What's new in heart failure treatment

ASSESSMENT OF LEFT VENTRICULAR FUNCTION

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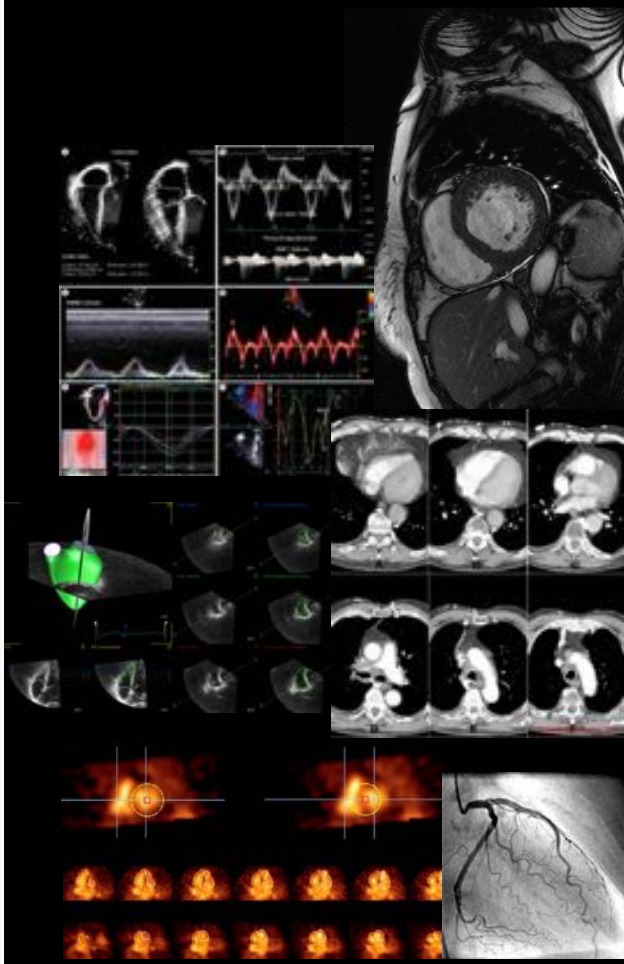
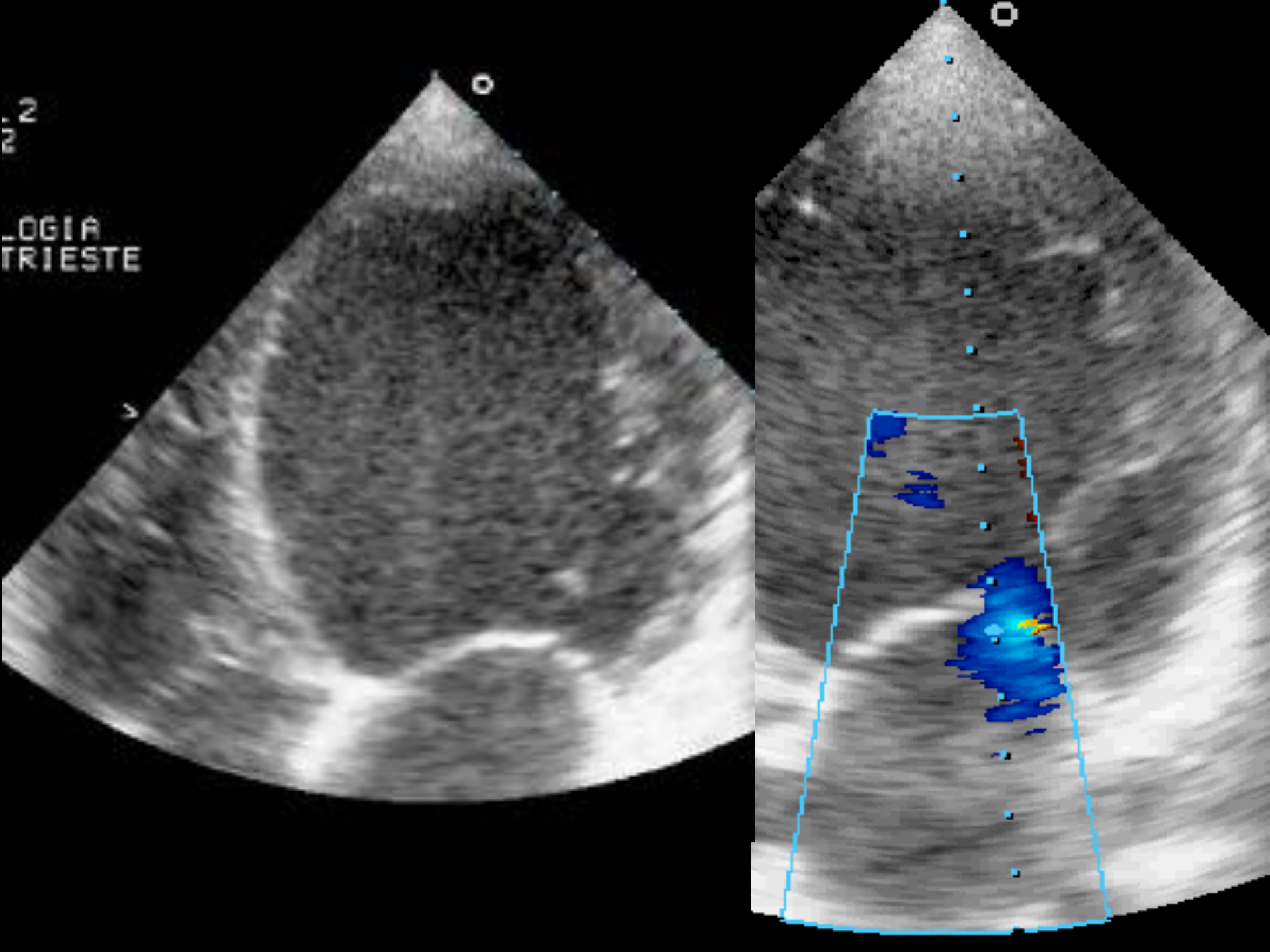
Recommendations for cardiac imaging in patients with suspected or established heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
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	

