiac arrest associated with metabolic imbalances from ipilimumab-induced diarrhea; 4 cases of hypertension (0.62)
Larkin et al., 2015	Melanoma	Nivolumab, ipilimumab, or nivolumab plus ipilimumab	937	0
Eggermont et al., 2015 and 2016	Melanoma (adjuvant)	Ipilimumab	471	1 case of myocarditis (0.21)
Borghaei et al., 2015	Non-squamous non–small-cell lung cancer	Nivolumab	287	1 case of cardiac tamponade; 1 case of pericardial effusion (0.70)
Brahmer et al., 2015	Squamous non–small-cell lung cancer	Nivolumab	131	0
Reck et al., 2016	Non–small-cell lung cancer	Pembrolizumab	154	0
Herbst et al., 2016	Non–small-cell lung cancer	Pembrolizumab	682	1 case of myocardial infarction (0.15)
Motzer et al., 2015	Renal-cell carcinoma	Nivolumab	406	0
Ferris et al., 2016	Head and neck squamous-cell carcinoma	Nivolumab	236	0

Edhery et al. NEJM.2017:376;3

Miocardite: manifestazioni cliniche ed evoluzione

Assenza di sintomi

Dolore toracico

Aritmie ipocinetiche/ ipercinetiche

Scompenso cardiaco

Forma fulminante

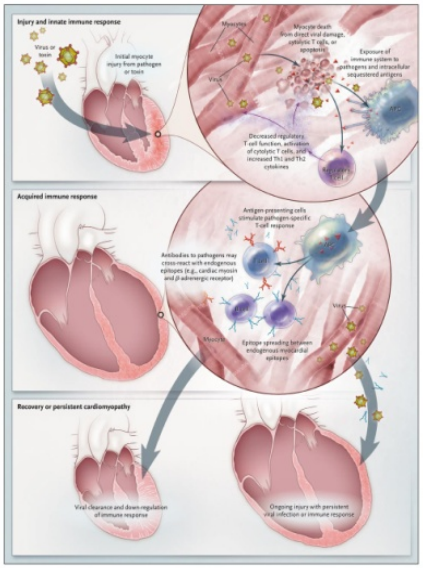
Guarigione completa o incompleta

CMPD

Morte improvvisa

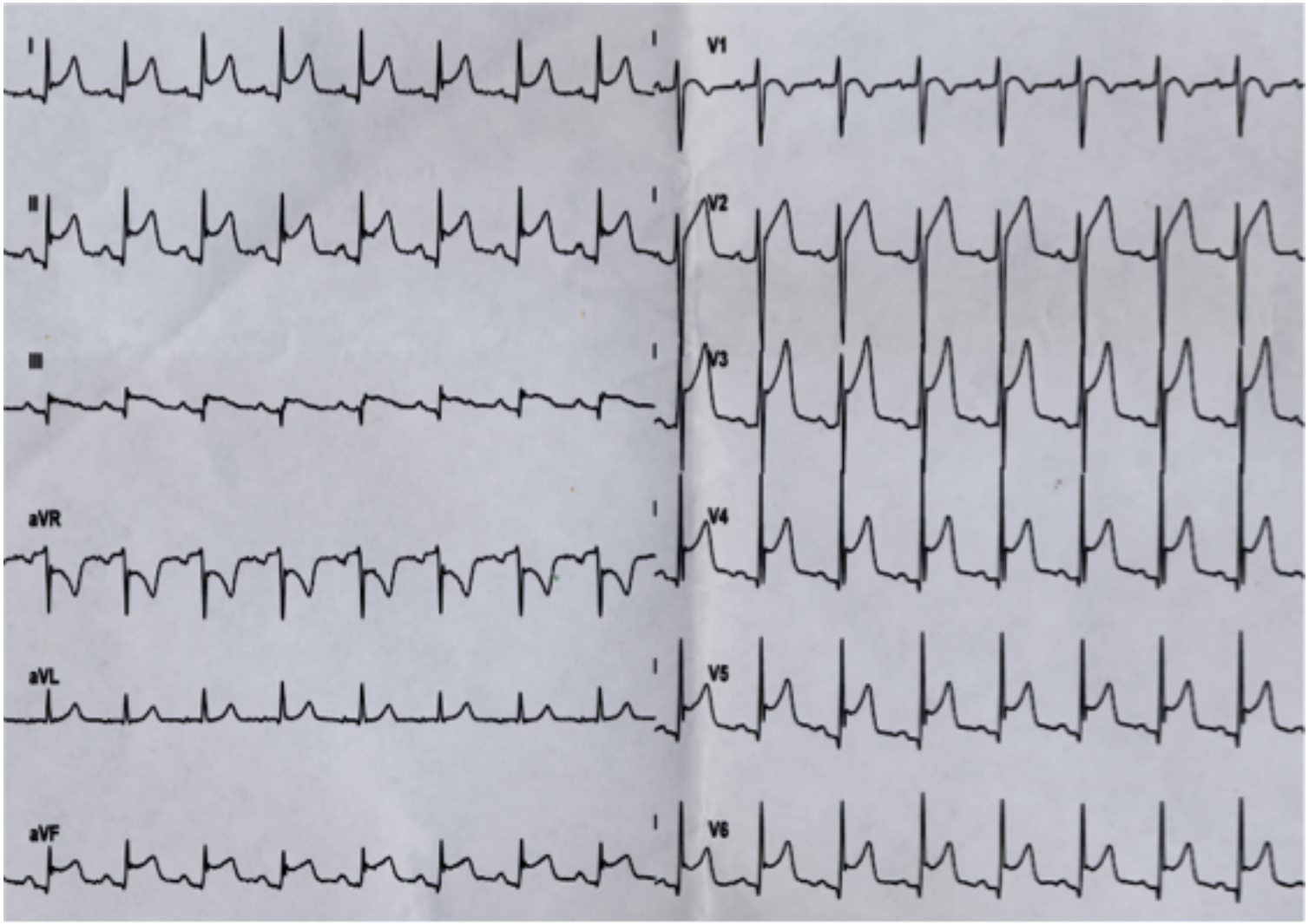
Morte in shock e MOF

-·-·-·- evoluzione possibile



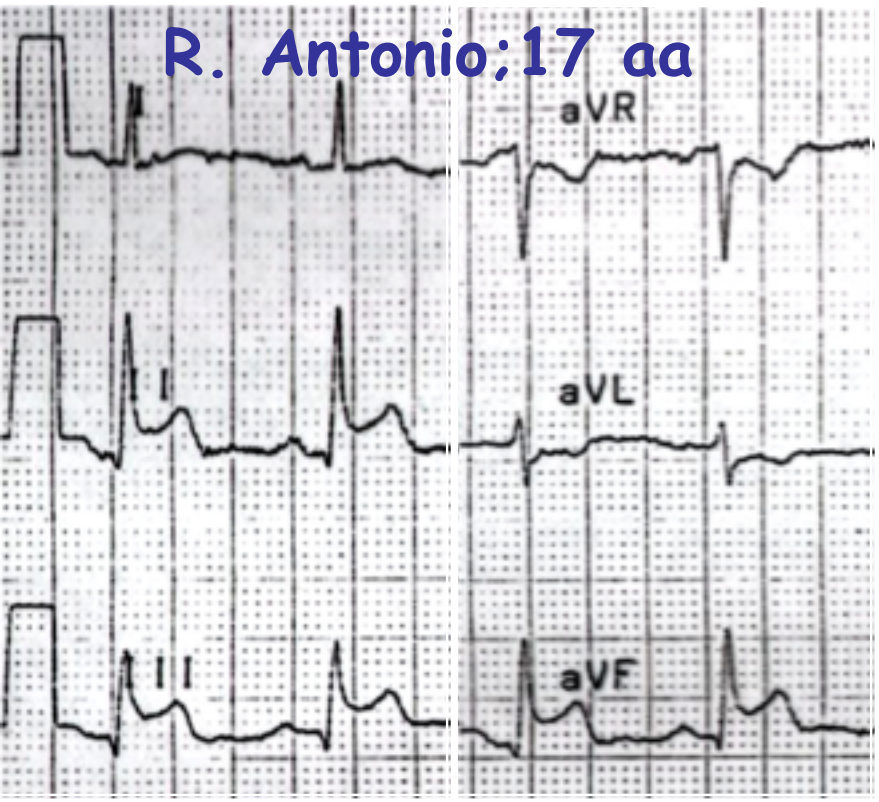
Sinagra et al. Trattato di Cardiologia; Excerpta Medica 2000;2013-33

