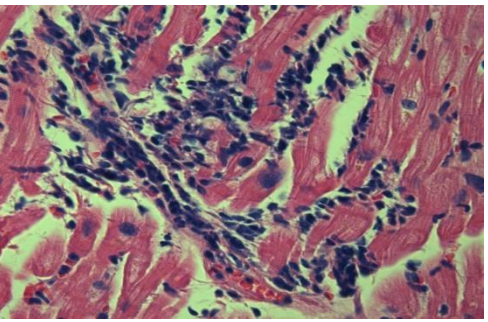
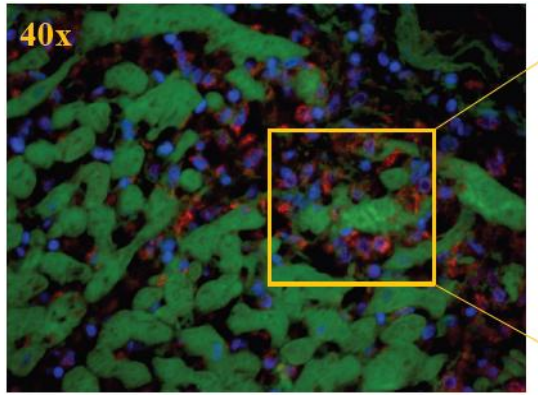
Fisiopatologia della “Miocardite”





First phase

Direct virus mediated myocardial damage

Second phase

Secondary viral mediated autoimmune myocardial injury

Third phase

Myocardial remodeling leading to DCM

Acute viral infection

Myocarditis

Genetic susceptibility

Fulminant

Asymptomatic

Chronic

Death

Recovery (complete or incomplete)

DCM

Dennert R, Crijns HJ, Heymans S. Acute viral myocarditis. Eur Heart J 2008;29:2073-82

Heart 2001;85:499–504 499

REVIEW

The fate of acute myocarditis between spontaneous improvement and evolution to dilated cardiomyopathy: a review

A D'Ambrosio, G Patti, A Manzoli, G Sinagra, A Di Lenarda, F Silvestri, G Di Sciascio

Assenza di sintomi

Dolore toracico

Aritmie ipocinetiche/ ipercinetiche

Scompenso cardiaco

Forma fulminante

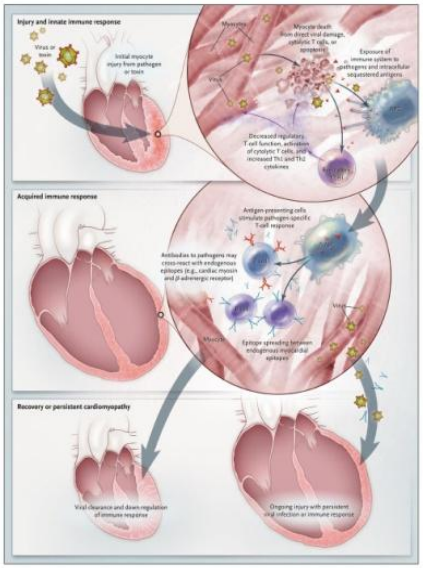
Guarigione completa o incompleta

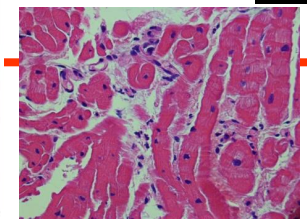
CMPD

Morte improvvisa

Morte in shock e MOF

-·-·-·- evoluzione possibile





Ospedali Riuniti di Trieste

Facoltà di Medicina e Chirurgia – Università degli Studi di Trieste

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

Registro Cardiomiopatie di Trieste - Miocarditi

	Pop. totale (82; 100%)	**SCC (53; 65%)**	**Aritmie (20; 24%)**	**Pseudo-IMA (9; 11%)**	**p value ***
Recente virosi – no. (%)	58(70)	39(74)	13(65)	6(67)	0.742
Puntura d'insetto – no. (%)	12(15)	4(8)	8(40)	0(0)	0.001
Durata sintomi – giorni	8[1-30]	15[5-54]	3.5[1-12]	1[1-14]	0.013
NYHA III-IV – no. (%)	39(48)	36(68)	3(15)	0(0)	<0.001
Press. Art. Sist. – mmHg	123±20	118±19	134±20	126±23	0.009
Frequenza cardiaca – bpm	88±28	98±26	64±19	84±22	<0.001
BBS – no. (%)	12(15)	10(19)	2(10)	0(0)	0.266
DASI – mm/m^2	22±5	24±5	18±3	19±3	<0.001
DTD VS I – mm/m^2	34[29-38]	36[33-40]	26[25-32]	27[26-30]	<0.001
FE VS – %	32[24-52]	28[21-32]	57[49-64]	56[53-64]	<0.001
FE VS < 50 % – no. (%)	59(72)	53(100)	5(25)	1(11)	<0.001

* p tra i gruppi (analisi della varianza)

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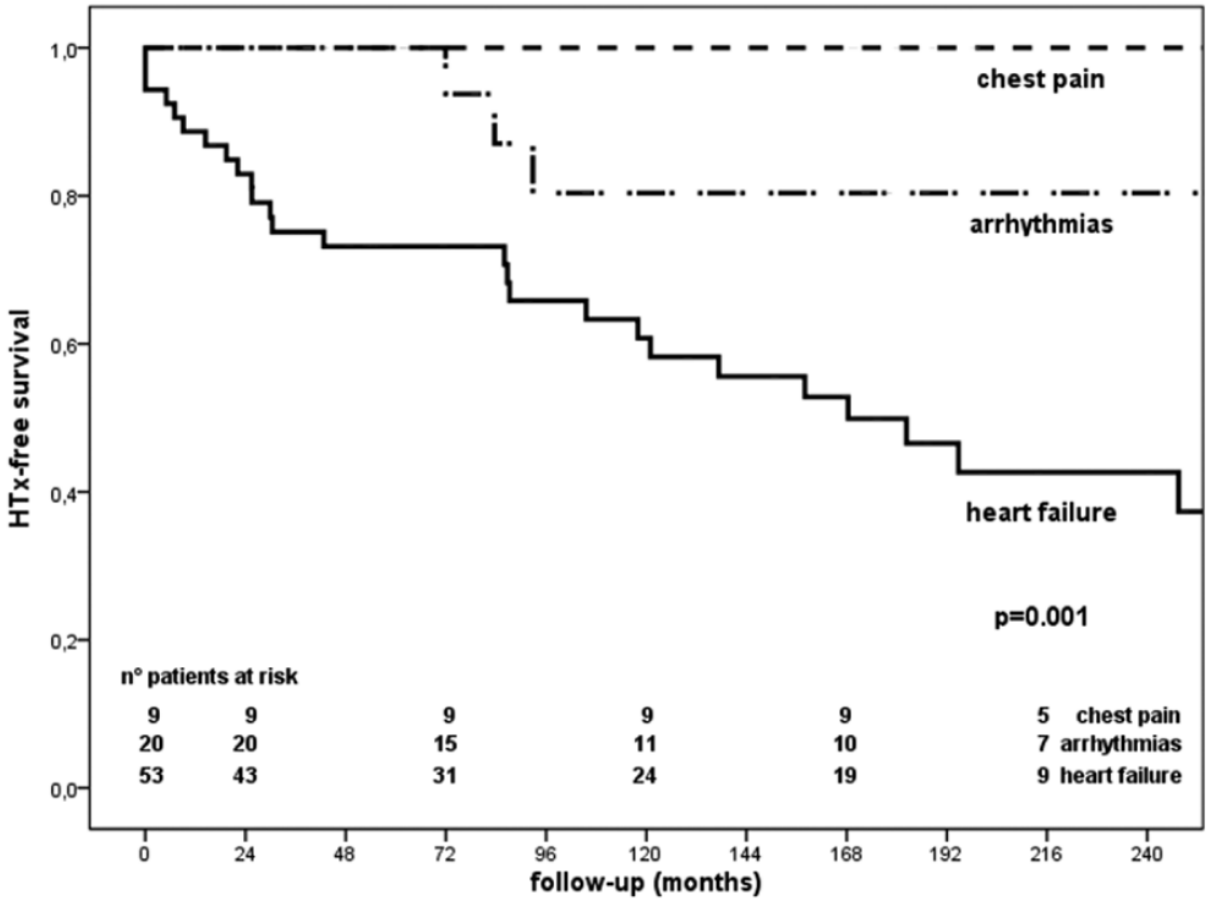
82 pts; Fup 147 mo; 5
53% 6 mo impr/norm
LVEF



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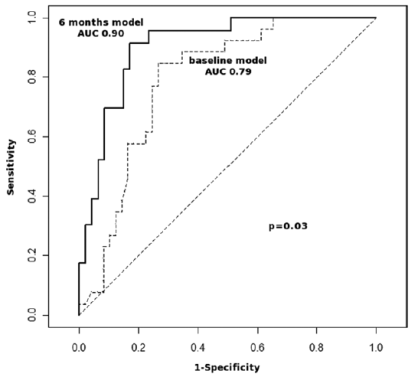
	Univariable Analysis			Multivariable Analysis			
	HR	CI 95%	*P* Value	HR	CI 95%	*P* Value	Missing, n (%)
Clinical findings							
NYHA functional class III–IV	37.153	7.362–187.507	<0.001	16.237	3.193–30.572	0.001	1 (1)
Echocardiographic findings							
LADI, mm/m (for 1 mm/m increase)	1.229	1.081–1.397	0.002	1.178	1.030–1.348	0.017	5 (6)
LVEF, % (for 5-U decrease)	1.560	1.347–1.808	<0.001				0
LVEF < 50%	41.175	5.523–304.625	<0.001				0
LVEDDI, mm/m (for 1 mm/m increase)	1.091	1.037–1.148	0.001				4 (5)
Improved/normal LVEF	0.020	0.003–0.152	<0.001	0.028	0.004–0.213	0.001	0

CI indicates confidence interval; HR, hazard ratio; HTx, heart transplantation; LADI, left atrium diameter indexed to height; LVEDDI, left ventricular end-diastolic diameter indexed to height; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.



