PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO
ROMA, 25 - 27 Giugno 2026

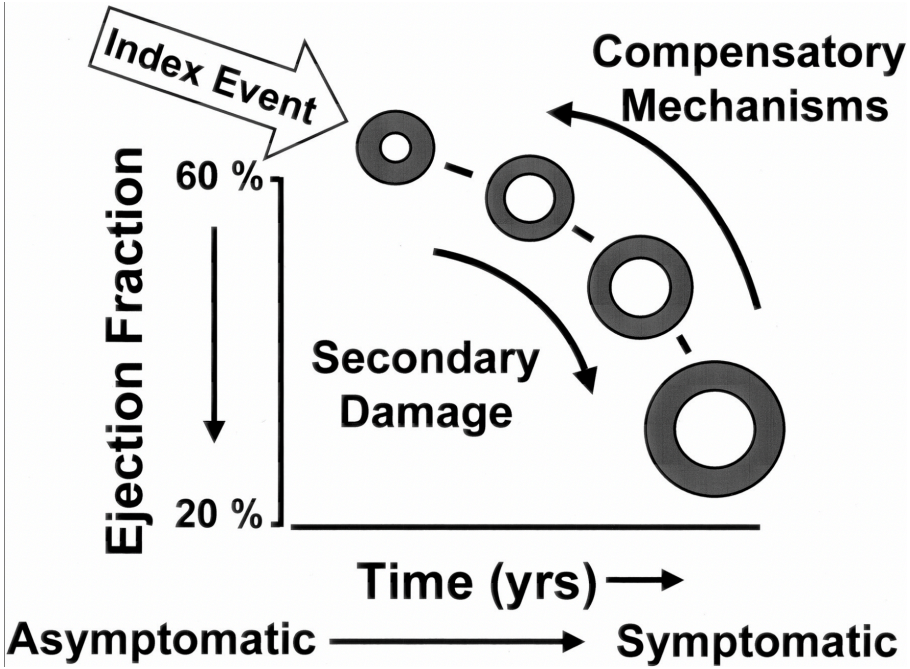
CARDIOMIOPATIE: HOT TOPICS

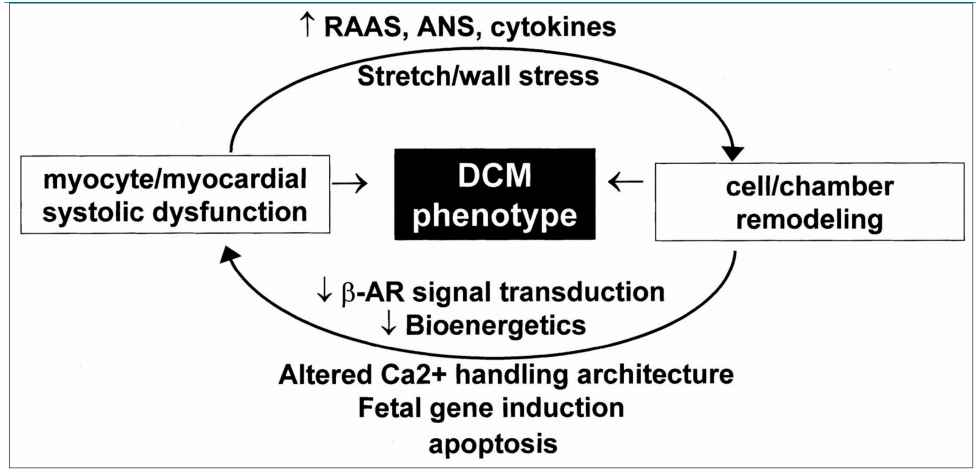
Ruolo integrato della risonanza magnetica cardiaca e della genetica nella previsione del rimodellamento inverso del ventricolo sinistro nella cardiomiopatia dilatativa e non dilatativa

Martina Setti
Ambulatorio Scompenso Cardiaco e Cardiomiopatie
Azienda Ospedale Universitaria integrata di Verona
- martina.setti@aovr.veneto.it

Adverse Remodelling

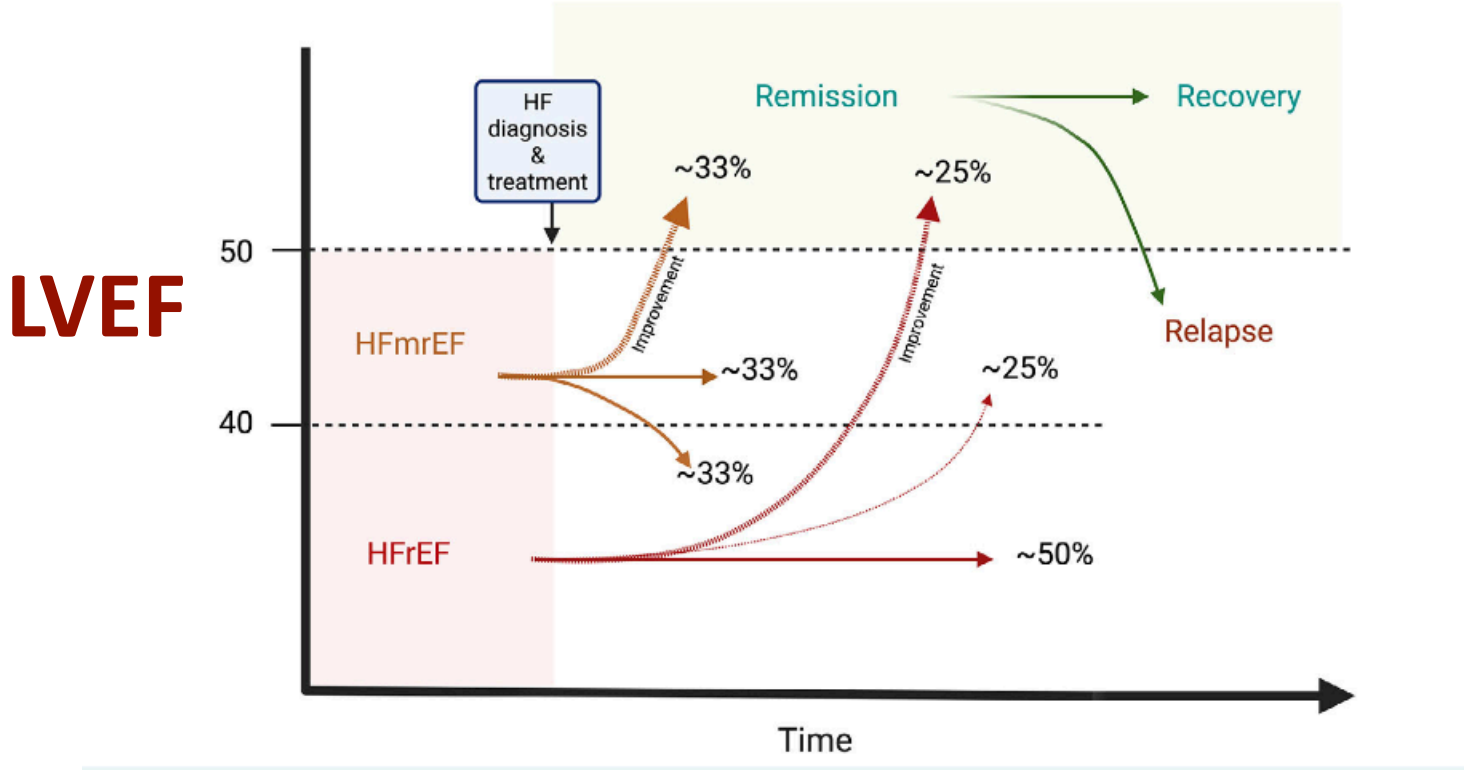
«Any changes to cardiac chamber geometry and function may occur in response to sustained physiological or pathophysiological stimuli such as cardiac injury, hemodynamic changes, and inflammation or neurohormonal activation»





Mann DL and Bristow MR, Circulation, 2005

Left Ventricular Reverse Remodelling (RR)



