



**ECOCARDIOCHIRURGIA®**  
ECO-RM-TC CHIRURGIA-INTERVENTISTICA

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# IX CONGRESSO NAZIONALE ECOCARDIOCHIRURGIA 2017

28 - 29 MARZO 2017 MILANO, 27 - 28 - 29 MARZO 2017 MILANO, 27 - 28 - 29 MARZO 2017 MILANO  
ILANO, 27 - 28 - 29 MARZO 2017 MILANO, 27 - 28 - 29 MARZO 2017 MILANO, 27 - 28 - 29 MARZO 20  
17 MILANO, 27 - 28 - 29 MARZO 2017 **MILANO, 27 - 28 - 29 MARZO 2017**

***Inquadrare il paziente con scompenso  
cardiaco***

**Dr. Francesca Macera**  
Cardiologia 2 – Insufficienza cardiaca e Trapianto

# CASO CLINICO

Uomo, 47 aa

65 Kg x 176 cm

Gruppo 0

Fumatore attivo, familiarità per CAD (padre IMA a 64 aa)

HCV + (genotipo 1b, no indicazione a th)

Portatore di protesi d'anca per osteocondrosi

**27/10/2010: accesso in PS per toracoalgie aspecifiche**

**15 gg prima sindrome influenzale, da allora dispnea per sforzi  
progressivamente più lievi**

# CASO CLINICO

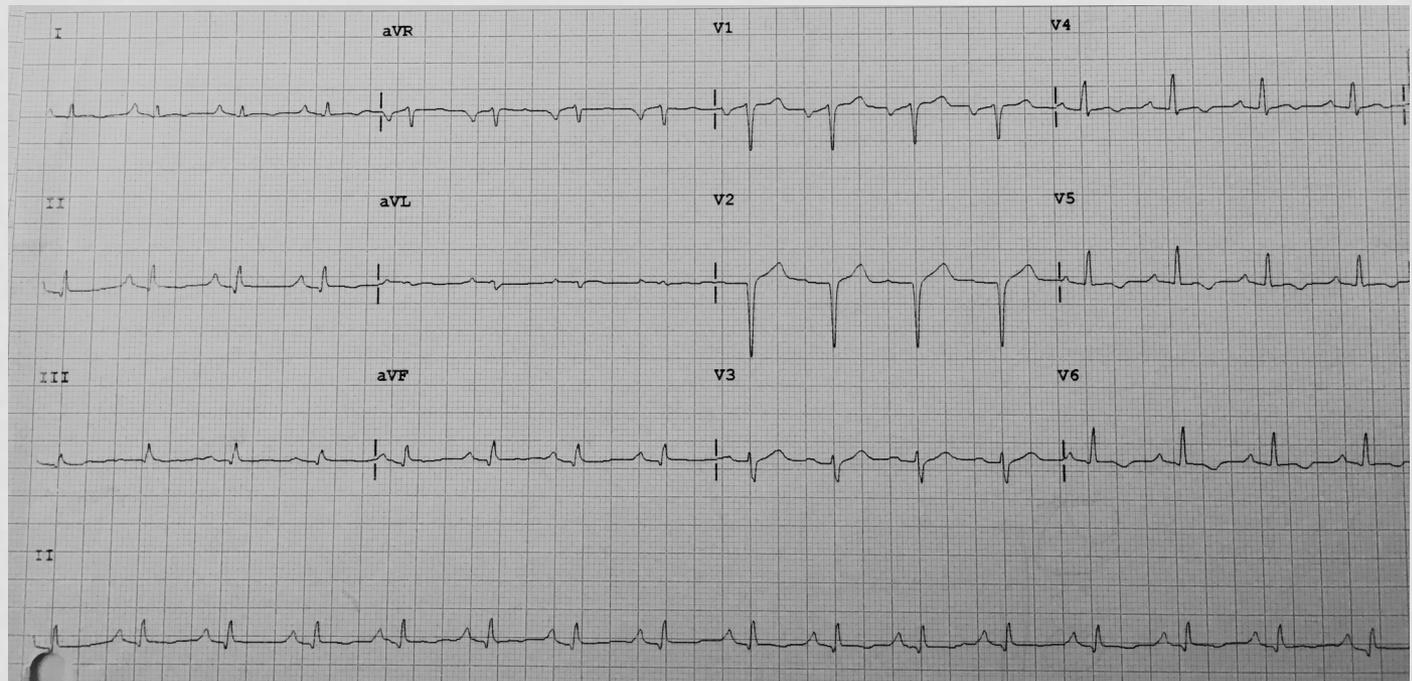
## Laboratorio

eGFR= 88  
 Crea= 0.92  
 BUN= 46  
 Na = 142  
 Bil.tot= 0.32  
 INR= 1.05  
 GB= 13.400  
 Hb= 14.6 (HcT 45.6%)  
 Urato= 7.7  
**PCR= 8**

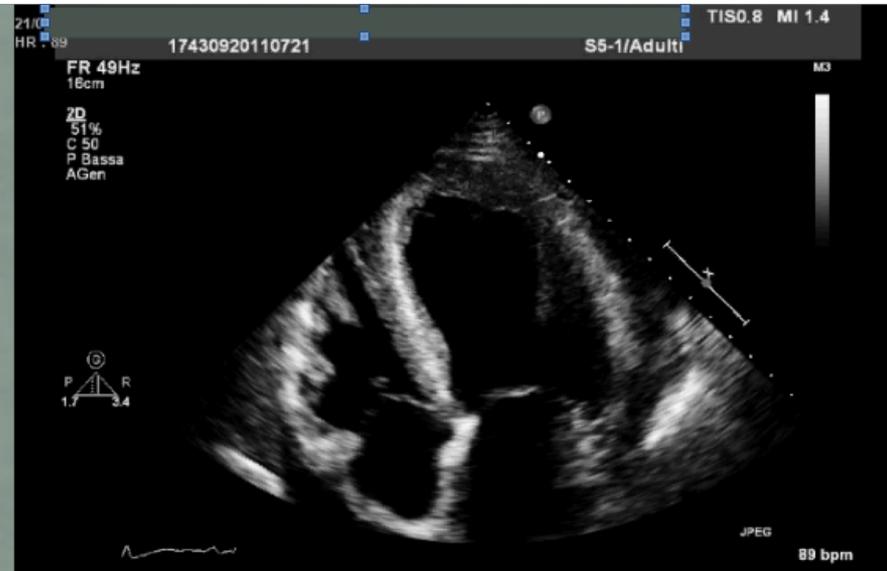
Colesterolo= 178  
 Col HDL= 38  
 Proteine tot= 7.7  
 Albumina= 4.67  
 Colinesterasi= 11727

CK-MB= 12  
TnT= 0.09 (0.00-0.03)

PA 140/80 mmHg, FC 95 bpm, eupnoico,  
 apiretico,  
 fini crepitazioni basali, T3



# ECOCARDIOGRAMMA



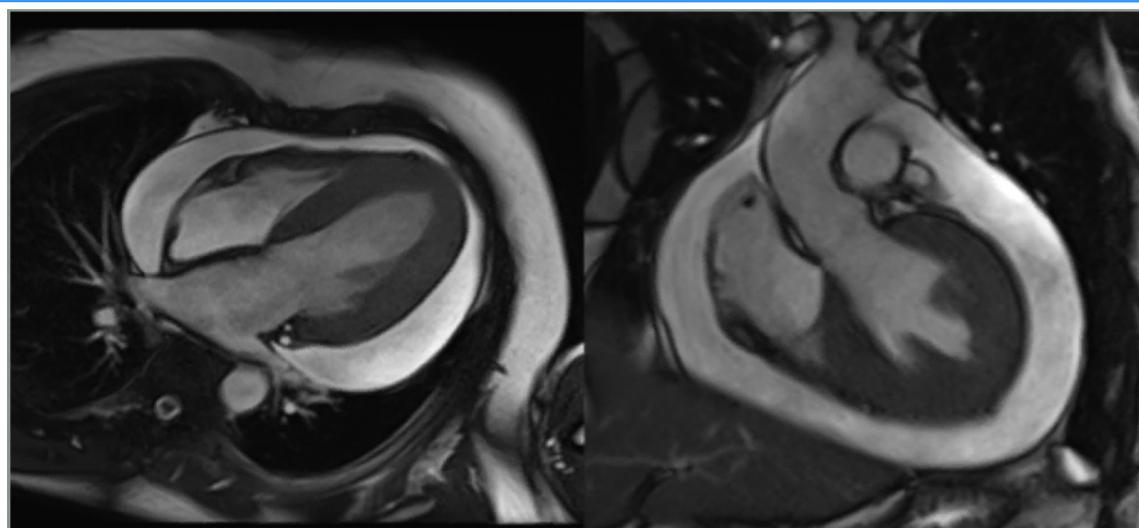
ECO: Vsn di **normali dimensioni** (DTD 48 mm, VTD/VTS 125/77 ml), moderato **aumento degli spessori** parietali (SIV basale 14 mm, medio 15 mm, PP basale 14 mm, media 17 mm), aumento dell'ecoriflettenza miocardica diffusamente. **FE 38%**. Pattern di flusso transmitralico restrittivo. Vdx di dimensioni nei limiti con aumento spessori parietali (parete libera 8 mm), ipocinesia diffusa (**TAPSE 14 mm**). Dilatazione atriale sn. IM 1+. IT lieve, P AP normale. Falda di **versamento pericardico** (max 15 mm).

CORO: non stenosi significative

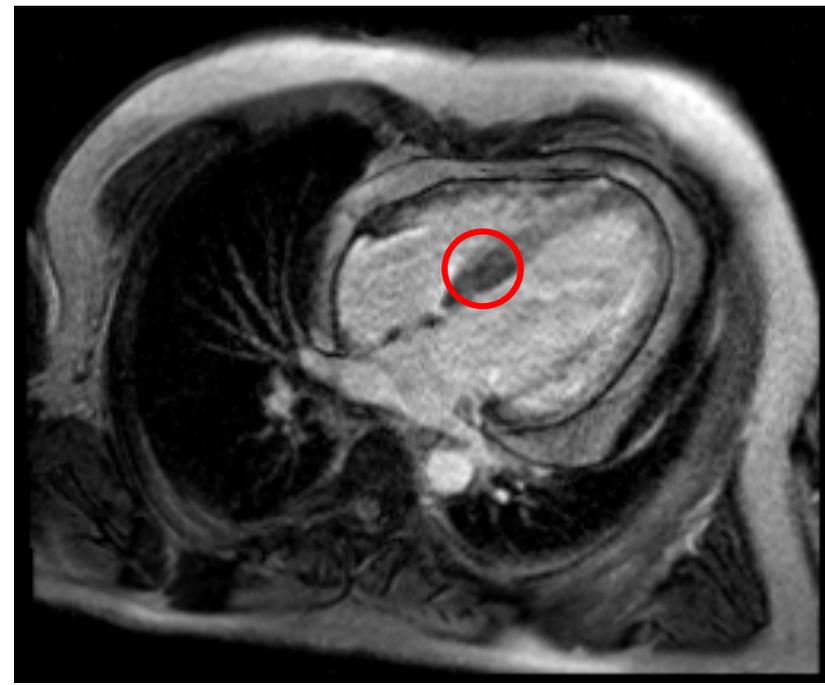
Sospetto di mio-pericardite

Avviata tp anti-infiammatoria + ACE-inibitore (ramipril)

Dimesso con programma di CMR in post-ricovero



Conferma di marcato aumento  
spessori/massa VS, disfunzione  
biventricolare, versamento  
pericardico ubiquitario  
→ Sospetta malattia infiltrativa  
(amiloidosi?)