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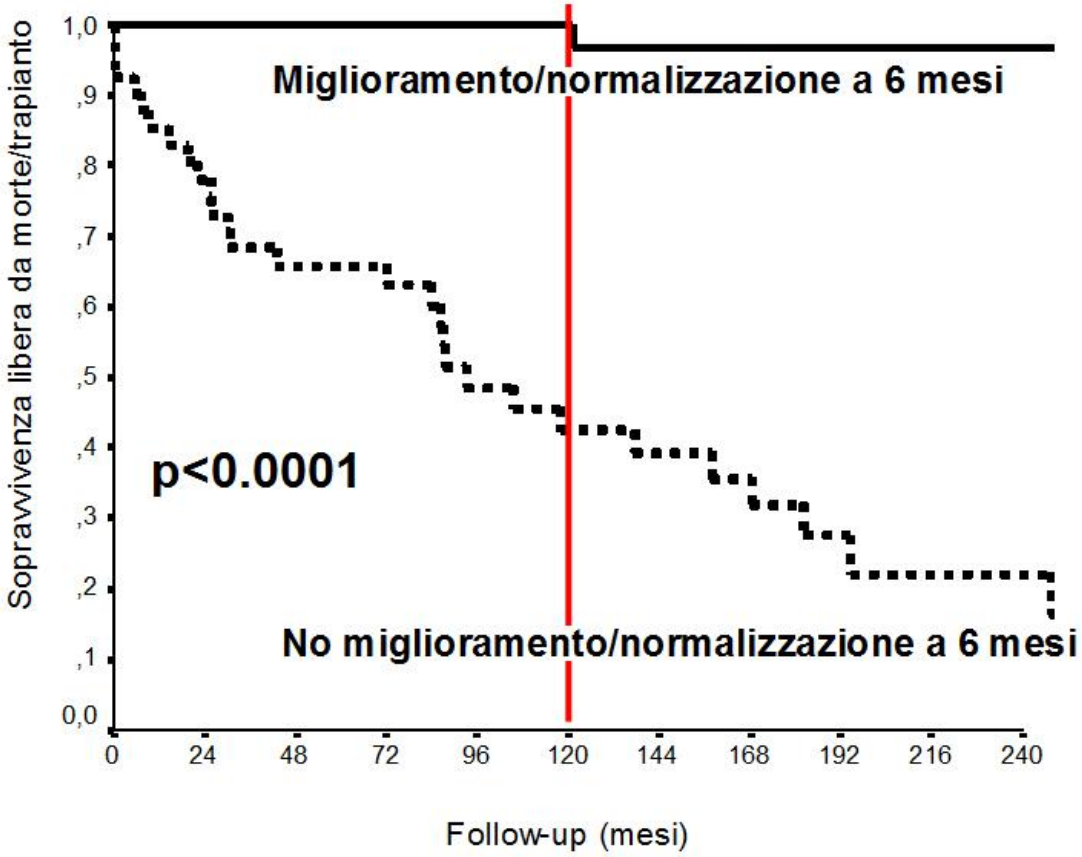
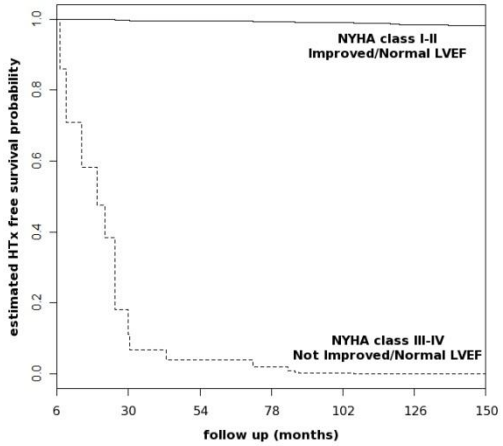
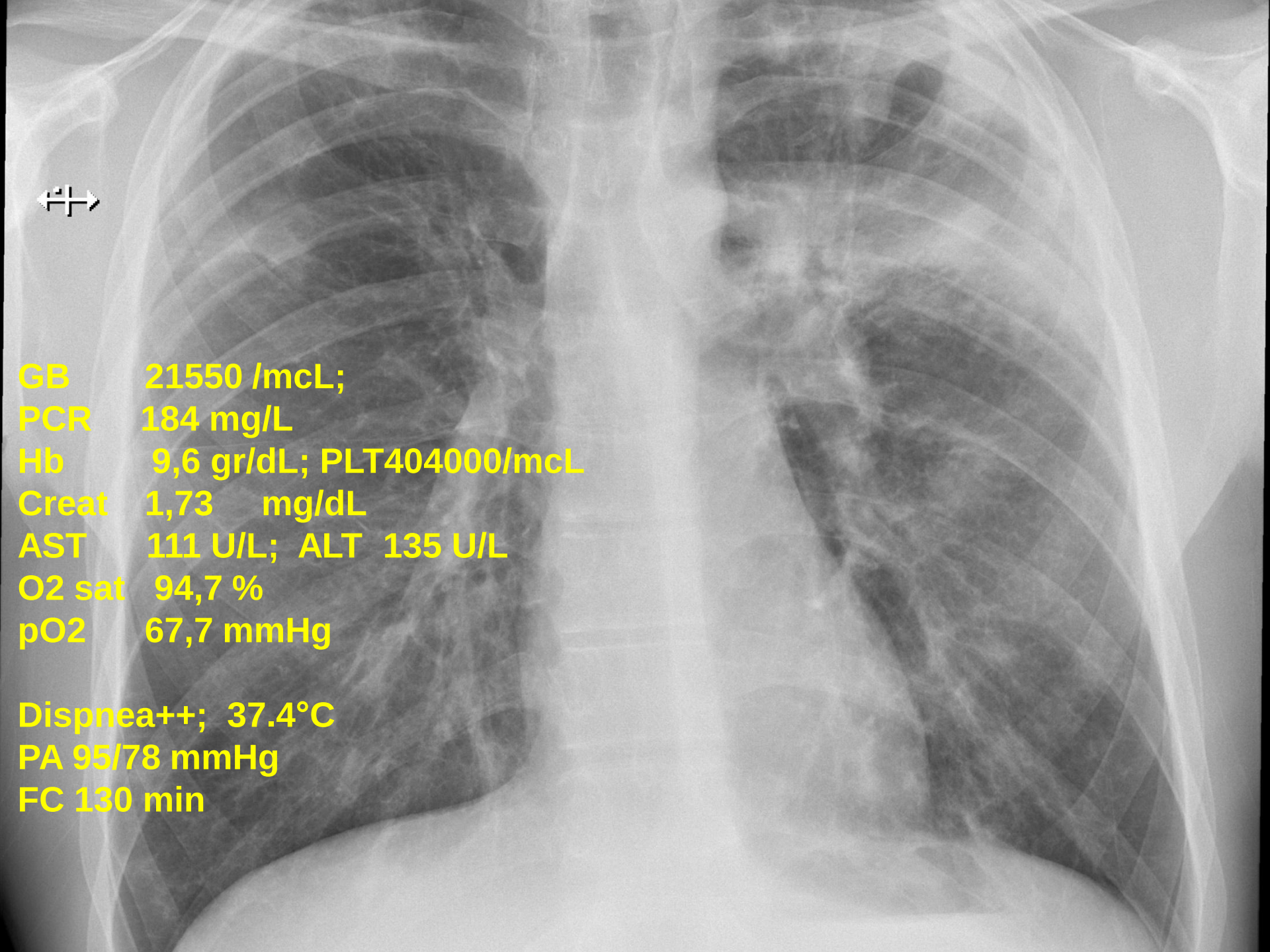
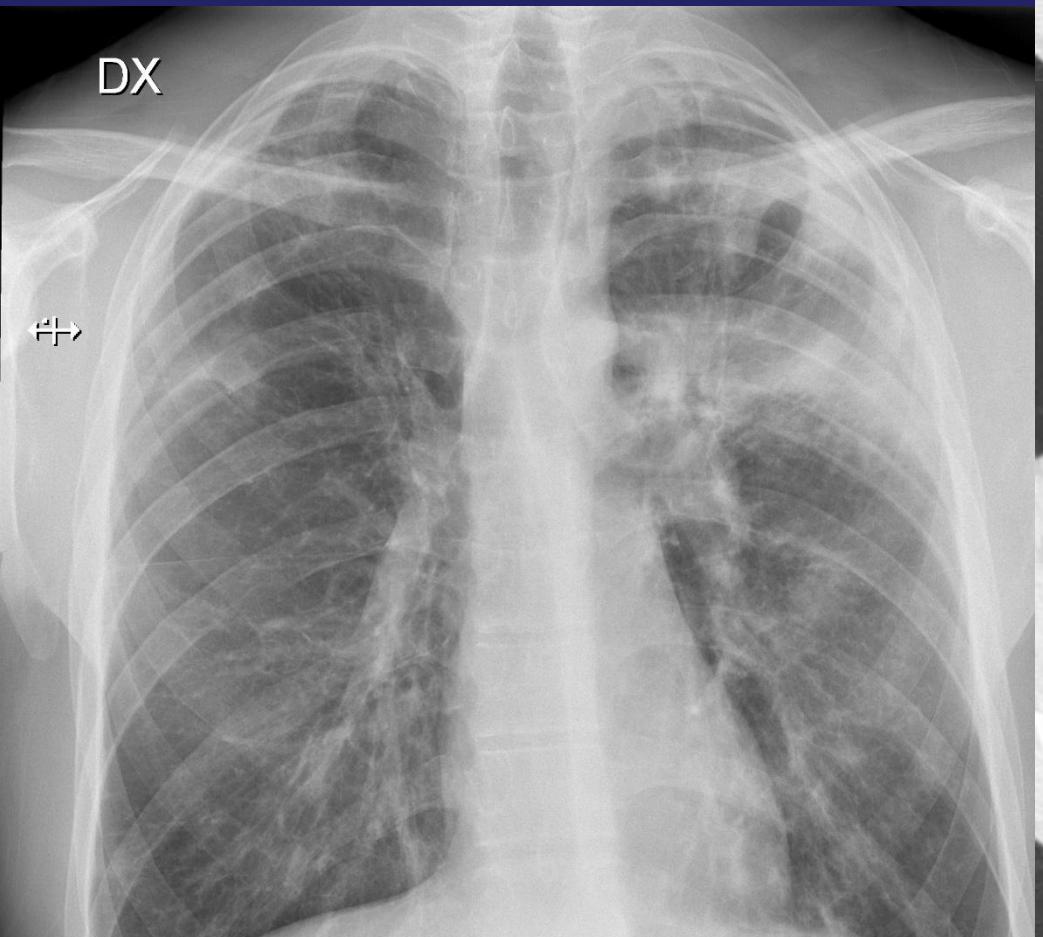
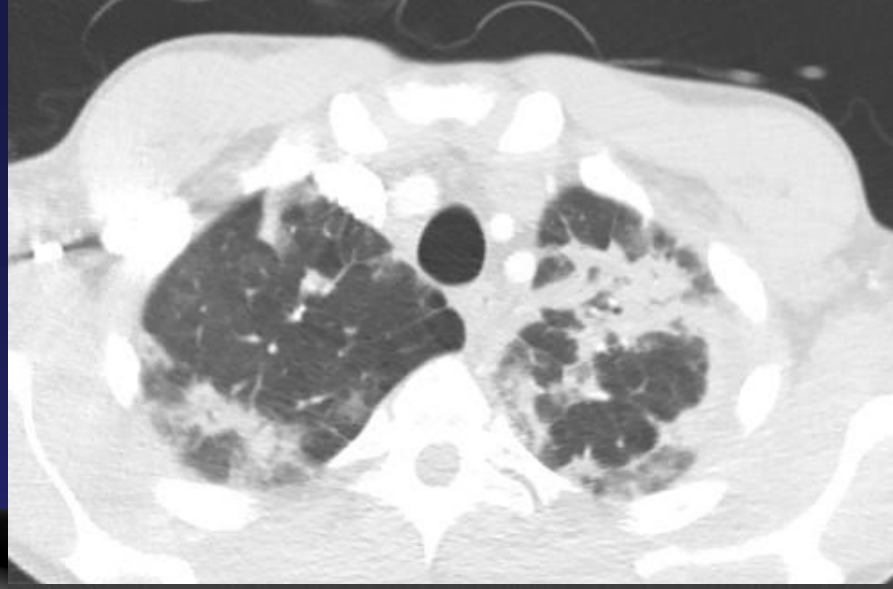


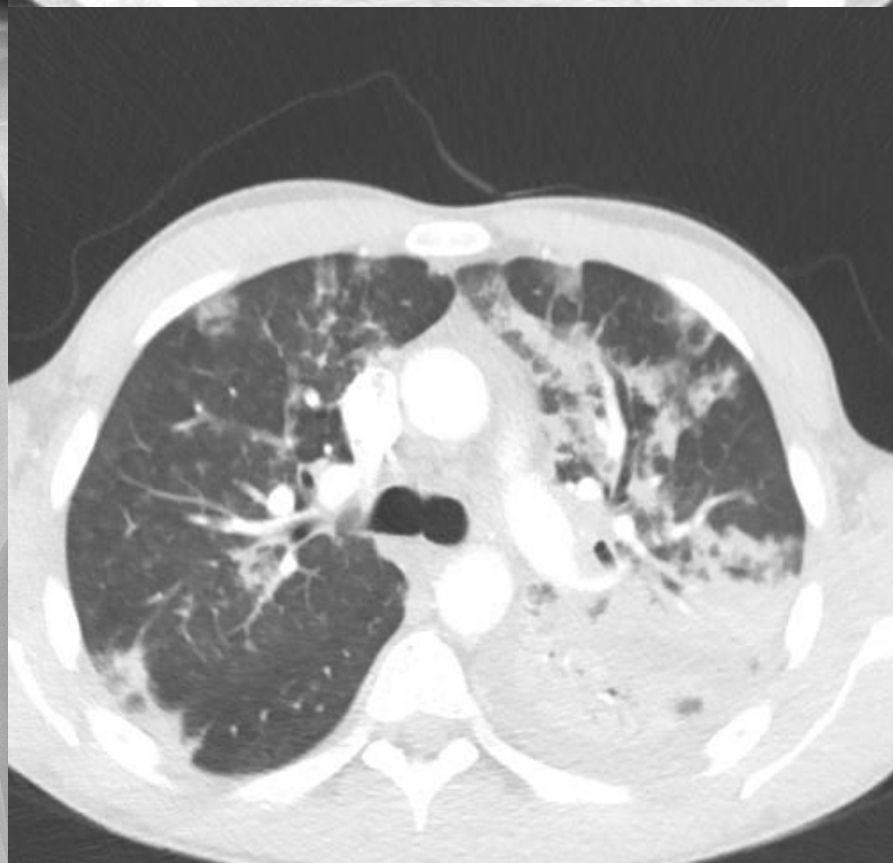


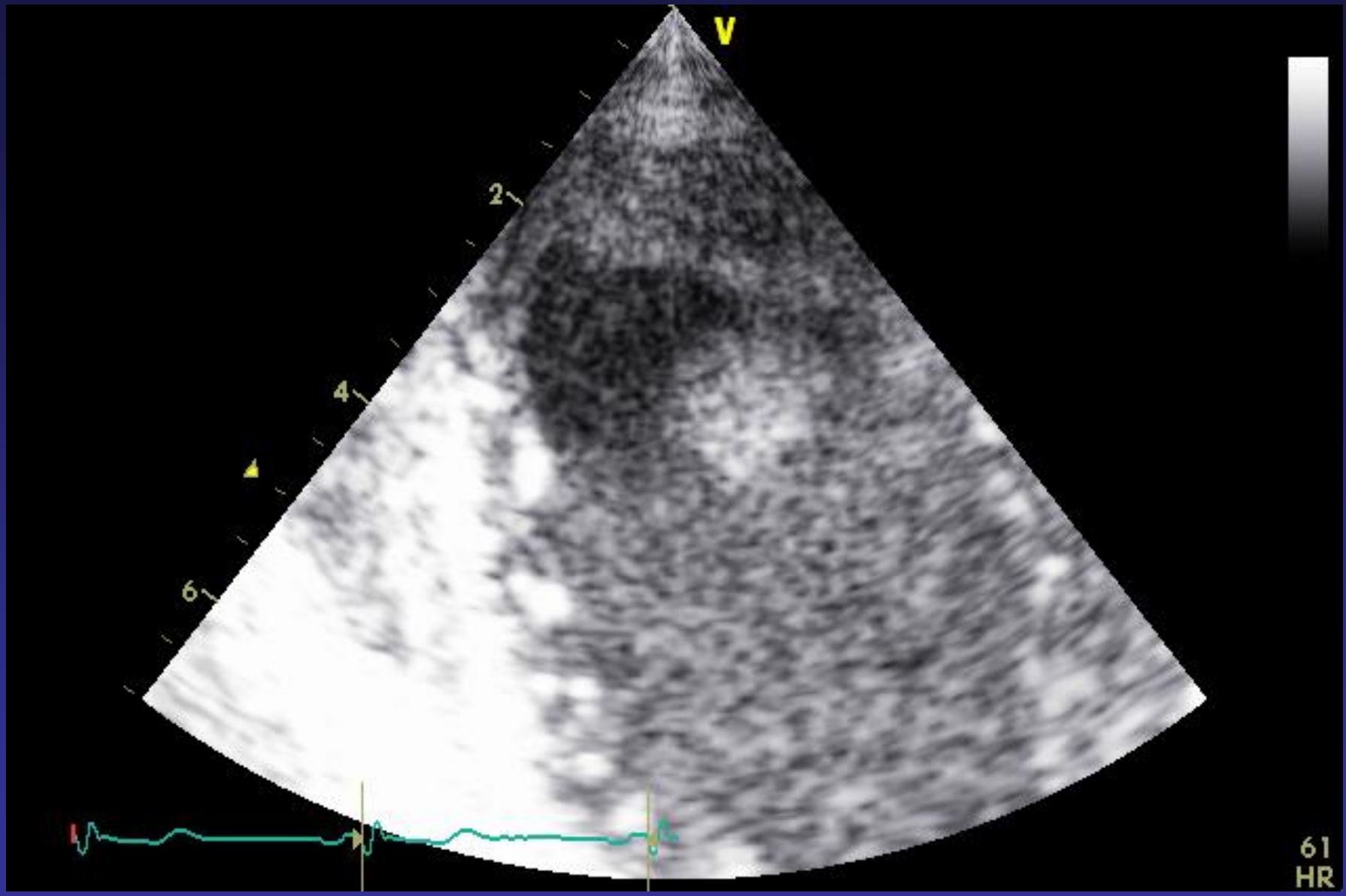

GB 21550 /mcL;
PCR 184 mg/L
Hb 9,6 gr/dL; PLT404000/mcL
Creat 1,73 mg/dL
AST 111 U/L; ALT 135 U/L
O2 sat 94,7 %
pO2 67,7 mmHg
Dispnea++; 37.4°C
PA 95/78 mmHg
FC 130 min

GB 21550 /mcL; N 6900;
L 2370; E 10340 /mcL
PCR 184 mg/L
BNP 1392 pg/ml

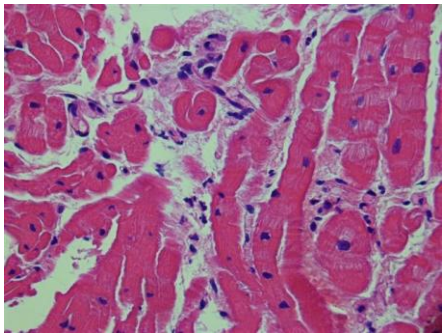







V
2
4
6
61
HR

Eterogeneità di evoluzione clinica (1)