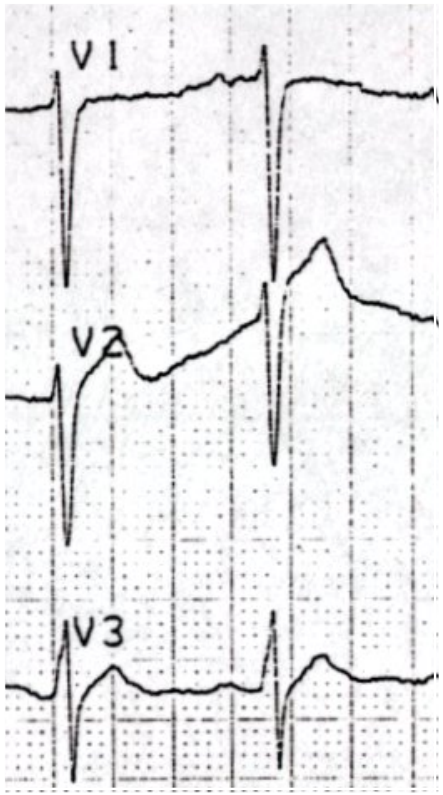
Ospedali Riuniti di Trieste

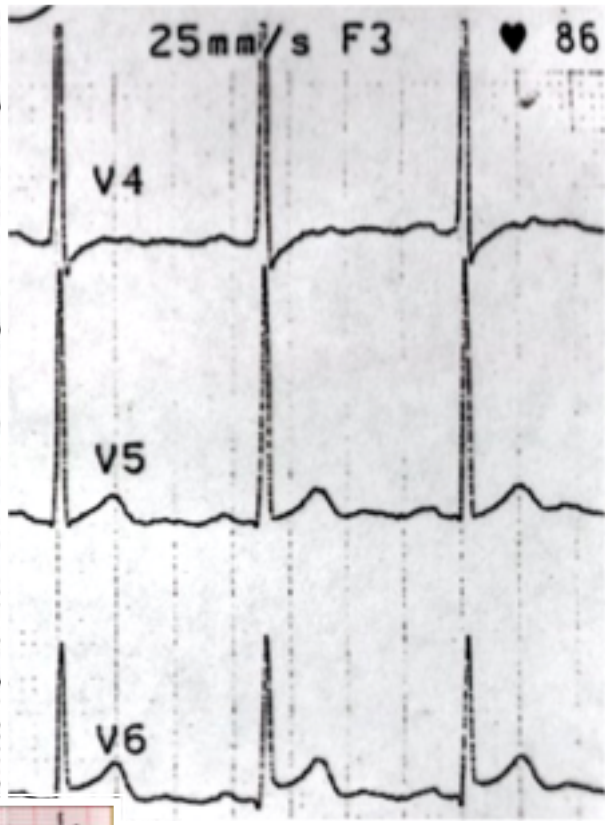


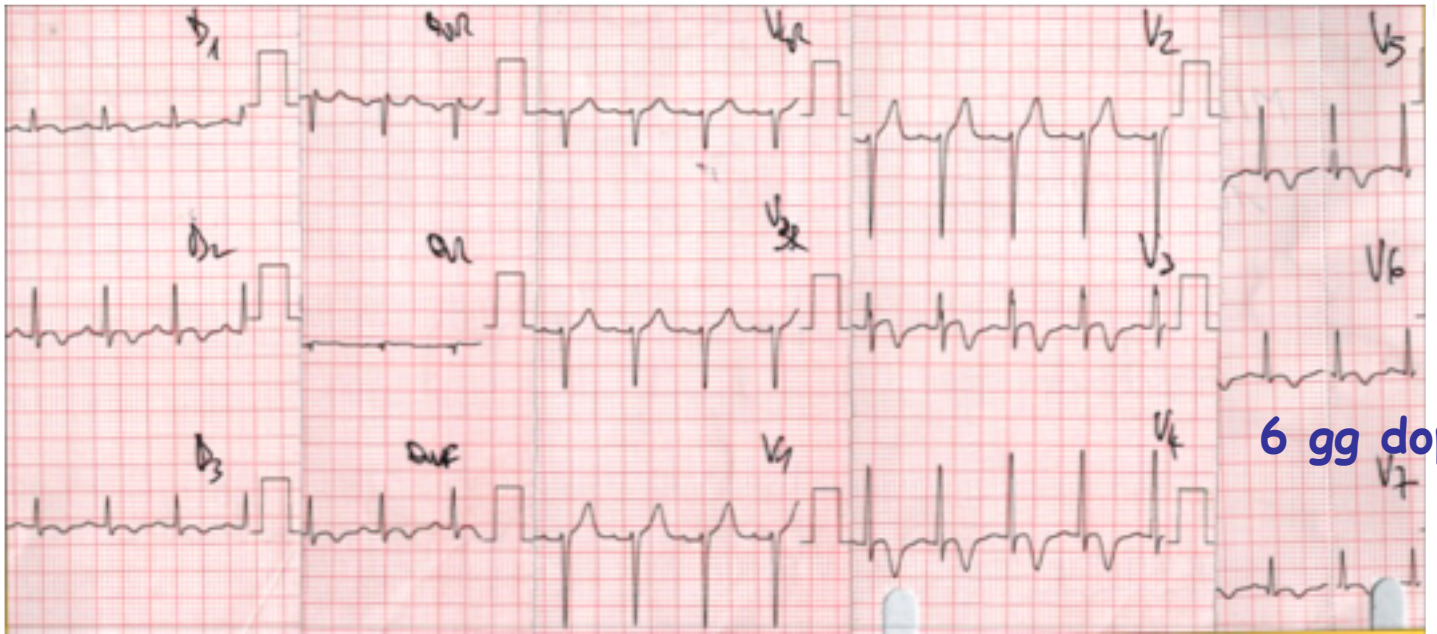
Ospedali Riuniti di Trieste

R. Antonio; 17 aa





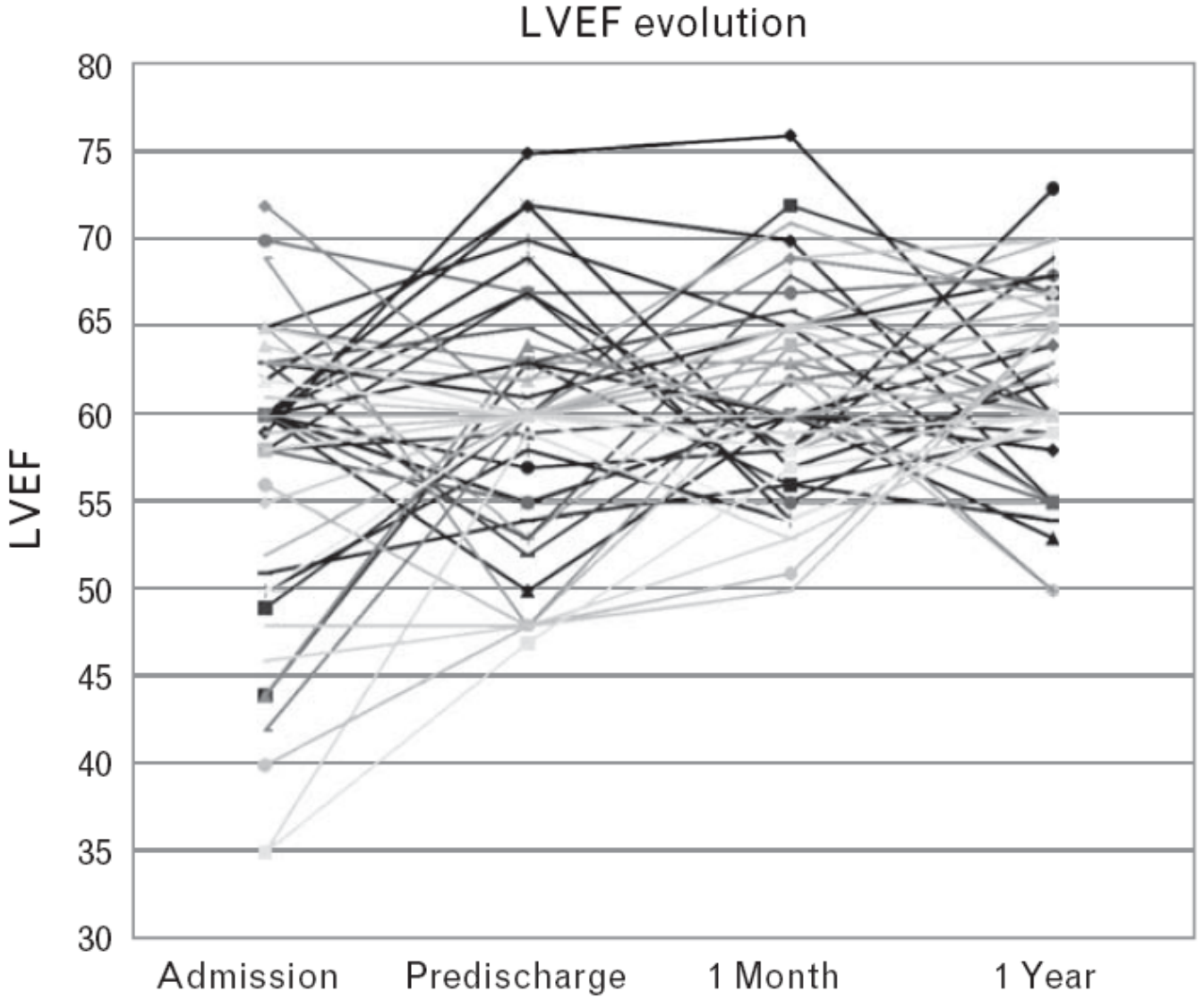




6 gg dopo; ASA 3 g ev/die

Clinical presentation and long-term follow-up of perimyocarditis

Buiatti, Sinagra et al
J Cardiovasc Med 2012, 13:000–000



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Good Prognosis for Pericarditis With and Without Myocardial Involvement : Results From a Multicenter, Prospective Cohort Study

Massimo Imazio, Antonio Brucato, Andrea Barbieri, Francesca Ferroni, Silvia Maestroni, Guido Ligabue, Alessandra Chinaglia, Davide Cumetti, Giovanni Della Casa, Federica Bonomi, Francesca Mantovani, Paola Di Corato, Roberta Lugli, Riccardo Faletti, Stefano Leuzzi, Rodolfo Bonamini, Maria Grazia Modena and Riccardo Belli

Circulation. 2013;128:42-49; originally published online May 24, 2013;
doi: 10.1161/CIRCULATIONAHA.113.001531

f-up 36 mo (6-88)	Pericarditis (n=346), n (%)	Myopericarditis (n=114), n (%)	Perimyocarditis (n=26), n (%)	P
Recurrence	110 (31.8)	12 (10.5)	3 (11.5)	<0.001
Cardiac tamponade	8 (2.3)	0 (0.0)	0 (0.0)	NS
Constrictive pericarditis	2 (0.6)	1 (0.9)	0 (0.0)	NS
Heart failure	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**NS**
LV dysfunction (EF <55%) at 12 mo	4 (1.1)	9 (7.9)	4 (15.4)	<0.001
All-cause death	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**NS**

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

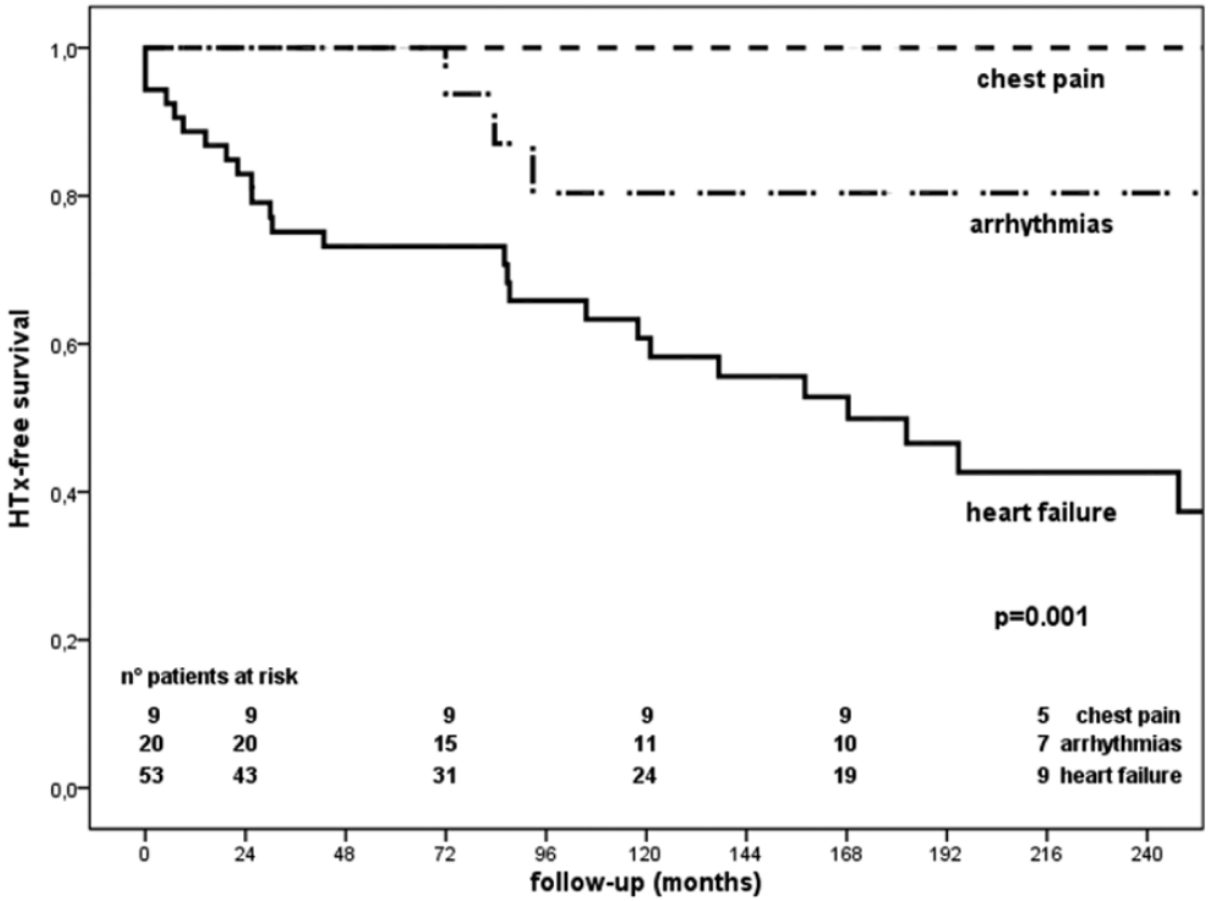
American Heart Association®

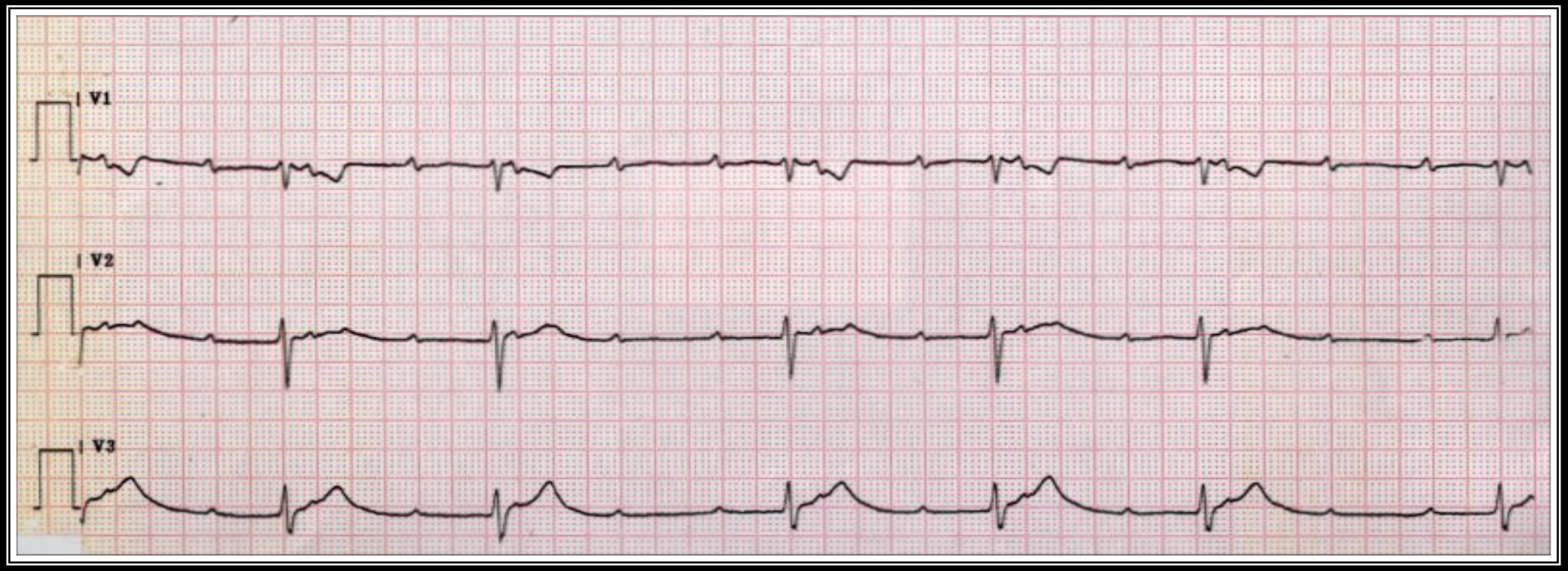
Long-Term Evolution and Prognostic Stratification of Biopsy-Proven Active Myocarditis