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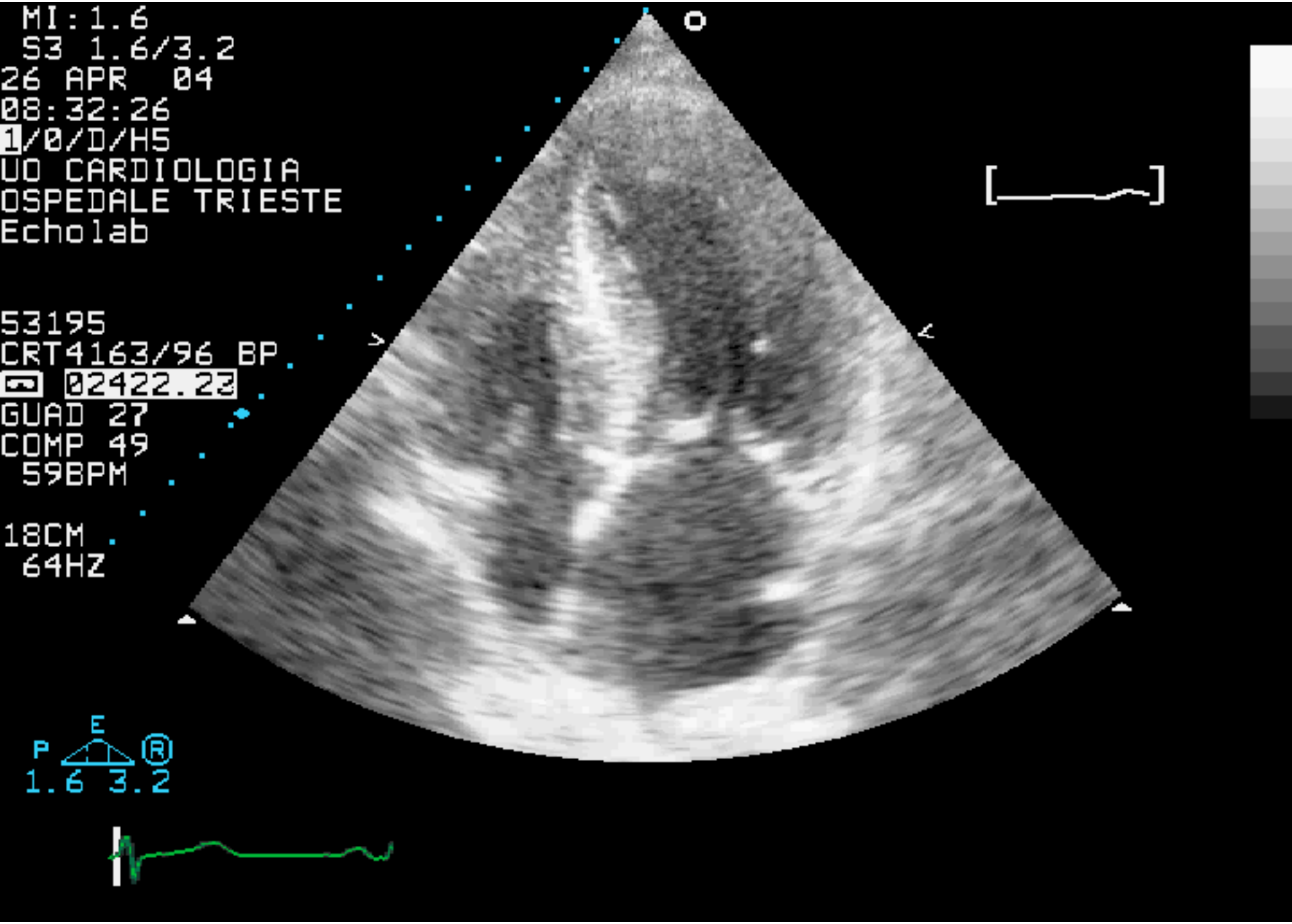
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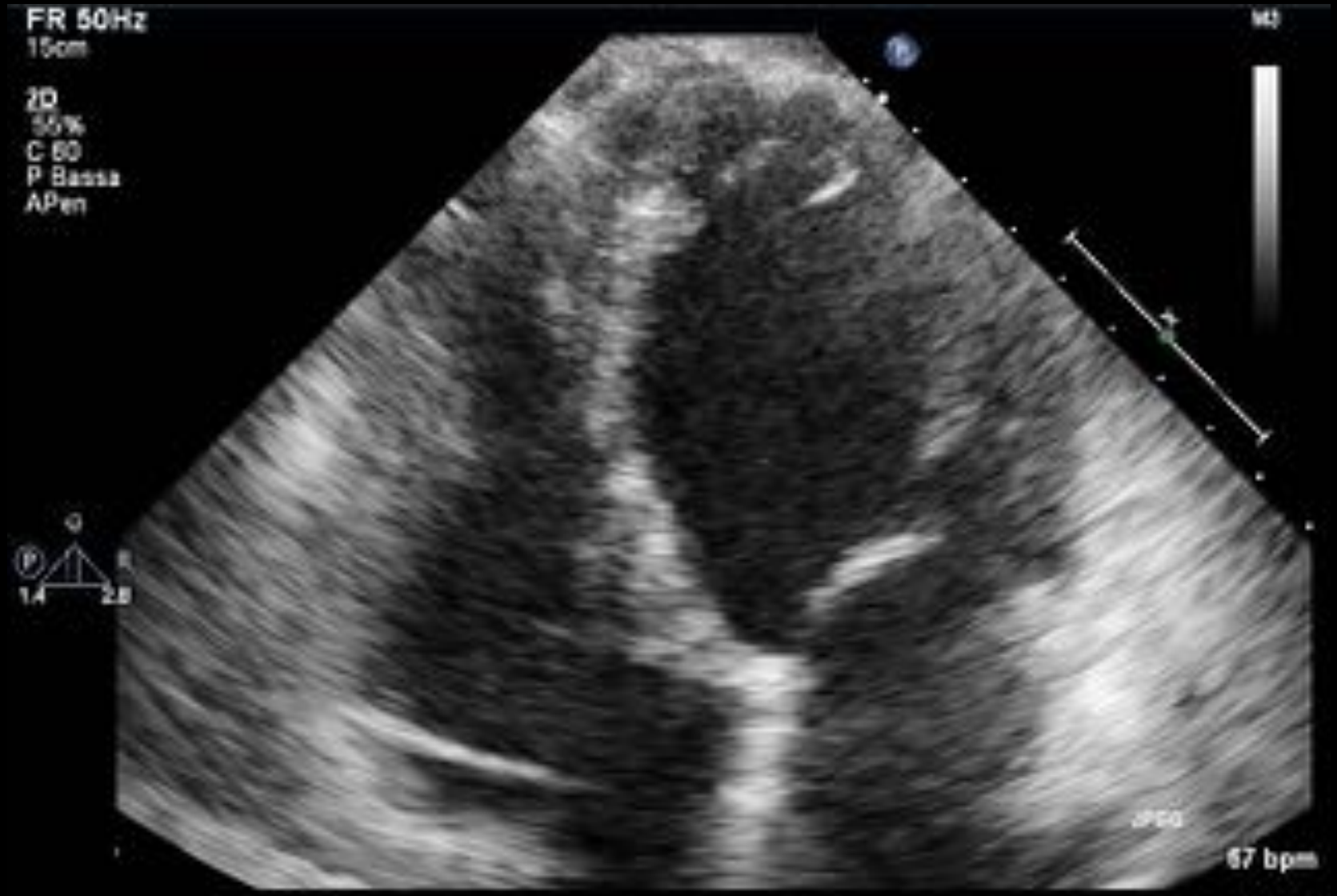
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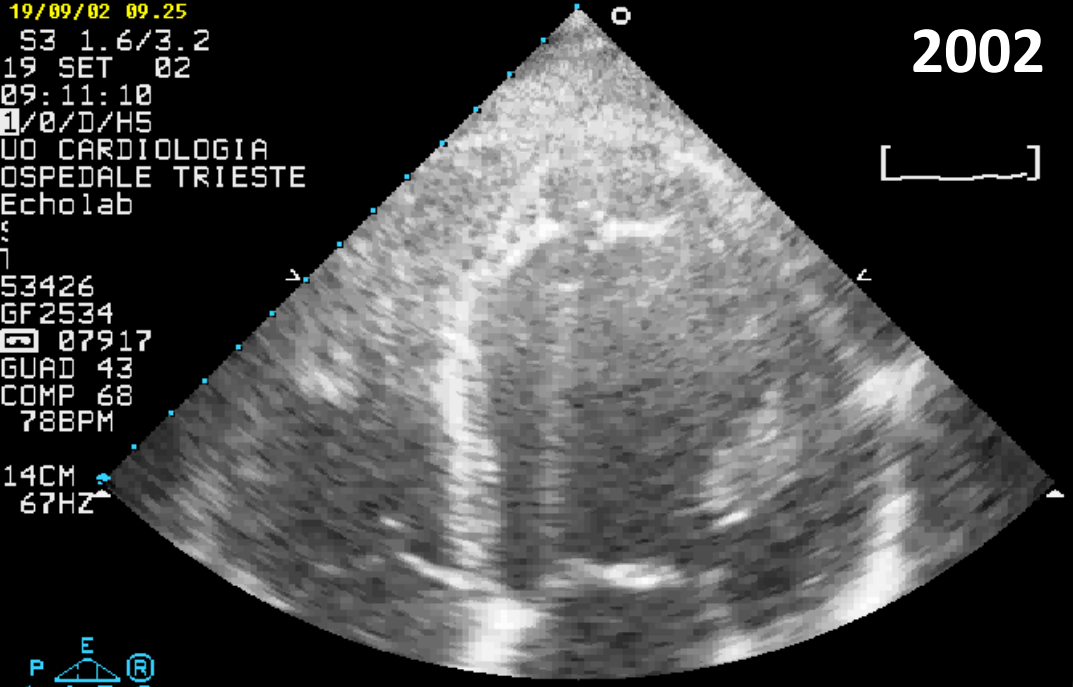
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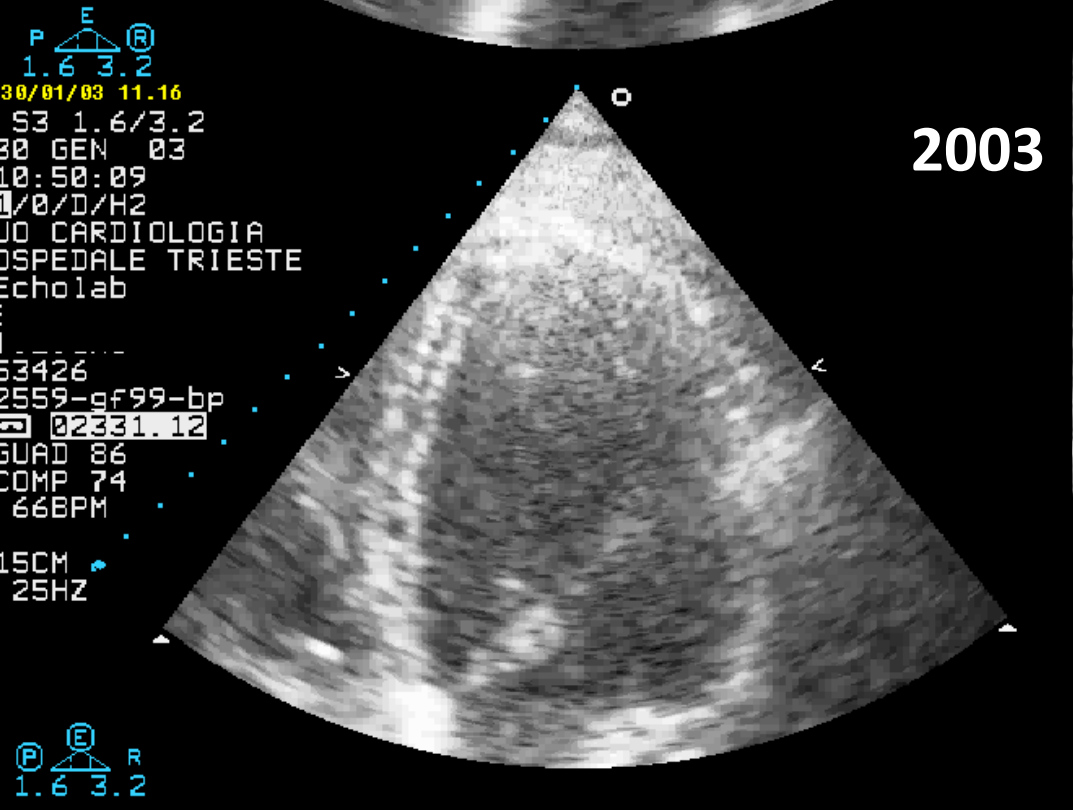
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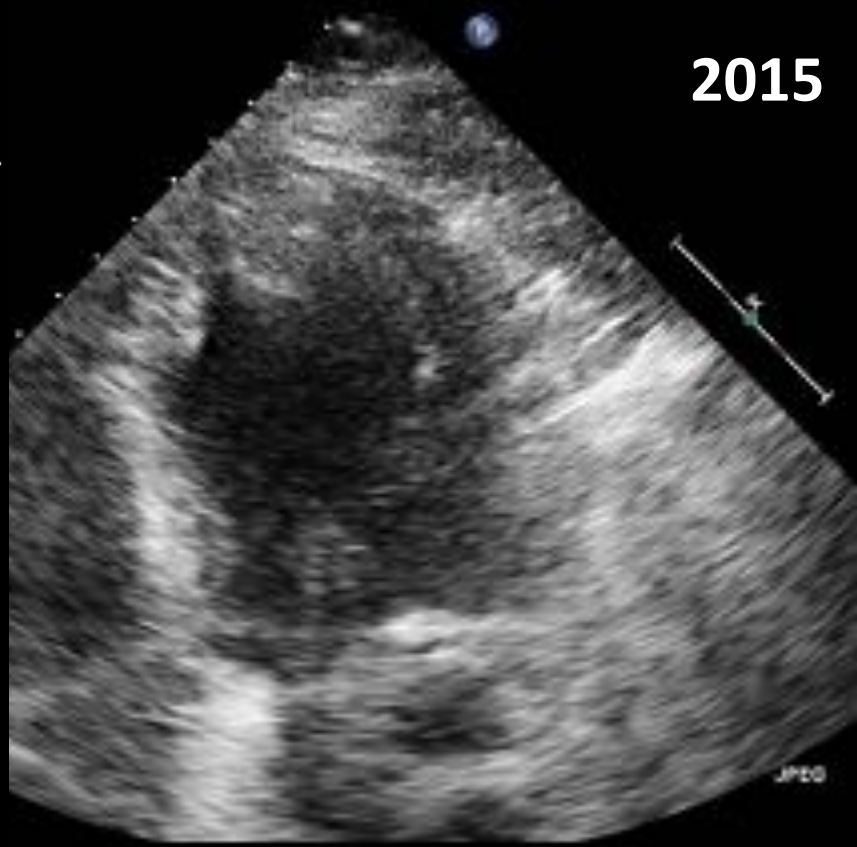