Hulot et al, *EJHF*, 2025

Diagnostic Criteria for RR in DCM

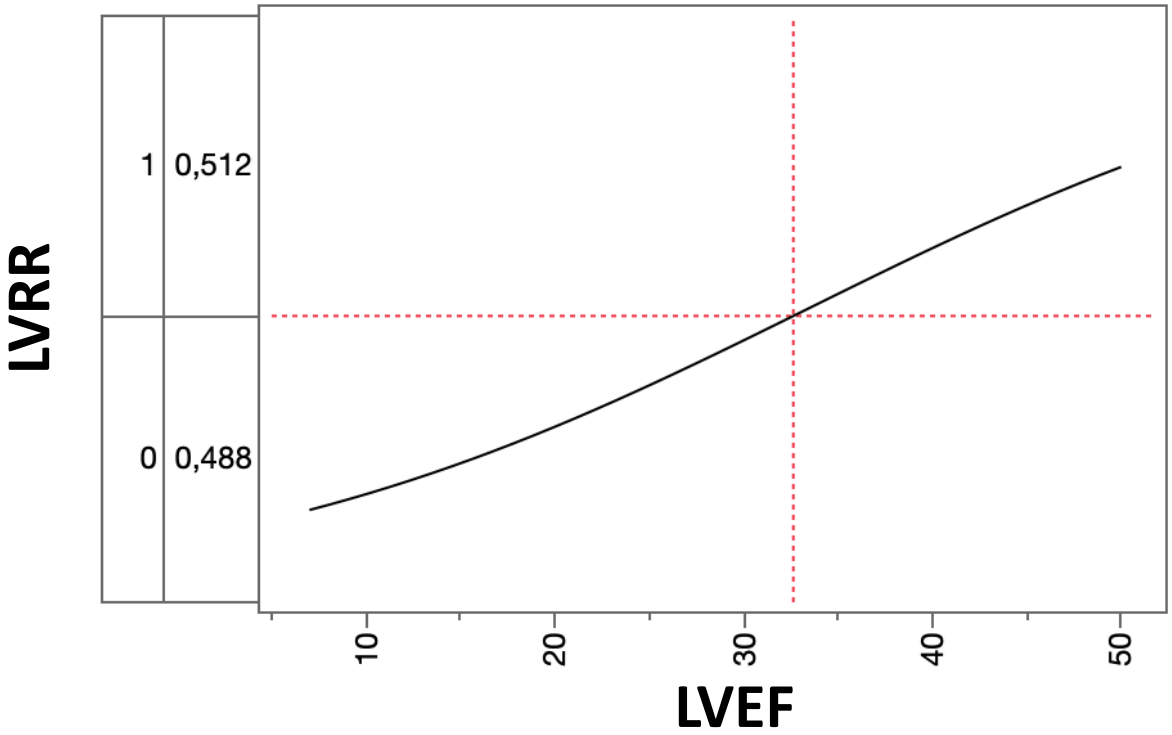
Table 1 Main observational studies on left ventricular reverse remodelling in dilated cardiomyopathy

Author	*n*	Definition of LVRR/impEF	Timing of assessment (months)	Prevalence (%)
Merlo[87]	242	LVEF increase ≥10% or LVEF ≥50% and LVEDDi reduction ≥10% or LVEDDi ≤33 mm/m^2	24	37
Amorim[88]	113	LVEF >10% and any decrease in LVEDD in absence of CRT	24	35
Matsumura[89]	19	LVEDD ≤55 mm and LV fractional shortening improved >25%	12	37
Kubanek[90]	44	LVEF increase ≥10% (>35%) and LVEDDi reduction ≥10%	12	45
McNamara[91]	373 (myocarditis)	LVEF increase ≥10% (1) and LVEF increase ≥20% (2)	6	70 (1) and 39 (2)
Hoshikawa[92]	33	LVEDD ≤55 mm and LV fractional shortening improved >25%	5 years	42
Ykeda[93]	207	LVEF increase >10% and LVEDDi reduction ≥10%	<24 and ≥24	40 + 12
Masci[94]	58	LVEF increase >10% and LVEDV reduction ≥10%, based on CMR data	24	38
Tayal[95]	34	LVEF increase >10%	12	59
Manca[37]	800 (NICM)	LVEF increase ≥10% and LVEF >40%	13 (median)	57

CRT, cardiac resynchronization therapy; impEF, improved ejection fraction; LV, left ventricular; LVEDD, left ventricular end-diastolic diameter; LVEDDi, indexed left ventricular end-diastolic diameter; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVRR, left ventricular reverse remodelling; NICM, non-ischaemic cardiomyopathy.

Gigli et al EJHF, 2025

RR diagnostic Criteria and baseline LVEF

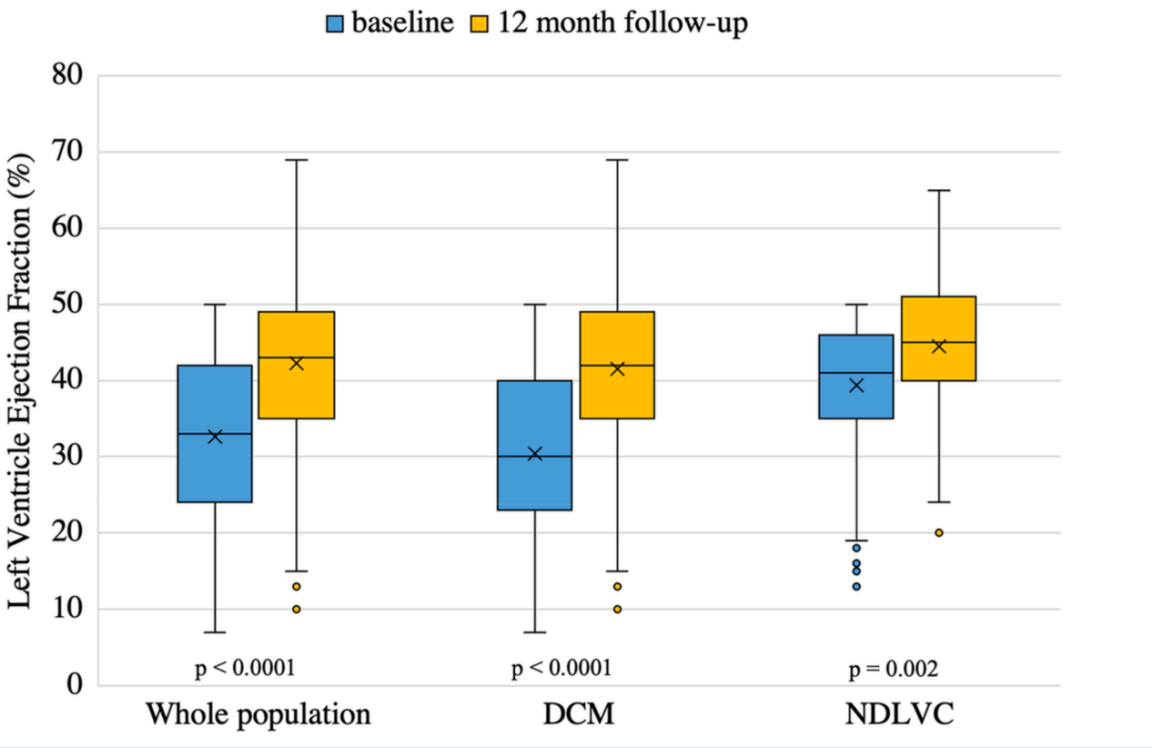


Trieste DCM Registry, *unpublished*

RR diagnostic Criteria in DCM and NDLVC

462 DCM, 154 NDLVC
- 289 Trieste
- 303 Maastricht
- 24 Denver US

LVRR at 12-month
= ↑ LVEF ≥10 %
or LVEF≥50% in pts
with LVEF <45%



RR: 54% in DCM vs. 41% in NDLVC

Setti et al, *EJHF*, 2025

HFrEF therapy

Beta-blockers

	Mean (SD) ejection fraction		
	Placebo	Metoprolol	p
All patients	(n=104)	(n=111)	
Baseline	0 22 (0 09)	0 22 (0 08)	0 63
6 months	0 26 (0 11)	0 32 (0·13)	<0 0001
12 months	0 28 (0 12)	0·34 (0 14)	<0·0001