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




V1
V2
V3

Venoarterial Extracorporeal Membrane Oxygenation for Acute Fulminant Myocarditis in Adult Patients: A 5-Year Multi-Institutional Experience

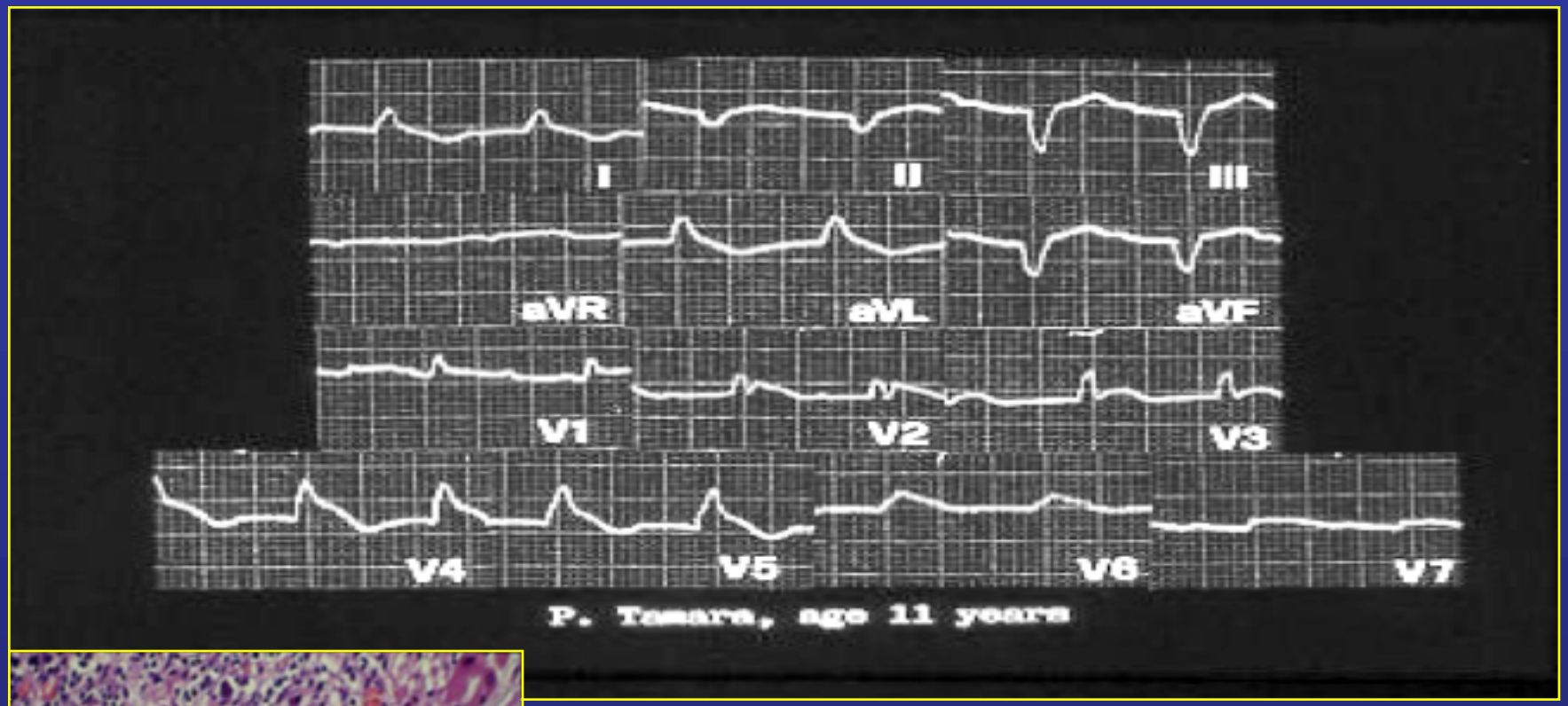
THE ANNALS OF THORACIC SURGERY

Table 5. Review of Published Studies That Included 6 or More Adults Patients Affected by Acute Fulminant Myocarditis and Supported by ECMO

Reference	Time Span	Patients, n	ECMO Weaning, n (%)	Survival to Hospital Discharge, n (%)	Postoperative Survival, % (follow-up, years)
Kawahito et al [19]	1991–1997	6	5 (80)	5 (80)	NA
Aoyama et al [5]	1989–2000	52	42 (80.7)	31 (59.6)	NA
Chen et al [9]	1994–2001	15	14 (93)	11 (73)	NA
Asaumi et al [13]	1993–2001	6	4 (67)	4 (67)	NA
Maejima et al [14]	1991–2000	8	NA	6 (75)	100 (range, 1.4–5.9)
Sezai et al [20]	1999–2006	7	7 (100)	7 (100)	NA
Pages et al [6]	2001–2006	6	5 (83)	5 (83)	80% (1)
Thiagarajan et al [21]	1992–2007	16	NA	9 (56)	NA
Hsu et al [10]	1994–2009	51	NA	31 (61)	NA
Mirabel et al [12]	2002–2009	35	NA	24 (69)	100 (1.5)
Beurtheret et al [22]	2005–2009	14	NA	9 (65)	NA
Diddle et al [6]	1995–2014	147	101 (69)	90 (61)	NA

Cardiopulmonary support with VA-ECMO provides an invaluable tool in the treatment of AFM, although major complications may characterize the hospital course. Long-term outcome appears favorable with rare episodes of recurrent myocarditis or cardiac related events.

Lorusso et al. Ann Thorac Surg 2016;101:919–26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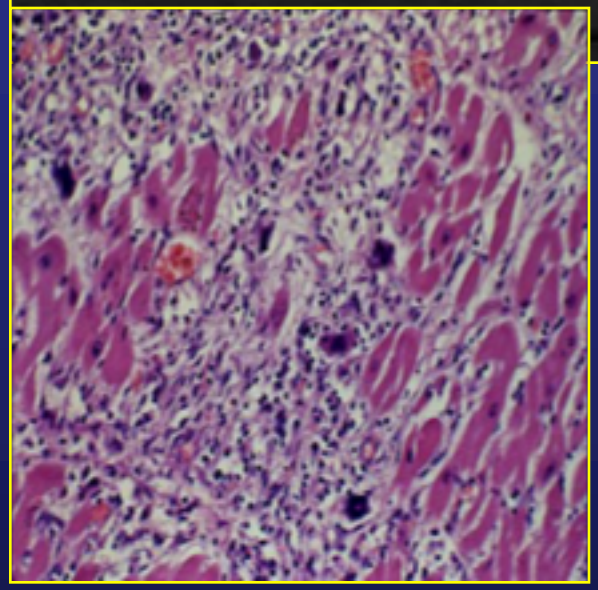
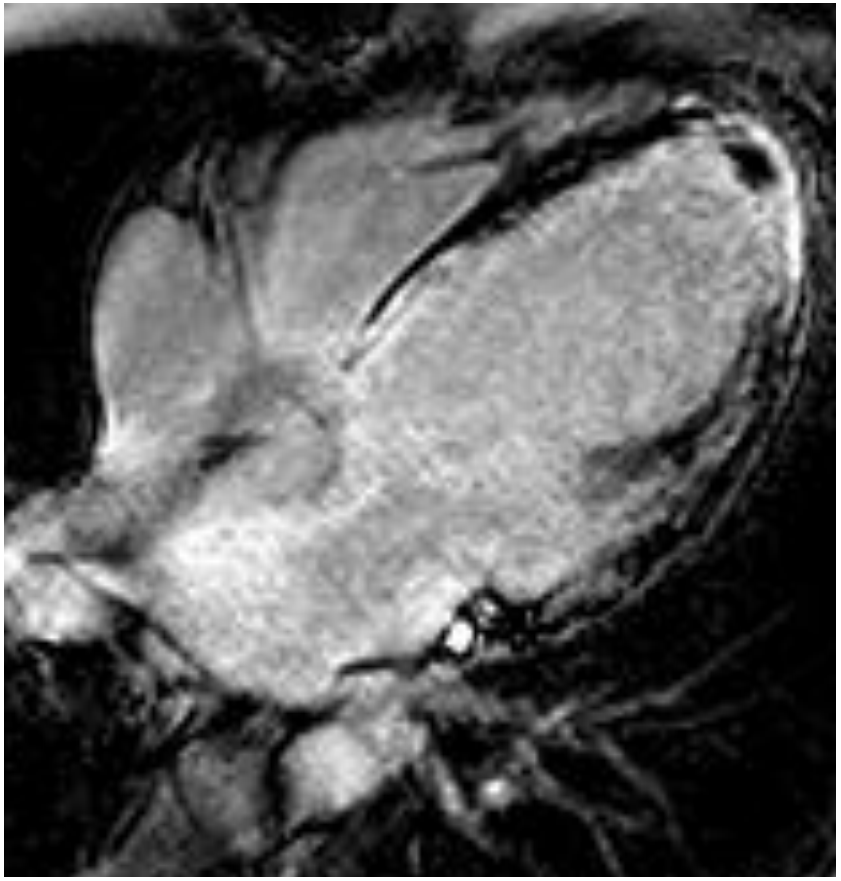
V7
P. Tamara, age 11 years