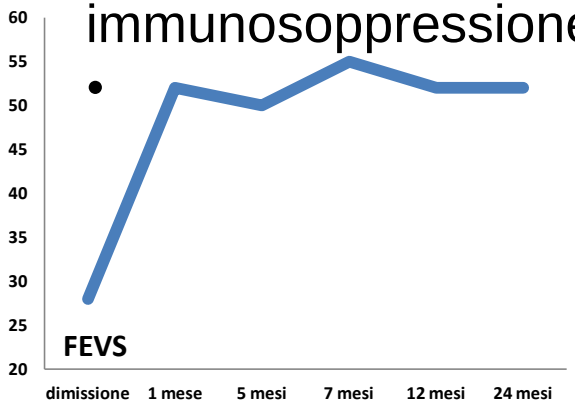


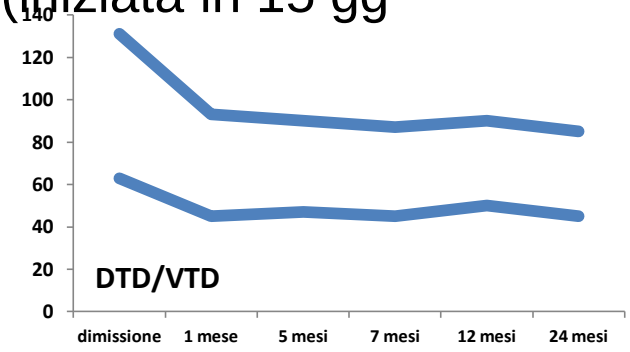
CS, m, 53 anni

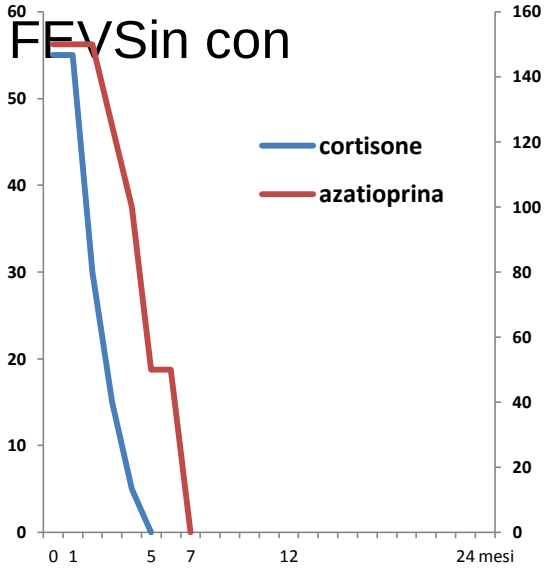
- Miocardite acuta esordita con shock
- FEVS 20%, DTD 63 mm, pattern restrittivo; FACCVDx 25%
- Necessità di inotropi e IABP
- Difficoltoso svezzamento da supporto emodinamico

- RMN (7 gg) negativa [T2/T1-LGE]
- BEM (10 gg): miocardite attiva; ricerca genoma virale negativa [RT-PCR]

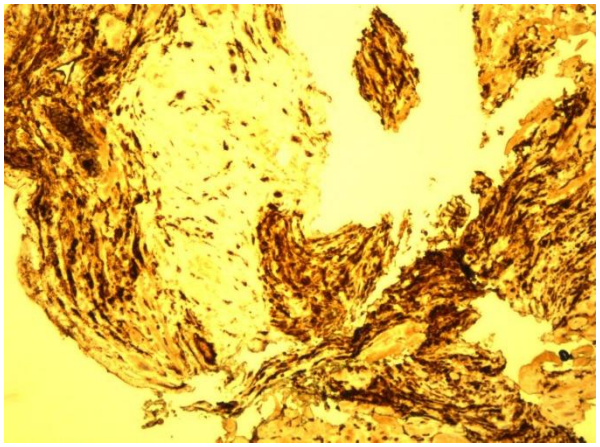
- Rapido miglioramento del quadro emodinamico e FEVSin con immunosoppressione (iniziata in 15 gg
-

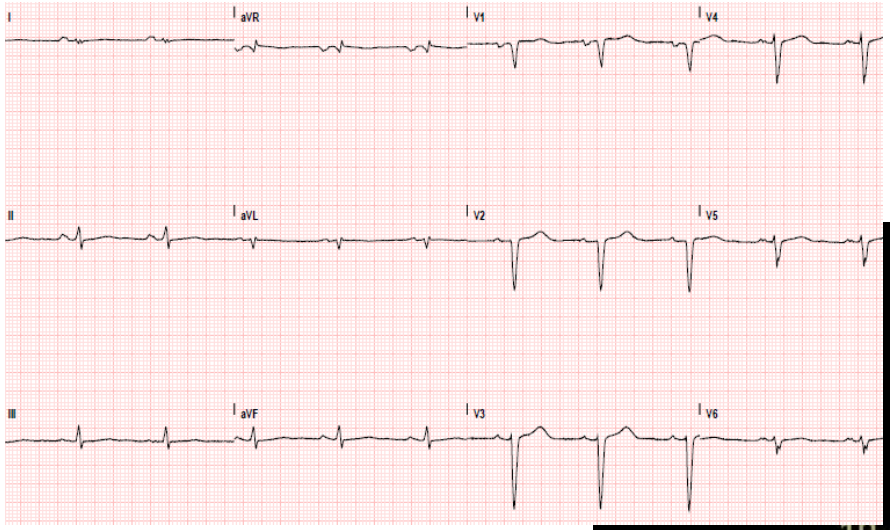


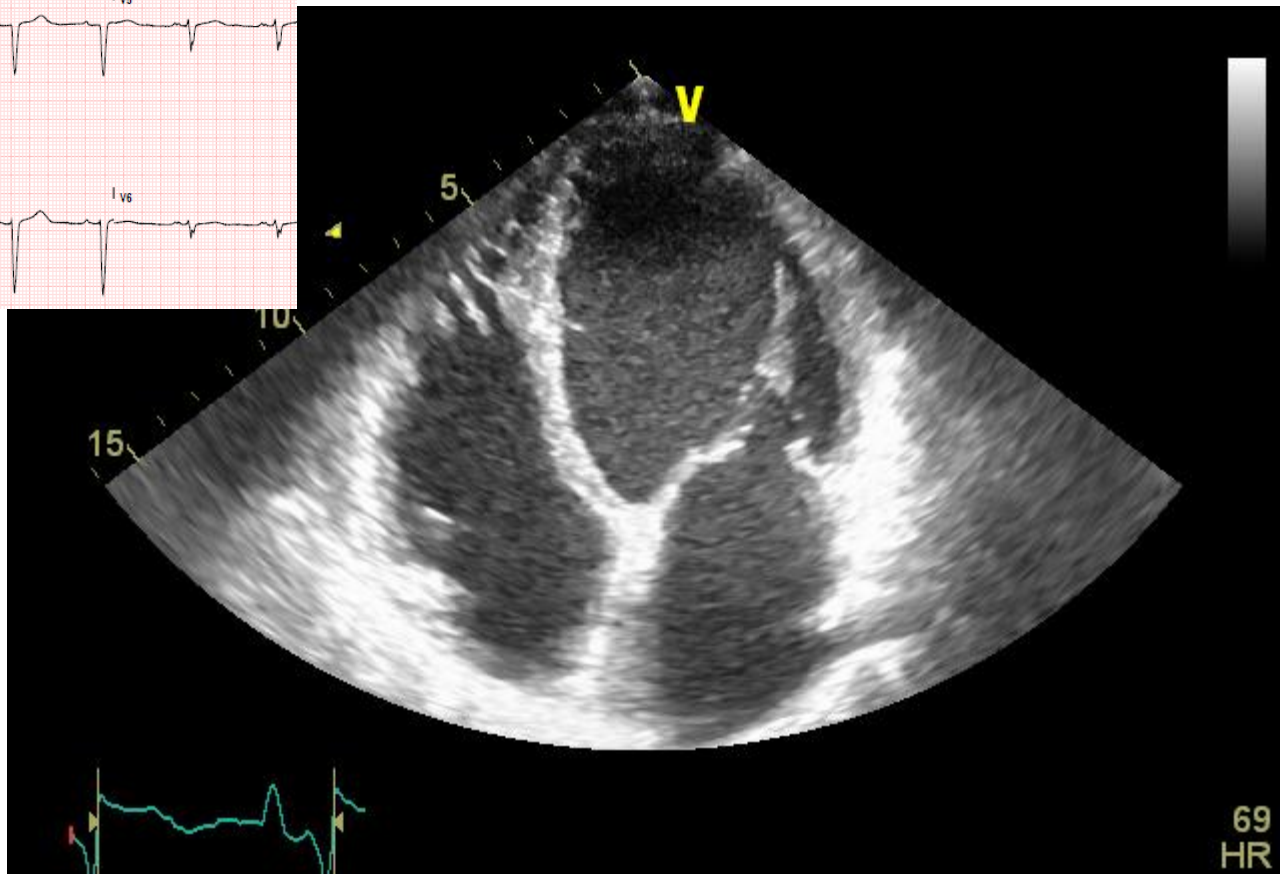


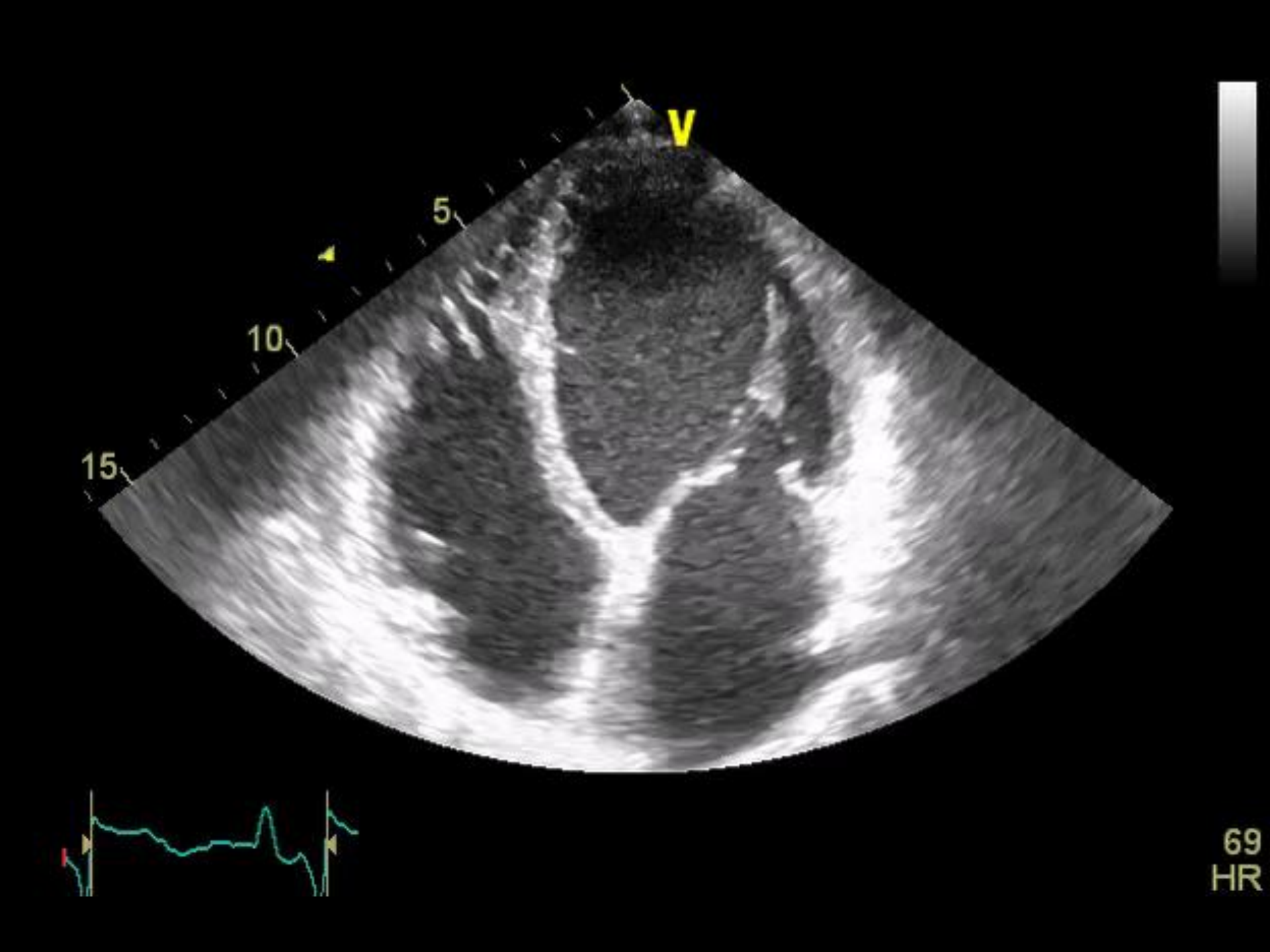


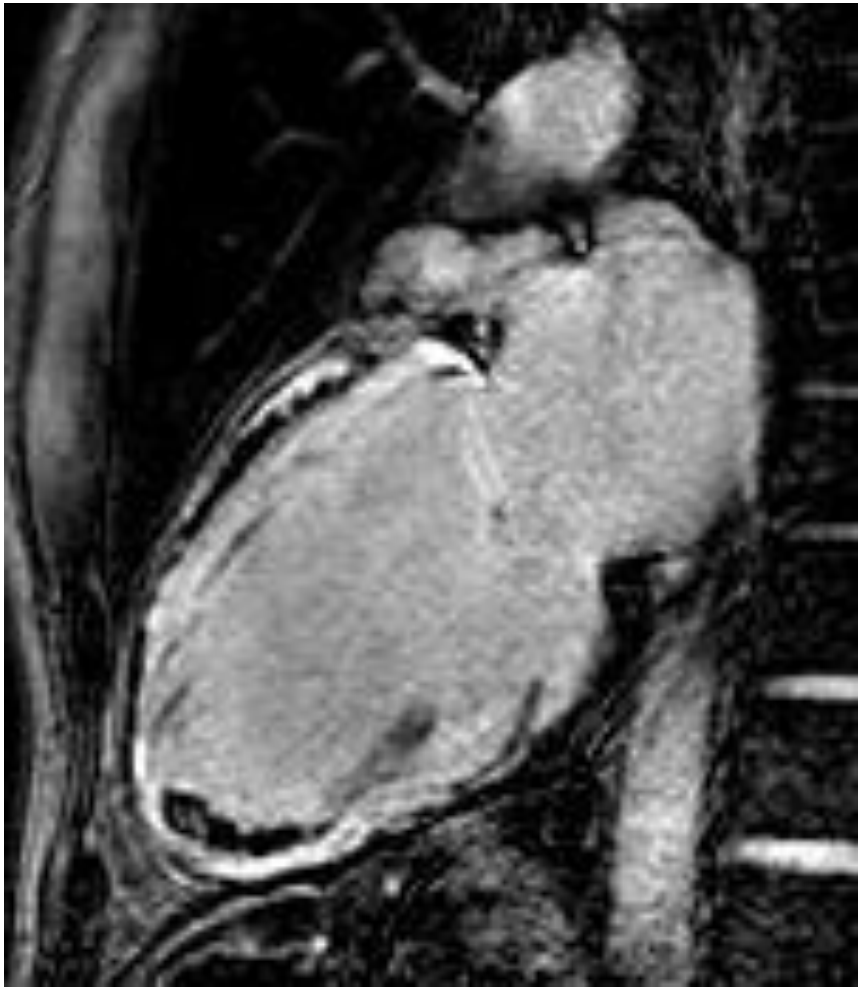
45 aa; shock cardiogeno; IABP, inotropi; TV++