MRA

ACEi/ARB

Sacubitril/Valsartan

	All Patients				
	Baseline Value, Median (25th to 75th Percentile)	6-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 6 mo (95% CI)	12-mo Value, Median (25th to 75th Percentile)	LS Mean Change From Baseline at 12 mo (95% CI)
LVEF, %	n = 757	n = 716		n = 648	
	28.2 (24.5 to 32.7)	34.1 (29.0 to 39.65)	5.2 (4.8 to 5.6)	37.8 (32.3 to 45.2)	9.4 (8.8 to 9.9)
LVEDVI, mL/m^2	n = 756	n = 716		n = 648	
	86.93 (76.17 to 100.43)	79.50 (69.34 to 93.52)	−6.65 (−7.11 to −6.19)	74.15 (63.46 to 86.30)	−12.25 (−12.92 to −11.58)

sGLT2i

	Baseline vs. 30 days			Baseline vs. 180 days		
	LS mean change (95% CI)	% change (95% CI)	*p*-value	LS mean change (95% CI)	% change (95% CI)	*p*-value
Left ventricle						
LVEDV	−2.12 (−4.49, 0.24)	−4.7 (−8.5, −0.8)	0.019	−4.92 (−7.34, −2.51)	−8 (−11.6, −4.2)	<0.001
LVESV	−1.75 (−3.58, 0.08)	−5.6 (−10.1, −0.9)	0.021	−4.4 (−6.27, −2.54)	−11.9 (−16.7, −6.8)	<0.001
LVI mass	−2.17 (−8.21, 3.87)	−2.2 (−7.2, 3)	0.398	−16.46 (−22.82, −10.11)	−13.9 (−18.7, −8.7)	<0.001
LVEF	0.84 (−0.68, 2.36)	2 (−1.6, 5.7)	0.285	2.29 (0.44, 4.15)	4.9 (0.2, 9.9)	0.040

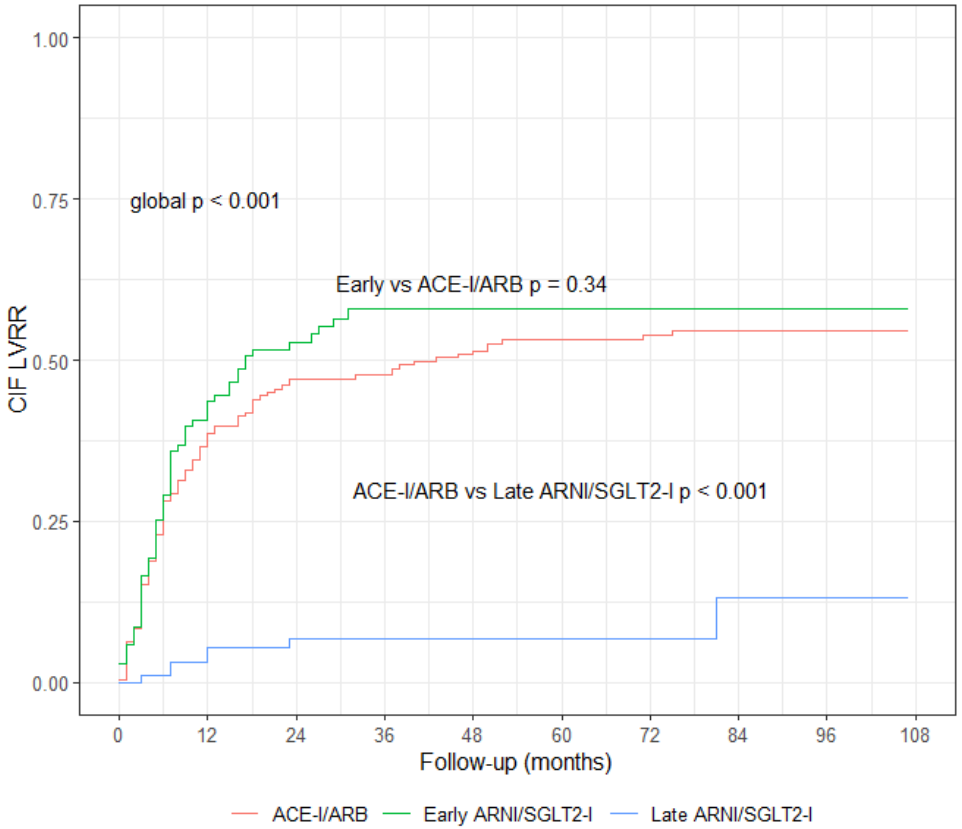
Waagstein et al, Lancet, 1993
Pascual-Figal et al, EJHF, 2023