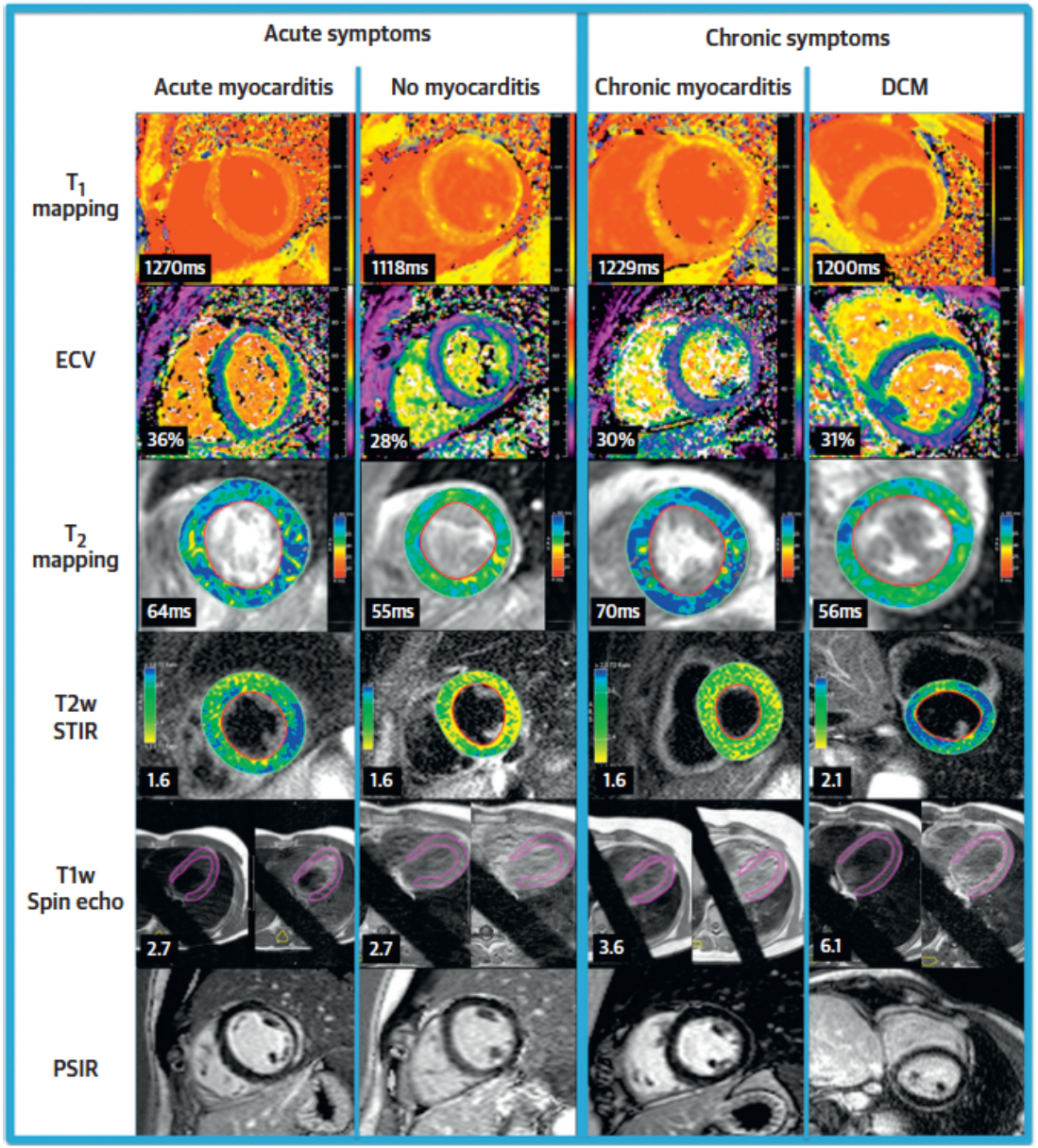


RM



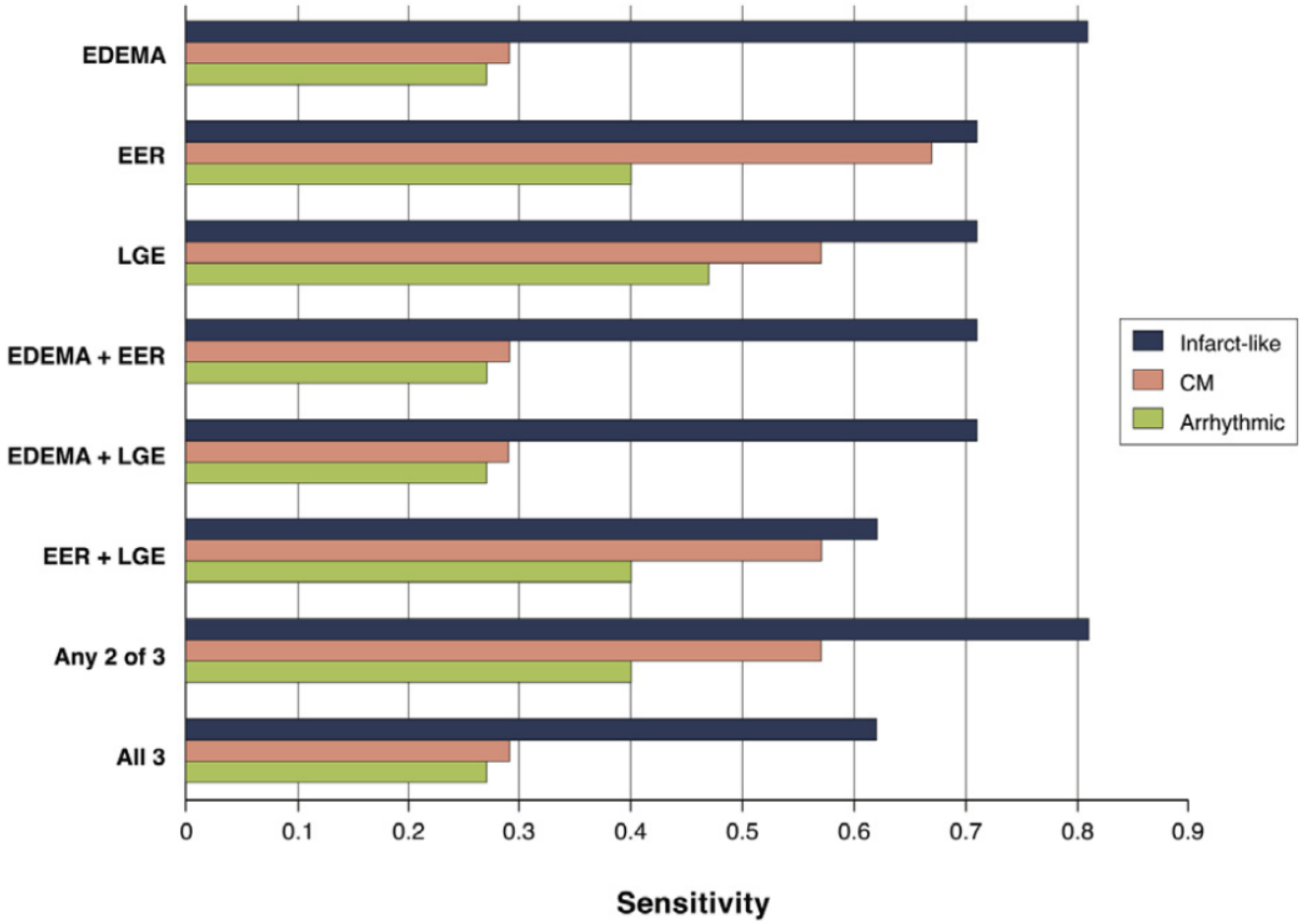
Comprehensive Cardiac Magnetic Resonance Imaging in Patients With Suspected Myocarditis

The MyoRacer-Trial



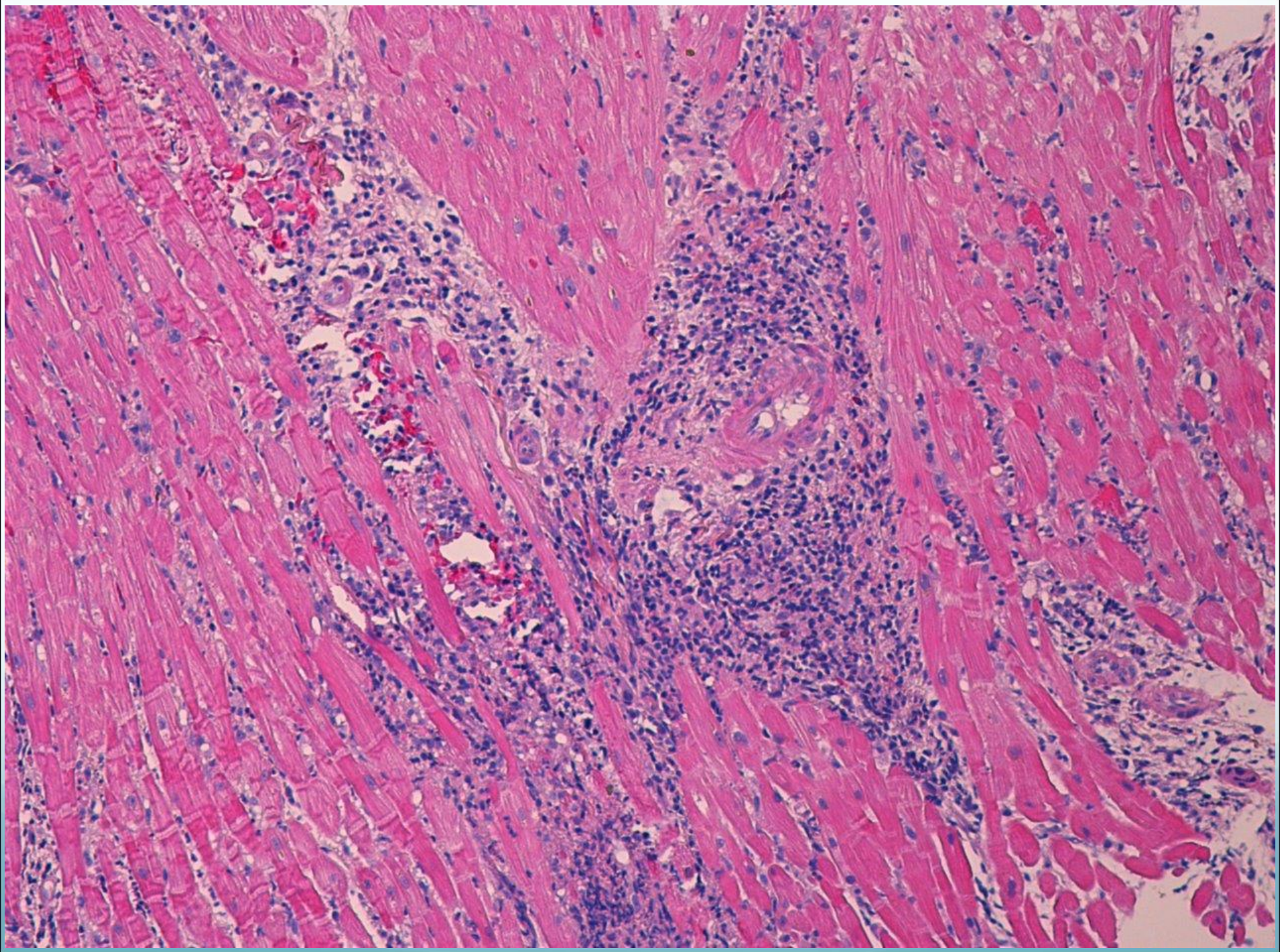
Lurz et al. J Am Coll Cardiol 2016;67:1800–11

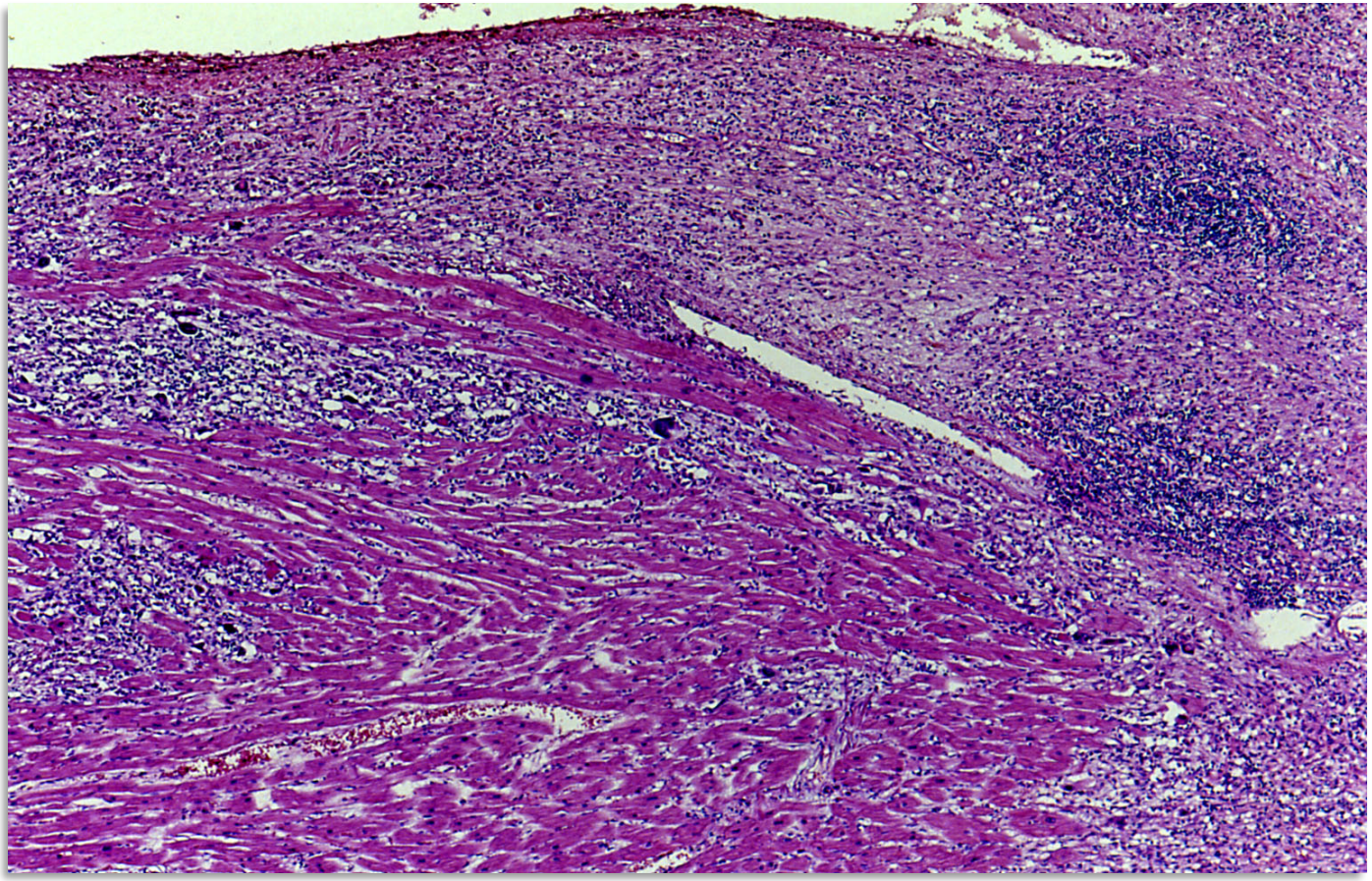
CMR Sensitivity Varies With Clinical Presentation and Extent of Cell Necrosis in Biopsy-Proven Acute Myocarditis