2015

European Heart Journal (2016) **37**, 2129–2200
doi:10.1093/eurheartj/ehw128

DEFINITION

2016 ESC GUIDELINES FOR THE DIAGNOSIS AND TREATMENT OF ACUTE AND CHRONIC HEART FAILURE

"HF is a **clinical syndrome** characterized by typical symptoms that may be accompanied by signs caused by a **structural and/or <u>functional cardiac abnormality</u>**, resulting in a reduced cardiac output and/ or elevated intracardiac pressures at rest or during stress"

Table 3.1 Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE); b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE); b. diastolic dysfunction (for details see Section 4.3.2).

BNP = B-type natriuretic peptide; HF = heart failure; HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LAE = left atrial enlargement; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; NT-proBNP = N-terminal pro-B type natriuretic peptide.
[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.
[b]BNP >35 pg/ml and/or NT-proBNP >125 pg/mL.

EF

Table 1 Comparison of imaging modalities for the evaluation of dilated cardiomyopathy

	2D echo	3D echo	CMR	CT	SPECT	PET
LV volumes and function	++	+++	++++	+++	++	++
Valvular disease	++++ (TOE optimal)	++++ (TOE optimal)	+++	+	–	–
Ischaemia/perfusion	+++	+++	+++	+	+++	++++
Morphology of the coronary arteries	–	–	++	+++	–	–
Imaging fibrosis	– (suspected using speckle tracking)	–	++++	++	–	++
Myocyte metabolism	–	–	++	–	++	++++
Clinical validation of prognostic tools	++++	++	+++	+	++	++
Spatial resolution	+++	++	+++	+++	++	++
Temporal resolution	++++	+++	++	+	+	+
Limitations	Operator dependence, acoustic window	Operator dependence, acoustic window	Availability, incompatible devices, renal failure	Availability, radiation, renal failure	Availability, radiation	Availability, radiation

CMR, cardiac magnetic resonance; echo, echocardiography; PET, positron emission tomography; SPECT, single photon emission CT; TOE, transoesophageal echocardiography.