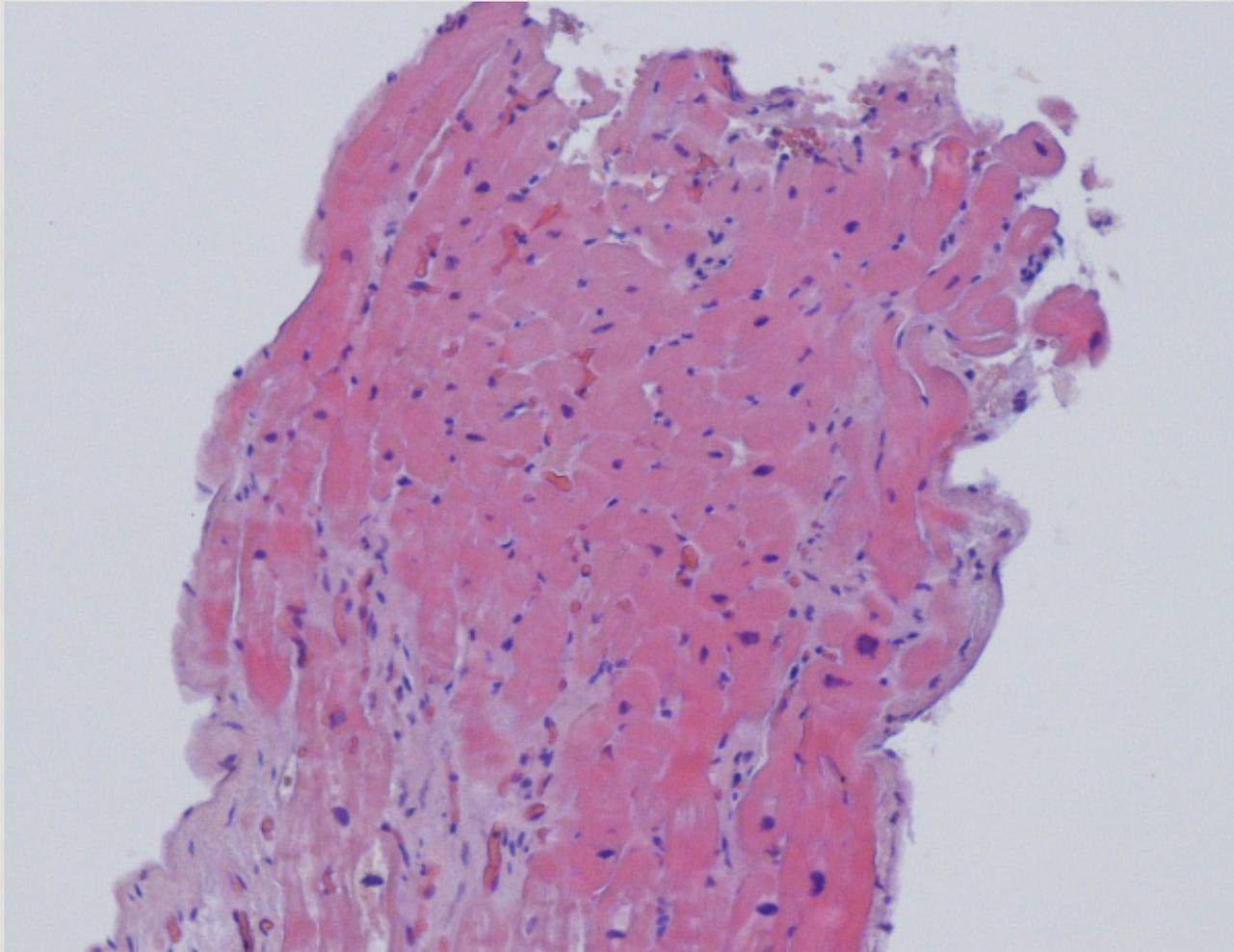


## Sospetto di cardiomiopatia (infiltrativa? ipertrofica?):

- **BEM**
- Periocardiocentesi + citologico → analisi liquido prelevato negativa per CTM/BK...
- Biologia molecolare: no mutazione gene TTR né gene GLA
- Indagini genetiche: neg MYBPC3, neg MYH7
- V. Ematologica: emometria nella norma, non CM all'elettroforesi, dosaggio Ig sieriche ndr, immunofissazione sierica ed urinaria, elettroforesi urinaria, ricerca catene leggere neg.

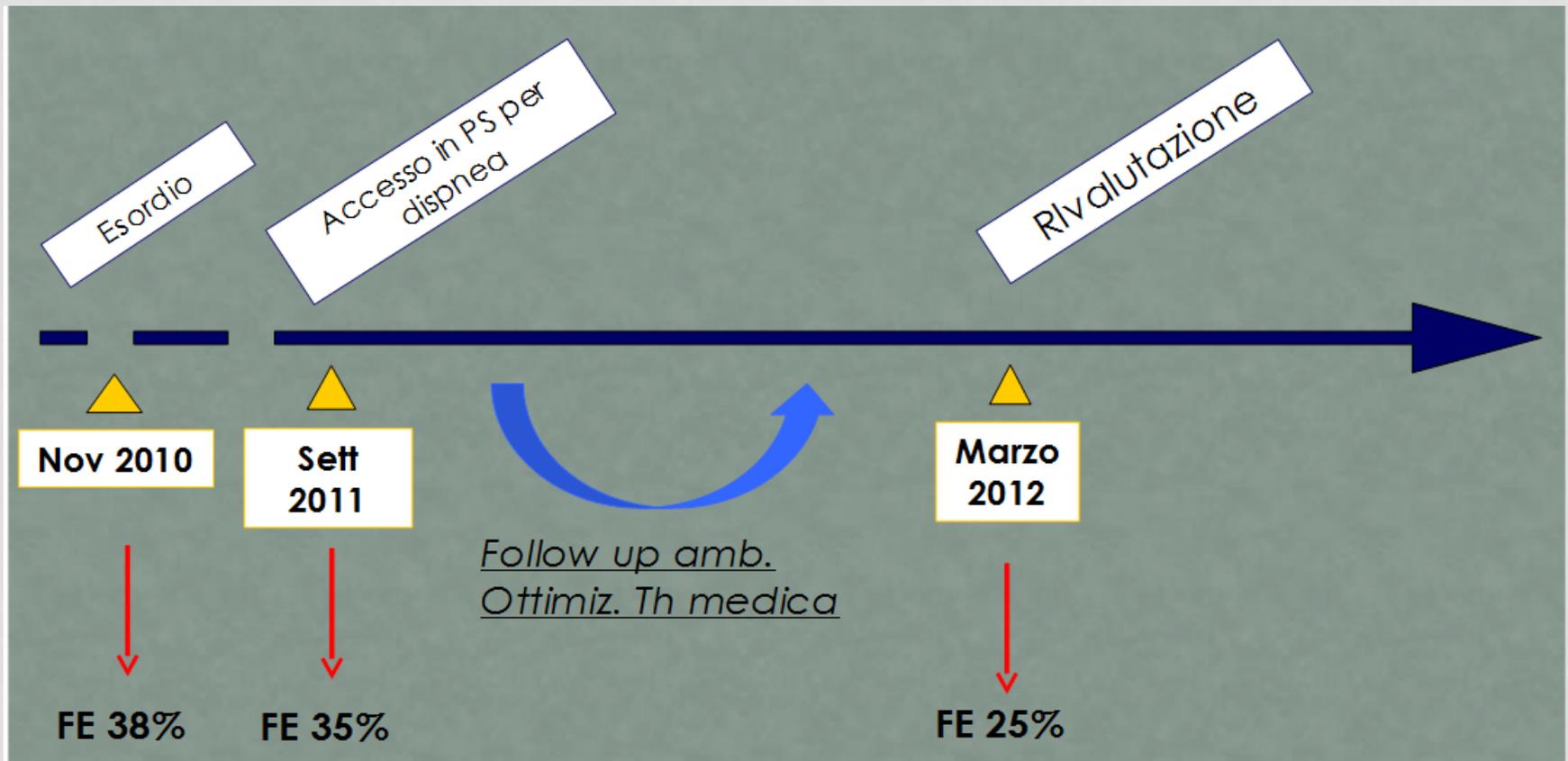
Th domiciliare: Enalapril 20 mg, Bisoprololo 2.5 mg, Indometacina + Colchicina

Dimesso con programma di follow up ambulatoriale presso ambulatori Cardiologia 2



Referto: in 4 su 4  
campioni  
“non depositi di  
sostanza amiloide,  
no disarray delle  
fibre muscolari, no  
fibrosi interstiziale”