Januzzi et al, JAMA, 2019
Pascual-Figal et al,

HFrEF therapy

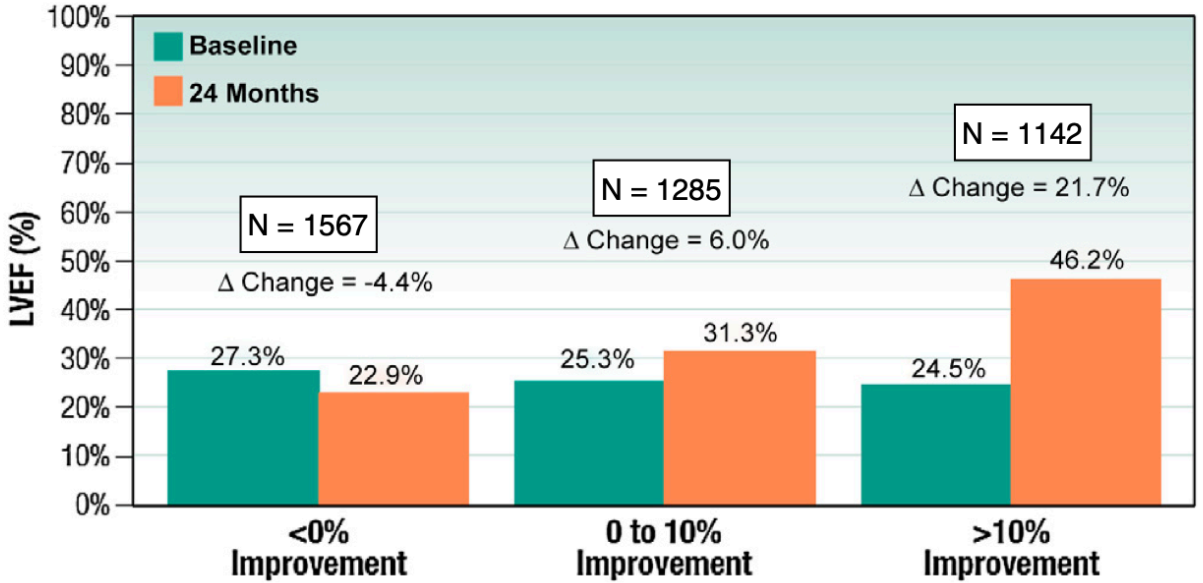
390 DCM patients from Trieste Registry

55% LVRR over 9 years



Pio Loco detto Gava et al., *unpublished*

Different grade of RR

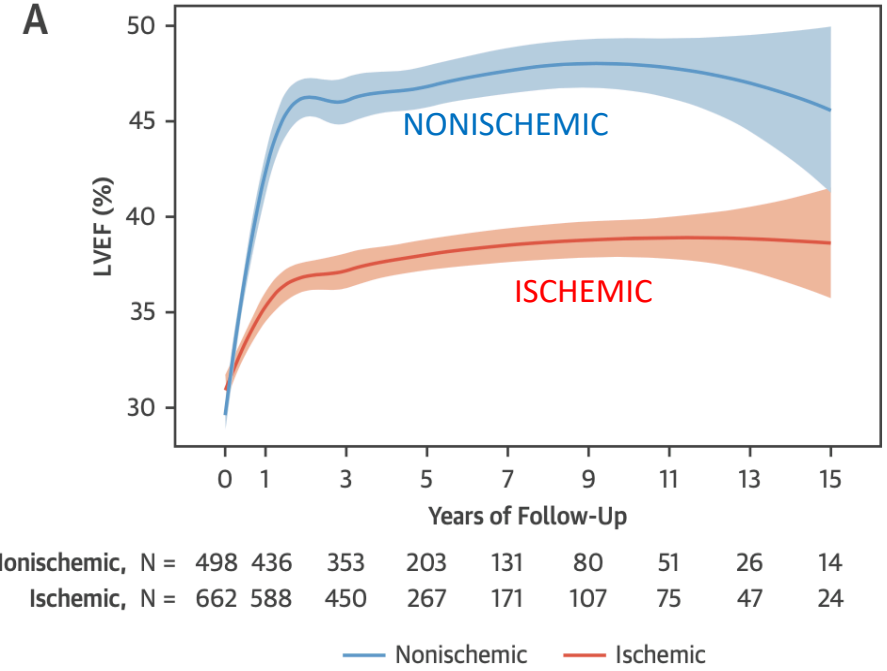


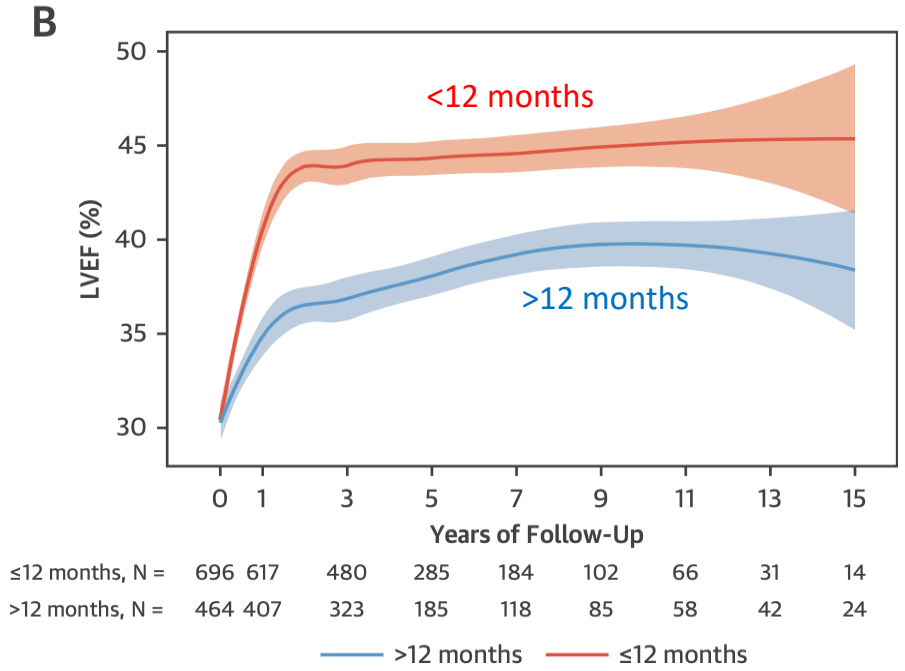
Left ventricular ejection fraction at baseline and 24 months according to tertile of LVEF improvement.

28.6% HFrEF pts

Wilcox et al, *American Heart Journal*, 2012

Clinical predictors of RR: DCM and HF duration





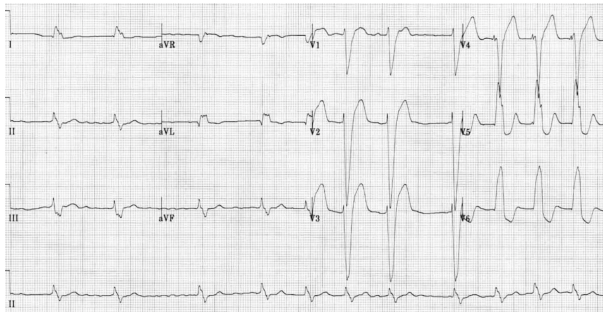
Lupon et al, *JACC*, 2018

ECG predictors of RR: left bundle branch block

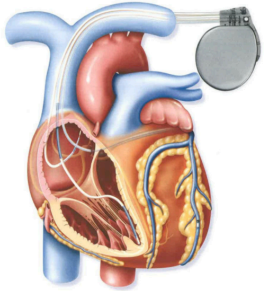
Absence LBBB

Table 3 Baseline Independent Predictors of LVRR at Mid-Term Follow-Up

	OR	95% CI	p Value
SBP, per 10-mm Hg increase	1.23	1.01–1.53	0.047
Absence of LBBB	2.47	1.25–4.87	0.009



CRT



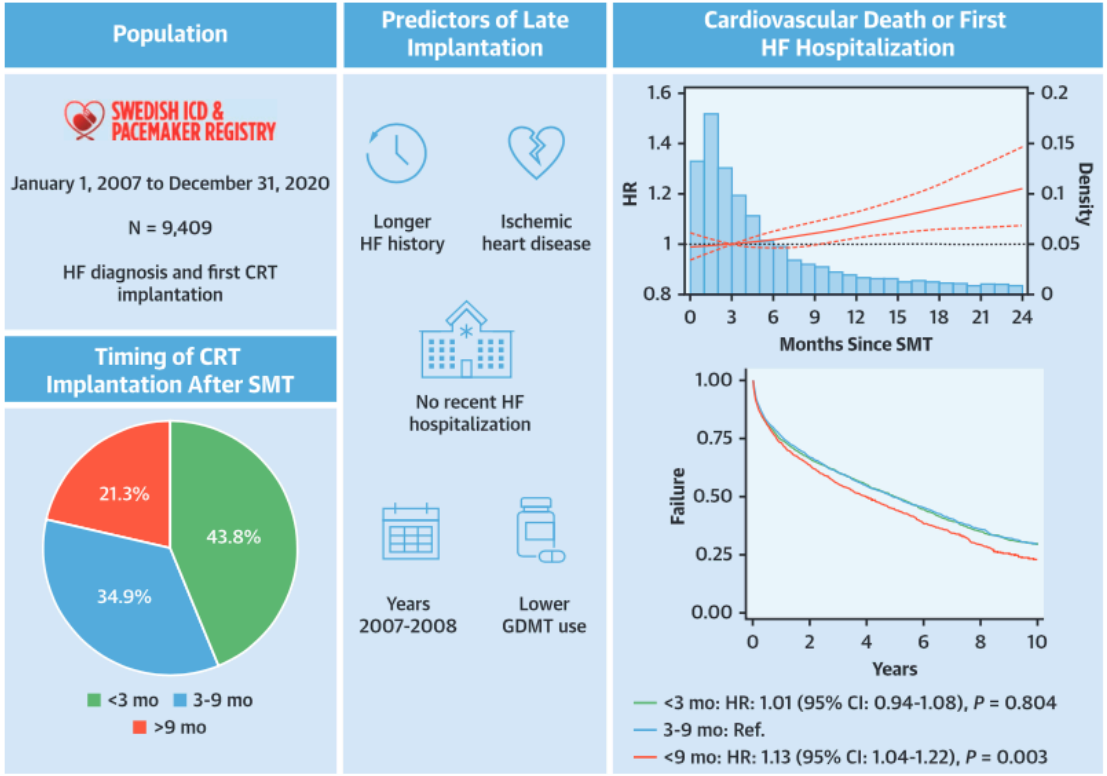
LBBB + CRT

Table 3 Multivariate Analysis of Predictors of LVEF Super-Response

Variable	Odds Ratio	95% Confidence Interval	p Value
Female	1.96	1.32–2.90	0.001
QRS duration ≥150 ms	1.79	1.17–2.73	0.007
LBBB	2.05	1.24–3.40	0.006
Body mass index <30 kg/m^2	1.51	1.03–2.20	0.035
No prior myocardial infarction	1.80	1.20–2.71	0.005
Left atrial volume index, SD*	1.47	1.21–1.79	<0.001

Merlo et al, *JACC*, 2011
Hsu et al, *JACC*, 2012

ECG predictors of RR: LBBB and CRT-D



Villaschi A, et al. JACC Heart Fail. 2025;13(10):102515.