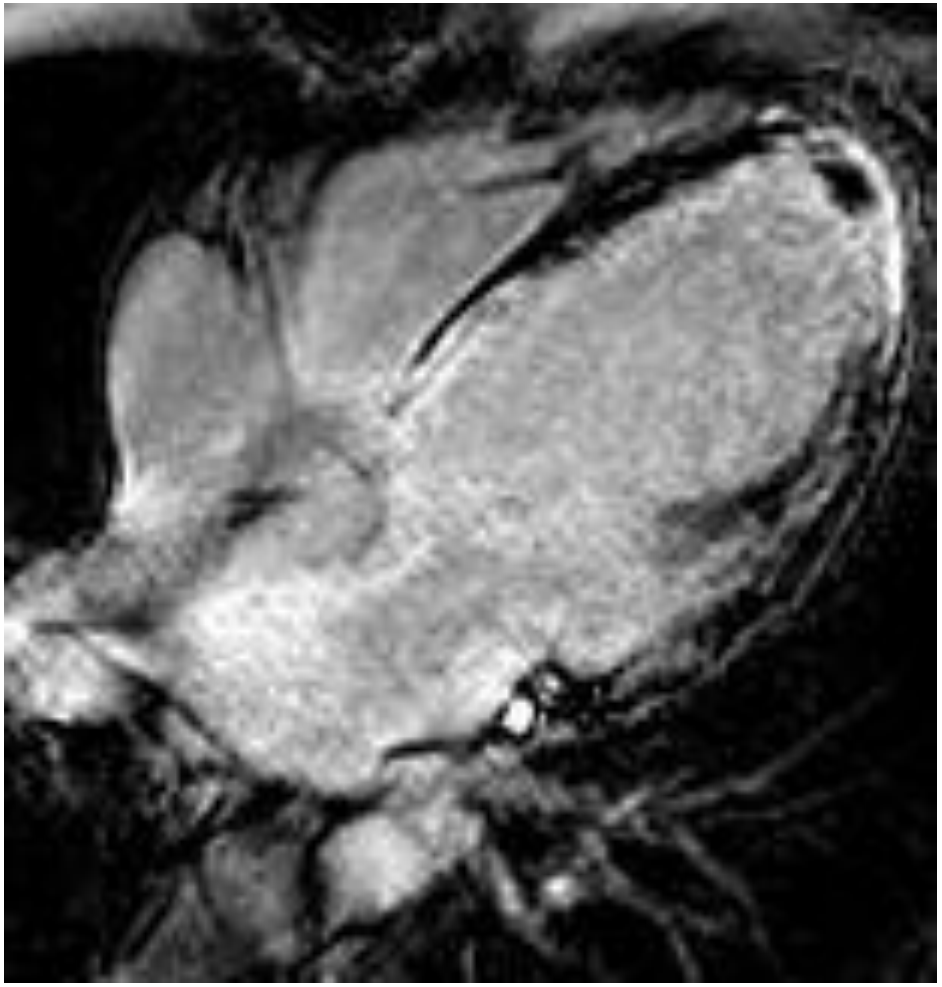




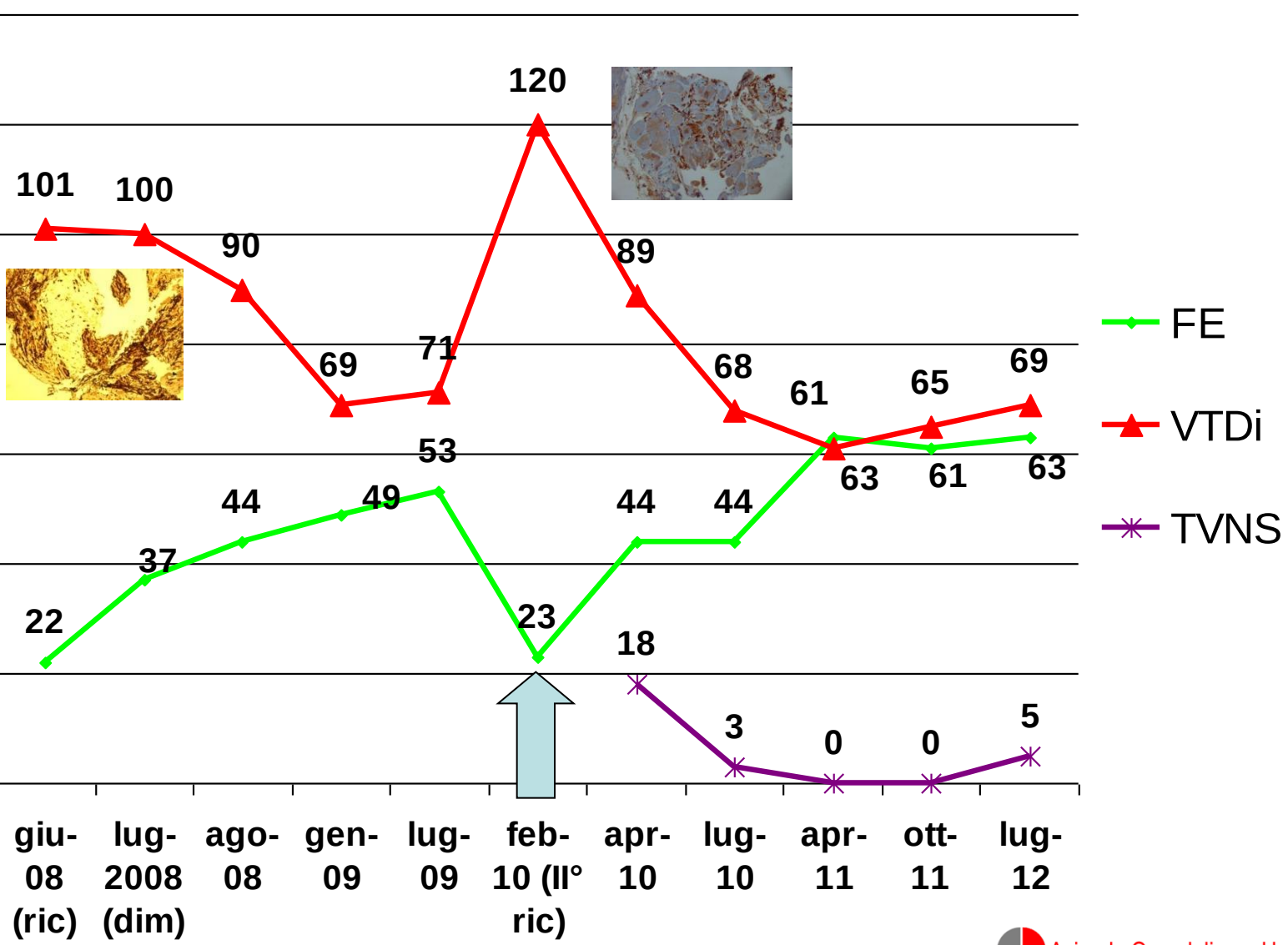



V
5
10
15
69
HR





Q.G; a.49



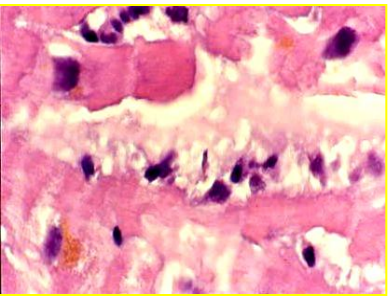
Eterogeneità di evoluzione clinica (2)

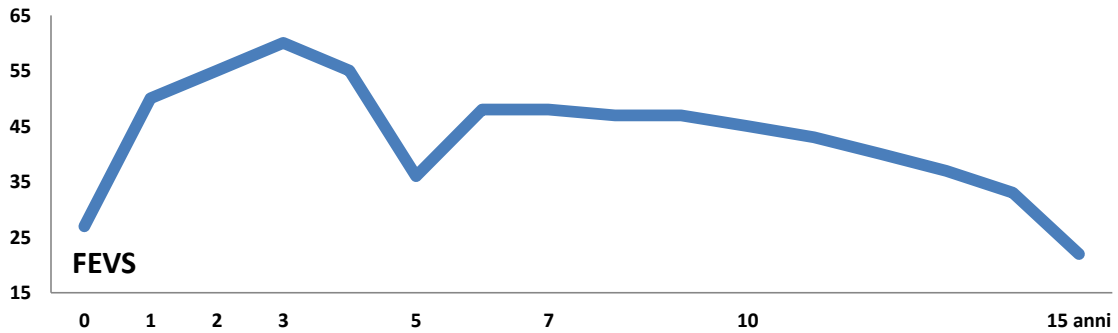
GM, m, 42 anni

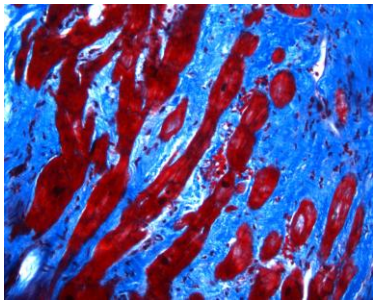
- **Miocardite acuta esordita con scompenso cardiaco NYHA III-IV**
- **FEVS 27%, DTD 60 mm, pattern restrittivo; FACCVDx 27%**
- **BEM: miocardite attiva (1997)**

- **Miglioramento clinico-strumentale in terapia immunosoppressiva**
- **FEVS 50-60% a 1, 3 e 5 anni di f-up; NYHA I**

- **Dal 10° anno peggioramento clinico-strumentale**
  - **FEVS 35-25%; NYHA II**
  - **RMN esiti ++ fibrotici meso-subepicardici [T1-LGE]; non edema (T2)**
  - **Holter-ECG: 1794 ExVe; 3 TVNS (17 batt 152 bpm, con cardiopalmo)**
  - **Impianto ICD bicamerale in prevenzione primaria.**

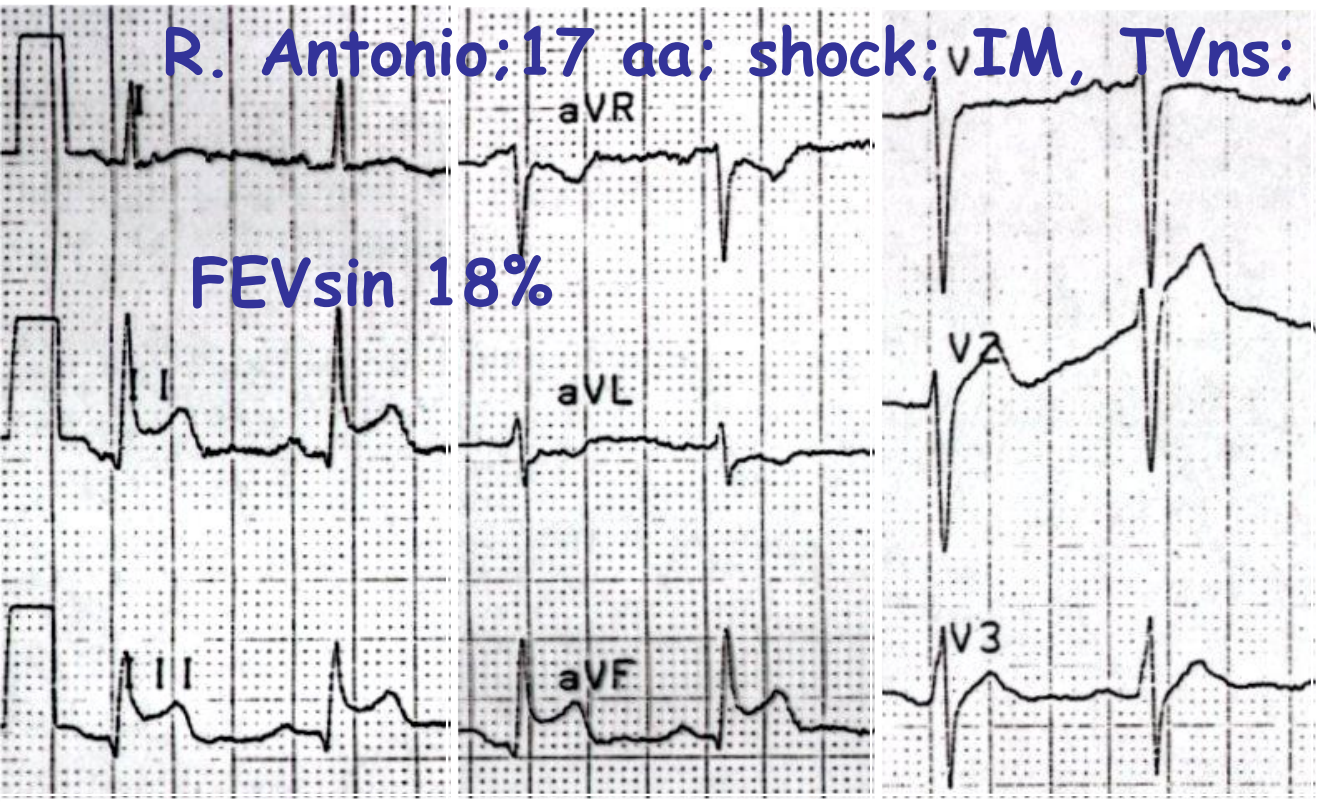


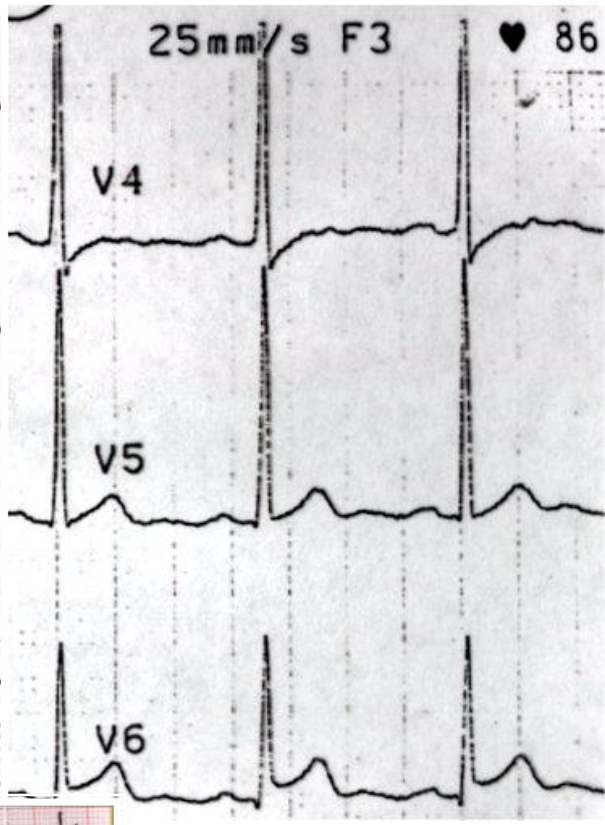


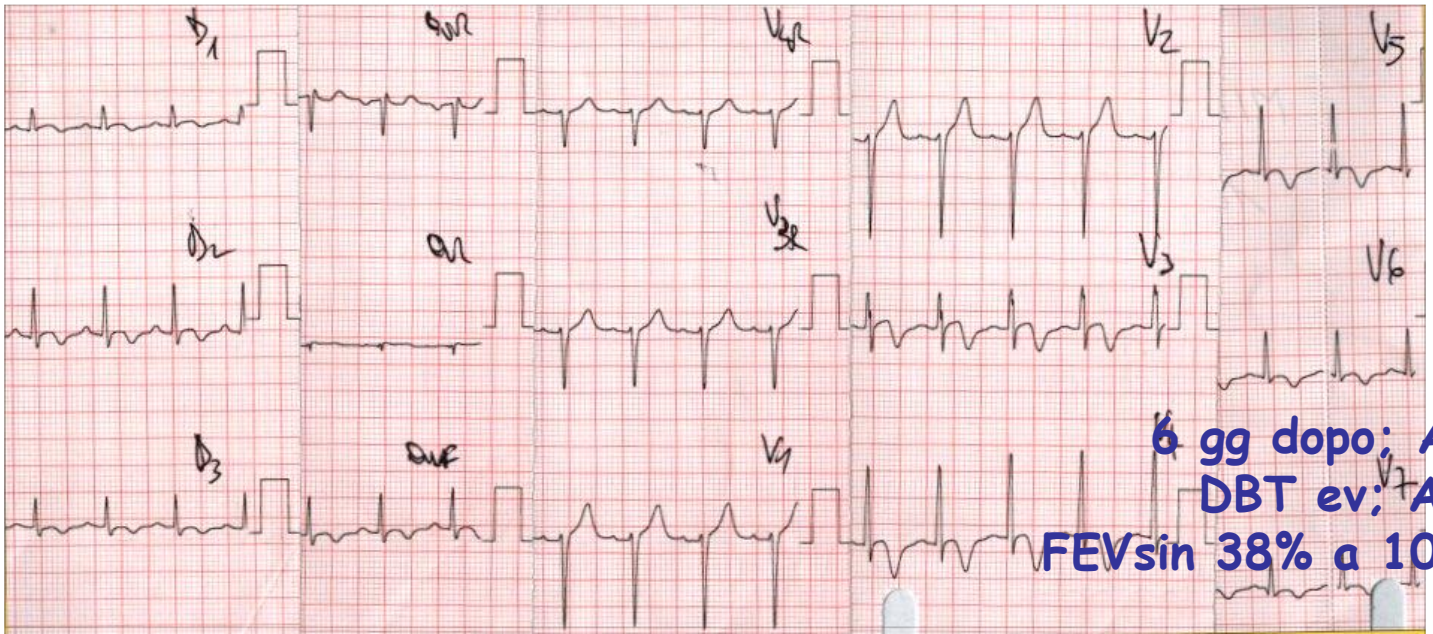


R. Antonio; 17 aa; shock; IM, TVns;

FEVsin 18%







6 gg dopo; ASA 3 g ev/die;
DBT ev; ACEi; LMWH;
FEVsin 38% a 10 gg→ 48% a 4 sett

Ruolo diagnostico del rilascio troponinico nella Miocardite (BEM) esordita con SCC