# ANAMNESI CARDIOLOGICA



# ANAMNESI CARDIOLOGICA

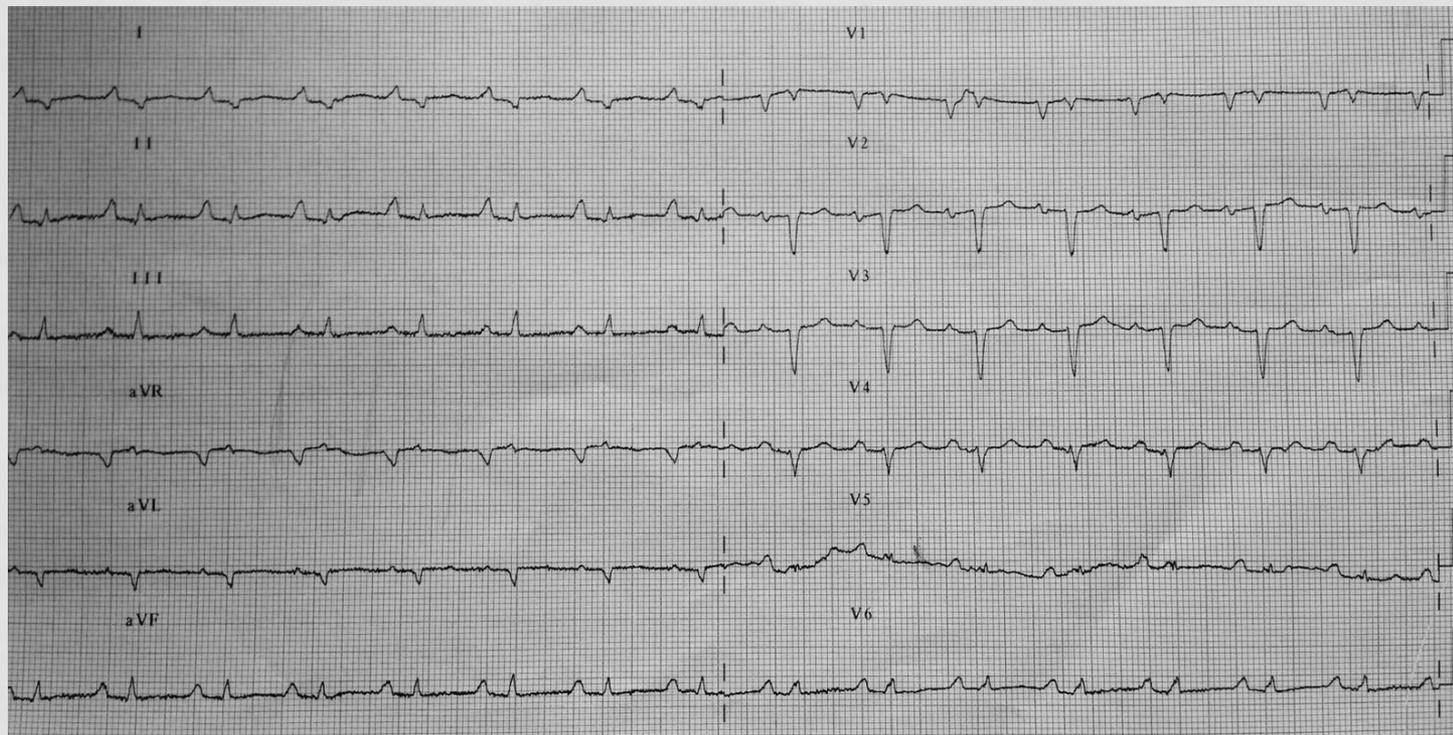
## Laboratorio

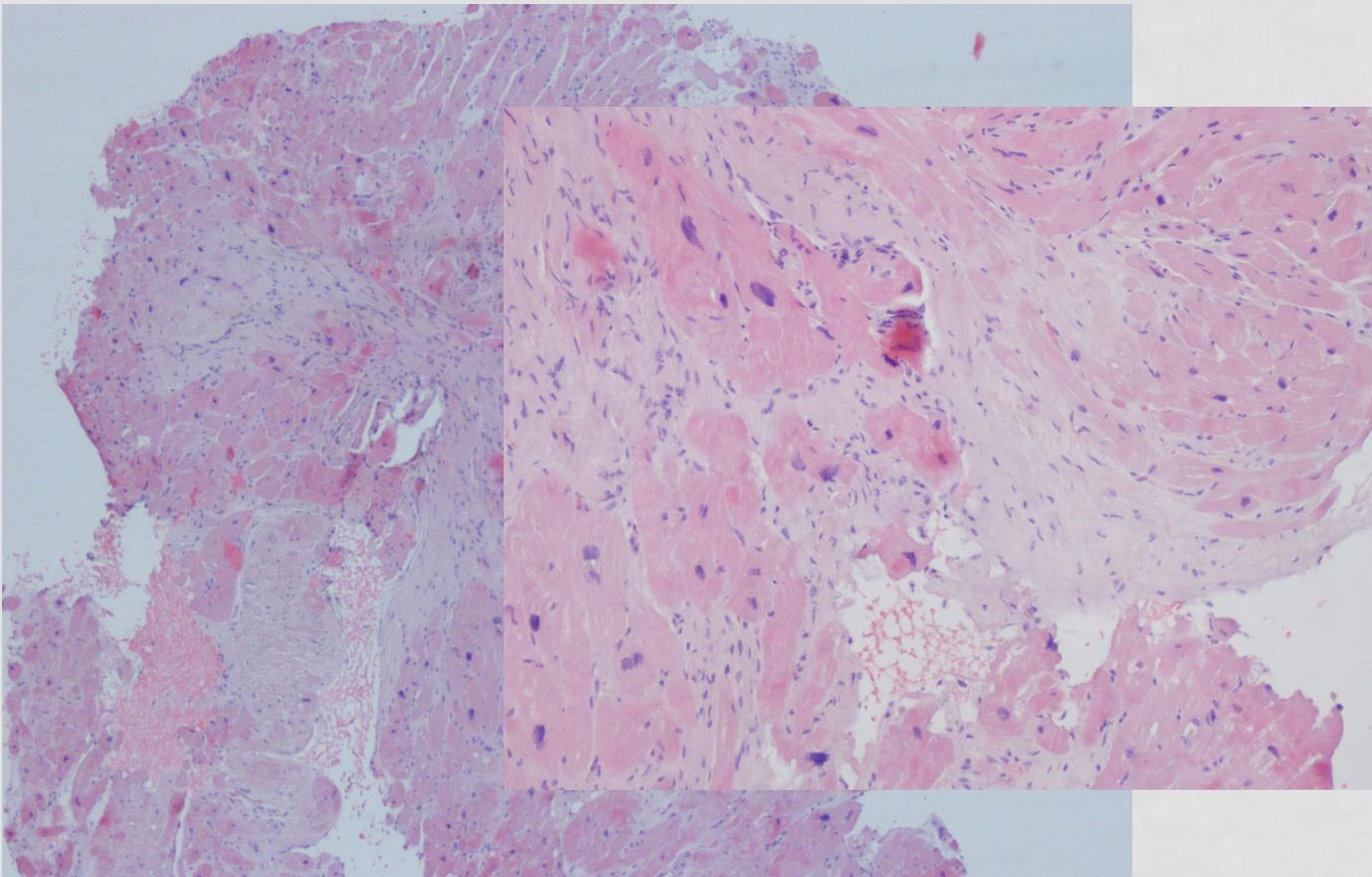
eGFR= 100  
Crea= 0.81  
BUN= 51  
Na = 139  
Bil.tot= 0.54  
INR= 1.04  
GB= 10.4  
Hb= 14.4 (HcT 43.9%)  
Urato= 9.2  
PCR= 0.6

Colesterolo= 195  
Proteine tot= 7  
Albumina= 4.17  
Colinesterasi= 10249

NTproBNP= 245  
CK-MB= 10  
TnT= 0,06

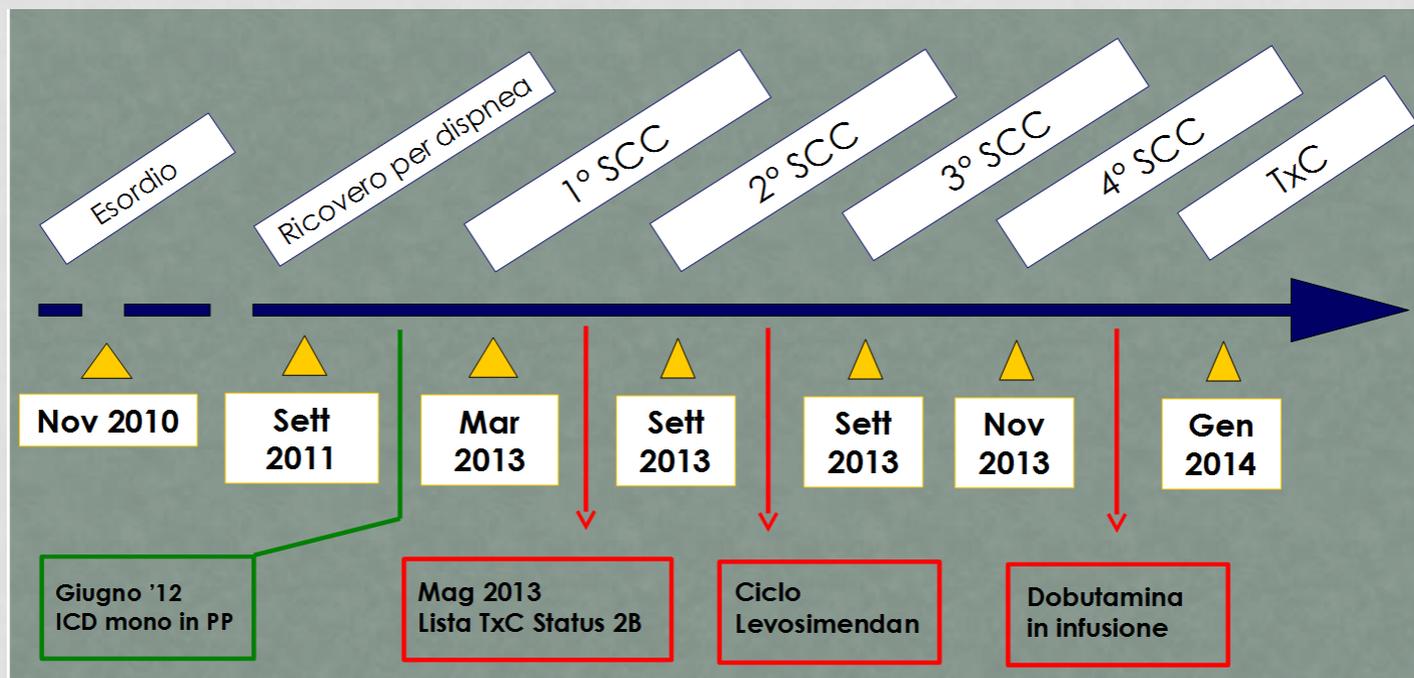
CAT dx 03/12	AD	PAP	WP	CI	PVR-i	PA <sub>s</sub>	FC
<b>BASALE</b>	15	48/21/31	32	1.3	7.2	100	68
<b>Dopo SNP 1 gamma</b>	7	39/16/26	19	1.47	4.7	90	65





Referto: in 4 campioni su 4  
“non depositi di sostanza amiloide, no disarray delle fibre muscolari, fibrosi interstiziale ed ipertrofia dei cardiomiociti”

# RICAPITOLANDO



Uomo giovane, no familiarità (per SCD, HF, HCM)

ECO e RMN compatibili con ipertrofia ventricolare sinistra vs CMIO infiltrativa (infiammatoria?)