PERSPECTIVES

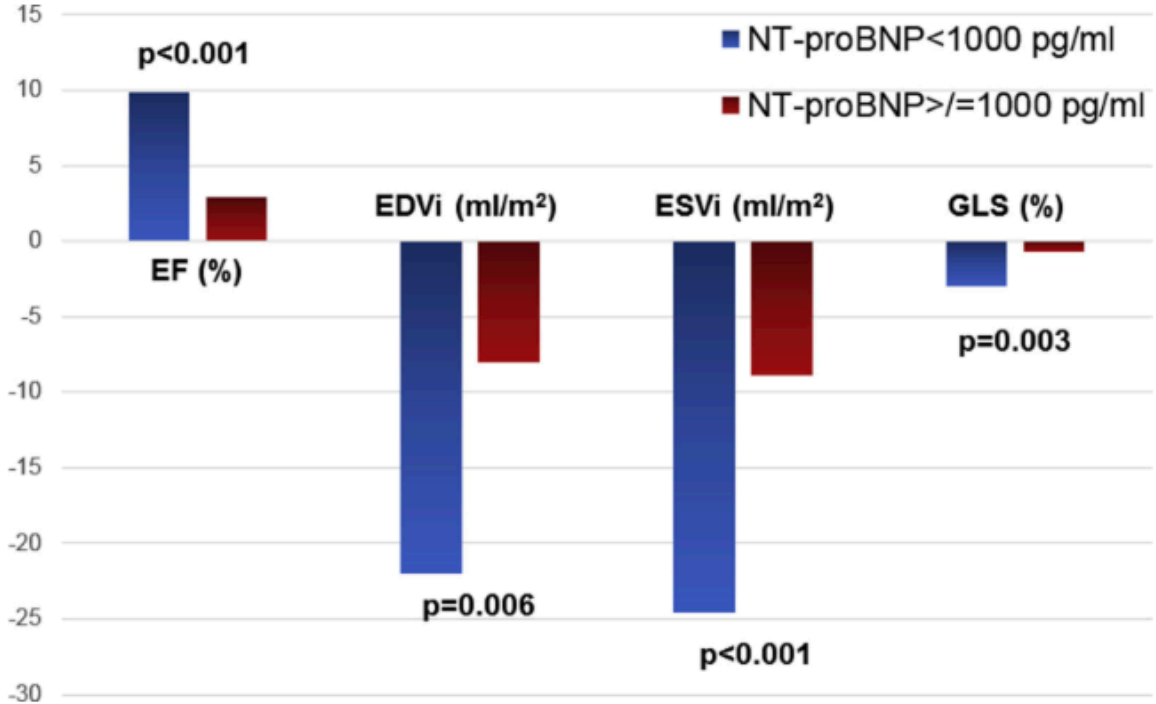
COMPETENCY IN PATIENT CARE AND MEDICAL KNOWLEDGE: Findings from this large national registry suggest that earlier CRT implantation is associated with a lower risk of morbidity and mortality whereas delayed CRT implantation (beyond 9 months) is associated with worse outcomes.

TRANSLATIONAL OUTLOOK: Although guidelines strongly recommend CRT for eligible patients, the actual timing of CRT post-OMT has remained unclear, and future prospective studies in diverse cohorts should better identify the optimal one.

Villaschi et al, *JACC HF*, 2025

Biomarker predictors of RR: NTproBNP

Changes in Left Ventricular Structure and Function by Achievement of NT-proBNP Goal at 12 Month

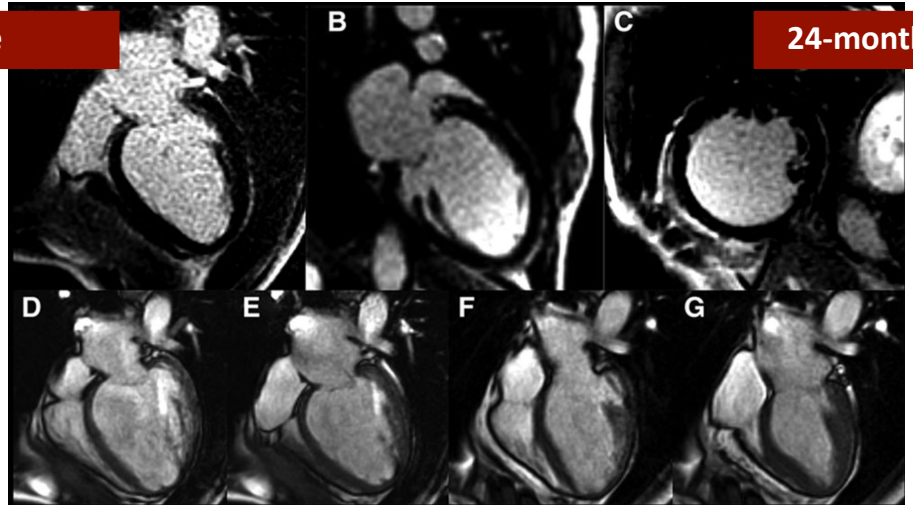


GUIDE IT - Daubert et al, *JACC HF*, 2019

CMR predictors of RR: LGE

58 patients with DCM

LVRR at 24-month
= ↑ LVEF ≥10 U
+ ↓ LV EDV ≥10%

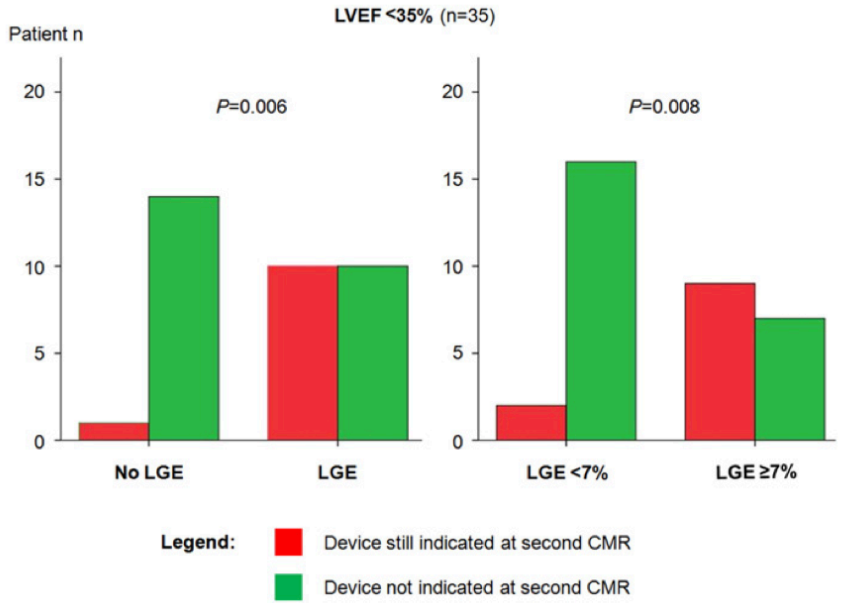


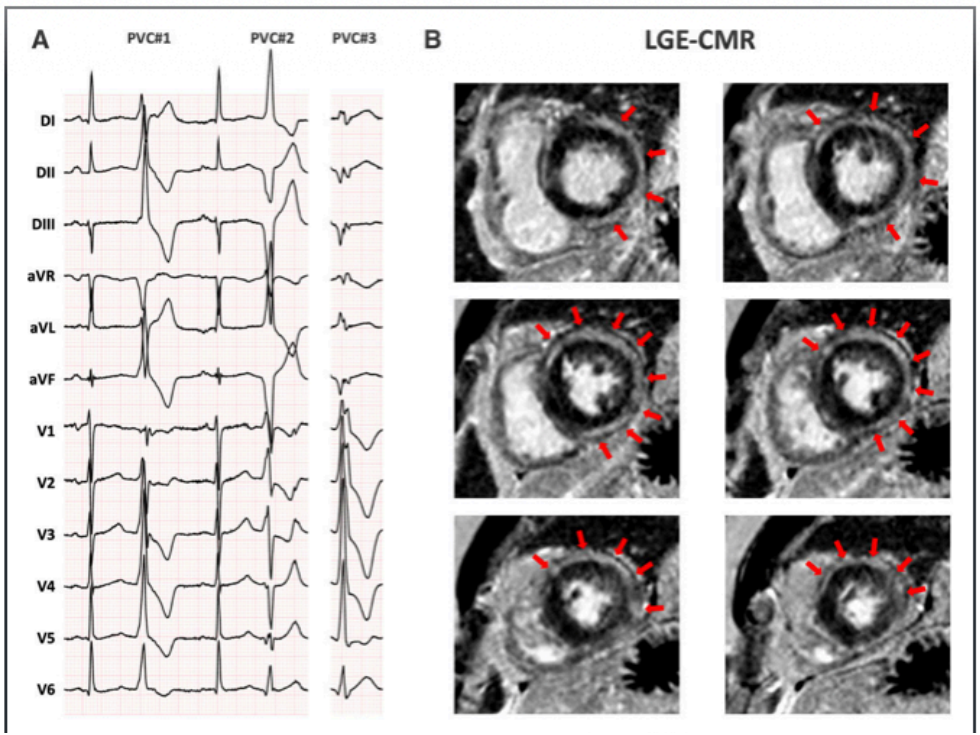
LVRR in 22 patients (38%)