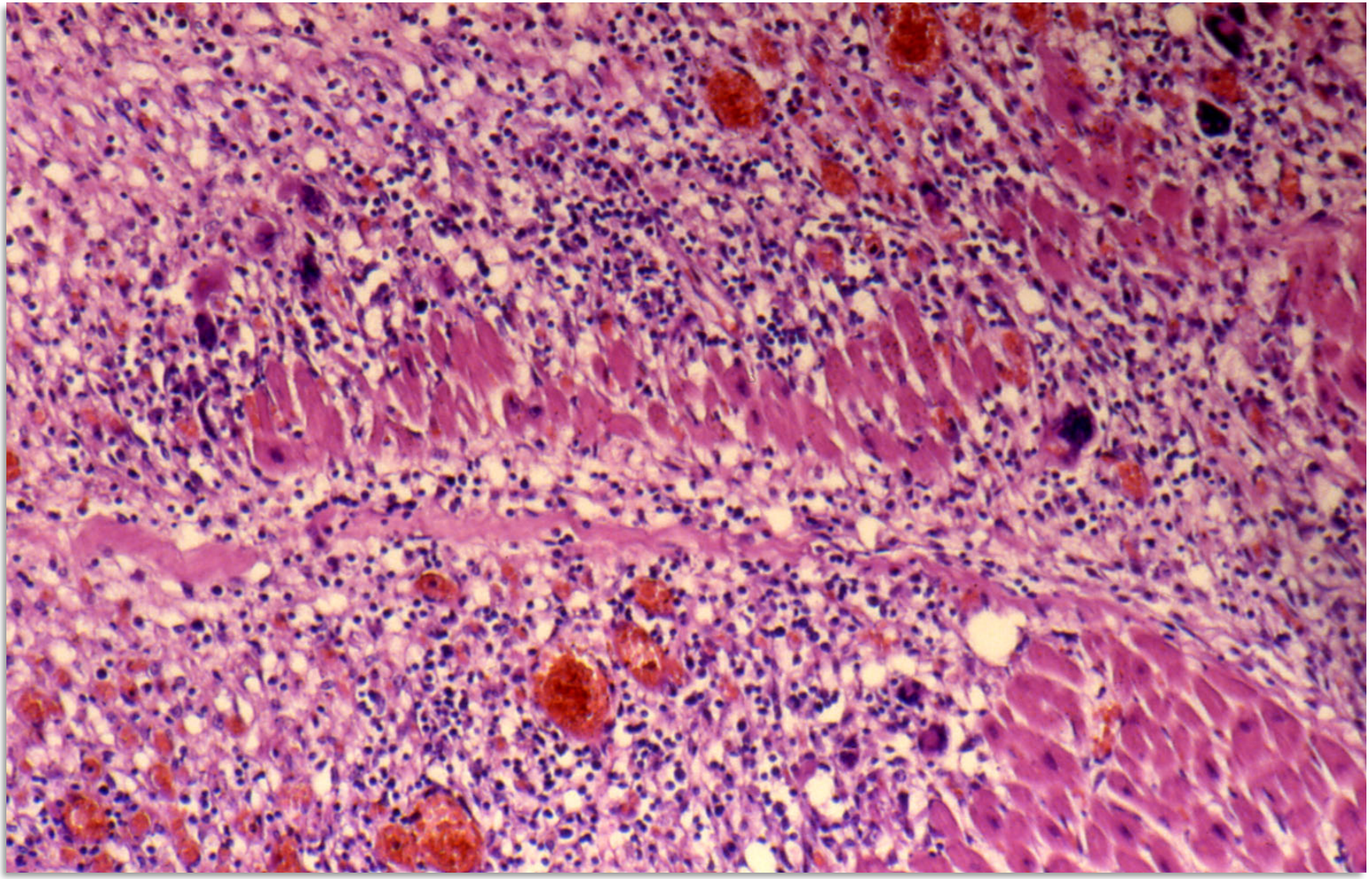


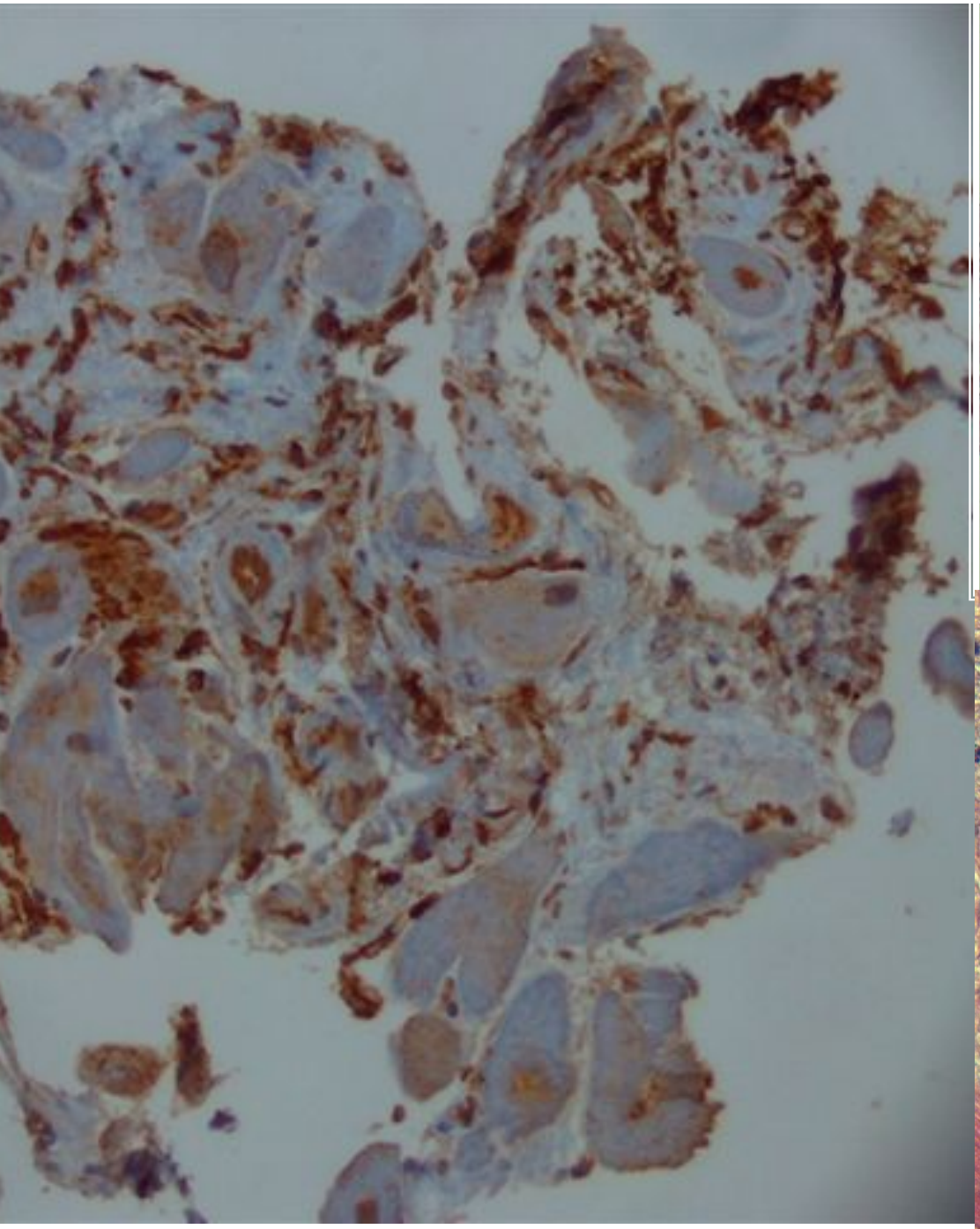
Francone M, Frustaci A et al;

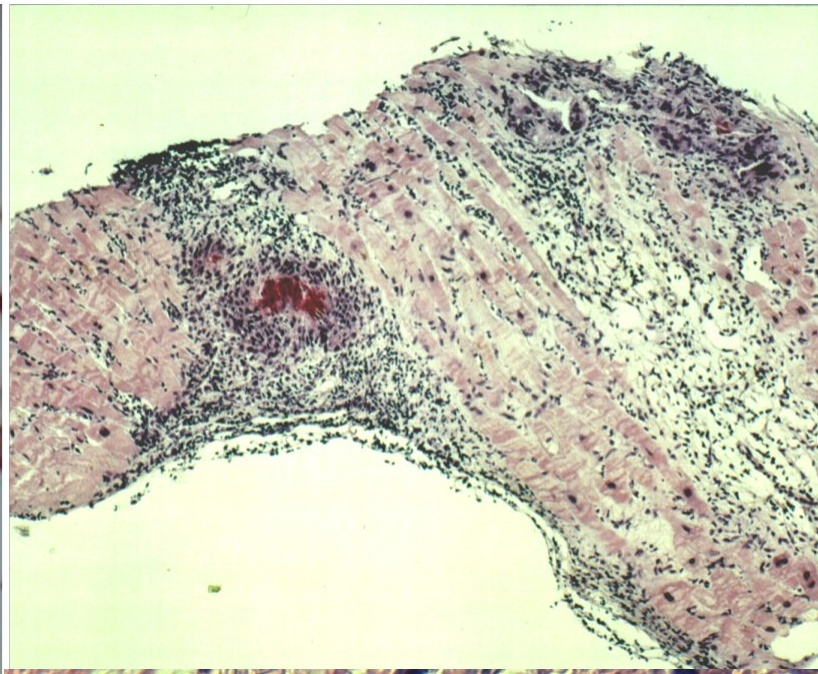
JACC: CARDIOVASCULAR IMAGING, VOL. 7, NO. 3, 2014
MARCH 2014:254–63