Test genetici e biomolecolari negativi (parziali), BEM mai diagnostica

Evoluzione rapidamente sfavorevole nonostante trattamenti raccomandati

# Approccio alla CMIO “de novo”

Diagnosi  
eziologica

Storia  
naturale

Risposta ai  
trattamenti

**TRAIETTORIA DI  
MALATTIA**

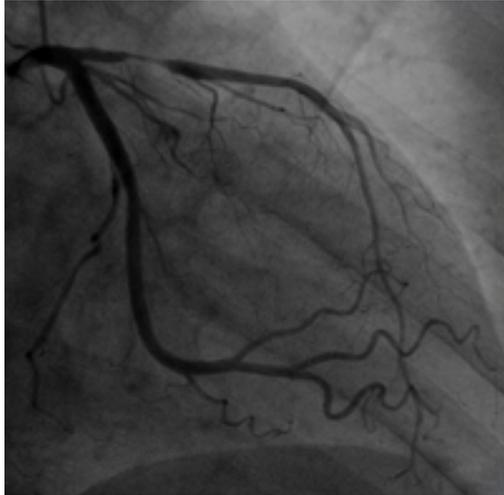


# Diagnosi eziologica

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>	Ref <sup>c</sup>
TTE is recommended for the assessment of myocardial structure and function in subjects with suspected HF in order to establish a diagnosis of either HFrEF, HFmrEF or HFpEF.	I	C	
TTE is recommended to assess LVEF in order to identify patients with HF who would be suitable for evidence-based pharmacological and device (ICD, CRT) treatment recommended for HFrEF.	I	C	
TTE is recommended for the assessment of valve disease, right ventricular function and pulmonary arterial pressure in patients with an already established diagnosis of either HFrEF, HFmrEF or HFpEF in order to identify those suitable for correction of valve disease.	I	C	
TTE is recommended for the assessment of myocardial structure and function in subjects to be exposed to treatment which potentially can damage myocardium (e.g. chemotherapy).	I	C	
Other techniques (including systolic tissue Doppler velocities and deformation indices, i.e. strain and strain rate), should be considered in a TTE protocol in subjects at risk of developing HF in order to identify myocardial dysfunction at the preclinical stage.	IIa	C	
CMR is recommended for the assessment of myocardial structure and function (including right heart) in subjects with poor acoustic window and patients with complex congenital heart diseases (taking account of cautions/contra-indications to CMR).	I	C	
CMR with LGE should be considered in patients with dilated cardiomyopathy in order to distinguish between ischaemic and non-ischaemic myocardial damage in case of equivocal clinical and other imaging data (taking account of cautions/contra-indications to CMR).	IIa	C	
CMR is recommended for the characterization of myocardial tissue in case of suspected myocarditis, amyloidosis, sarcoidosis, Chagas disease, Fabry disease non-compaction cardiomyopathy, and haemochromatosis (taking account of cautions/contra-indications to CMR).	I	C	
Non-invasive stress imaging (CMR, stress echocardiography, SPECT, PET) may be considered for the assessment of myocardial ischaemia and viability in patients with HF and CAD (considered suitable for coronary revascularization) before the decision on revascularization.	IIb	B	116-118
Invasive coronary angiography is recommended in patients with HF and angina pectoris recalcitrant to pharmacological therapy or symptomatic ventricular arrhythmias or aborted cardiac arrest (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity.	I	C	
Invasive coronary angiography should be considered in patients with HF and intermediate to high pre-test probability of CAD and the presence of ischaemia in non-invasive stress tests (who are considered suitable for potential coronary revascularization) in order to establish the diagnosis of CAD and its severity.	IIa	C	
Cardiac CT may be considered in patients with HF and low to intermediate pre-test probability of CAD or those with equivocal non-invasive stress tests in order to rule out coronary artery stenosis.	IIb	C	
Reassessment of myocardial structure and function is recommended using non-invasive imaging: - in patients presenting with worsening HF symptoms (including episodes of AHF) or experiencing any other important cardiovascular event; - in patients with HF who have received evidence-based pharmacotherapy in maximal tolerated doses, before the decision on device implantation (ICD, CRT); - in patients exposed to therapies which may damage the myocardium (e.g. chemotherapy) (serial assessments).	I	C	

ESC guide-lines 2016





Stenosi critiche  
→ CMIO ischemica



Non stenosi critiche  
→ CMIO “dilatativa”

- ✓ Vasi epicardici più brevi in rapporto a massa VS
- ✓ Minori rami collaterali di IVA e Cx
- ✓ Anomalie microcircolo (low-flow, FFR ridotta)

*Gil KE et al. Adv Med Sci  
2016;61:331*

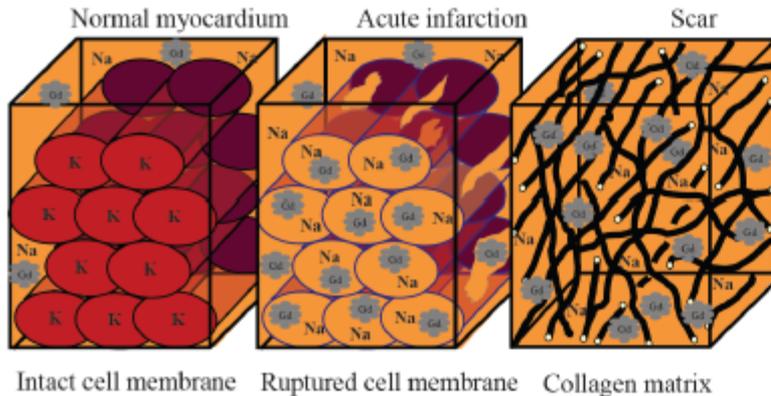
# Risonanza magnetica cardiaca

## Immagini cine:

- ✓ Precisa identificazione del bordo endocardico
- ✓ Stima riproducibile di volumi, cinesi e funzione biventricolari, spessori, massa cardiaca
- ✓ Valutazione morfologica accurata di valvole e pericardio
- ✓ Informazioni anche su strutture extracardiache



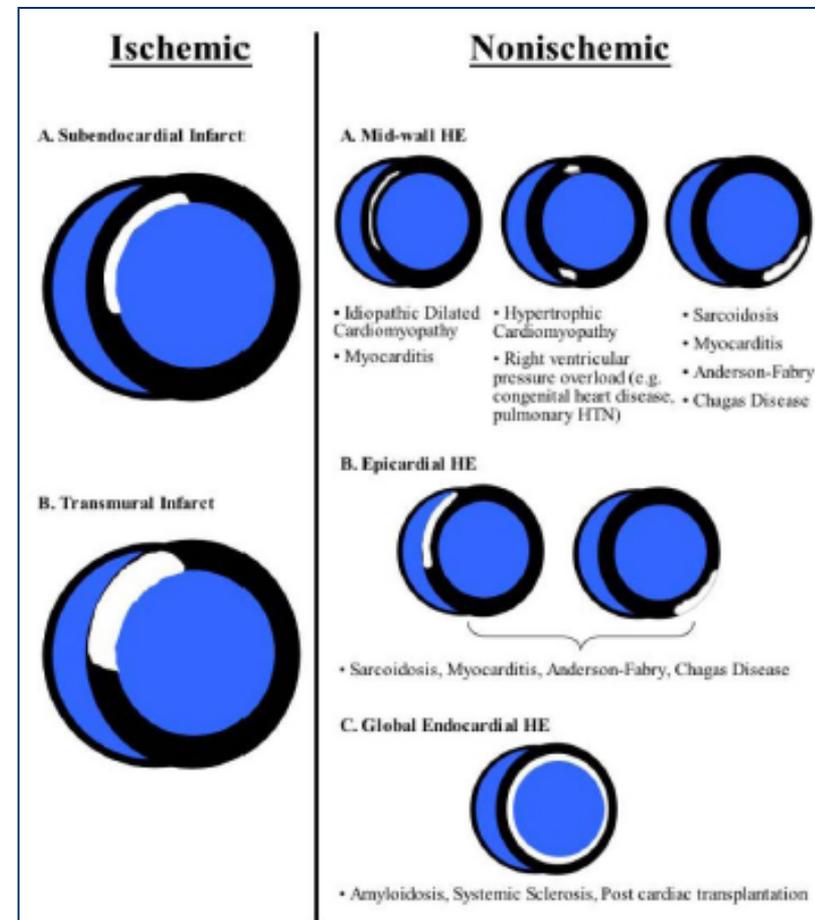
# Risonanza magnetica cardiaca



## Gadolinio:

- ✓ si distribuisce nello spazio extracellulare
- ✓ se lisi di membrana si distribuisce tra le cellule
- ✓ persiste nel tessuto se aumenta la matrice collagene (cicatrice, fibrosi)

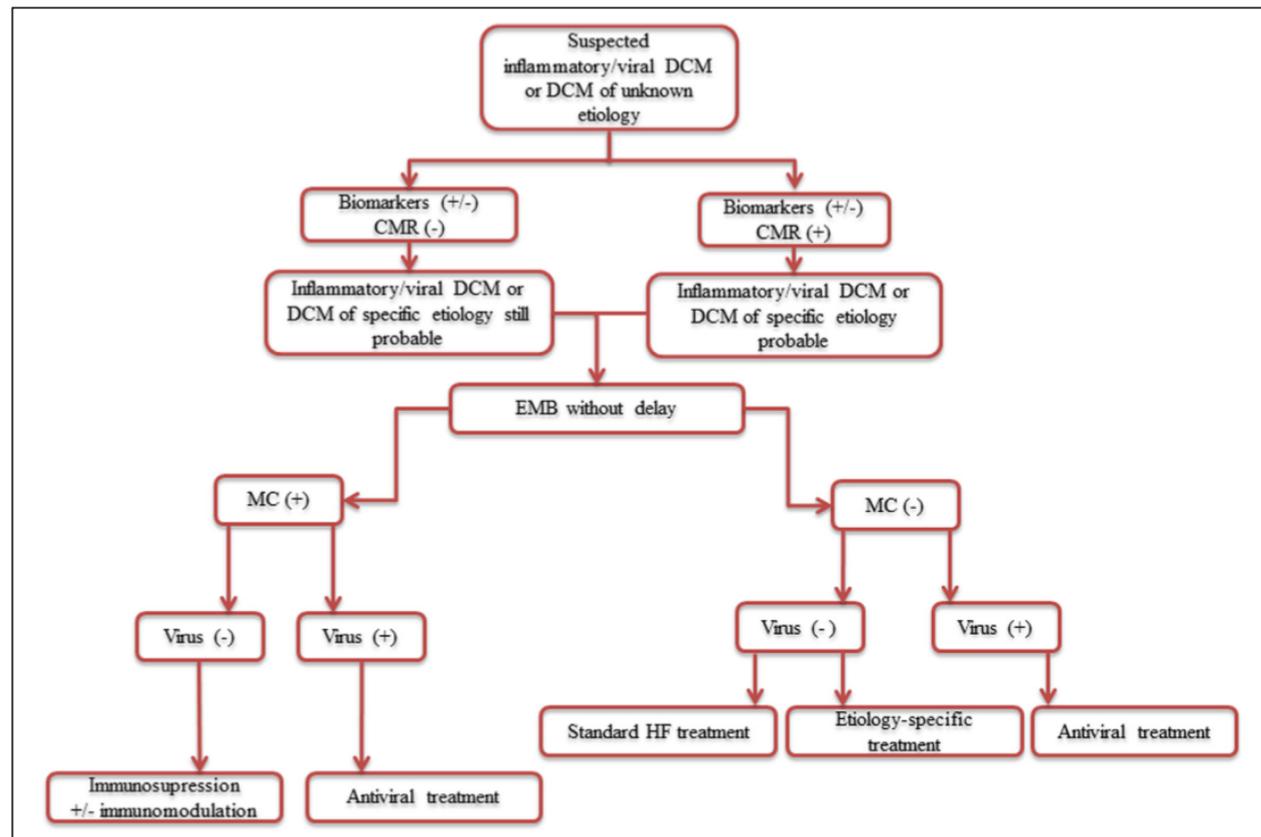
## Pattern di LGE



# Biopsia endomiocardica

## BEM:

- ✓ Esame istologico, colorazioni classiche e specifiche (Rosso Congo), evidenza di necrosi cell, infiltrato infiammatorio
- ✓ Immunoistochimica (ricerca di popolazioni leucocitarie, auto-anticorpi)
- ✓ PCR per genomi virali