Variables at Baseline	Model 1		Model 2	
OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	
Age, y	…	…	…	…
Heart rate, bpm	…	…	…	…
NYHA class >I				
Absence of LGE	10.857 (1.844–63.911)	0.008	23.743 (2.887–195.298)	0.003
LV-EDVi, mL/m^2	…	…	…	…
LV-ESVI, mL/m^2	1.071 (1.026–1.119)	0.002	N/A	N/A
LV-EF, %	N/A	N/A	0.830 (0.748–0.921)	<0.001
RV-EF, %	…	…	…	…

Masci et al, *Circ HF*, 2013

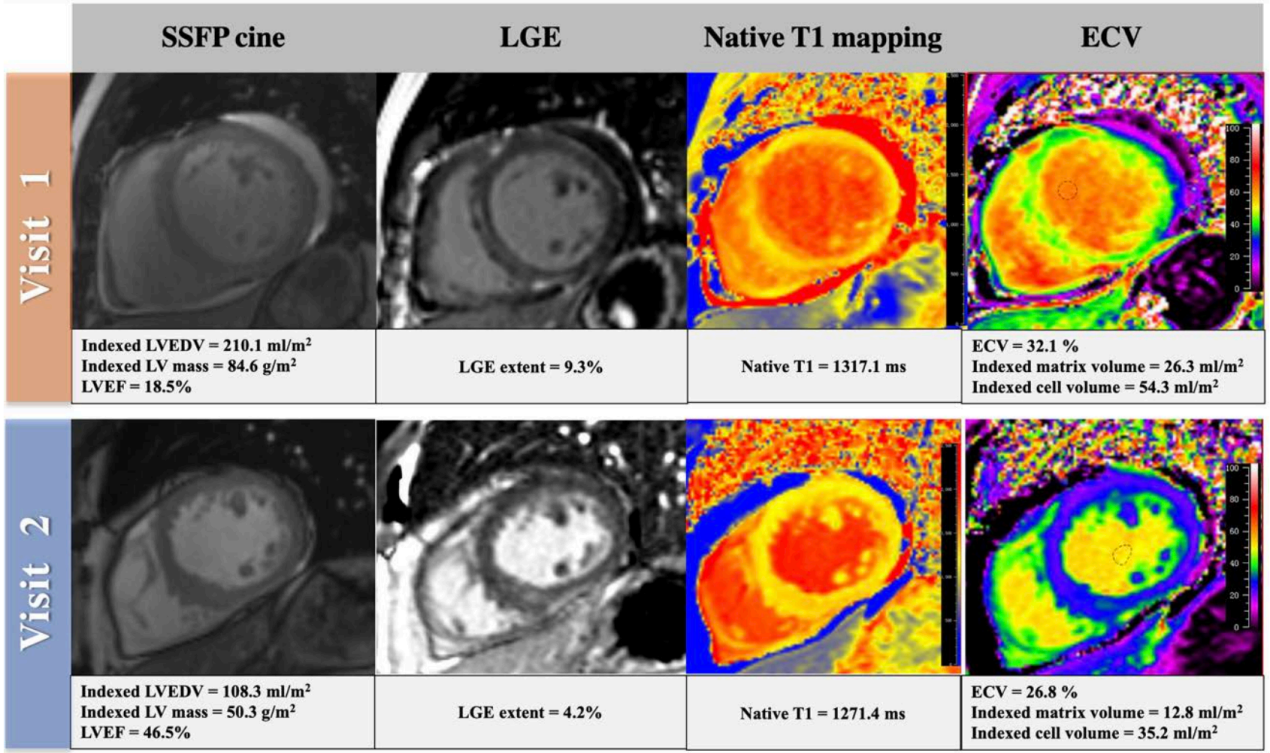
CMR predictors of RR: LGE





Barison et al, *IJC*, 2018
Muser et al., *Circulation*, 2021

CMR predictors of RR: ECV, T1 mapping, LGE

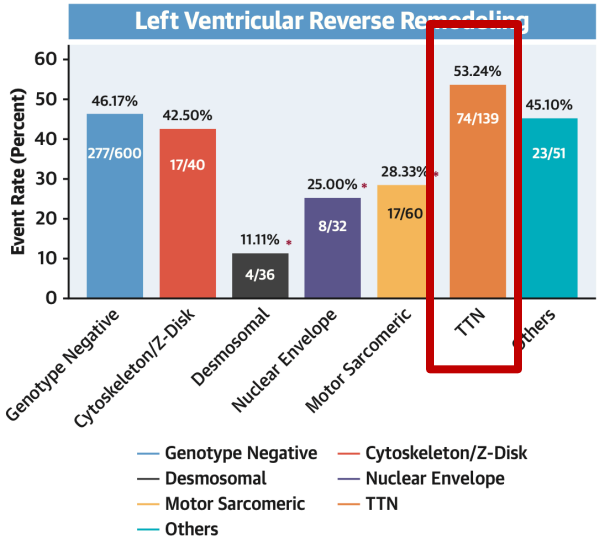


Xu et al, *Circulation HF*, 2021

Genetic predictors of RR

Table 3 Echocardiographic metrics and LVRR assessment at follow-up

	Total	No/unknown mutation	Titin	Lamin A/C	Structural cytoskeleton Z-disk genes	Desmosomal genes	Motor sarcomeric genes	Other genes
		0	1	2	3	4	5	6
	n=139	n=62	n=24	n=5	n=16	n=9	n=17	n=7
LVEDDI (mm/m²)	32 (29–35)	31 (28–35)	31 (28–35)	33 (29–38)	32 (33–39)	33 (31–34)	33 (29–37)	31 (26–34)
LVEF (%)	43 (33–51)	45 (36–52)	44 (36–51)	32 (30–58)	34 (27–41)*[6]	40 (31–50)	42 (25–50)	51 (46–53)
LVRR (%)	29 (38)	28 (45)	14 (58)*[3]	1 (20)	1 (6)*[0,1,6]	4 (44)	4 (24)*[6]	6 (86)*[3,5]
LVRR-PPrV carriers included (n=127) (%)	57 (41)	10 (43)	14 (58)*[3]	1 (20)	3 (12)*[0,1,6]	8 (50)	8 (33)	13 (57)



Dal Ferro et al, *Heart*, 2017

Escobar-Lopez et al., *JACC*, 2

Predictors of RR: Genotype and CMR

616 pts with
DCM/NDLVC
From Trieste and Maastricht cohort

Overall
314 (51%) LVRR
at 12-month follow-up

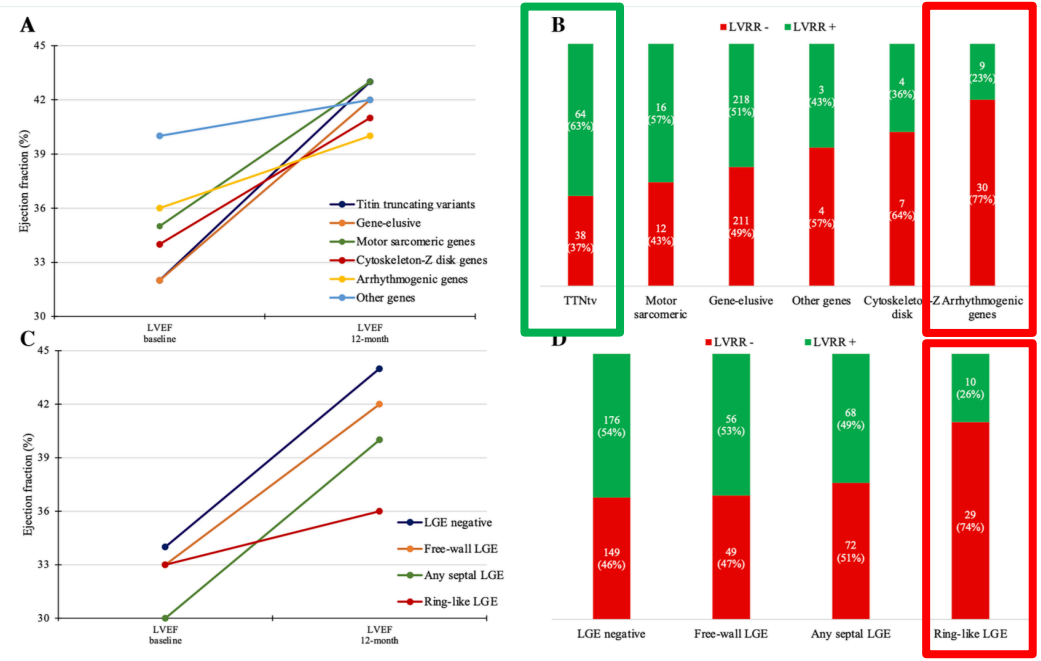


Table 3 Predictors of left ventricular reverse remodelling in univariable and multivariable analysis