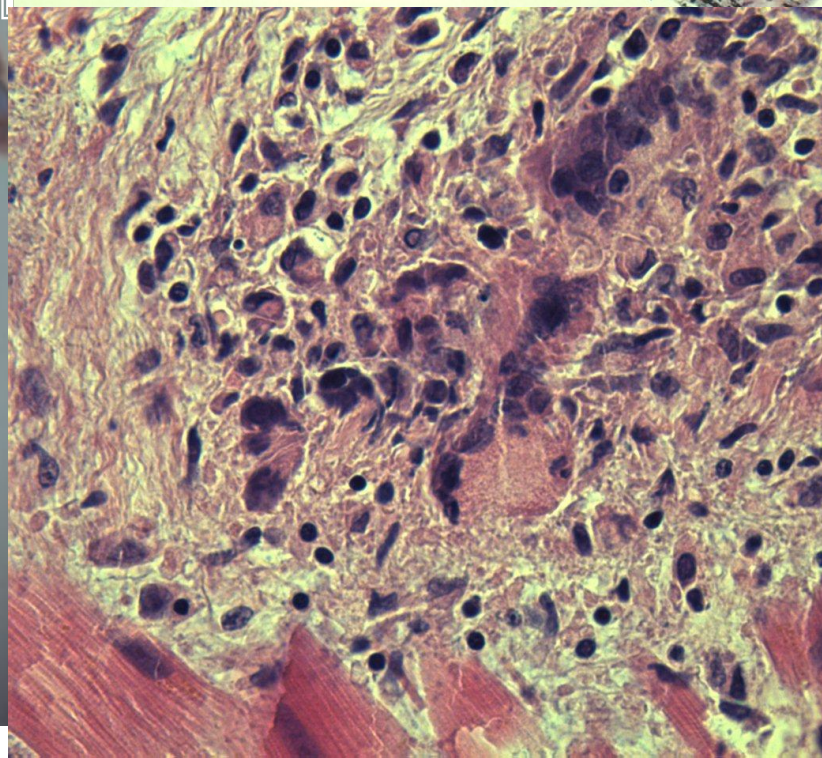


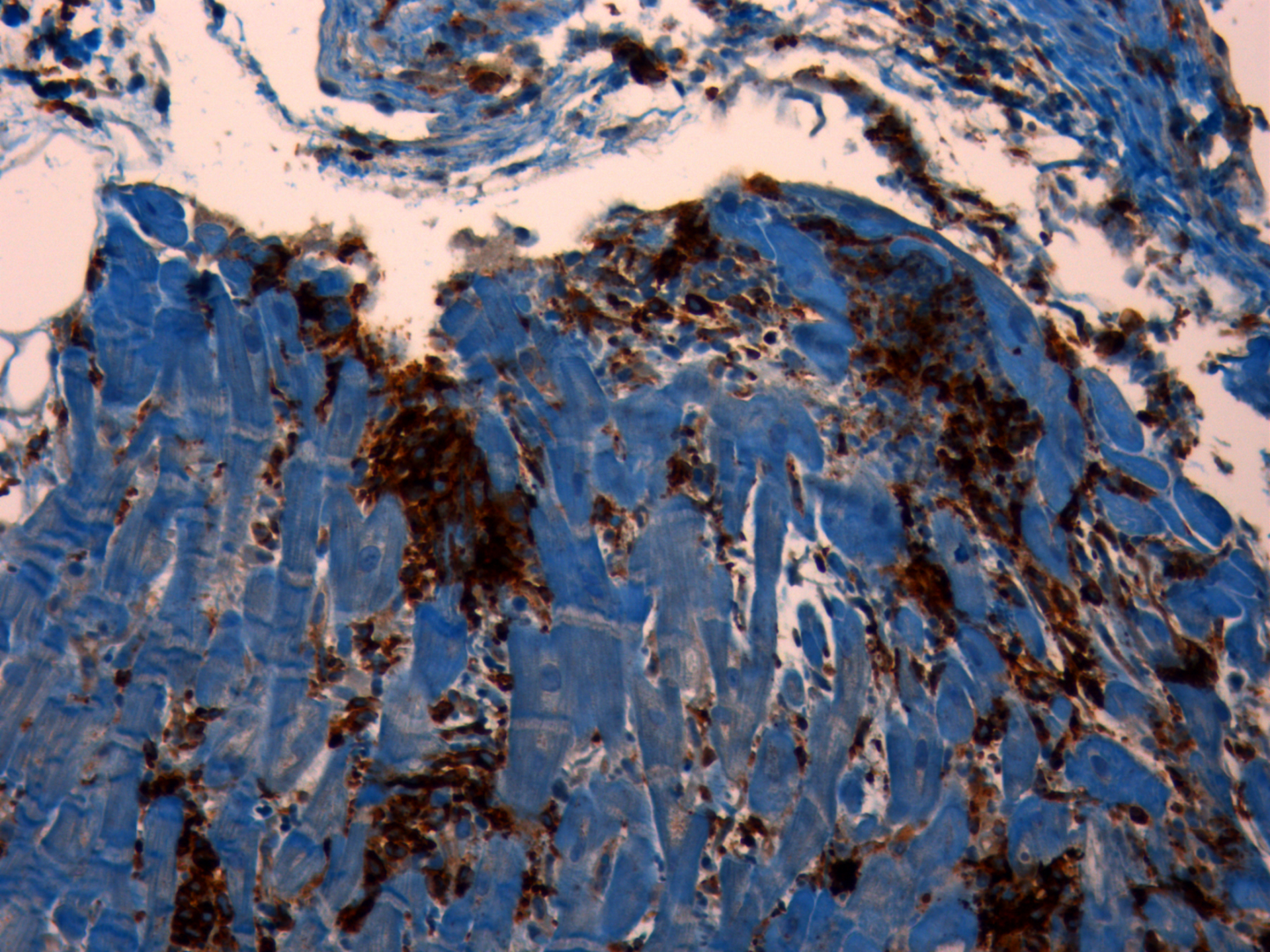












Federazione Italiana di Cardiologia

Documento di consenso sulla biopsia endomiocardica promosso dall'Associazione per la Patologia Cardiovascolare Italiana

Frequency: 0,3-1,7%

- Type: arrhythmias, free wall perforation, haemopericardium, pneumothorax, coronary fistulae, valve chordal rupture, embolism
- Overall risk of death: 0-0,13%

(G Ital Cardiol 2009; 10 (Suppl 1-9): 3S-4S)

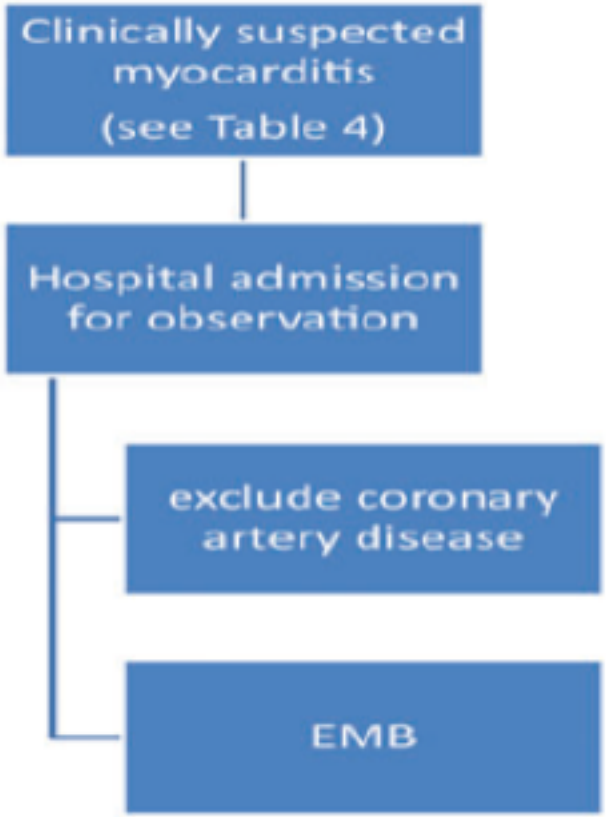
Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases

Alida L. P. Caforio[1]*, Sabine Pankuweit[2], Eloisa Arbustini[3], Cristina Basso[4], Juan Gimeno-Blanes[5], Stephan B. Felix[6], Michael Fu[7], Tiina Heliö[8], Stephane Heymans[9], Roland Jahns[10], Karin Klingel[11], Ales Linhart[12], Bernhard Maisch[1], William McKenna[13], Jens Mogensen[14], Yigal M. Pinto[15], Arsen Ristic[16], Heinz-Peter Schultheiss[17], Hubert Seggewiss[18], Luigi Tavazzi[19], Gaetano Thiene[4], Ali Yilmaz[20], Philippe Charron[21], and Perry M. Elliott[22]

EUROPEAN SOCIETY OF CARDIOLOGY®

Table 4 Diagnostic criteria for clinically suspected myocarditis

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



Recommendations

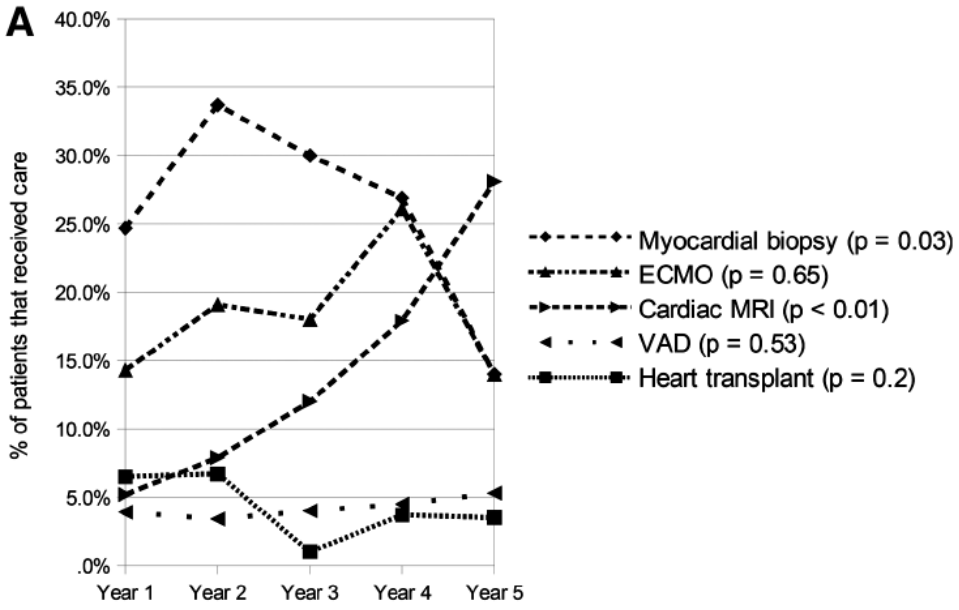
11. Tissue obtained from EMB should be analysed using histology, immunohistochemistry, and viral PCR (on heart tissue and a blood sample).
12. At least three myocardial samples, each 1–2 mm in size, should be taken (from the right or from the left ventricle) and immediately fixed in 10% buffered formalin at room temperature for light microscopy; additional samples should be taken, snap frozen in liquid nitrogen, and stored at −80°C, or stored in RNA later tubes at room temperature, for viral PCR.[2,149]
13. Endomyocardial biopsy may be repeated if necessary to monitor response to aetiology-directed therapy, or if a sampling error is suspected in a patient with unexplained progression of heart failure.

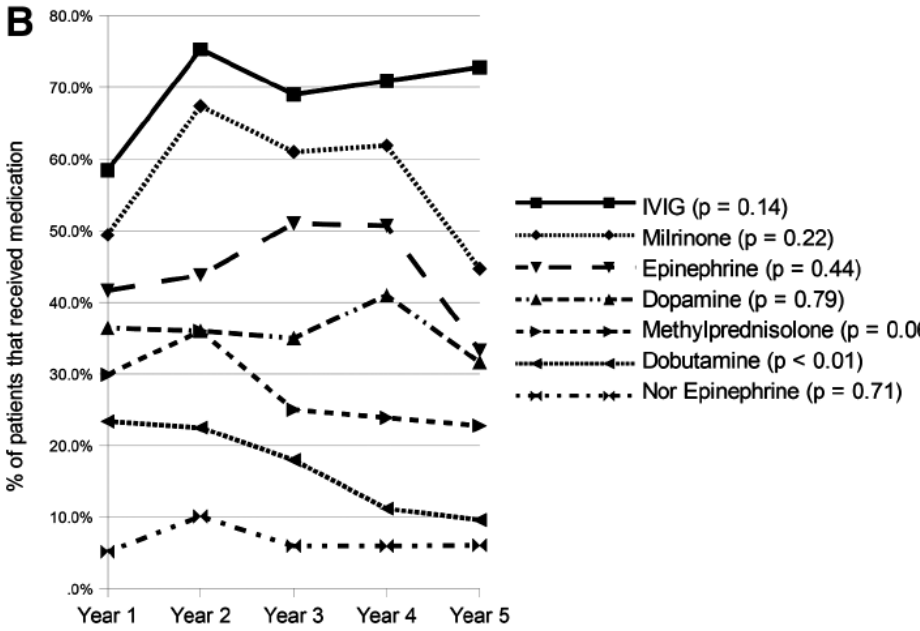
European Heart Journal (2013) **34**, 2636–2648

Demographics, Trends, and Outcomes in Pediatric Acute Myocarditis in the United States, 2006 to 2011

Sunil J. Ghelani, MBBS, MD; Michael C. Spaeder, MD, MS; William Pastor, MA, MPH; Christopher F. Spurney, MD; Darren Klugman, MD, MMS

Circ Cardiovasc Qual Outcomes. 2012;5:622-627.