*Gil KE et al. Adv Med Sci  
2016;61:331*

## Raccomandazioni

GIORNALE  
ITALIANO  
DI CARDIOLOGIA

**Tabella III.** Malattie del miocardio diagnosticabili mediante biopsia endomiocardica con provata terapia specifica.

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Sarcoidosi cardiaca  
Miocardite a cellule giganti  
Sindrome ipereosinofila a coinvolgimento miocardico  
Infezioni batteriche a coinvolgimento miocardico  
Rigetto post-trapianto  
Cardiotossicità da antracicline

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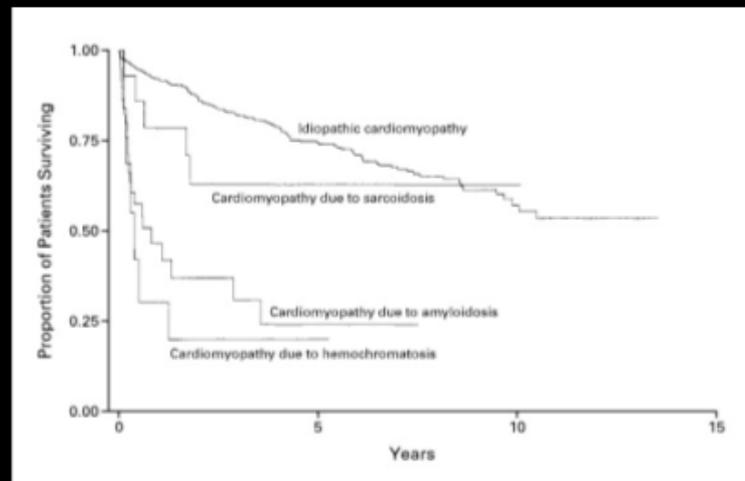
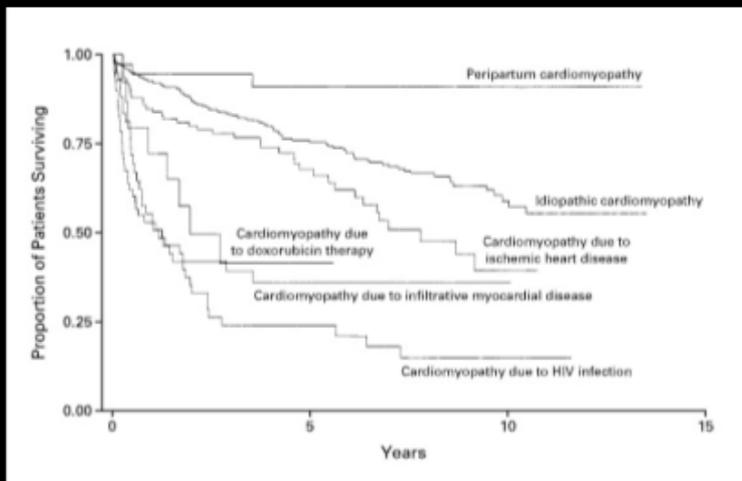
*Perkan A et al. Ital Heart J  
2002;3:419*

2011 Consensus statement on endomyocardial biopsy from the Association for European Cardiovascular Pathology and the Society for Cardiovascular Pathology

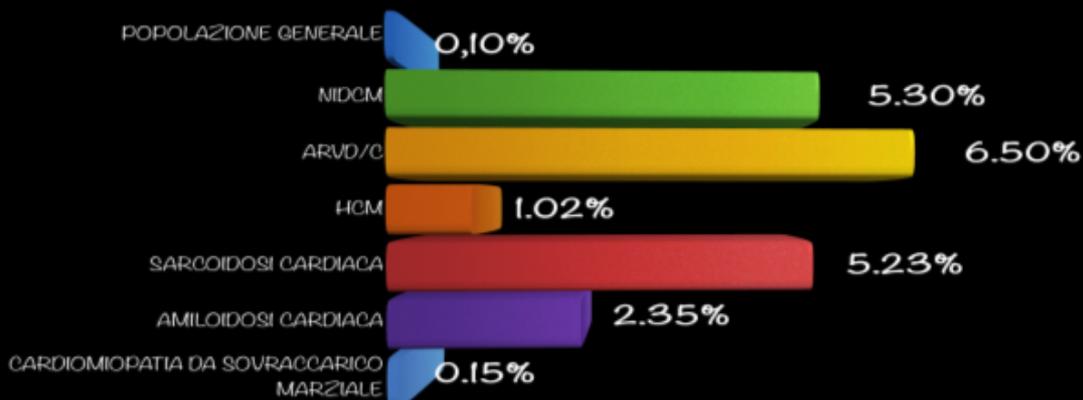
- ✓ Miocarditi, CMIO infiammatorie, miocarditi da ipersensibilità
- ✓ Sarcoidosi, amiloidosi
- ✓ Mal di Anderson-Fabry
- ✓ Glicogenosi
- ✓ Endocardite fibroblastica di Loeffler
- ✓ Sovraccarico marziale
- ✓ Displasia aritmogena del VD
- ✓ Tumori cardiaci

*Leone O et al. Cardiovasc  
Pathol 2012;245*

# Eziologia e "traiettoria"



Felker GM et al. N Engl J Med 2000;342:1077-1084.



Diagnosi  
eziologica

Storia  
naturale

Risposta ai  
trattamenti

**TRAIETTORIA DI  
MALATTIA**

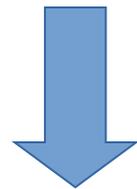


# Predittori di outcome

## Indicatori prognostici

- ✓ Clinici (HR, SBP, comorbidità)
- ✓ Strumentali (dilatazione VS, FE%, caratteristiche tissutali a CMR, capacità funzionale)
- ✓ Biochimici (attivazione neuro-ormonale, marcatori di danno cell, anemia)
- ✓ Genetici (tipizzazione genotipica)

*ESC guide-lines 2016*



Score  
prognostici

Numerous prognostic markers of death and/or HF hospitalization have been identified in patients with HF (*Web Table 3.5*). However, their clinical applicability is limited and precise risk stratification in HF remains challenging.

In recent decades, several multivariable prognostic risk scores have been developed for different populations of patients with HF,<sup>36-41</sup> and some are available as interactive online applications. Multivariable risk scores may help predict death in patients with HF, but remain less useful for the prediction of subsequent HF hospitalizations.<sup>37,38</sup> A systematic review examining 64 prognostic models<sup>37</sup> along with a meta-analysis and meta-regression study of 117 prognostic models<sup>38</sup> revealed only a moderate accuracy of models predicting mortality, whereas models designed to predict the combined endpoint of death or hospitalization, or only hospitalization, had an even poorer discriminative ability.

# Parametri Clinici: frequenza cardiaca

- ✓ Nella fase intraospedaliera: durante episodio di SC acuto o alla dimissione, FC è maggiore che nella fase cronica (dati ESC-HF Pilot, IN-HF)
- ✓ Sempre in acuto, FC troppo bassa ( $< 70$ ) o elevata ( $> 80$ ) in acuto è predittiva di eventi a 7 giorni (studio PROTECT, score prognostico che contiene anche biomarcatori)
- ✓ FC elevata alla dimissione sembra essere predittore di eventi CV nella fase “vulnerabile” (30 gg post-dimissione)
- ✓ Riduzione di FC ottenuta in ricovero è prognosticamente favorevole, indipendentemente dal valore raggiunto