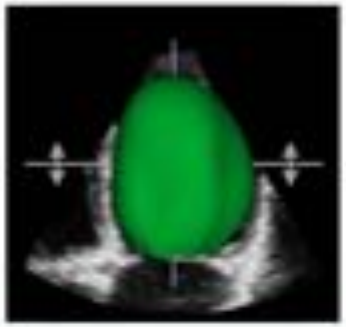
Heart. 2015 Apr;101(7):565-72.

GUIDELINES AND STANDARDS

Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

Roberto M. Lang, MD, FASE, FESC, Luigi P. Badano, MD, PhD, FESC, Victor Mor-Avi, PhD, FASE, Jonathan Afilalo, MD, MSc, Anderson Armstrong, MD, MSc, Laura Ernande, MD, PhD, Frank A. Flachskampf, MD, FESC, Elyse Foster, MD, FASE, Steven A. Goldstein, MD, Tatiana Kuznetsova, MD, PhD, Patrizio Lancellotti, MD, PhD, FESC, Denisa Muraru, MD, PhD, Michael H. Picard, MD, FASE, Ernst R. Rietzschel, MD, PhD, Lawrence Rudski, MD, FASE, Kirk T. Spencer, MD, FASE, Wendy Tsang, MD, and Jens-Uwe Voigt, MD, PhD, FESC, *Chicago, Illinois; Padua, Italy; Montreal, Quebec and Toronto, Ontario, Canada; Baltimore, Maryland; Créteil, France; Uppsala, Sweden; San Francisco, California; Washington, District of Columbia; Leuven, Liège, and Ghent, Belgium; Boston, Massachusetts*

3D data sets



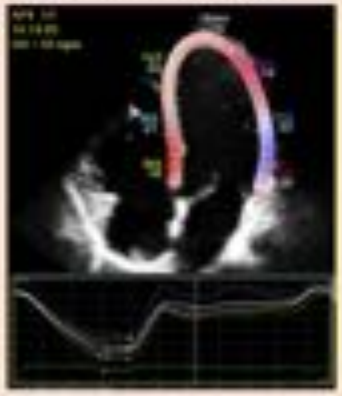
- No geometrical assumption
- Unaffected by foreshortening
- More accurate and reproducible compared to other imaging modalities

- Lower temporal resolution
- Less published data on normal values
- Image quality dependent

Recommendations. In laboratories with experience in 3DE, 3D measurement and reporting of LV volumes **is recommended** when feasible depending on image quality.

LV systolic function **should be** routinely assessed using 2DE or 3DE by calculating EF from EDV and ESV.

Global Longitudinal Strain



- Angle independent
- Established prognostic value

- Vendor dependent

Recommendations. Two-dimensional STE-derived GLS appears to be reproducible and feasible for clinical use and offers **incremental prognostic data** over LV EF in a variety of cardiac conditions, although measurements vary among vendors and software versions.

J Am Soc Echocardiogr 2015;28:1-39

Novel Approach to Three-Dimensional Echocardiographic Quantification of Right Ventricular Volumes and Function from Focused Views

Diego Medvedofsky, MD, Karima Addetia, MD, Amit R. Patel, MD, Anke Sedlmeier, MS, Rolf Baumann, MS, Victor Mor-Avi, PhD, and Roberto M. Lang, MD, *Chicago, Illinois; and Unterschleissheim, Germany*

J Am Soc Echocardiogr 2015;28:1222-31.

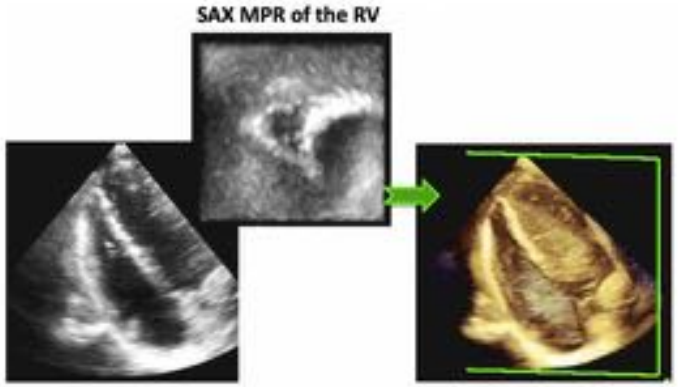
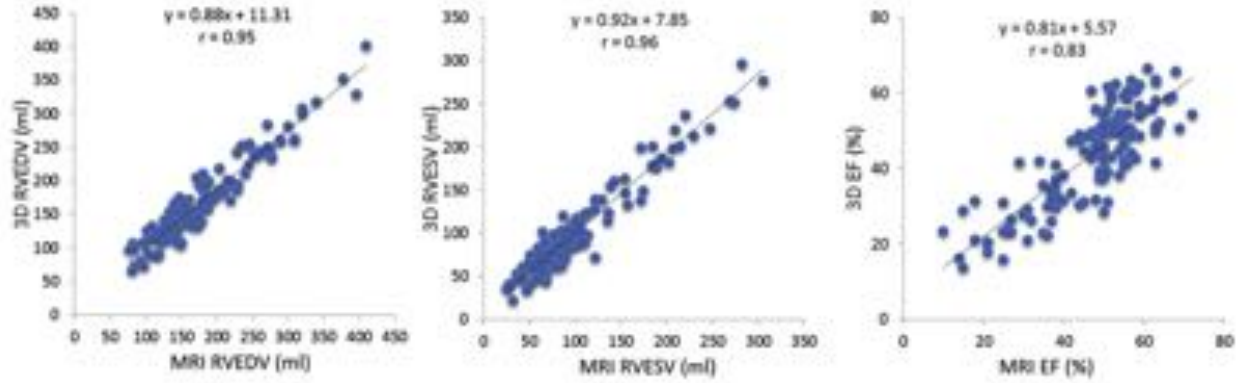


Figure 1 Three-dimensional echocardiographic imaging of the right ventricle (RV). For full coverage of the RV by the 3D pyramidal scan volume, the observer should use a modified two-dimensional (2D) apical view (left): compared with the standard apical view, the transducer must be positioned more laterally. This position allows coverage of the entire right ventricular free wall. Simultaneous real-time short-axis (SAX) multiplanar reconstruction (MPR) (middle) was used to ensure optimal visualization of the entire free wall. This results in a RV-focused 3D data set (right).

Table 2 RV volumes and function measurements by CMR and 3DE analysis and intertechnique agreement (n = 131)

Variable	r	CMR	3DE	Bias ± SD	P	Bias (% mean) ± SD
EDV (mL)	0.95	183 ± 66	172 ± 61	−11 ± 20	.17	−6 ± 11
ESV (mL)	0.96	102 ± 57	101 ± 55	−0.3 ± 15.3	.96	0 ± 15
EF (%)	0.83	47 ± 13	44 ± 13	−3.3 ± 7.6	.04	−7 ± 17

Data are expressed as mean ± SD.



European Heart Journal (2016) 37, 1196–1207
doi:10.1093/eurheartj/ehv529

REVIEW

Imaging

Myocardial strain imaging: how useful is it in clinical decision making?