Ospedali Riuniti di Trieste

ACCF/AHA Practice Guideline

2013 ACCF/AHA Guideline for the Management of Heart Failure

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines

Table 11. Recommendations for Invasive Evaluation

Recommendations	COR	LOE
Monitoring with a pulmonary artery catheter should be performed in patients with respiratory distress or impaired systemic perfusion when clinical assessment is inadequate	I	C
Invasive hemodynamic monitoring can be useful for carefully selected patients with acute HF with persistent symptoms and/or when hemodynamics are uncertain	IIa	C
When ischemia may be contributing to HF, coronary arteriography is reasonable	IIa	C
Endomyocardial biopsy can be useful in patients with HF when a specific diagnosis is suspected that would influence therapy	IIa	C
Routine use of invasive hemodynamic monitoring is not recommended in normotensive patients with acute HF	III: No Benefit	B[305]
Endomyocardial biopsy should not be performed in the routine evaluation of HF	III: Harm	C

COR indicates Class of Recommendation; HF, heart failure; and LOE, Level of Evidence.

Class IIa

3. **Endomyocardial biopsy can be useful in patients presenting with HF when a specific diagnosis is suspected that would influence therapy.** ***(Level of Evidence: C)***

Class III: Harm

1. **Endomyocardial biopsy should not be performed in the routine evaluation of patients with HF.** ***(Level of Evidence: C)***

European Heart Journal
doi:10.1093/eurheartj/ehw128

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

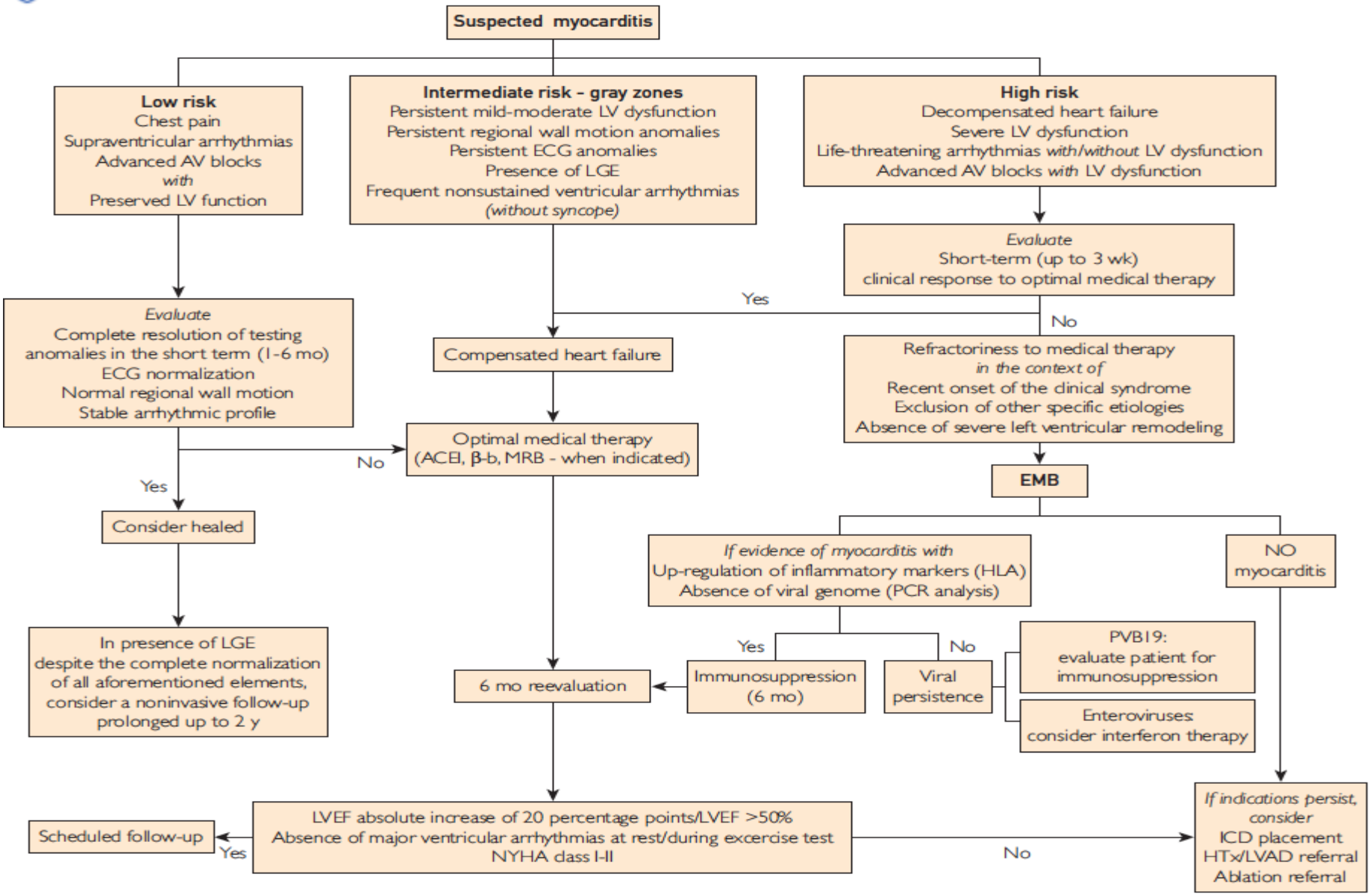
The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

EMB should be considered in patients with rapidly progressive HF despite standard therapy when there is a probability of a specific diagnosis which can be confirmed only in myocardial samples and specific therapy is available and effective.	IIa	C	93

Cooper et al. Eur Heart J 2007;28:3076-3093

MAYO CLINIC

Myocarditis in Clinical Practice



Sinagra et al Mayo Clin Proc. ■ September 2016;91(9):1256-1266

[Intervention Review]

Corticosteroids for viral myocarditis

Huai Sheng Chen[1], Wei Wang[2], Sheng Nan Wu[3], Jian Ping Liu[4]

[1]Intensive Care Unit, Shenzhen People's Hospital, The Second Affiliated Hospital of Ji Nan University, Shenzhen City, China. [2]Endocrinology, Shenzhen People's Hospital, Shenzhen City, China. [3]Intensive Care Unit, Shenzhen People's Hospital, The Second Affiliated Hospital of Ji Nan University, Shenzhen City, China. [4]Centre for Evidence-Based Chinese Medicine, Beijing University of Chinese Medicine, Beijing, China

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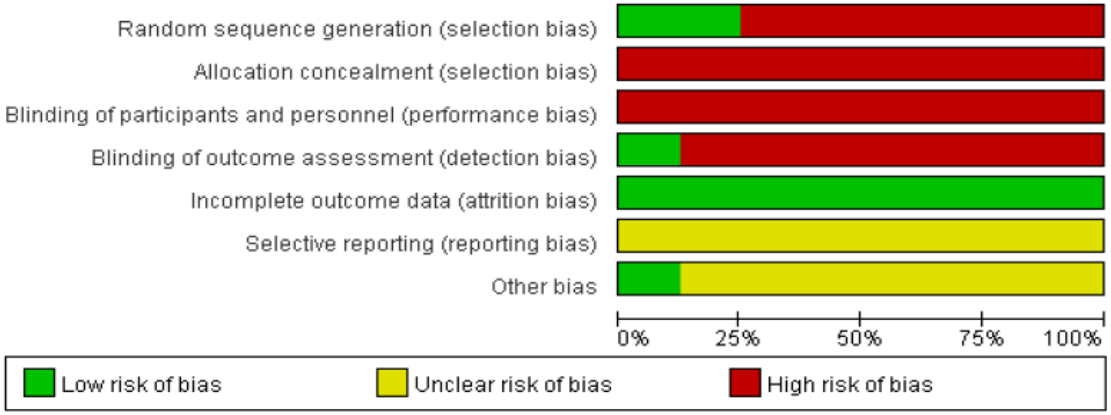
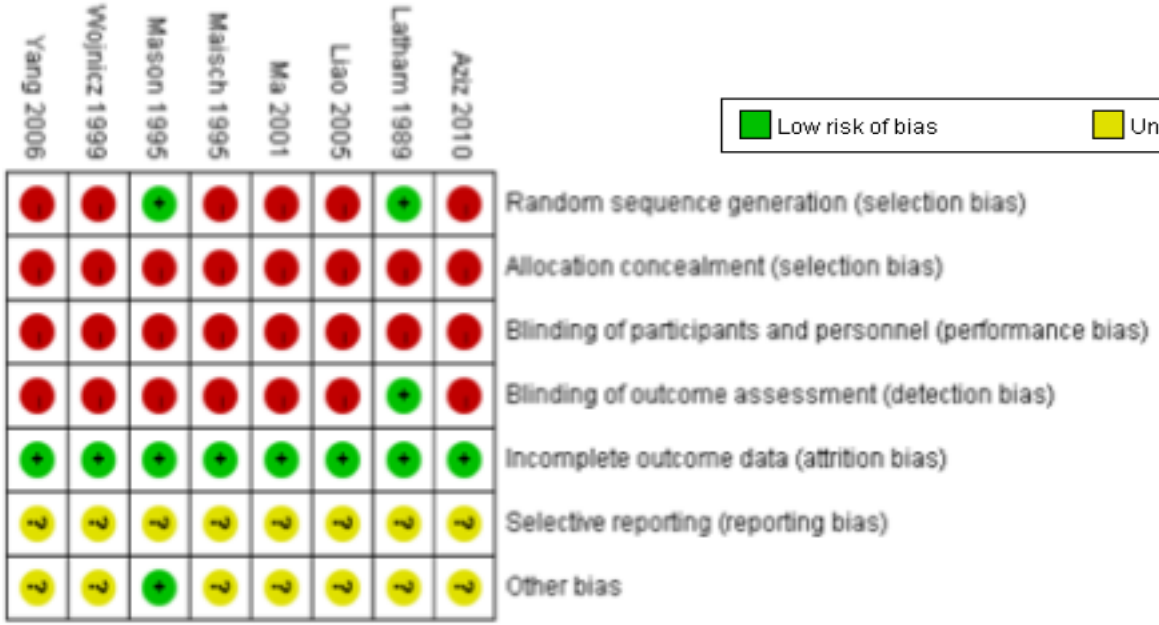


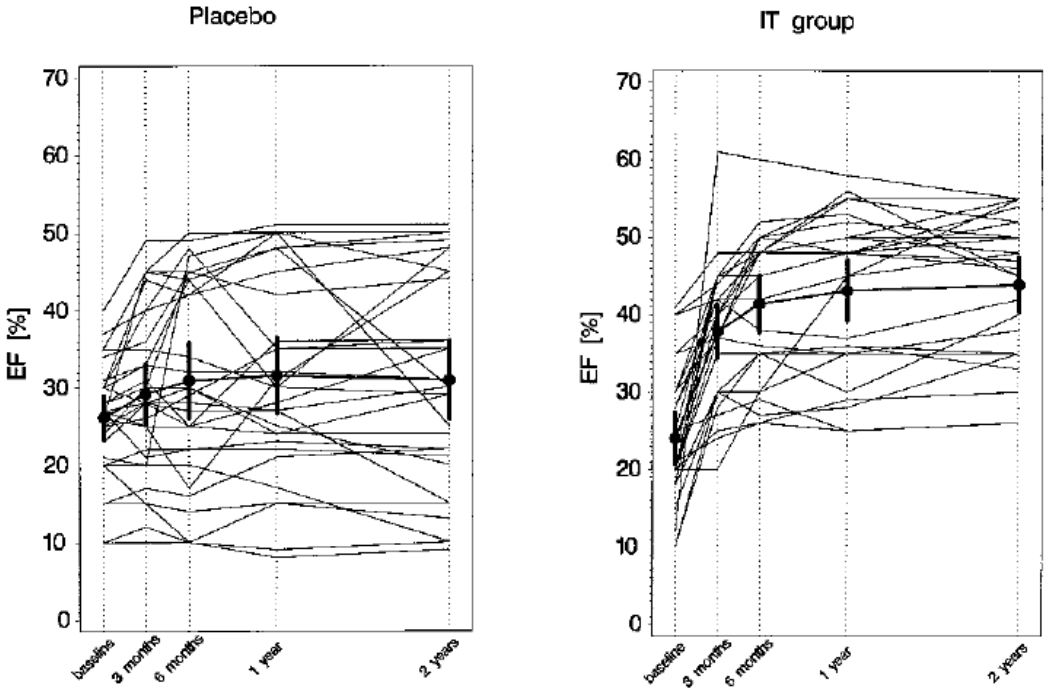


Chen, et al. Cochrane Database of Systematic Reviews 2013, Issue 10.