**Frequenza  
cardiaca**

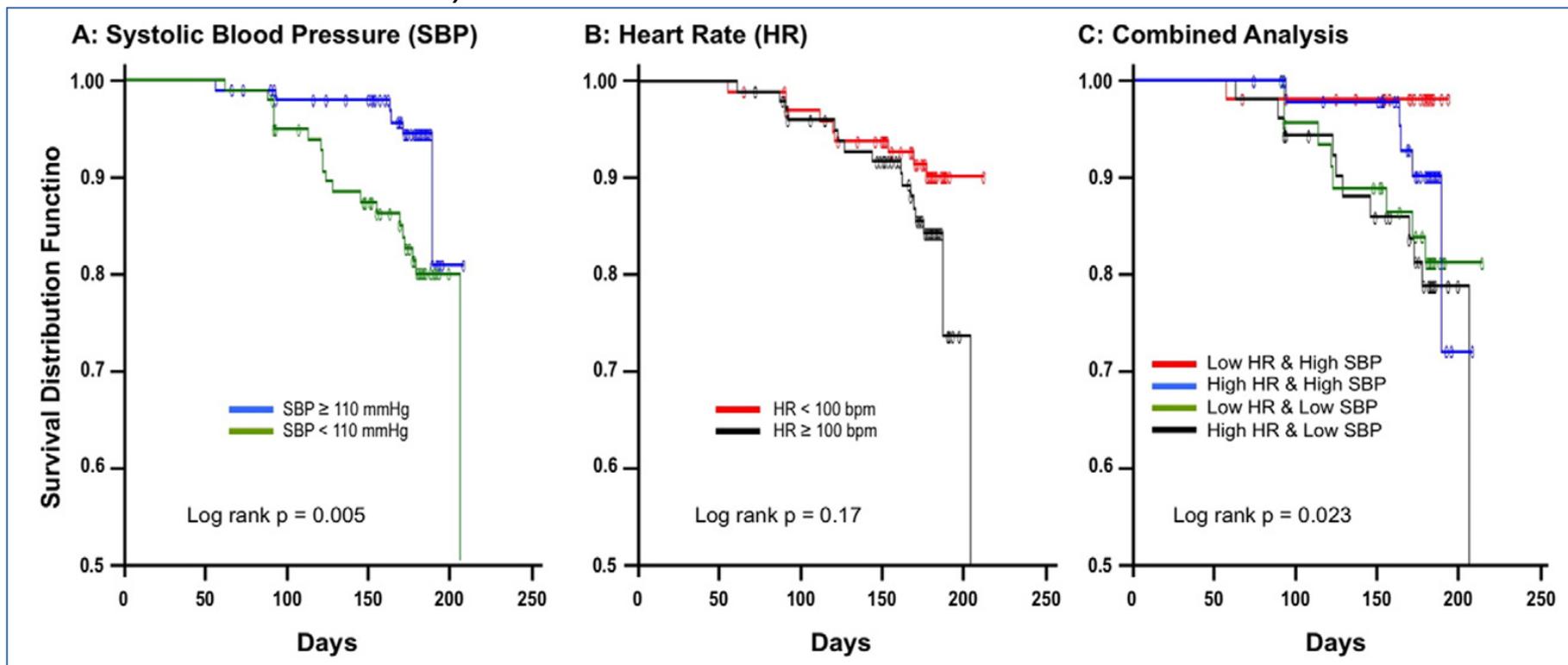


**Fattore prognostico**

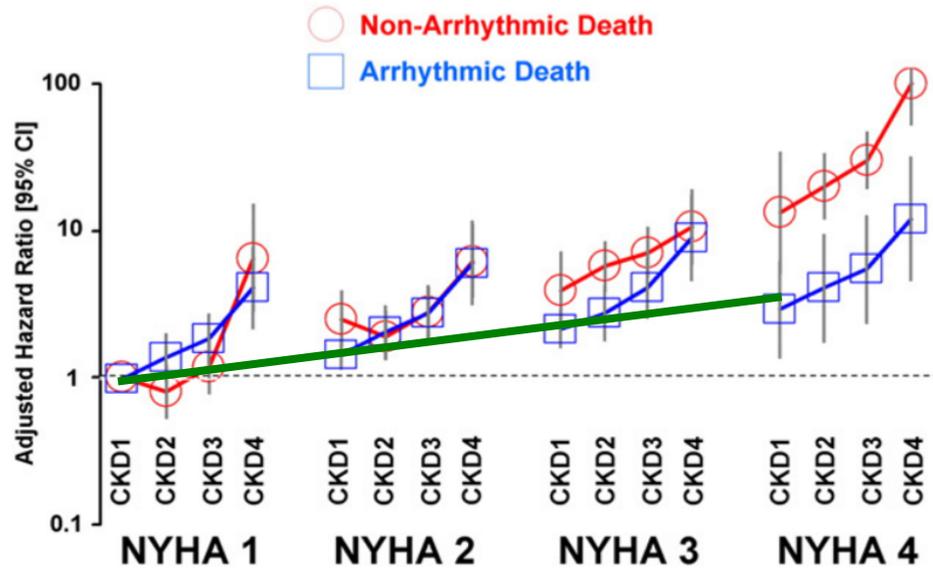
**Target terapeutico**

# Parametri Clinici

- ✓ 206 pts, PPCM, caratteristiche di base simili
- ✓ Trattamenti raccomandati, dosaggi simili
- ✓ SBP < 110 e HR > 100 predittori di peggiore outcome (comb: morte, FE < 35%, NYHA III-IV a 6 mesi)



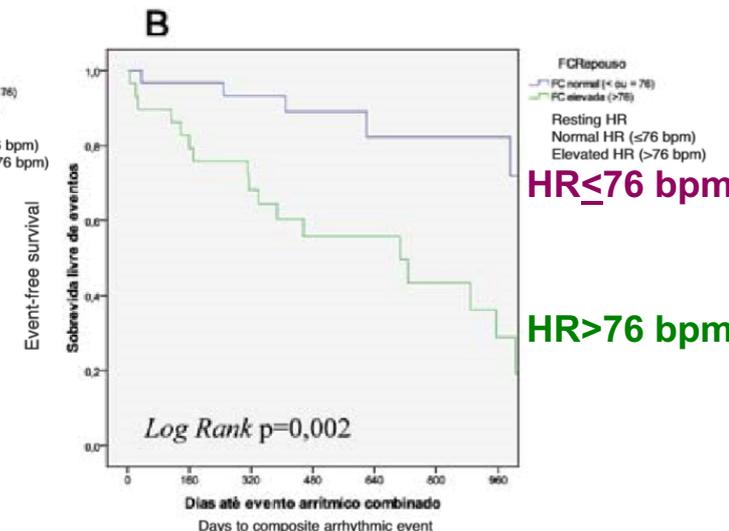
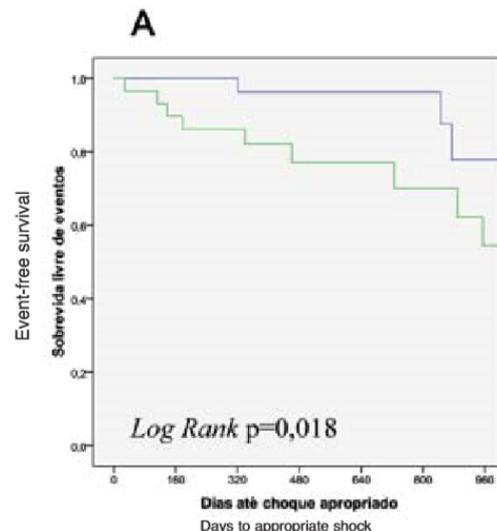
# Parametri clinici



- ✓ Classe NYHA
- ✓ IRC
- ✓ HR a riposo (OMT)

Alsheikh-Ali AA, et al.  
Am Heart J 2011;161:204

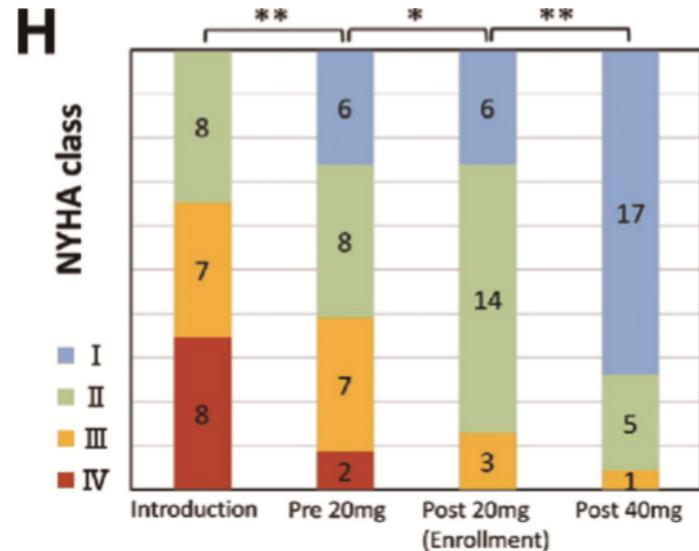
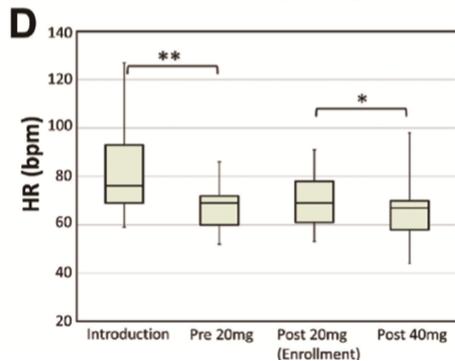
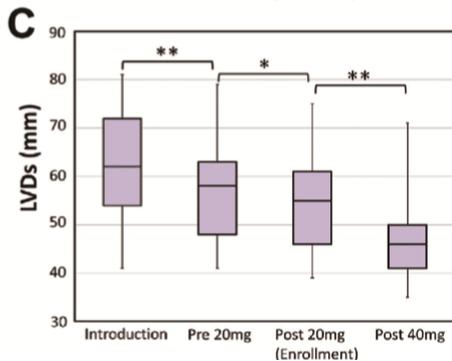
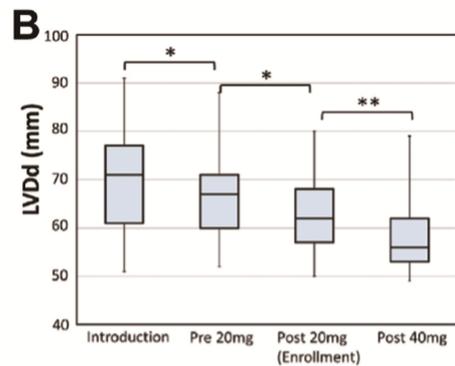
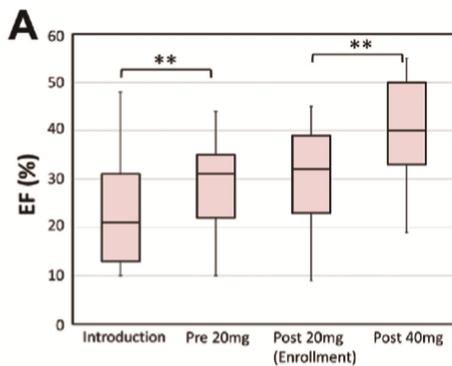
Calè R, et al  
Rev Port Cardiol 2011



# Trattamenti farmacologici

- ✓ CMIO non ischemica, severa disfunzione VS
- ✓ Già avviato carvedilolo LD da 6 mesi, persistenza di disfunzione VS

➔ Ulteriore rimodellamento inverso (Dd, FE) e miglioramento clinico (NYHA, BNP)



**TABLE 3** CMR Results and Patient Clinical Outcomes

	All Patients (N = 113)	Patients With Events (n = 36)	Patients Without Events (n = 77)	p Value
Pathological LVEDV	60 (53)	28 (78)	32 (42)	<0.001
LVEDV, ml/m <sup>2</sup>	149 ± 96	225 ± 122	112 ± 50	<0.001
Pathological LVESV index	89 (79)	31 (86)	58 (75)	0.190
LVESV index, ml/m <sup>2</sup>	90 ± 85	153 ± 117	60 ± 40	0.001
Pathological LVSV index	48 (42)	21 (58)	27 (35)	0.019
LVSV index, ml/m <sup>2</sup>	56 ± 24	66 ± 30	51 ± 19	0.25
Pathological LVEF	82 (73)	31 (86)	51 (66)	0.027
LVEF, %	45 ± 15	39 ± 18	48 ± 13	0.001
Pathological LV mass	35 (31)	8 (22)	27 (35)	0.168
LV mass, g	116 ± 39	123 ± 36	113 ± 40	0.574
Total LV-MMI, g/m <sup>2</sup>	68 ± 22	67 ± 21	69 ± 22	0.825
LV-MMI compacted, g/m <sup>2</sup>	52 ± 22	52 ± 21	53 ± 22	0.99
LV-MMI noncompacted, g/m <sup>2</sup>	13 ± 8	11 ± 8	13 ± 9	0.249
Percent LV-MM noncompacted	19 ± 10	16 ± 7	20 ± 11	0.137
Percent LV-MM noncompacted >20%	24 (21)	12 (33)	12 (16)	0.031
Percent LV-MM noncompacted >25%	21 (19)	5 (14)	16 (21)	0.38
Total LV-MMI noncompacted >15 g/m <sup>2</sup>	33 (29)	10 (28)	23 (30)	0.819
NC/C ratio ≥3:1 in at least 1 of segments 1-3, 7-16	32 (28)	7 (19)	25 (32)	0.152
NC/C ratio ≥2:1 in at least 1 of segments 4-6	4 (3.5)	1 (3)	3 (4)	0.764
Patients with LGE	11 (9.7)	10 (28)	1 (1.3)	<0.001
Patients with RVNC	20 (18)	5 (14)	15 (19)	0.246
RV abnormalities (RVNC, LGE, low EF, dilation)	29 (26)	8 (21)	21 (27)	0.124
Patients with RV LGE	0	0	0	-