Otto A. Smiseth[1]*, Hans Torp[2], Anders Opdahl[1], Kristina H. Haugaa[1] and Stig Urheim[1]

- CARDIOMYOPATHIES AND SUB-CLINICAL LEFT VENTRICULAR DYSFUNCTION
- CARDIOTOXICITY DURING CHEMOTHERAPY
- VALVULAR HEART DISEASE
- CORONARY ARTERY DISEASE: DETECTION OF MYOCARDIAL ISCHEMIA AND VIABILITY
- CARDIAC RESYNCHRONIZATION THERAPY
- HEART FAILURE WITH PRESERVED EJECTION FRACTION
- LEFT ATRIAL STRAIN

European Heart Journal
doi:10.1093/eurheartj/ehw211

2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines

Technique	Currently available diagnostic criteria	Advantages	Major limitations
Echocardiography: **- 3D-based LVEF** **- 2D Simpson's LVEF** **- GLS**	• LVEF: >10 percentage points decrease to a value below the LLN suggests cardiotoxicity. • GLS: >15% relative percentage reduction from baseline may suggest risk of cardiotoxicity.	• Wide availability. • Lack of radiation. • Assessment of haemodynamics and other cardiac structures.	• Inter-observer variability. • Image quality. • GLS: inter-vendor variability, technical requirements.

Echocardiography. Echocardiography is the method of choice for the detection of myocardial dysfunction before, during and after cancer therapy (see *Table 6*).[85,95] Unless three-dimensional (3D) echocardiography is used, which is the best echocardiographic method for measuring LVEF when endocardial definition is clear, the two-dimensional (2D) biplane Simpson method is recommended for estimation of LV volumes and ejection fraction in these patients. Cancer therapeutics–related cardiac dysfunction (CTRCD) is defined as a decrease in the LVEF of >10 percentage points, to a value below the lower limit of normal.[85,97] This decrease should be confirmed by repeated cardiac imaging done 2–3 weeks after the baseline diagnostic study showing the initial decrease in LVEF. The LVEF decrease

to cancer therapy.[92] Global systolic longitudinal myocardial strain (GLS) has been reported to accurately predict a subsequent decrease in LVEF.[101,102] A relative percentage reduction of GLS of >15% from baseline is considered abnormal and a marker of early LV subclinical dysfunction. Until standardization of strain imaging through different vendors is fully achieved, the current recommendation is to use the same equipment for the longitudinal follow-up of patients with cancer to facilitate the interpretation of results. These

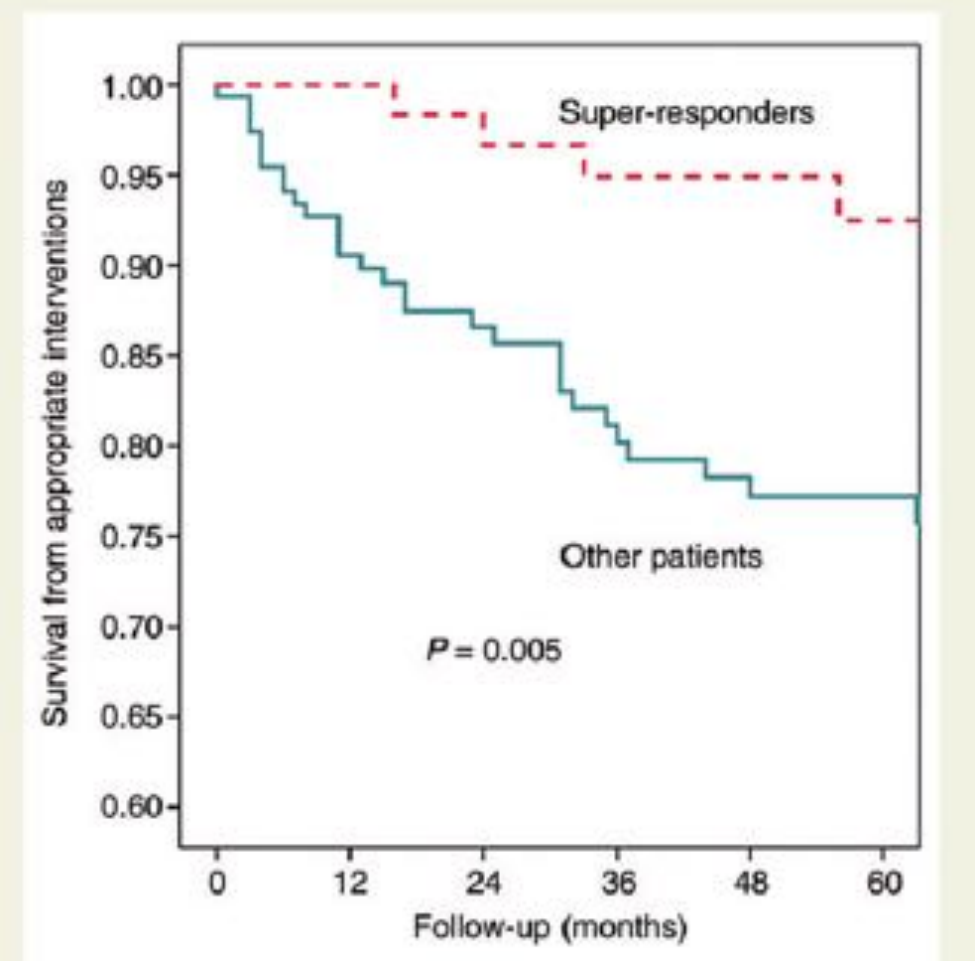
3.1.4 Patients with asymptomatic reduction in global longitudinal strain during chemotherapy

Currently there is no evidence to guide specific cardioprotection if early signs of subclinical myocardial dysfunction are detected during echocardiography-based GLS surveillance.[85,90,250] GLS may be a more sensitive tool to detect early cardiotoxicity, but based on currently available evidence, cancer treatment should not be stopped, interrupted or reduced in dose based on a new GLS reduction alone.

Europace (2014) 16, 363–371
doi:10.1093/europace/eut339

Long-term outcome of 'super-responder' patients to cardiac resynchronization therapy

Massimo Zecchin[1]*, Alberto Proclemer[1], Silvia Magnani[1], Laura Vitali-Serdoz[1], Domenico Facchin[2], Daniele Muser[2], Andrea Nordio[1], Giulia Barbati[1], Ilaria Puggia[1], Gianfranco Sinagra[1], and Alessandro Proclemer[2]