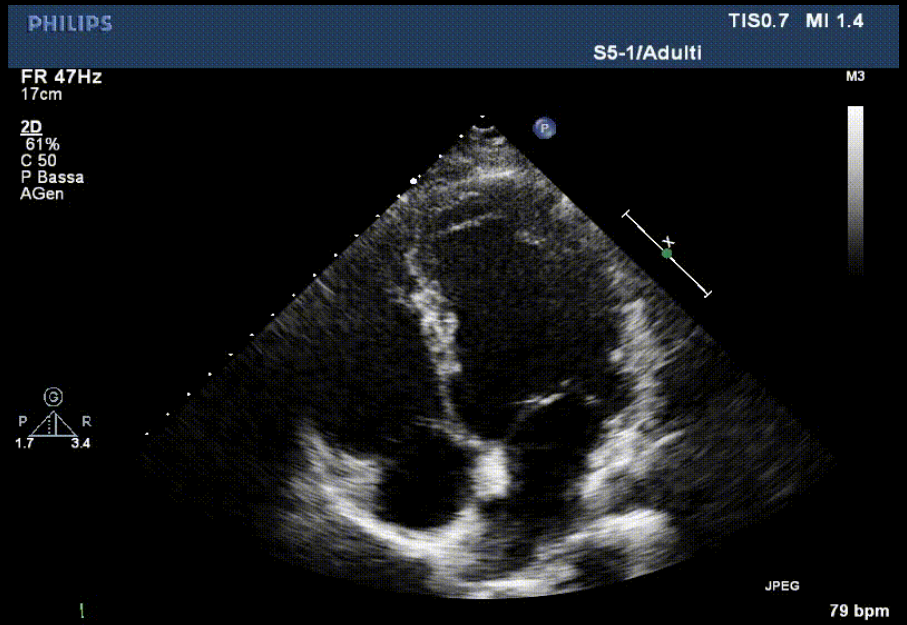
	Univariable analysis			Multivariable analysis		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
TTNtv[a]	1.78	1.15–2.75	**0.009**	1.57	1.01–2.45	**0.04**
Arrhythmogenic genes[a]	0.27	0.13–0.57	**0.0007**	0.27	0.12–0.60	**0.001**
LGE ring-like pattern	0.31	0.15–0.69	**0.002**	0.33	0.16–0.71	**0.004**

TTNtv
63%
LVRR +

Arrhythmogenic genes
23%
LVRR -

Ring-like LGE
26%
LVRR -

Setti et al, *EJHF*, 2025



50 yrs
no LGE
TTNtv

47 yrs
Ringlike LGE
LMNA

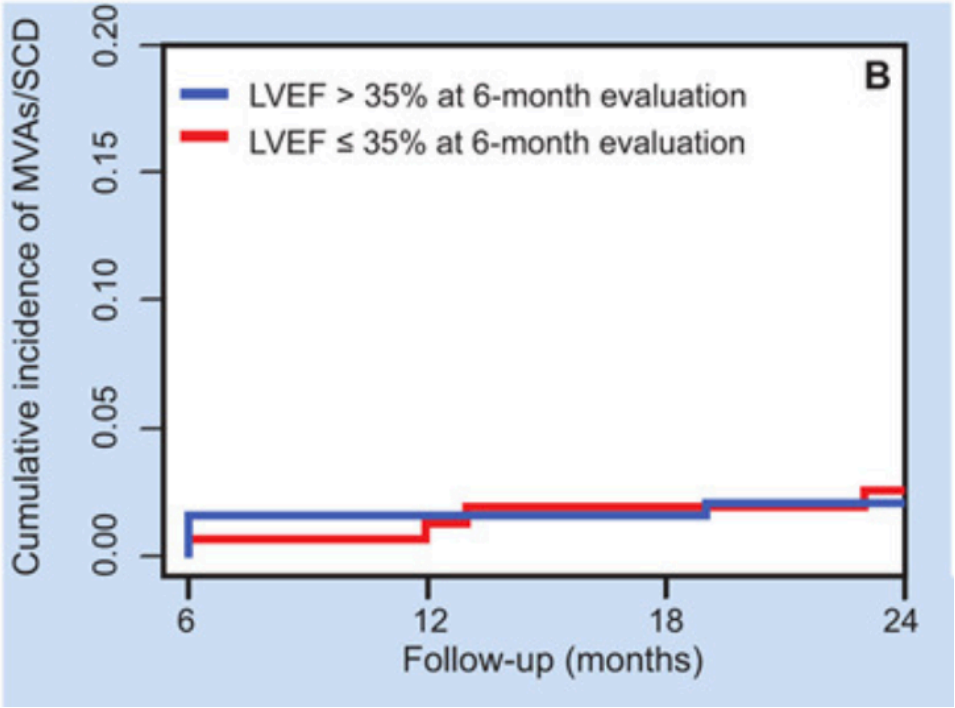
Timing of assessment RR in DCM

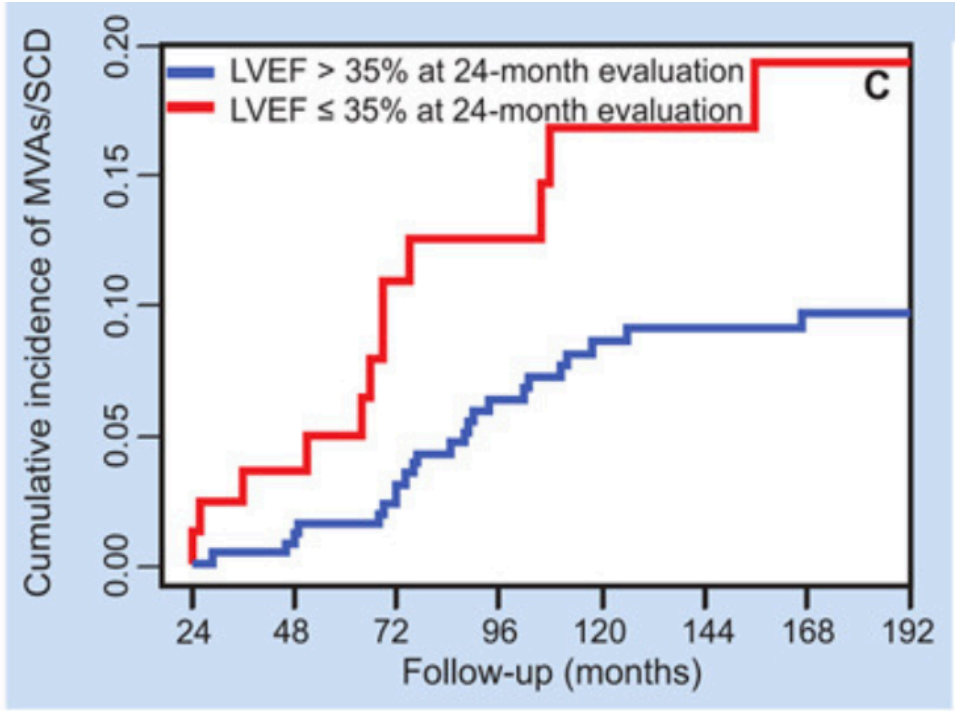
Primary prevention		
An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of an ischaemic aetiology (unless they have had a MI in the prior 40 days—see below), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.[161,165]	I	A
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of a non-ischaemic aetiology, and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.[161,166,167]	IIa	A