	All Patients (N = 132)	Group 1 (Symptoms ≤14 Days; n = 70)	Group 2 (Symptoms >14 Days; n = 62)	Group 1 vs. 2, p Value
Age, yrs	47 ± 16	44 ± 17	52 ± 13	0.004
Female	28 (21.2)	9 (13.0)	19 (30.6)	0.02
Duration of symptoms in days	14 (3–40)	3 (1–7)	42 (28–90)	<0.001
Pathological ECG findings				
Block	23 (17.7)	9 (13.2)	14 (23.7)	0.17
ST-segment elevation	45 (34.1)	39 (57.4)	6 (10.2)	<0.001
ST-segment depression	74 (56.1)	42 (61.8)	32 (54.2)	0.38
Elevated troponin	37 (38.5)	31 (51.7)	6 (17.1)	<0.001
Elevated creatine kinase-MB	42 (42.4)	35 (58.3)	7 (17.9)	<0.001
Elevated C-reactive protein	58 (68.2)	43 (86.0)	15 (44.1)	<0.001

Lurz P et al. JACC Cardiovasc Imaging 2012;5:513-24

Miocardite attiva ad esordio con SCC e rilascio troponinico

Utility of Combination of Cardiac Magnetic Resonance Imaging and High-Sensitivity Cardiac Troponin T Assay in Diagnosis of Inflammatory Cardiomyopathy

Marek Šramko, MD[a,*], Miloš Kubánek, MD, PhD[a], Jaroslav Tintěra, MSc, PhD[b], Dana Kautznerová, MD[b], Jiří Weichet, MD, PhD[c], Jana Malušková, MD[d], Janka Franeková, MD[e], and Josef Kautzner, MD, PhD[a]

Am J Cardiol 2013;111:258–264

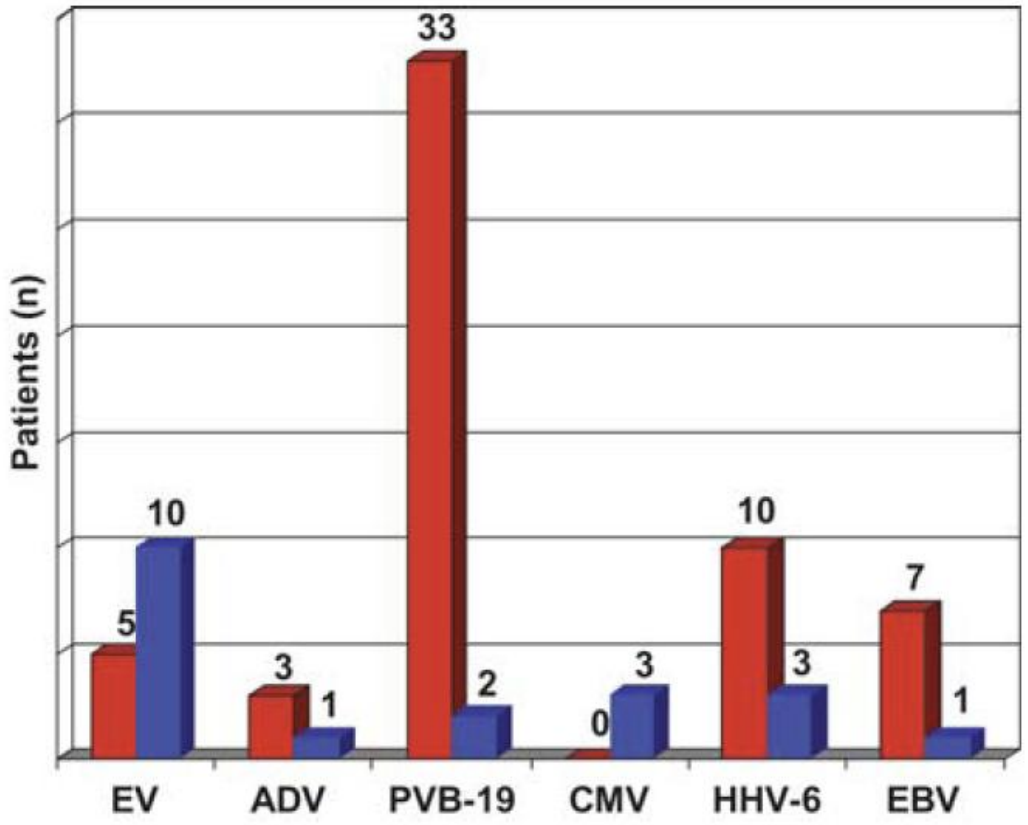
Baseline clinical, biochemical, and biopsy findings

Variable	Idiopathic DC (n = 27)	Inflammatory DC (n = 15)
High-sensitivity troponin T level (ng/L)	11 (5–32)	17 (5–30)
High-sensitivity troponin T >13.5 ng/L	12 (44%)	10 (67%)
Conventional troponin I >0.03 μg/L	7 (26%)	6 (40%)
Maximum conventional troponin I (μg/L)	1.27	3.61
C-reactive protein (mg/L)	2 (1–7)	3 (2–9)
B-type natriuretic peptide (ng/L)	963 (240–1,508)	647 (279–1,180)
Viral genome in biopsy specimen	16 (59%)	11 (73%)

Virus serology in patients with suspected myocarditis: utility or futility?

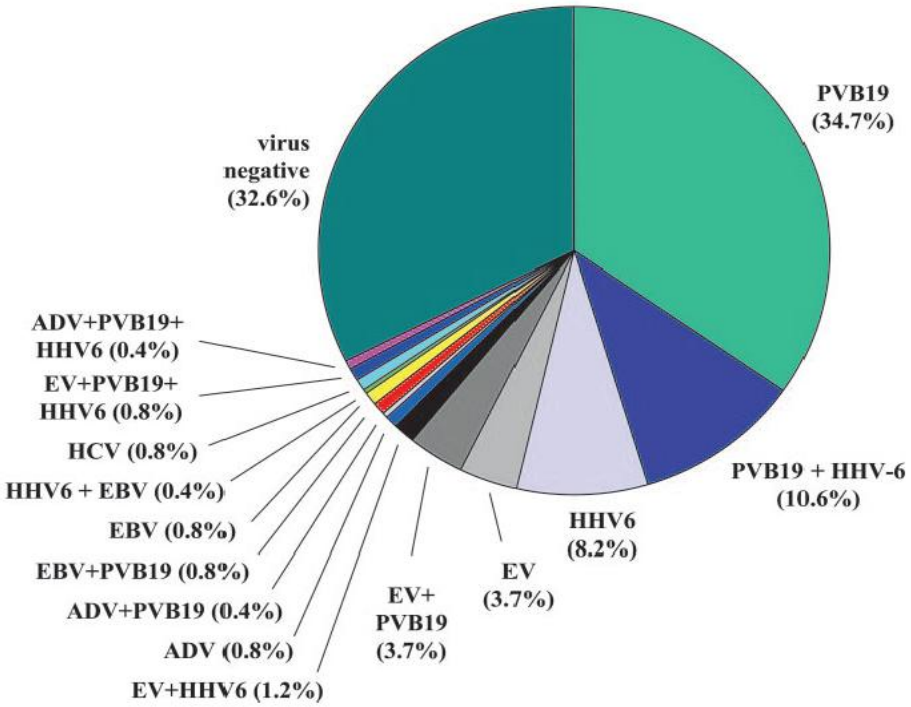
Felix Mahfoud[1]*, Barbara Gärtner[2], Michael Kindermann[1], Christian Ukena[1], Katharina Gadomski[1], Karin Klingel[3], Reinhard Kandolf[3], Michael Böhm[1], and Ingrid Kindermann[1]

European Heart Journal (2011) **32**, 897–903



High Prevalence of Viral Genomes and Multiple Viral Infections in the Myocardium of Adults With "Idiopathic" Left Ventricular Dysfunction

Uwe Kühl, PhD, MD; Matthias Pauschinger, MD; Michel Noutsias, MD; Bettina Seeberg, MD; Thomas Bock, PhD; Dirk Lassner, PhD; Wolfgang Poller, MD; Reinhard Kandolf, PhD, MD; Heinz-Peter Schultheiss, MD



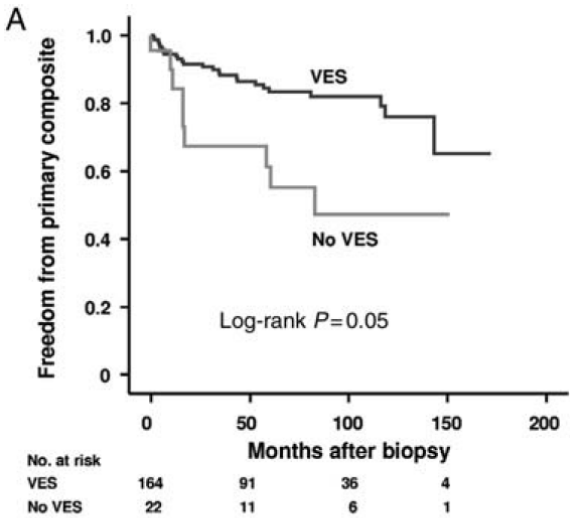
Distribution of viral genomes in 245 consecutive patients with clinical presentation of "idiopathic" DCM.

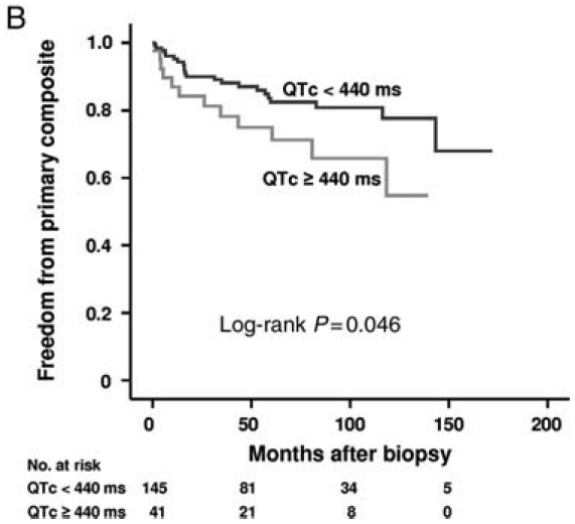
Circulation 2005;111;887-893

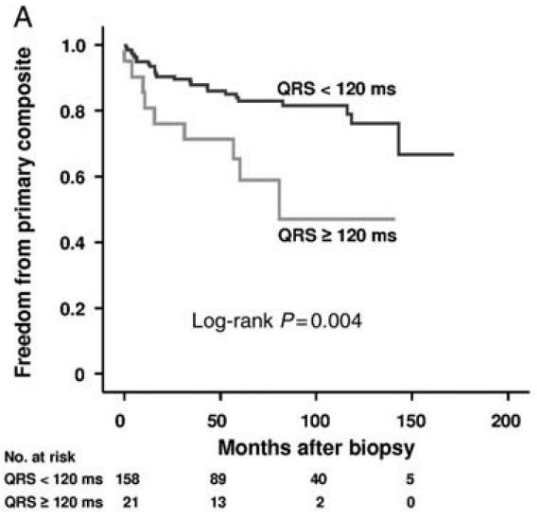
Ospedali Riuniti di Trieste

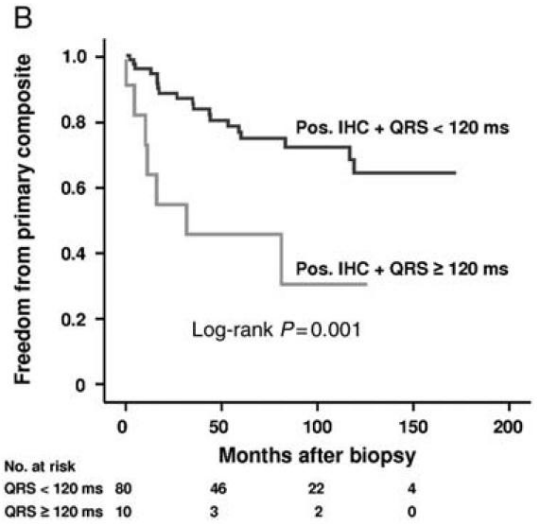
Prognostic electrocardiographic parameters in patients with suspected myocarditis