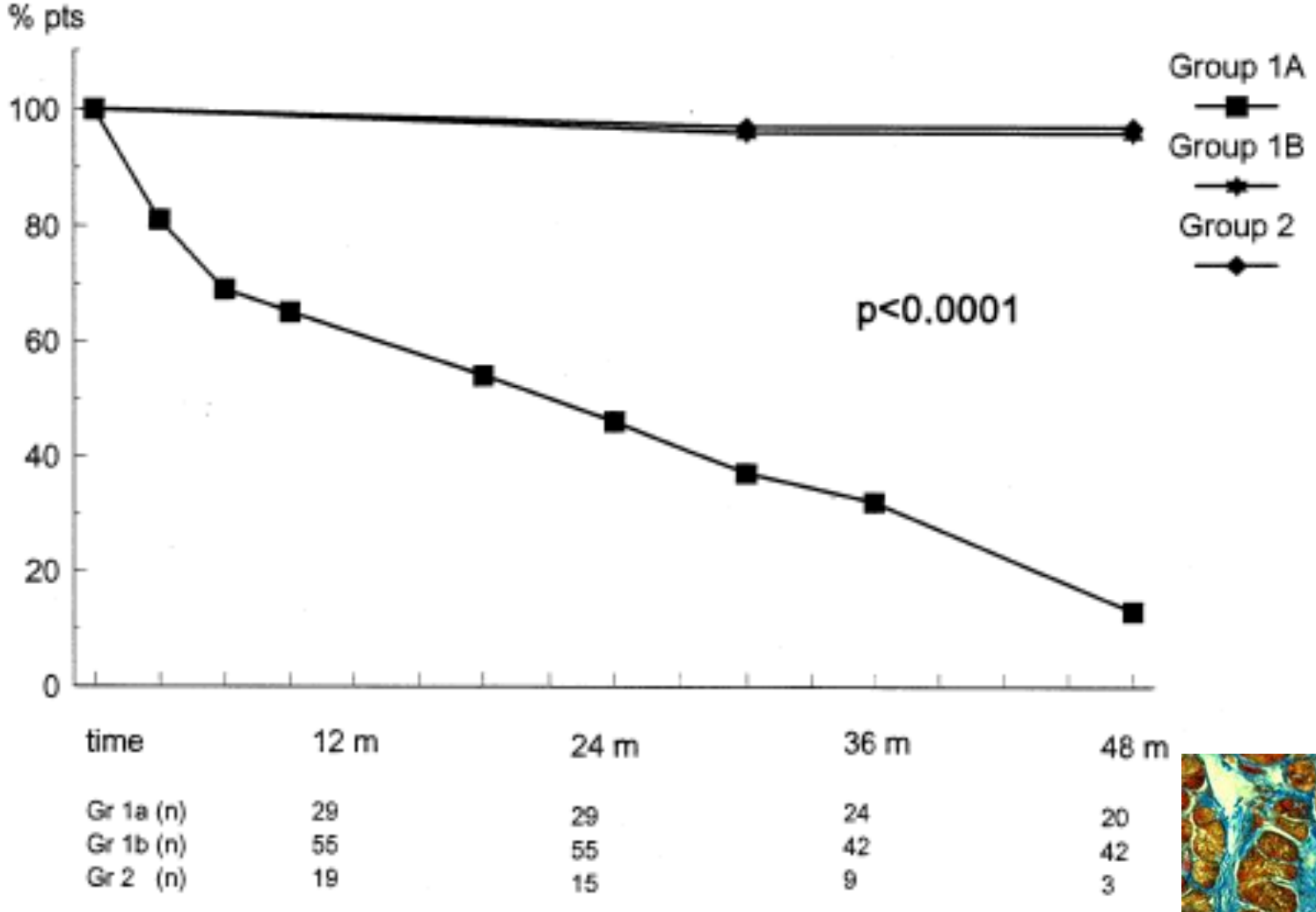


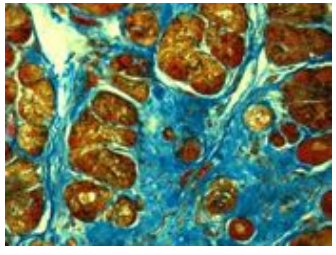
Persistence of Restrictive Left Ventricular Filling Pattern in Dilated Cardiomyopathy: An Ominous Prognostic Sign

JACC

(J Am Coll Cardiol 1997;29:604–12)

BRUNO PINAMONTI, MD, MASSIMO ZECCHIN, MD, ANDREA DI LENARDA, MD,
DARIO GREGORI, MA, PHD, GIANFRANCO SINAGRA, MD, FULVIO CAMERINI, MD



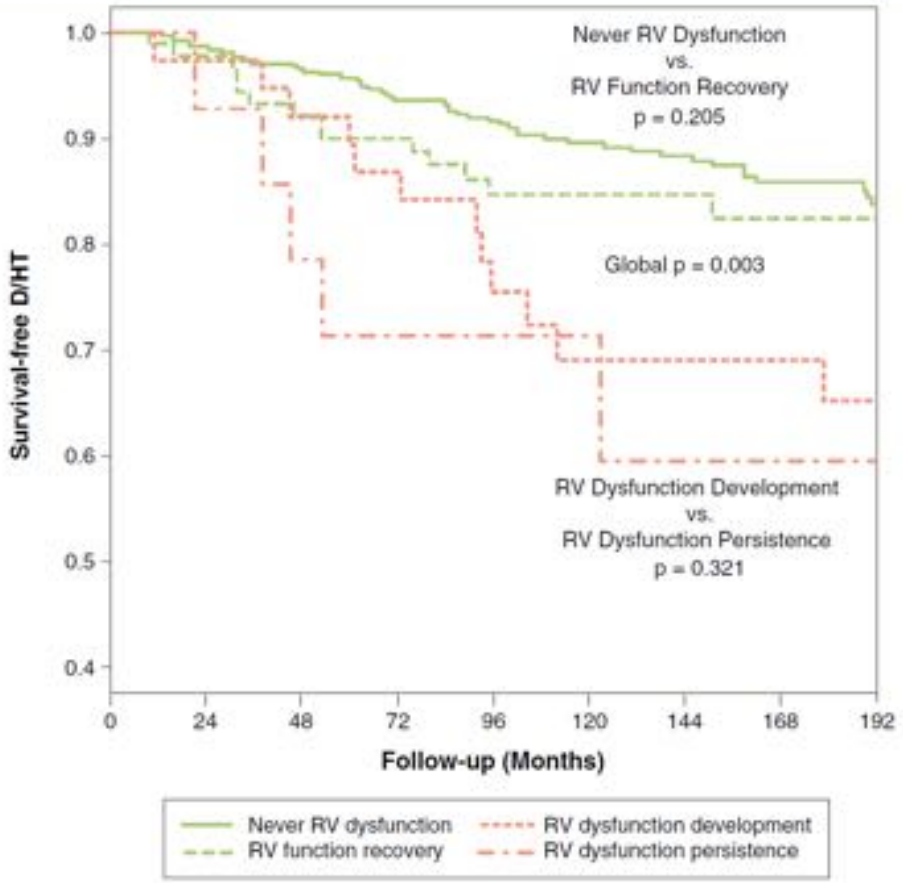


The Prognostic Impact of the Evolution of RV Function in Idiopathic DCM

Marco Merlo, MD,[a] Marco Gobbo, MD,[a] Davide Stolfo, MD,[a] Pasquale Losurdo, MD,[a] Federica Ramani, PhD,[a] Giulia Barbati, PhD,[a,b] Alberto Pivetta, MD,[a] Andrea Di Lenarda, MD,[b] Marco Anzini, MD,[a] Marta Gigli, MD,[a] Bruno Pinamonti, MD,[a] Gianfranco Sinagra, MD[a]

JACC Cardiovasc Imaging. 2016 Sep;9(9):1034-42.