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 3599–3726
doi:10.1093/eurheartj/ehab368

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

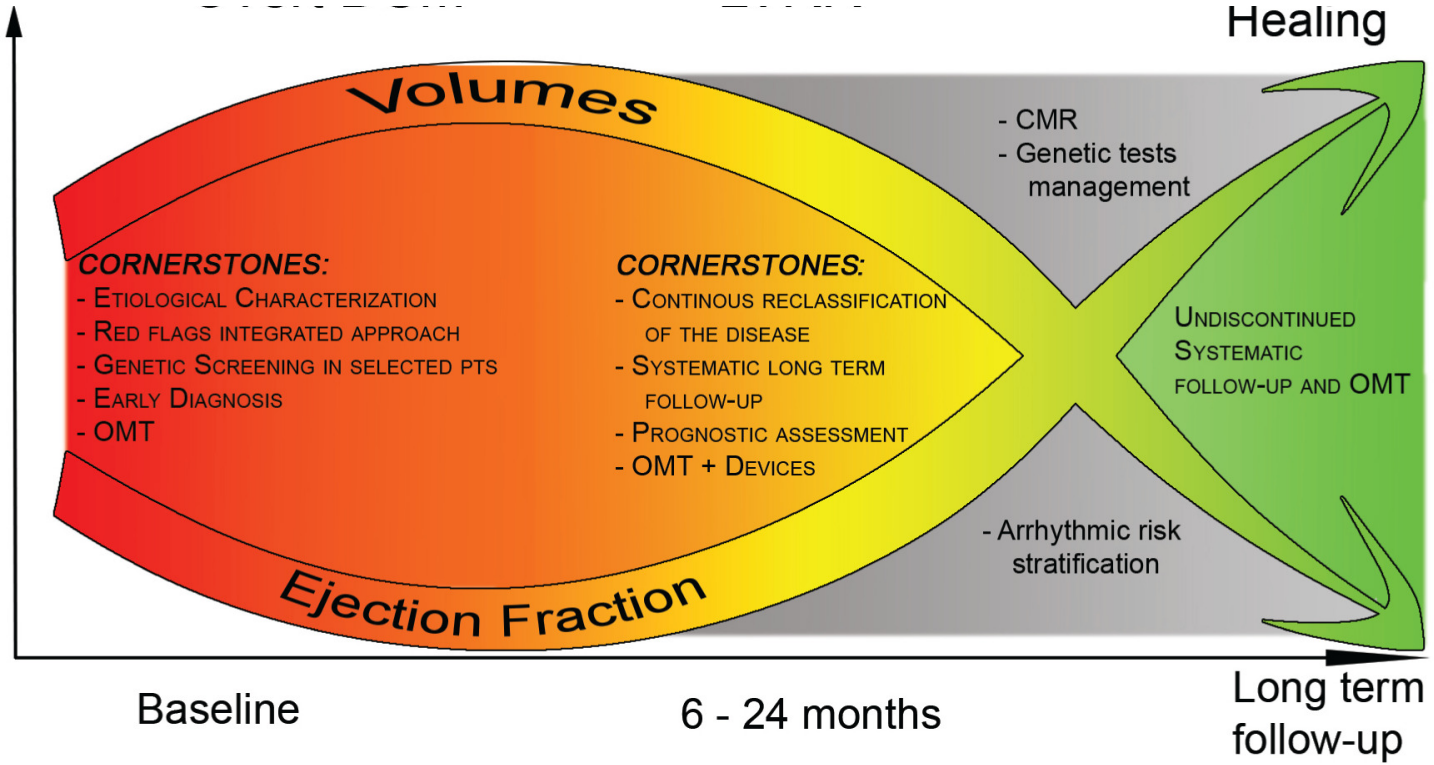
Timing of assessment RR in DCM





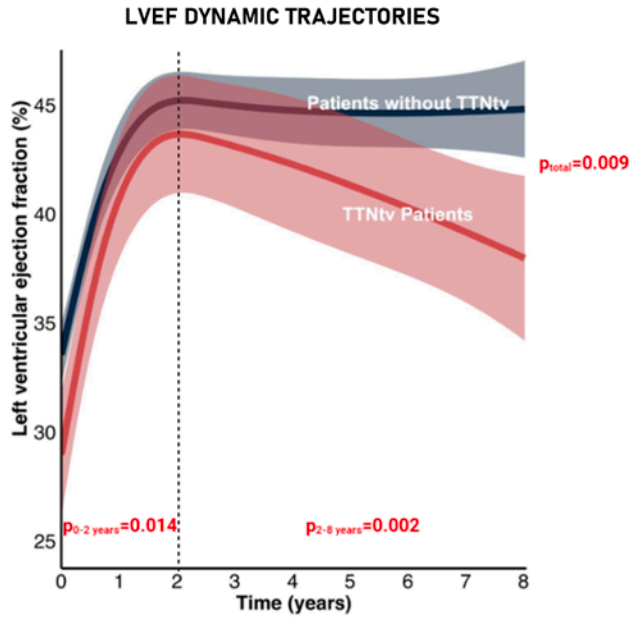
De Angelis et al, *JASE*, 2022

Dynamic disease

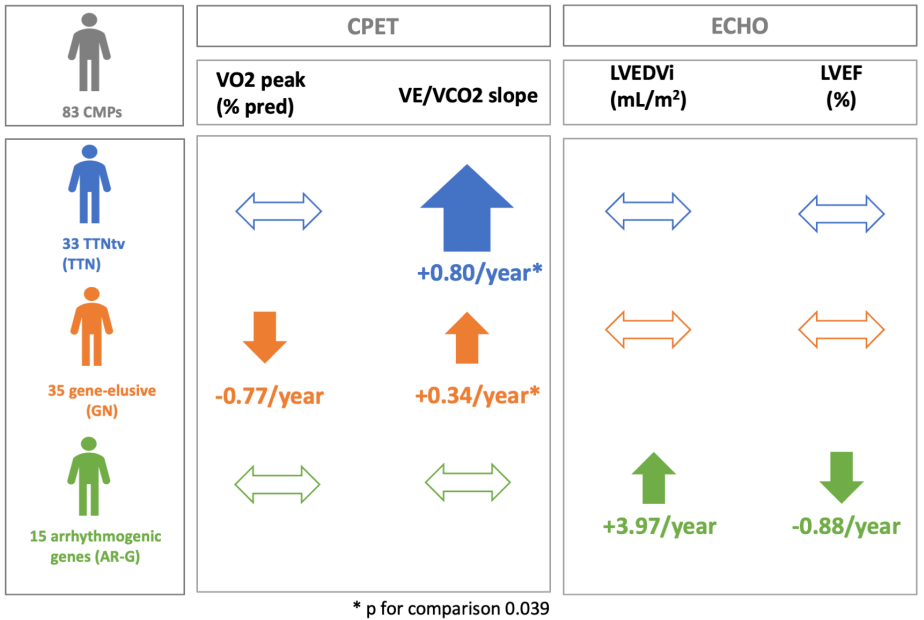


Merlo et al, EJHF, 2017

Dynamic disease in TTNtv-DCM



Henkens et al, Circ HF, 2022



Setti et al, *under review*

Take-home messages

- Lack of standard definition of Reverse Remodelling (RR) in DCM/NDLVC.
- Multiparametric assessment of RR, including genetics and CMR.
- RR does not imply full myocardial recovery.

Ambulatorio Scompenso Cardiaco e Cardiomiopatie – Borgo Trento,

Dr.ssa Martina Setti
Dr.ssa Caterina Butturini
Dr.ssa Anna Carrer
cardiologia.scompensocardiaco@aovr.veneto.it

Day Hospital Scompenso Cardiaco – Borgo Roma

Dr.ssa Anna Piccoli
Dr. Enrico Tadiello
cardiologia.dayservice.br@aovr.veneto.it

Genetica cardiovascolare

Dott.ssa Giorgia Beffagna

Azienda Ospedaliera Universitaria Integrata Verona

CardioVr.it

Italian Cardiologists Of Tomorrow

GRAZIE!

martina.setti@aovr.veneto.it