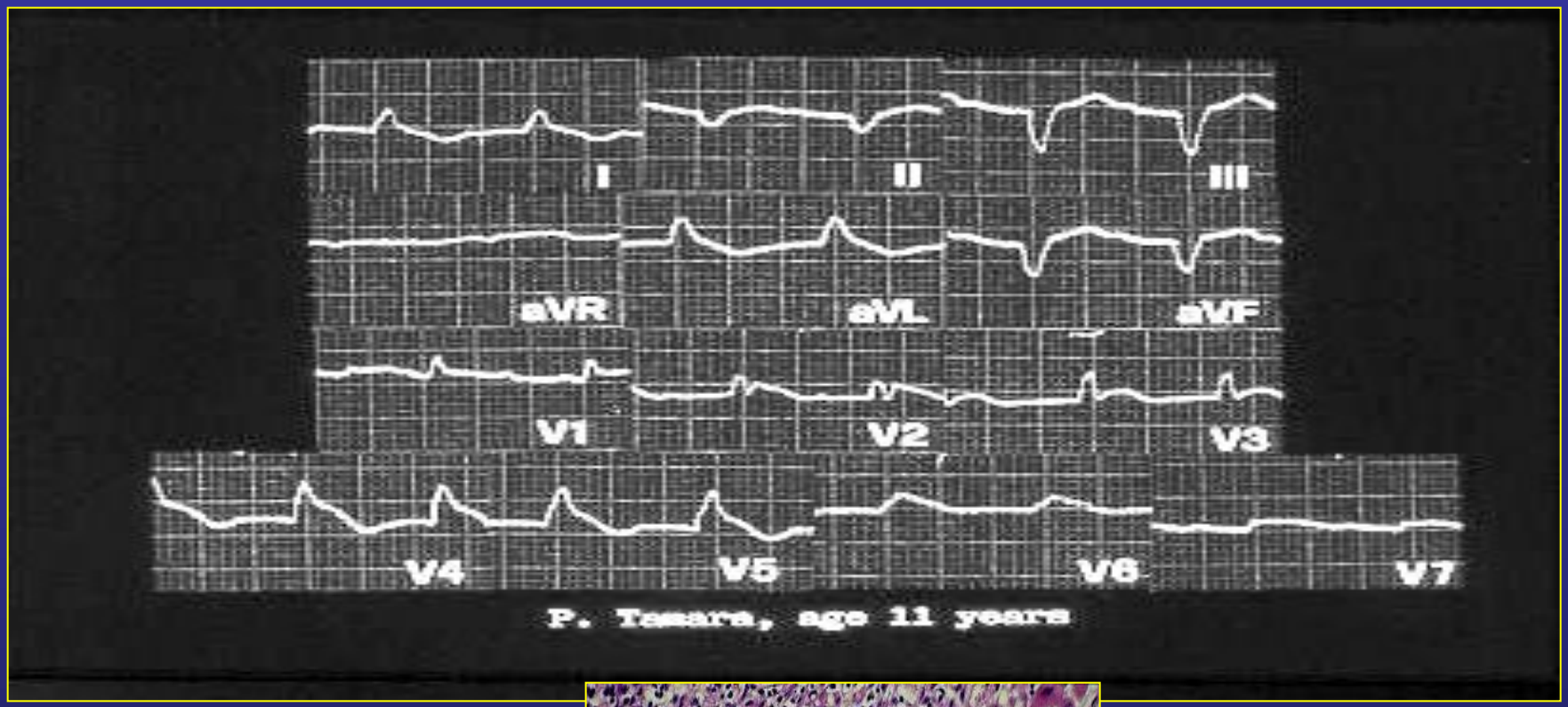
Christian Ukena[1*†], Felix Mahfoud[1†], Ingrid Kindermann[1], Reinhard Kandolf[2], Michael Kindermann[1†], and Michael Böhm[1†]

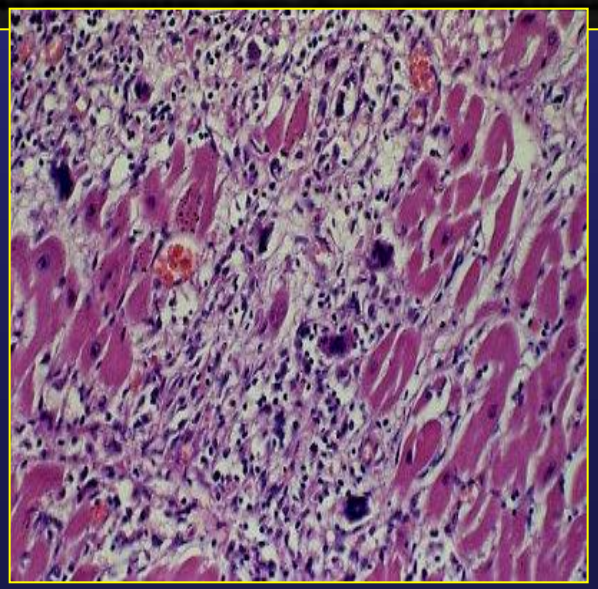









I
II
III
aVR
aVL
aVF
V1
V2
V3
V4
V5
V6
V7
P. Tamara, age 11 years



Am J Cardiol. 1988 Aug 1;62(4):285-91.

Echocardiographic findings in myocarditis.

Pinamonti B, Alberti E, Cigalotto A, Dreas L, Salvi A, Silvestri F, Camerini F.

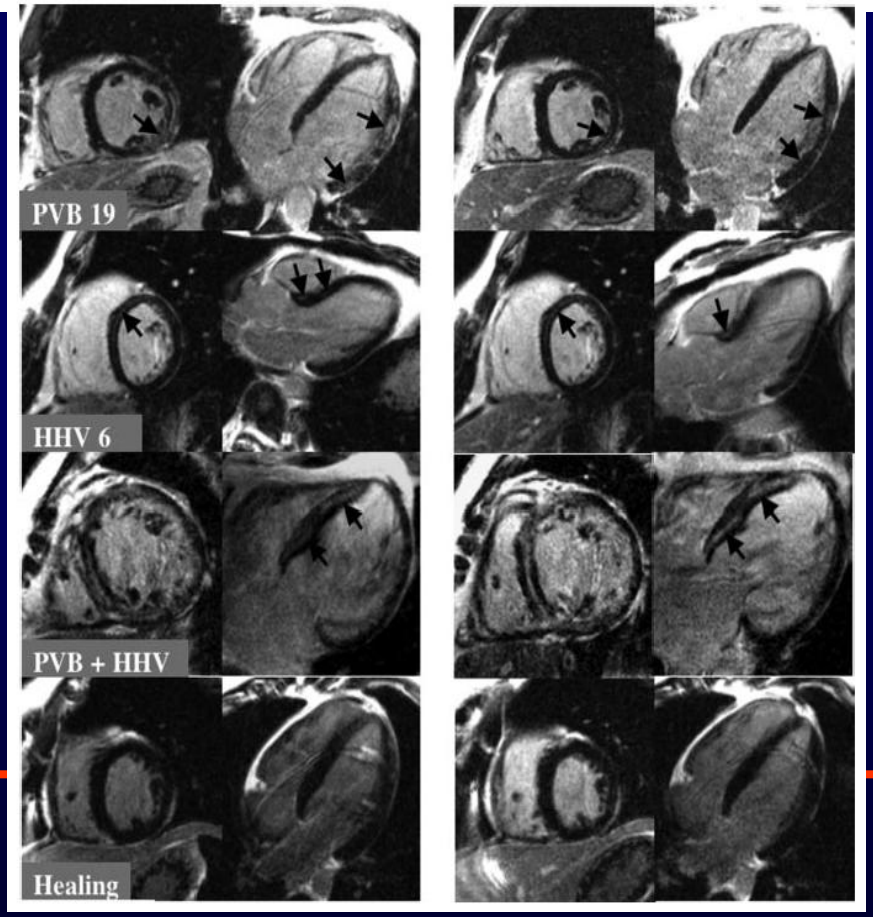
Divisione di Cardiologia, Università degli Studi, Trieste, Italy.

Scompenso cardiaco di recente insorgenza: reperti suggestivi di miocardite

- Disfunzione ventricolare sinistra
- Rimodellamento lieve/assente con Mantenimento shape ellissoidale
- Spessori e volumi delle pareti conservati
- Anomalie disomogenee della cinetica
- Versamento pericardico
- Pseudoipertrofia delle pareti (edema) in segmenti remoti a quelli asinergici
- Alterata ecoriflettenza del tessuto miocardico
- Disfunzione diastolica
- Trombosi endoventricolare

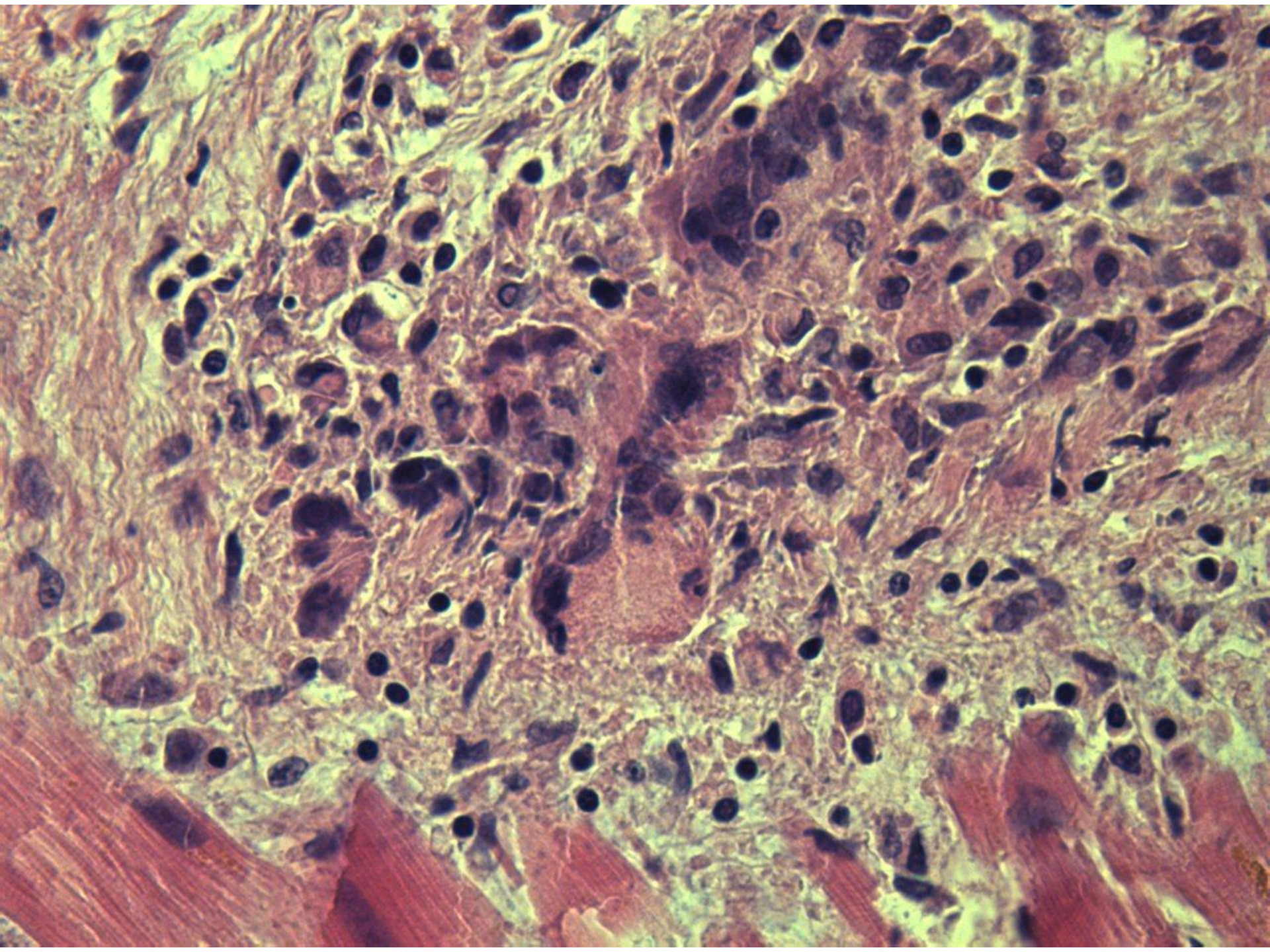
Presentation, Patterns of Myocardial Damage, and Clinical Course of Viral Myocarditis

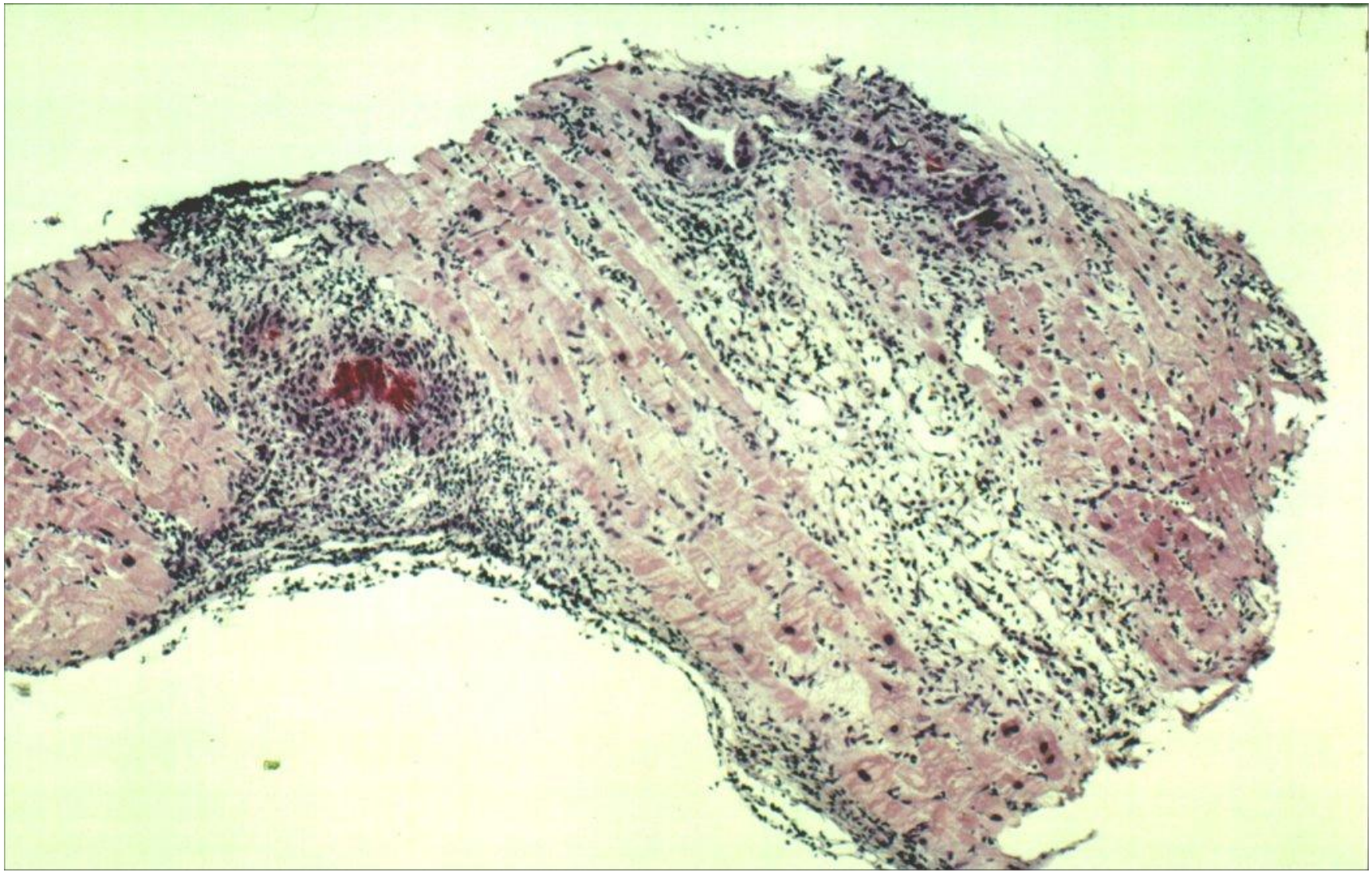
Heiko Mahrholdt, MD; Anja Wagner, MD; Claudia C. Deluigi, MD; Eva Kispert, RN; Stefan Hager, MD; Gabriel Meinhardt, MD; Holger Vogelsberg, MD; Peter Fritz, MD; Juergen Dippon, PhD; C.-Thomas Bock, PhD; Karin Klingel, MD; Reinhard Kandolf, MD; Udo Sechtem, MD