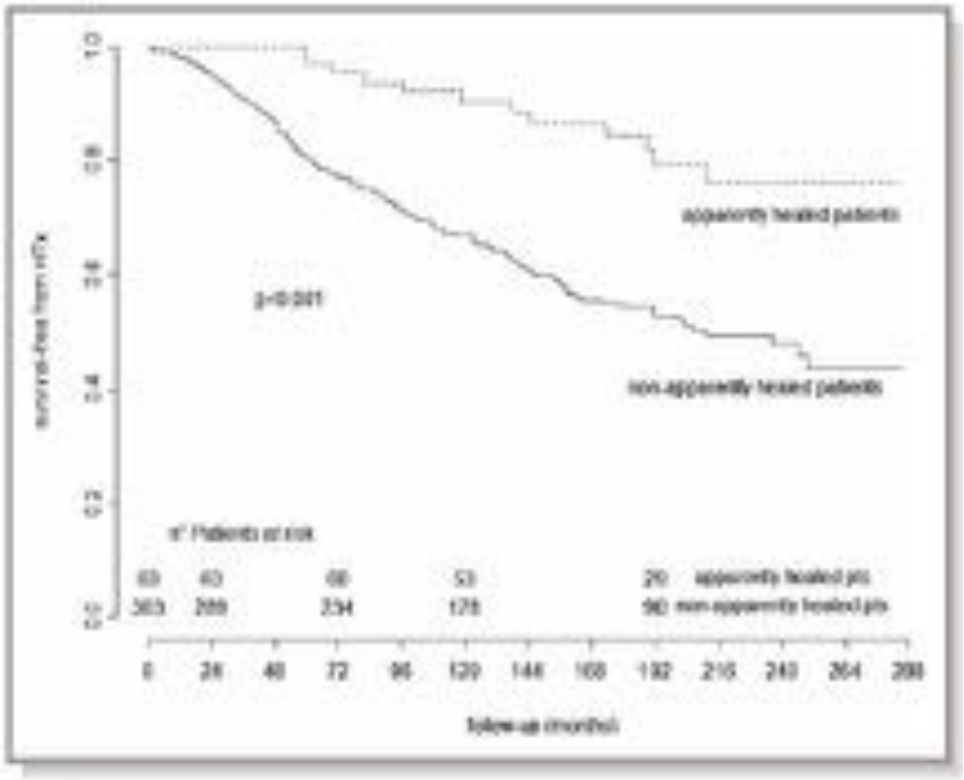
FIGURE 4 Kaplan-Meier Survival Curves: Long-Term Prognostic Role of RV Dysfunction Revaluation



JACC Cardiovascular Imaging

Persistent Recovery of Normal Left Ventricular Function and Dimension in Idiopathic Dilated Cardiomyopathy During Long-Term Follow-up: Does Real Healing Exist?

Marco Merlo, MD; Davide Stolfo, MD; Marco Anzini, MD; Francesco Negri, MD; Bruno Pinamonti, MD; Giulia Barbati, PhD; Federica Ramani, PhD; Andrea Di Lenarda, MD; Gianfranco Sinagra, MD, FESC



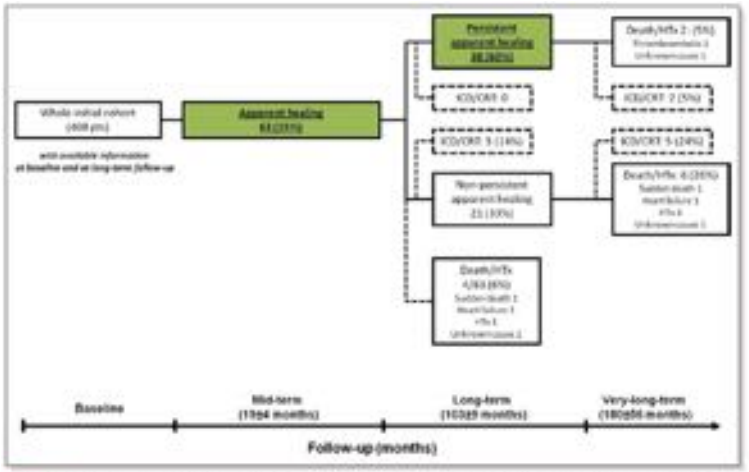


Figure 2. Flowchart of the long-term evolution of the study population. All analyzed patients underwent a complete echocardiographic evaluation at each follow-up. CRT indicates cardiac resynchronization therapy; HTx, heart transplant; ICD, implantable cardioverter-defibrillator.

Persistent apparent healing was defined as left ventricular ejection fraction ≥50% and indexed left ventricular end-diastolic diameter ≤33 mm/m2 at both mid-term (19±4 months) and long-term (103±9 months) follow-up.

J Am Heart Assoc. 2015 Jan; 4(1): e001504.

LVRR in DCM – PROGNOSTIC ROLE

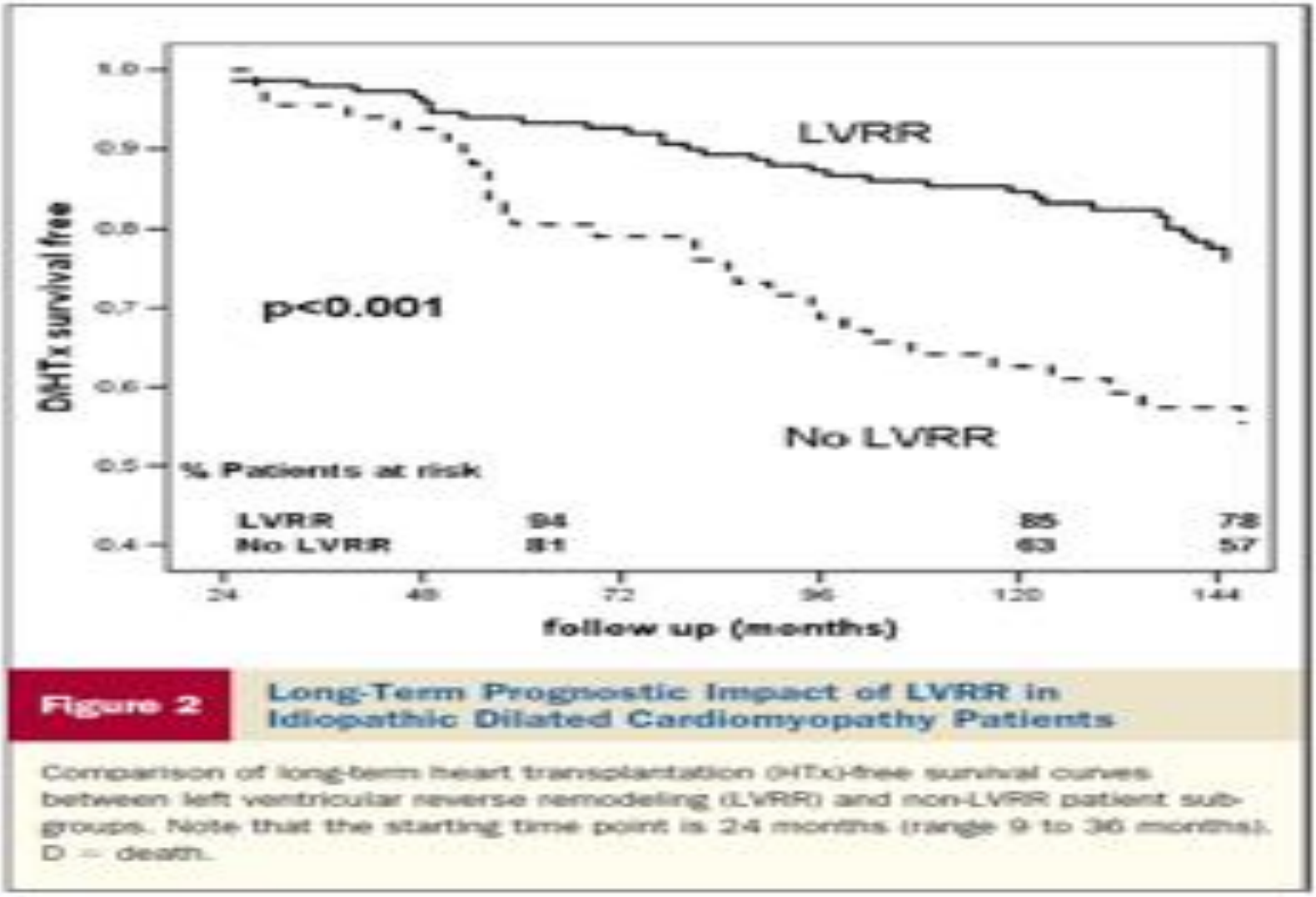


Figure 2 **Long-Term Prognostic Impact of LVRR in Idiopathic Dilated Cardiomyopathy Patients**

Comparison of long-term heart transplantation (HTx)-free survival curves between left ventricular reverse remodeling (LVRR) and non-LVRR patient subgroups. Note that the starting time point is 24 months (range 9 to 36 months). D = death.