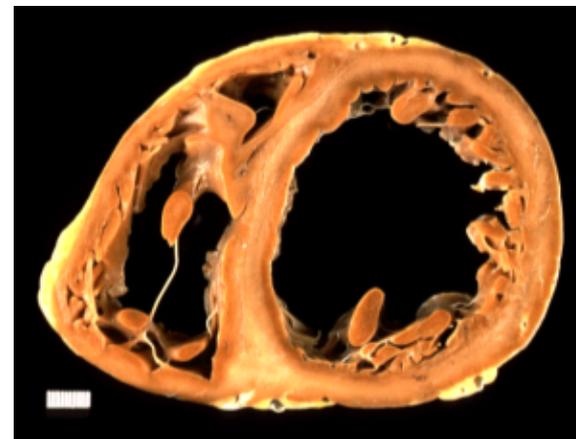
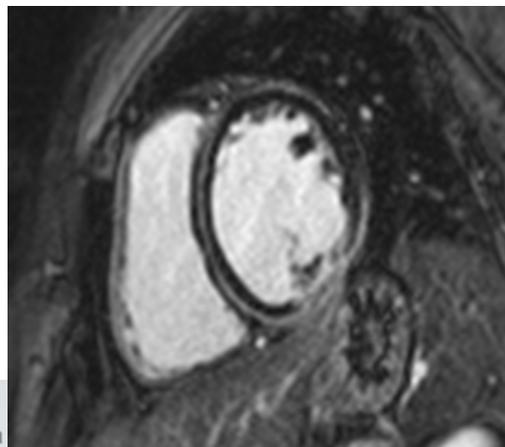
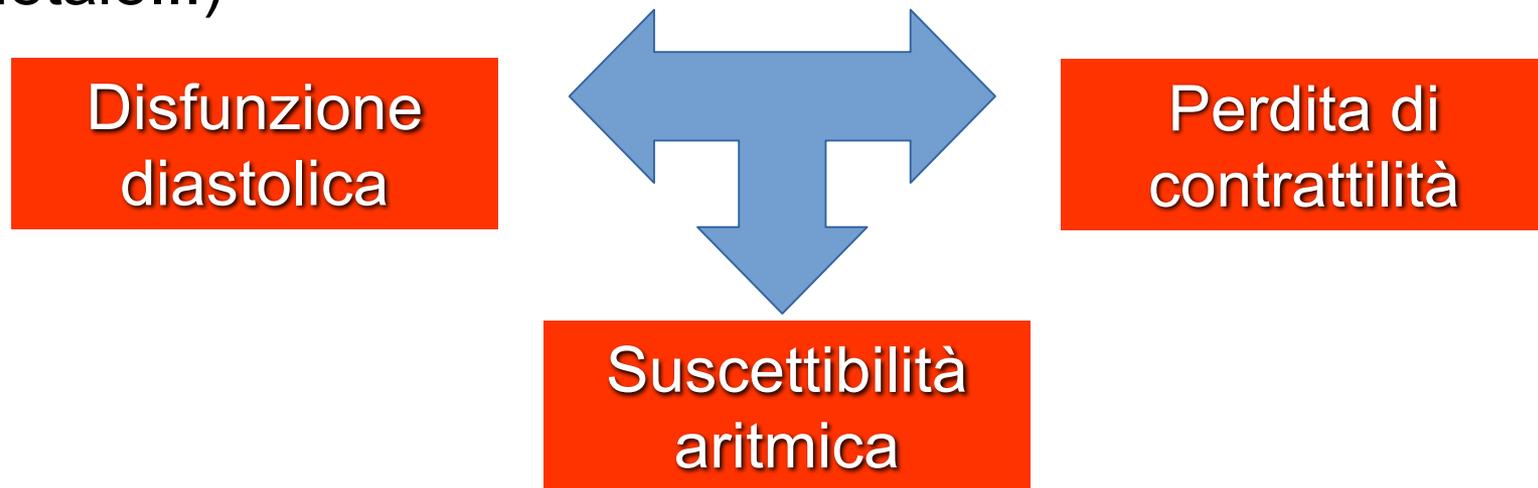
133 pts

Eventi:

- ricovero per HF
- aritmie V
- morte aritmica o per HF
- eventi tromboembolici

# LGE = Fibrosi miocardica

**Fibrosi:** punto di arrivo istologico (irreversibile) di molti processi patologici (ischemia, infiammazione, diabete, stress parietale...)

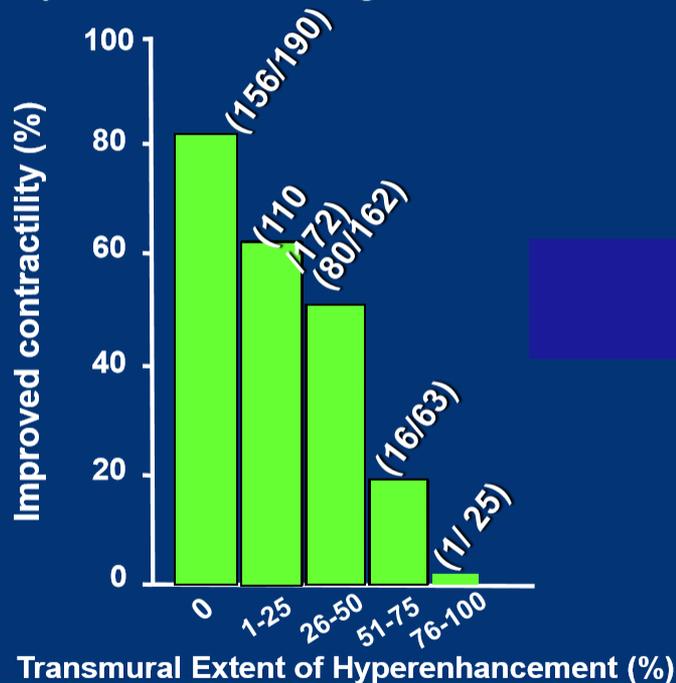


# Fibrosi miocardica: CMIO ischemica

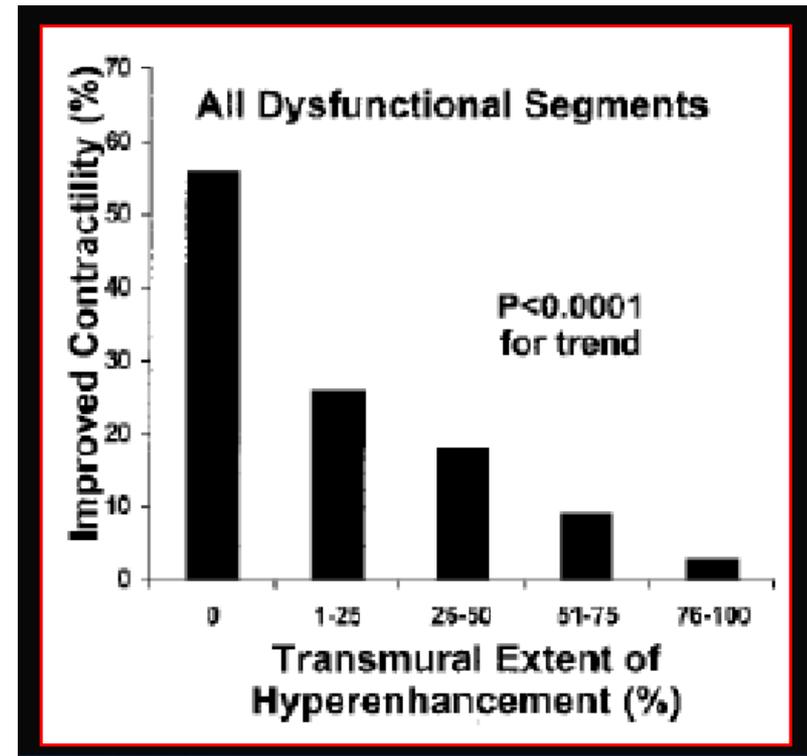
Nella **CMIO ischemica** estensione e quantità di fibrosi (LGE) predice il recupero di funzione contrattile dopo:

## Rivascolarizzazione

All Dysfunctional Segments



## Tp beta-bloccante



Selvanajagam et al. *Circ* 2004; Bello et al. *Circ* 2003

Inquadrare il paziente con SC

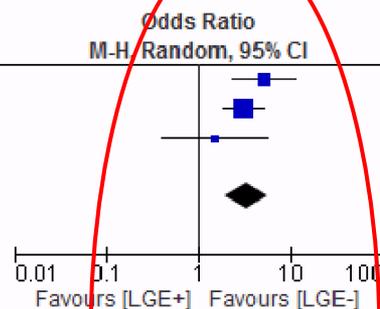
F. Macera – Milano, 29 marzo 2017

# Fibrosi miocardica: CMIO dilatativa

## A. Presence of LGE and All-Cause Mortality

Study or Subgroup	LGE+		LGE-		Weight	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
Cheong BYC 2009	16	37	23	178	31.8%	5.13 [2.34, 11.25]
Gulati A 2013	38	142	35	330	54.1%	3.08 [1.85, 5.13]
Muller KAL 2013	6	94	4	91	14.1%	1.48 [0.40, 5.44]
<b>Total (95% CI)</b>		<b>273</b>		<b>599</b>	<b>100.0%</b>	<b>3.27 [1.94, 5.51]</b>

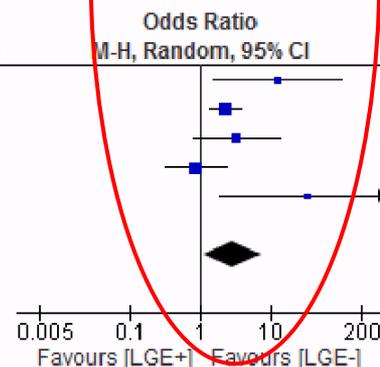
Total events 60 62  
 Heterogeneity:  $\text{Tau}^2 = 0.06$ ;  $\text{Chi}^2 = 2.76$ ,  $\text{df} = 2$  ( $P = 0.25$ );  $I^2 = 28\%$   
 Test for overall effect:  $Z = 4.45$  ( $P < 0.00001$ )