Randomized, Placebo-Controlled Study for Immunosuppressive Treatment of Inflammatory Dilated Cardiomyopathy : Two-Year Follow-Up Results

Romuald Wojnicz, Ewa Nowalany-Kozielska, Celina Wojciechowska, Grazyna Glanowska, Przemyslaw Wilczewski, Tomasz Niklewski, Marian Zembala, Lech Polonski, Marius M. Rozek and Jan Wodniecki

Circulation 2001, 104:39-45



Studio Randomizzato Controllato

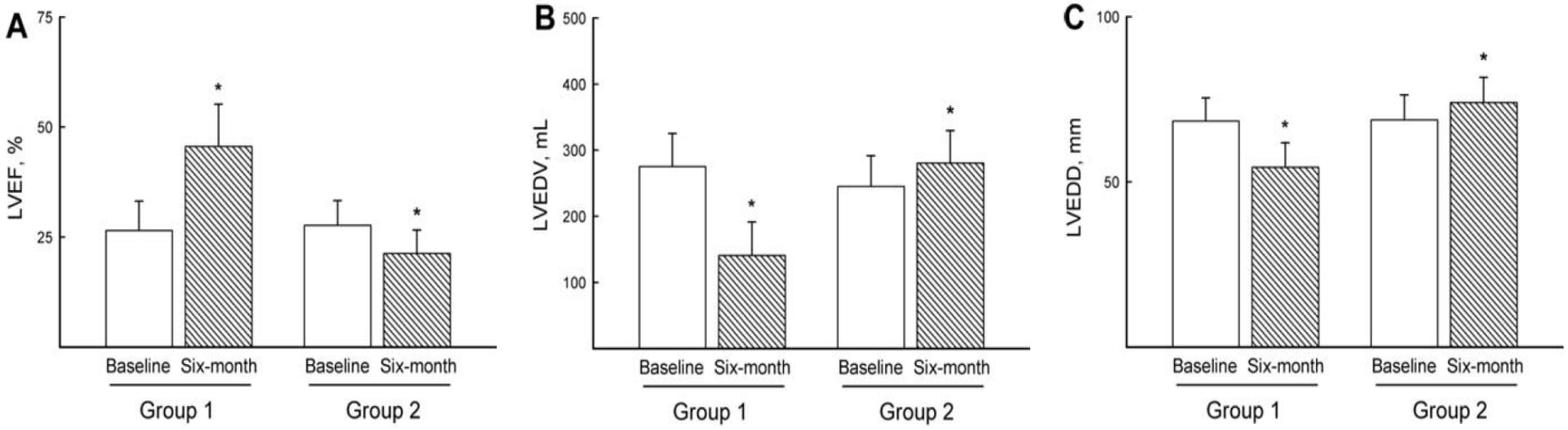
Pazienti con sintomi di SCC da almeno 6 mesi

Arruolameno in base a Immunoistochimica (Immunoattivazione)

Randomized study on the efficacy of immunosuppressive therapy in patients with virus-negative inflammatory cardiomyopathy: the TIMIC study

European Heart Journal (2009) **30**, 1995–2002

Andrea Frustaci[1,2]*, Matteo A. Russo[3,4], and Cristina Chimenti[1,2,4]

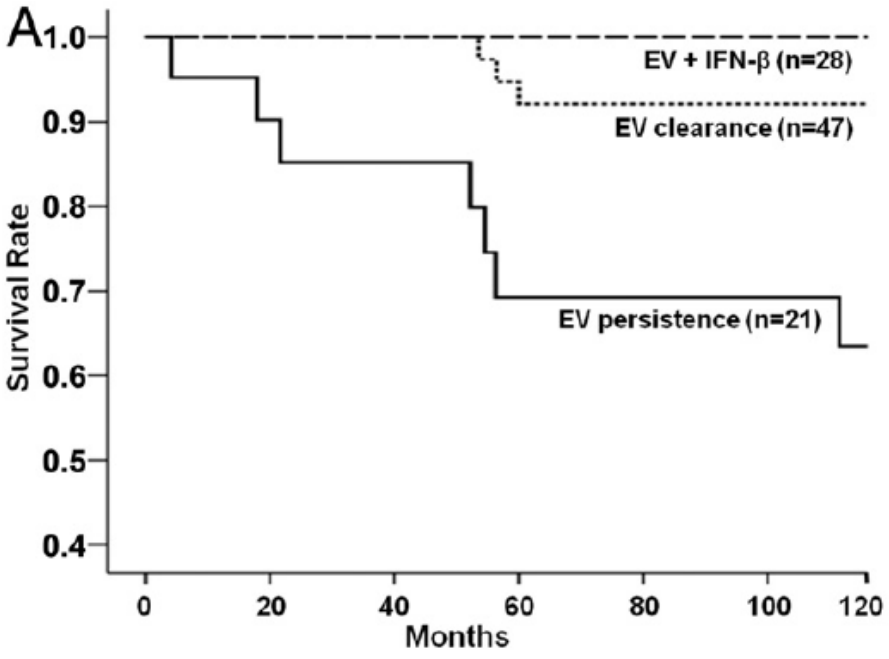


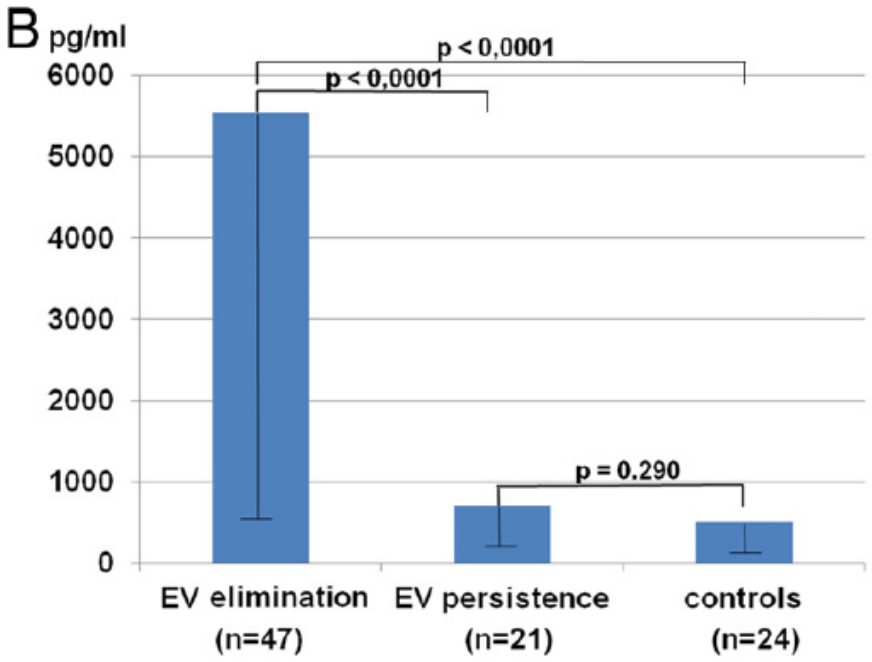
Studio Randomizzato Controllato
Pazienti con sintomi di SCC da almeno 6 mesi
Eleggibilità se Immunoistochimica positiva e Virologia negativa

Research Correspondence

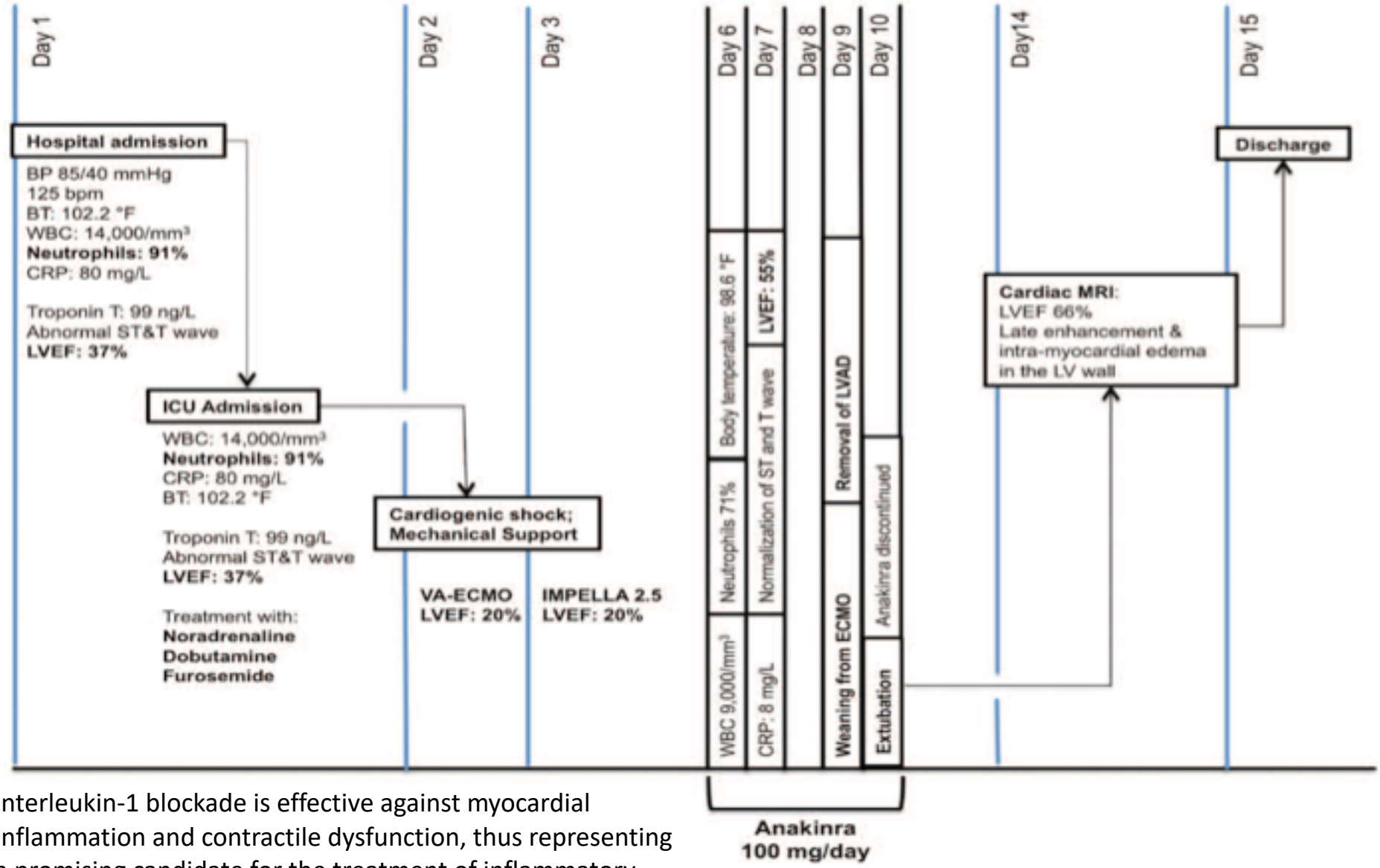
JACC Vol. 60, No. 14, 2012
October 2, 2012:1295–6

Interferon-Beta Improves Survival in Enterovirus-Associated Cardiomyopathy





Treating Life-Threatening Myocarditis by Blocking Interleukin-1



interleukin-1 blockade is effective against myocardial inflammation and contractile dysfunction, thus representing a promising candidate for the treatment of inflammatory heart failure

Cavalli et al. Crit Care Med 2016;

Take home message: quali indicazioni a BEM a scopo clinico?

- Shock cardiogeno;
- OHCA;
- HF/aritmie VE minacciose persistenti malgrado terapia convenzionale;
- perimiocarditi ricorrenti anche senza HF/Aritmie;
- quadri migliorati con persistente severa disfunzione (LVEF <40%);
- malattie infiammatorie sistemiche in immunosoppressione con sospetto di forme infettive specifiche o ausilio all'intensità di immunosoppressione;
- dati controversi su protocolli di terapia specifica e responders a IS;
- spazio per terapia convenzionale ed osservazione evoluzione (prime 2-4 settimane);
- CRM nelle prime 2 sett;
- se BEM + con immunoistochimica+ e virologia molecolare -, vi sono indicazioni a tp immunosoppressiva (steroide+AZA)