Circulation 2006;114;1581-1590

Ospedali Riuniti di Trieste





Usefulness of Pericardial Effusion as New Diagnostic Criterion for Noninvasive Detection of Myocarditis

Peter Ong, MD[a,*], Anastasios Athansiadis, MD[a], Stephan Hill, MD[a], Eva-Maria Kispert[a], Gabor Borgulya, MD, MSc[b], Karin Klingel, MD[c], Reinhard Kandolf, MD[c], Udo Sechtem, MD[a], and Heiko Mahrholdt, MD[a]

(Am J Cardiol 2011;108:445–452)

35 patients with biopsy proven viral-associated myocarditis
onset of symptoms within 3 months
normal left ventricular function

Table 2
Comparison of sensitivity of different approaches

Protocol for Diagnostic Approach	Sensitivity (%)
LGE + T_2	49%
LGE + PE	66%
LGE + T_2 + PE	69%
Echocardiography vs CMR	
Sensitivity for echocardiography to detect PE	29%
Specificity for echocardiography to detect PE	100%

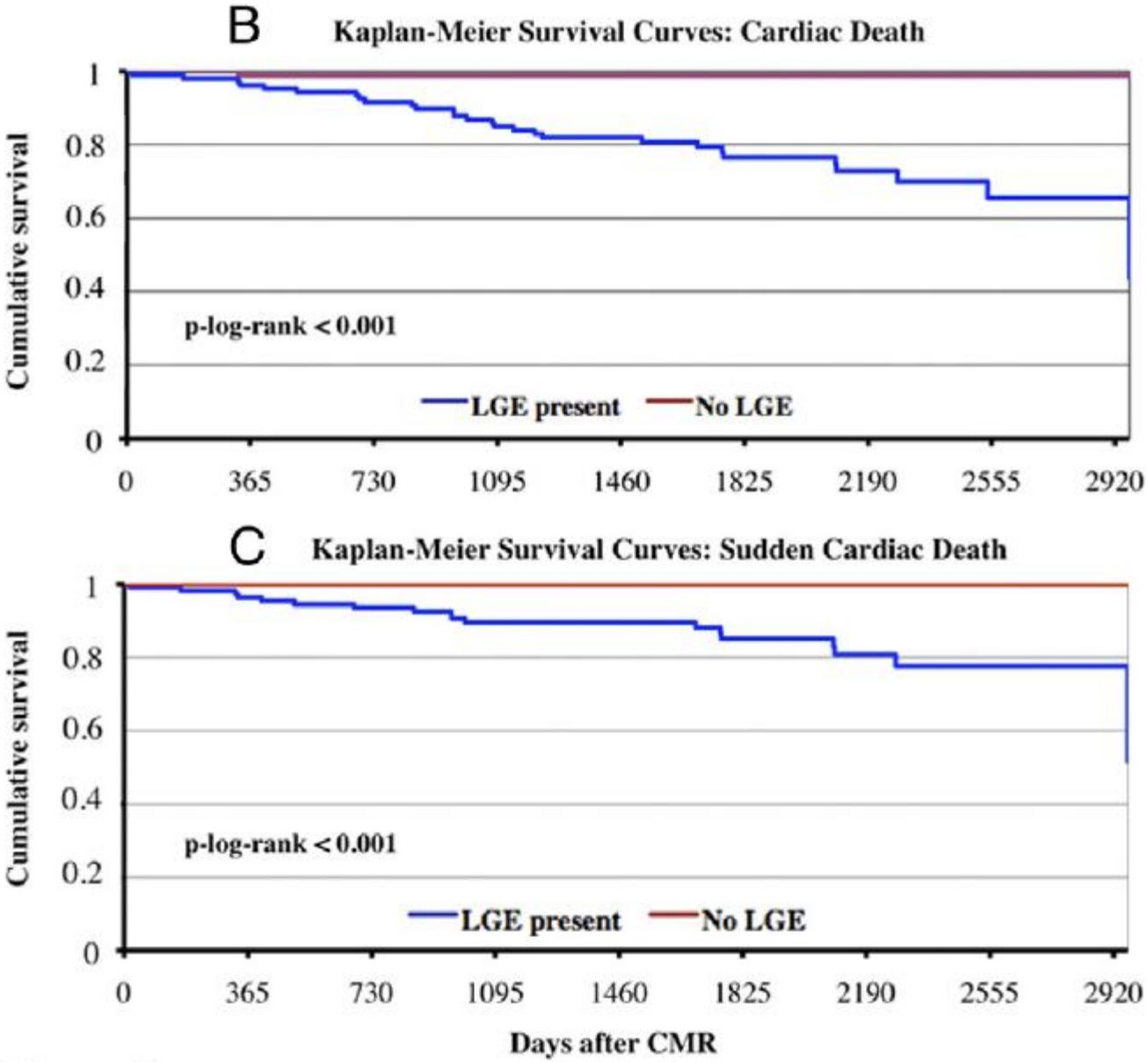
LGE = T_1-weighted images with late gadolinium contrast enhancement; PE = pericardial effusion; T_2 = T_2-weighted images for detection of myocardial edema (abnormal by either visual assessment or ratio calculation).

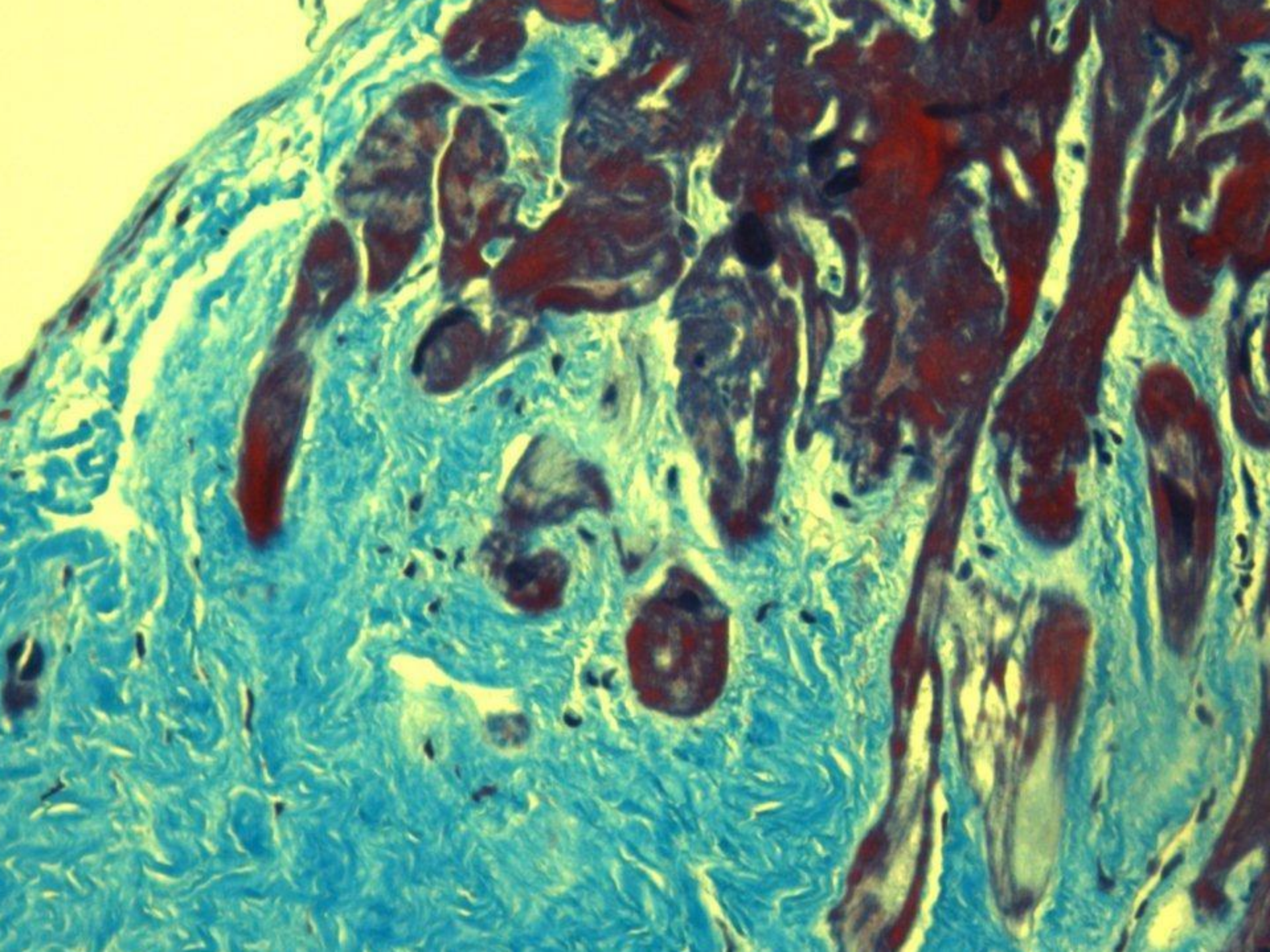
PE = pericardial effusion.

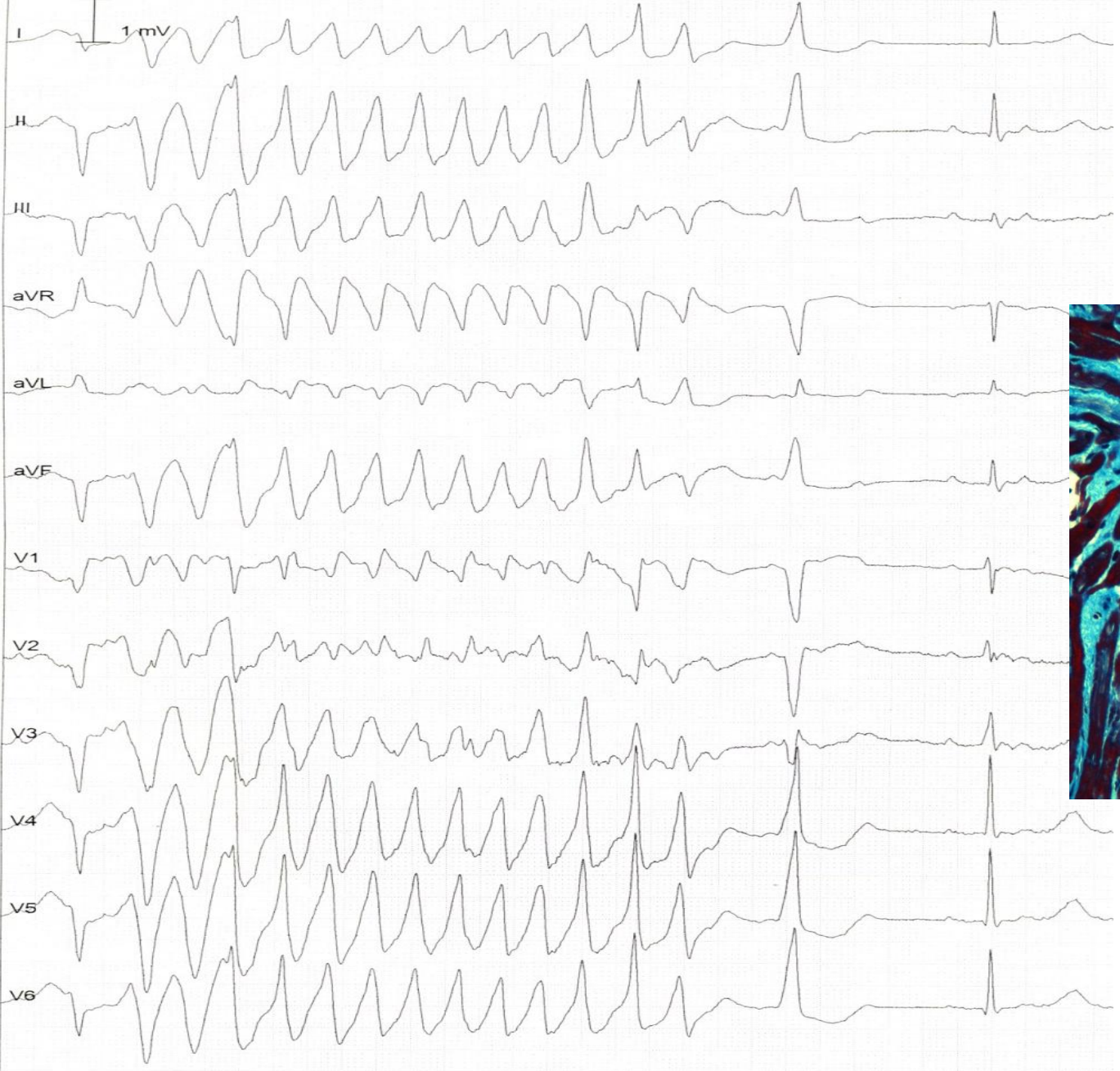
Long-Term Follow-Up of Biopsy-Proven Viral Myocarditis

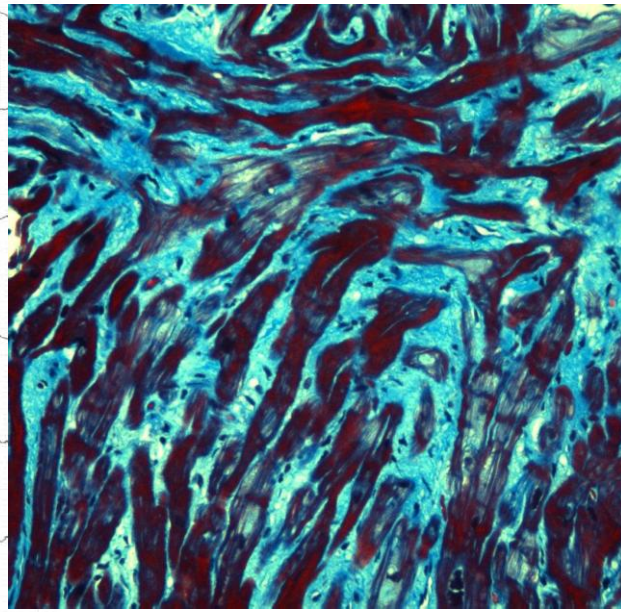
Predictors of Mortality and Incomplete Recovery

JACC Vol. 59, No. 18, 2012
May 1, 2012:1604–15









ECG 12 Derivazioni (calcolate EASI) Larghezza di banda: 0.05-40 Hz 25 mm/s 10 mm/mV 15

Long-Term Follow-Up of Biopsy-Proven Viral Myocarditis

Predictors of Mortality and Incomplete Recovery

JACC Vol. 59, No. 18, 2012
May 1, 2012:1604–15

Stefan Grün, MD,* Julia Schumm, MD,* Simon Greulich, MD,* Anja Wagner, MD,† Steffen Schneider, PHD,‡ Oliver Bruder, MD,‡ Eva-Maria Kispert, RN,* Stephan Hill, MD,* Peter Ong, MD,* Karin Klingel, MD,§ Reinhardt Kandolf, MD,§ Udo Sechtem, MD,* Heiko Mahrholdt, MD*