## B. Presence of LGE and Heart Failure Hospitalization

Study or Subgroup	LGE+		LGE-		Weight	Odds Ratio M-H, Random, 95% CI
	Events	Total	Events	Total		
Cho JR 2010	11	42	1	37	12.7%	12.77 [1.56, 104.60]
Gulati A 2013	30	142	35	330	33.5%	2.26 [1.32, 3.85]
Lehrke S 2011	6	72	3	112	19.8%	3.30 [0.80, 13.65]
Muller KAL 2013	8	94	9	91	26.1%	0.85 [0.31, 2.30]
Wu KC 2008	8	27	0	38	7.9%	33.56 [1.84, 612.28]
<b>Total (95% CI)</b>		<b>377</b>		<b>608</b>	<b>100.0%</b>	<b>2.91 [1.16, 7.27]</b>

Total events 63 48  
 Heterogeneity:  $\text{Tau}^2 = 0.58$ ;  $\text{Chi}^2 = 10.24$ ,  $\text{df} = 4$  ( $P = 0.04$ );  $I^2 = 61\%$   
 Test for overall effect:  $Z = 2.28$  ( $P = 0.02$ )



Morte per  
tutte le cause

Ricoveri per  
scompenso

Kuruvilla S, et al. *Circ Cardiovasc Imaging* 2014;7(2):250

## LGE:

✓ Identifica popolazione a maggior rischio (5% HF se LGE+; <2% eventi se LGE-)

✗ No consenso sulla definizione/quantificazione di LGE (> in LGE diffuso, più frequente in CMIO non-ischemica)

Dilatazione, disfunzione e fibrosi ventricolare sono condizioni tardive nel processo fisiopatologico

Utili marcatori correlati con i meccanismi cellulari di dilatazione o *reverse remodeling*.

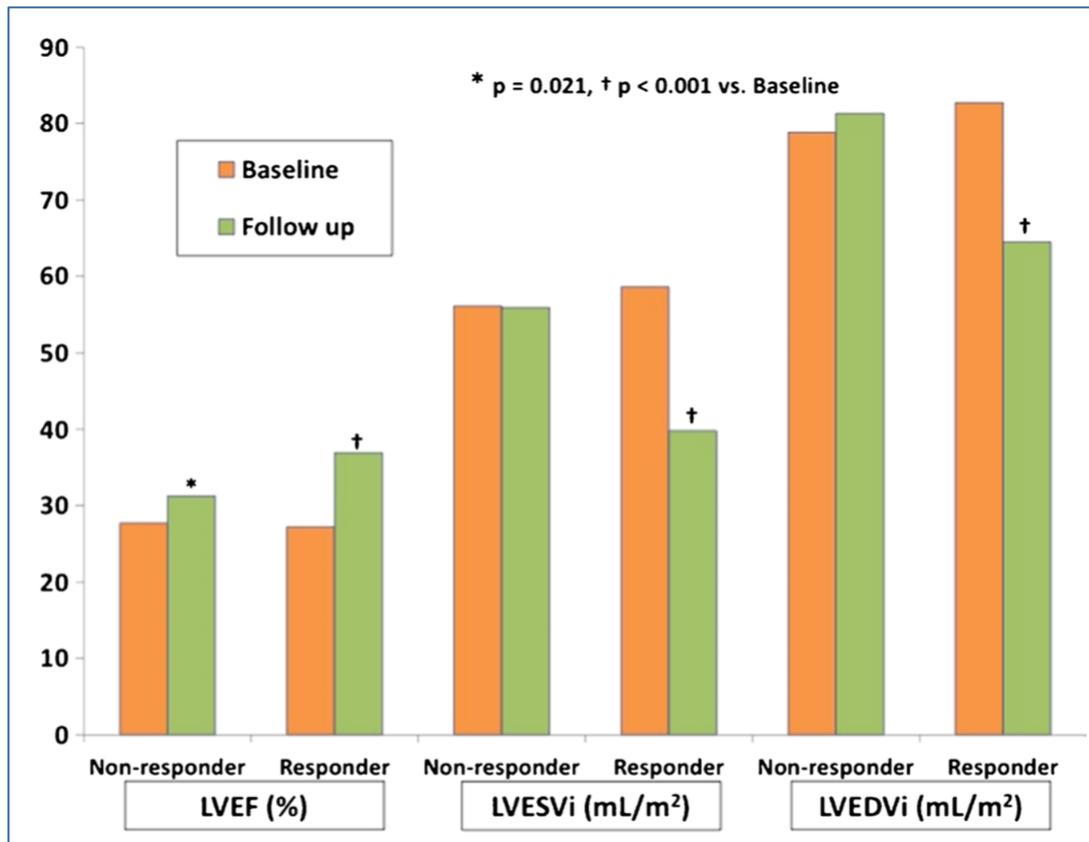
- ➔ **Troponine:** marcatori di progressione del danno cellulare
- ➔ **Peptidi natriuretici:** marcatori di stress di parete, aumento pressioni endocavitarie
- ➔ **Altri:** markers di infiammazione, fibrosi interstiziale (sST2, galectina-3)

# Troponina

- ➔ Nello scompenso cronico, rialzo persistente di troponina è marcatore di prognosi sfavorevole
- ➔ Nota correlazione tra picco di troponina post-infarto e successivo rimodellamento sfavorevole
- ➔ Alcuni studi hanno associato il rialzo di troponina con outcome avverso (eventi CV, rimodellamento sfavorevole) anche in cardiopatie di eziologia non ischemica

**Table 1** Strength of evidence for use of serum biomarkers to predict clinical outcomes, left ventricular remodeling, and reverse remodeling

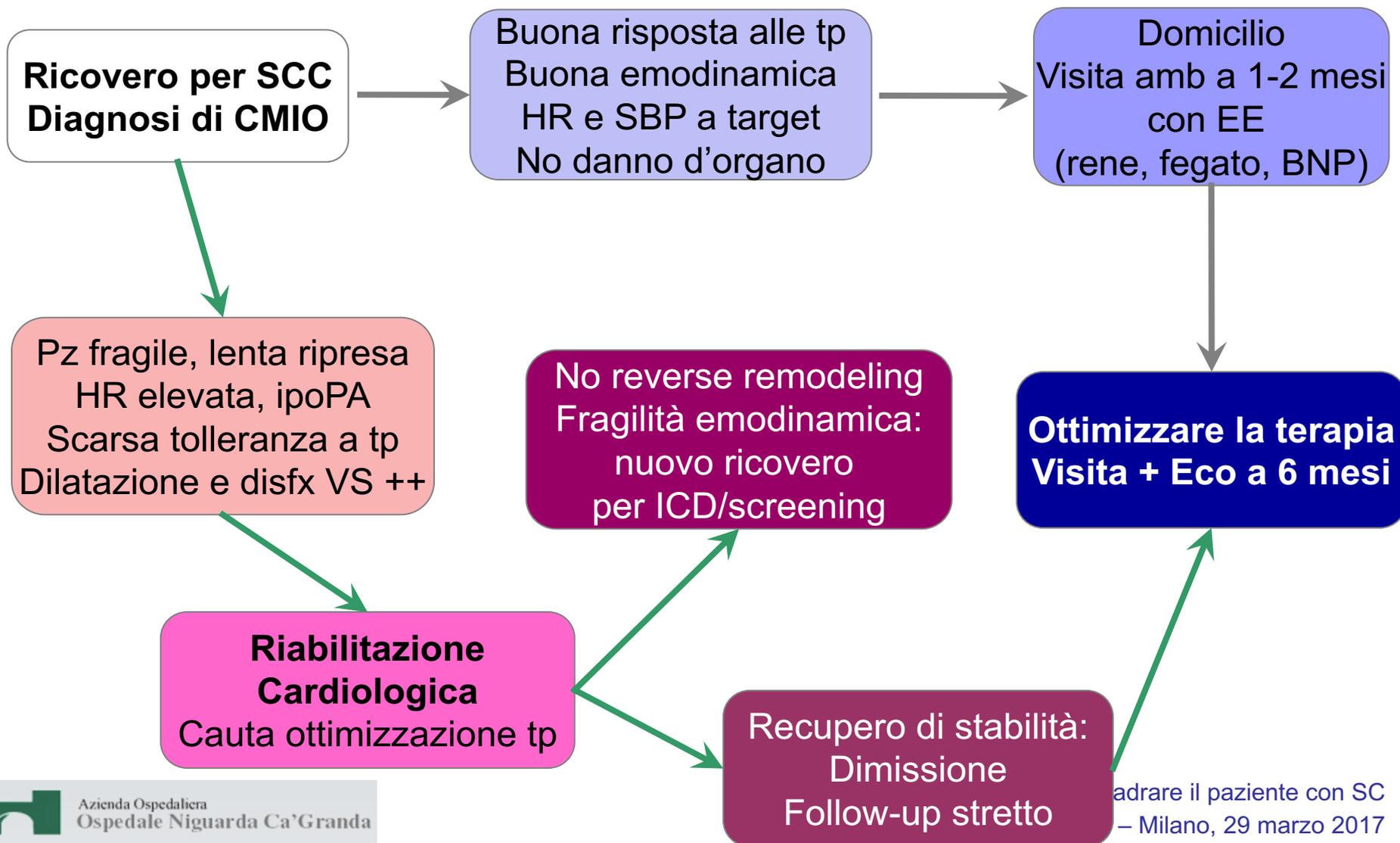
Category	Candidate biomarkers	Clinical outcomes	Left ventricular remodeling	Reverse remodeling	
(1)	Myocyte stretch and stress	BNP, NT-proBNP	+++	+++	++
(2)	Myocyte injury	cTnT, cTnI	+++	+++	++
(3)	Inflammation and fibrosis	sST2	+++	+++	+++
		Galectin-3	++	++	+
(4)	Extracellular matrix proteins	MMP9, TIMP1	+	++	+
		BMP1	+	++	+
		PICP, PIIINP	+	++	+



Riduzione, in terapia, di Nt-proBNP < 1000  
→ predittore di migliore risposta in termini di *reverse remodeling*

➔ Risultati non univoci in diversi studi, ma il trend conferma l'utilità di monitorare i peptidi natriuretici come indicatore di outcome

# Follow-up: la nostra proposta



Non disponibili parametri che riescano a predire con precisione il tipo di evoluzione della cardiopatia al suo esordio

Il primo passo verso una stratificazione prognostica attendibile è il corretto inquadramento eziologico

Alcune caratteristiche cliniche (profilo di FC, pressione arteriosa), strumentali (dilatazione VS, LGE alla CMR) e biochimiche (rialzo persistente di troponina, scarsa risposta di BNP alla terapia) aiutano ad identificare i pazienti a maggior rischio, meritevoli di follow-up più stretto