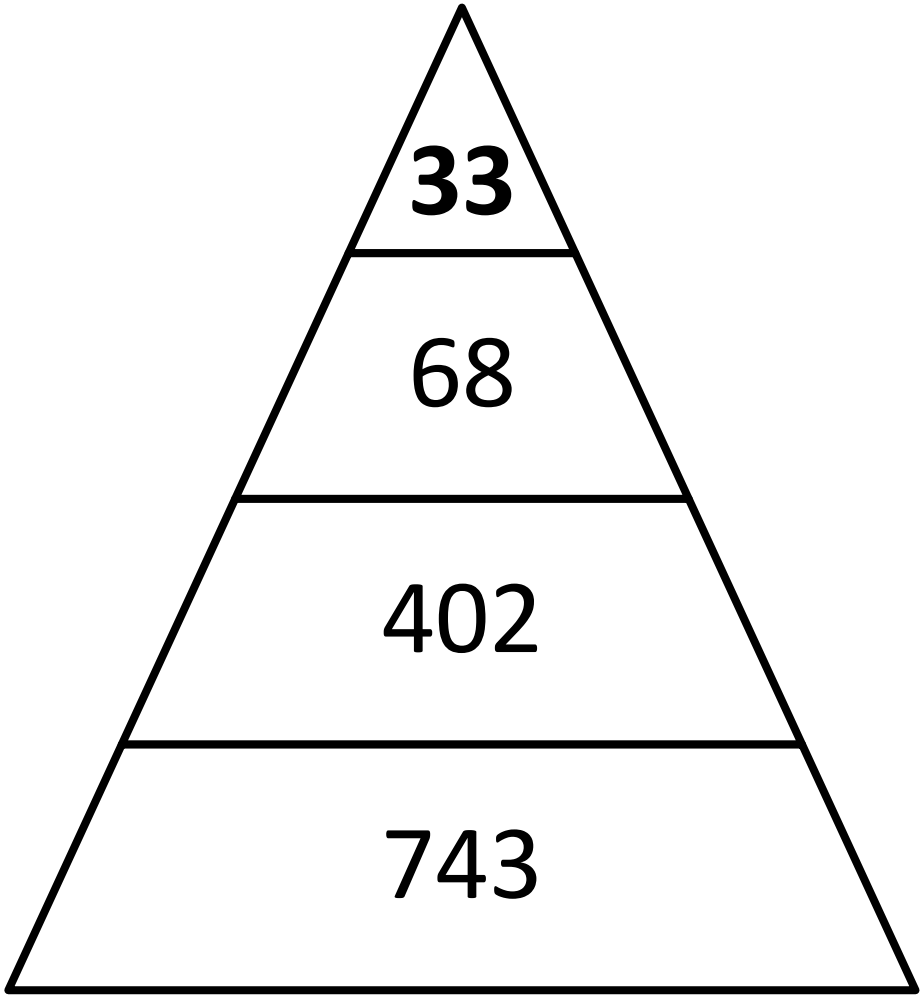
Stuttgart, Essen, and Tübingen, Germany; and Stamford, Connecticut

Table 2 Characteristics of Patients With and Without LGE

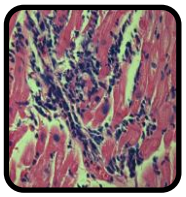
	LGE Present (n = 108)	No LGE (n = 95)	p Value	OR (95% CI)
Primary clinical presentation				
Symptoms of ACS	37 (34.3)	37 (38.9)	0.49	0.82 (0.46–1.45)
Subacute new-onset heart failure	37 (34.3)	25 (26.3)	0.22	1.46 (0.80–2.67)
Reoccurring episodes of overt HF	11 (10.2)	7 (7.4)	0.48	1.43 (0.53–3.84)
Combination of palpitations, fatigue, dyspnea on exertion	23 (21.3)	26 (27.4)	0.31	0.72 (0.38–1.37)
Aborted SCD	0 (0)	0 (0)	1.00	
BNP, pg/ml	336 (82–983)	67 (27–457)	<0.001	
NT-proBNP, pg/ml	2,359 (547–18,092)	1,938 (38–4,391)	0.55	
CMR imaging parameter				
LVEF, %	37.5 (24.5–57.0)	53.0 (39.0–64.0)	<0.0001	
EF indexed, %/m^2	19.9 (12.7–28.4)	26.8 (19.6–33.8)	<0.0001	
LV-EDV, ml	187.5 (140–263)	155.0 (120–193)	<0.001	
LV-ESV, ml	119.5 (57.5–179.0)	73.0 (43.0–113.0)	<0.0001	
LGE mass, g	5.3 (3.2–18.6)	—		
LGE, % of LV mass	4.2 (2.3–9.3)	—		

Rilevanza nella pratica clinica reale

Dati dal Registro delle Malattie del Miocardio di Trieste

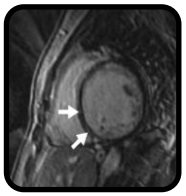


BEM con miocardite attiva (2002-2012)

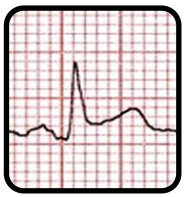


BEM effettuate (2002-2012)

Nuove CMPD (2002-2012)



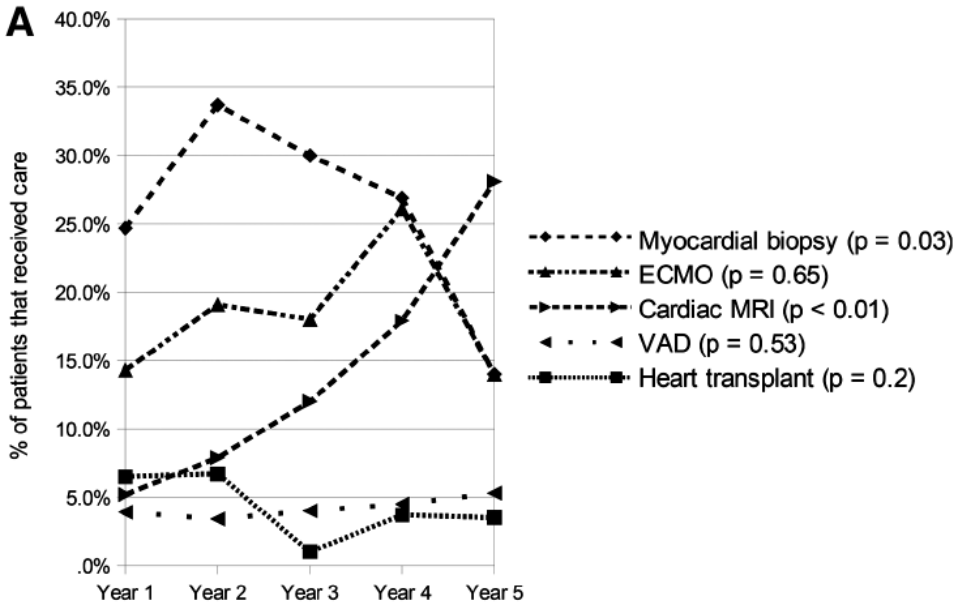
Pericarditi/Perimiocarditi (2002-2012)

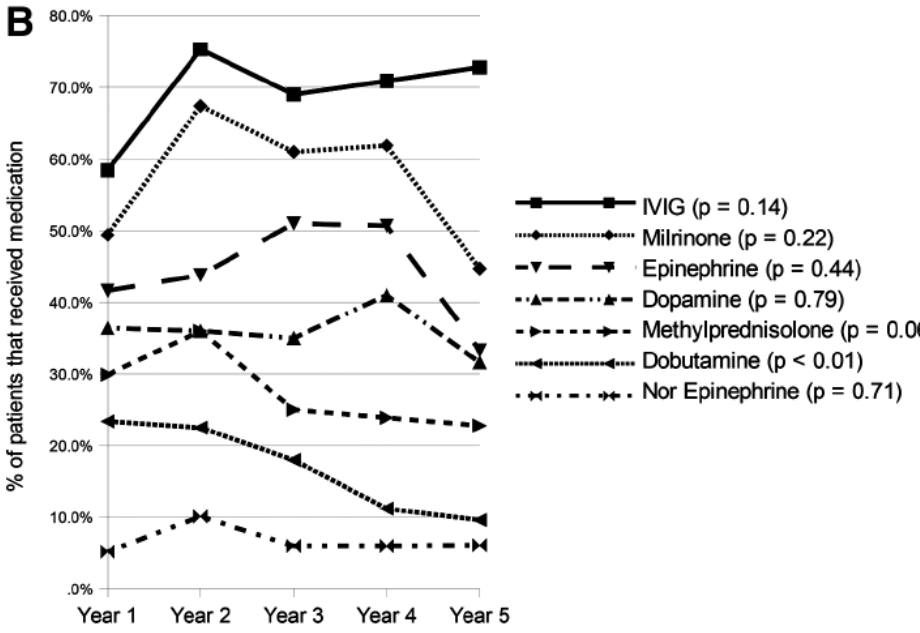


Demographics, Trends, and Outcomes in Pediatric Acute Myocarditis in the United States, 2006 to 2011

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

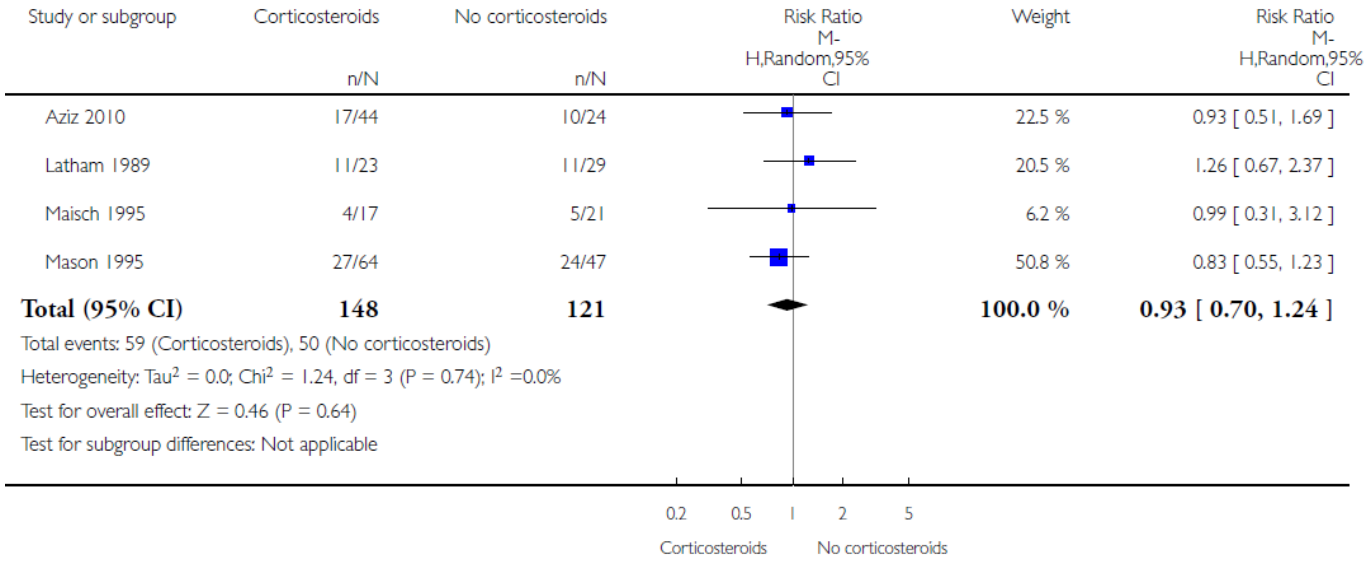
Circ Cardiovasc Qual Outcomes. 2012;5:622-627.

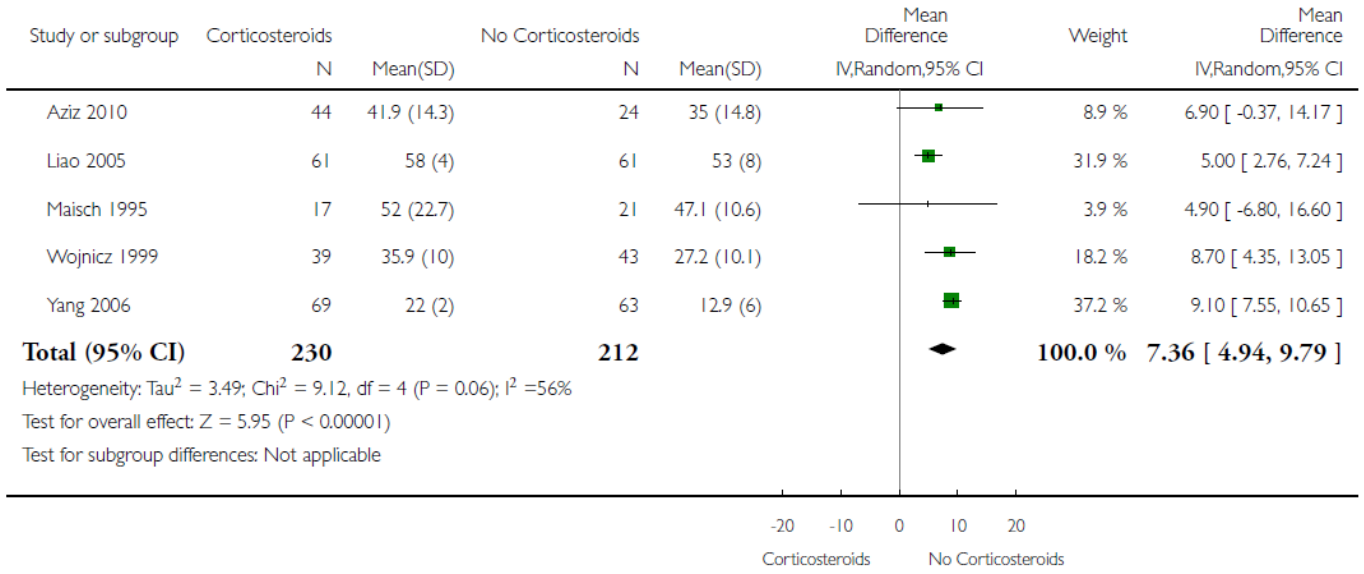




Corticosteroids for viral myocarditis (Review)

The Cochrane Library 2013, Issue 10





Protocolli di immunosoppressione

Protocollo utilizzato da Wojnicz R et al. Circulation 2001

FARMACO	DOSAGGIO
Prednisone	1 mg/kg/die per 12 giorni, ndi riduzione della dose di 5 mg/die ogni 5 giorni fino alla dose di 0,2 mg/kg/die, per un totale di 90 giorni
Azatioprina	1 mg/kg/die per un totale di 100 giorni

Protocollo utilizzato da Frustaci et al. Eauropean Heart Journal 2009

FARMACO	DOSAGGIO
Prednisone	1 mg/kg/die per 4 settimane, quindi 0.33 mg/kg/die per 5 mesi
Azatioprina	2 mg/kg/die per 6 mesi

Protocollo utilizzato presso la SC Cardiologia di Trieste

FARMACO	DOSAGGIO
Prednisone	50 mg/m^2/die per 2 settimane indi scalo di 0,3 mg/kg per due mesi, indi scalo gradualmente fino allo stop (6°mese)
Azatioprina	75 mg/m^2/die per 6 mesi
Ciclosporina*	10 mg/kg/die (2 somministrazioni) per 6 mesi

Controllo con biopsia endomiocardica a 2 e 6 mesi.
*** In casi selezionati (es. miocardite a cellule giganti) o in caso di persistente attività infiammatoria nonostante terapia con prednisone.**

“Approach to the patient” (Harrison; Principles of Internal Medicine; 1950)

- “….. ***In the care of the suffering he needs technical skill, scientific knowledge and human understanding. He who uses these with courage,with umilty and with wisdom will provide a unique service….”***