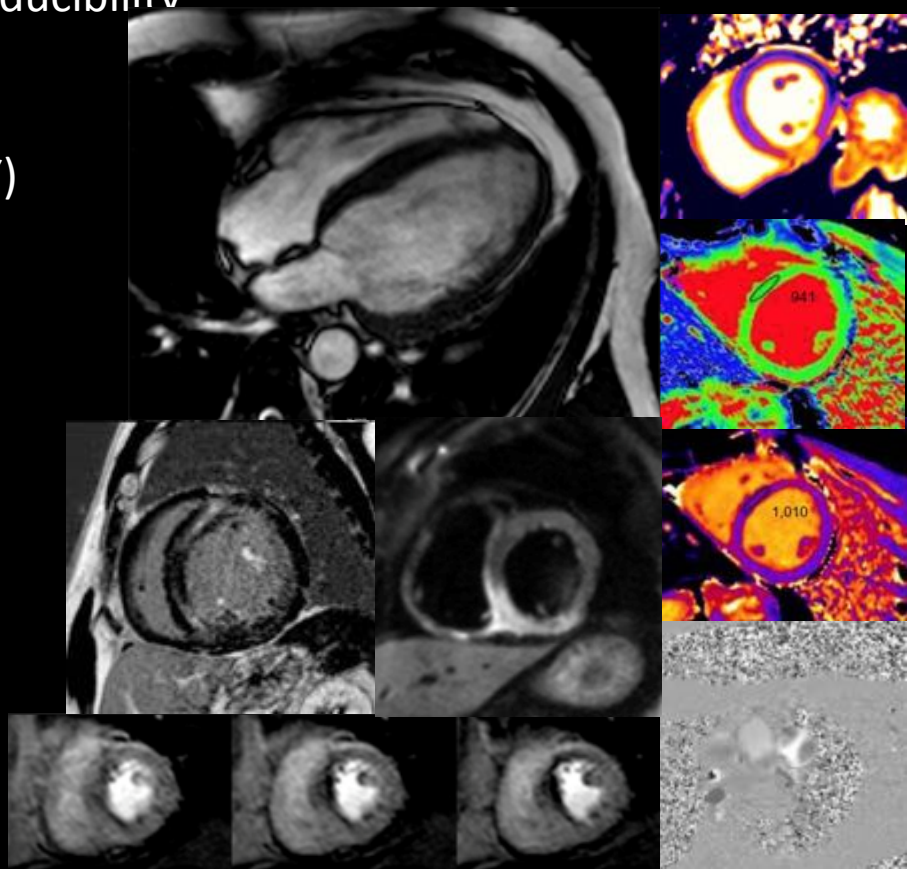
Merlo M, Sinagra G, et al. J Am Coll Cardiol,2011;57:1468-76

CARDIOVASCULAR MAGNETIC RESONANCE

- High spatial and temporal resolution. Multiplanary. No ionizing radiation.

- ANATOMICAL AND FUNCTIONAL EVALUATION: Gold Standard for quantification of volumes, mass, and systolic function with the highest inter- intra-observer reproducibility

  DIRECT FLOW MEASUREMENT
- TISSUE CHARACTERIZATION (ETIOLOGY)
- PERFUSION, ISCHEMIA AND VIABILITY



Myocardial Fibrosis Assessment by LGE Is a Powerful Predictor of Ventricular Tachyarrhythmias in Ischemic and Nonischemic LV Dysfunction

A Meta-Analysis

JACC
Journal of the American College of Cardiology

TABLE 3 Tachyarrhythmic Event Rate and Odds Ratio in the Different Subgroups of Studies

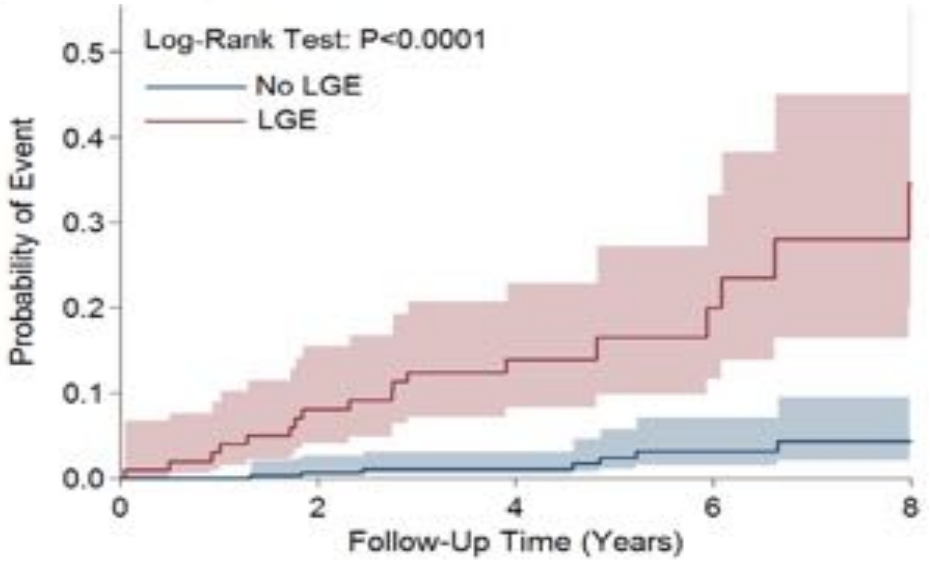
Subgroups	Studies	Patients	% AER	LGE-CMR		OR (95% CI)	p Value
				% of LGE− AER+	% LGE− AER+		
Total	19	2,850	5.3	8.6	1.7	5.62 (4.20-7.51)	<0.00001
ICM	5	358	8.9	13.2	3.3	5.05 (2.73-9.36)	<0.00001
NICM	8	1,443	3.7	7.6	1.3	6.27 (4.15-9.47)	<0.00001
Mixed population	6	1,049	6.8	8.8	1.8	4.92 (2.70-8.98)	<0.00001
Mean EF ≤30%	11	1,178	6.6	10.3	1.2	9.56 (5.63-16.23)	<0.00001
Mean EF >30%	8	1,672	4.6	7.4	2.0	4.48 (3.17-6.33)	<0.00001

Disertori et al. JACC Imaging 2016 I

Association Between Midwall Late Gadolinium Enhancement and Sudden Cardiac Death in Patients With Dilated Cardiomyopathy and Mild and Moderate Left Ventricular Systolic Dysfunction

Circulation

Primary End Point: Sudden Cardiac Death and Aborted Sudden Cardiac Death



Outcome	LGE Status	Events n (%)	Univariable		Multivariable*	
			HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
SCD or Aborted SCD	LGE−	7 (2.3)	9.2 (3.9, 21.8)	<0.0001	9.3 (3.9, 22.3)	<0.0001
	LGE+	18 (17.8)				
SCD	LGE−	6 (2.0)	4.9 (1.8, 13.5)	0.002	4.8 (1.7, 13.8)	0.003
	LGE+	9 (8.9)				
Aborted SCD	LGE−	1 (0.3)	34.8 (4.6, 266.6)	<0.0001	35.9 (4.8, 271.4)	<0.001
	LGE+	10 (9.9)				

Halliday B, et al. Circulation. 2017;135:2106–2115

RESEARCH Open Access

Value of scar imaging and inotropic reserve combination for the prediction of segmental and global left ventricular functional recovery after revascularisation

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46 Patients
Mean LVEF 35%
CMR before and after revascularization (6 m)

LDD-CMR is superior to LGE-CMR alone as a predictor of segmental recovery

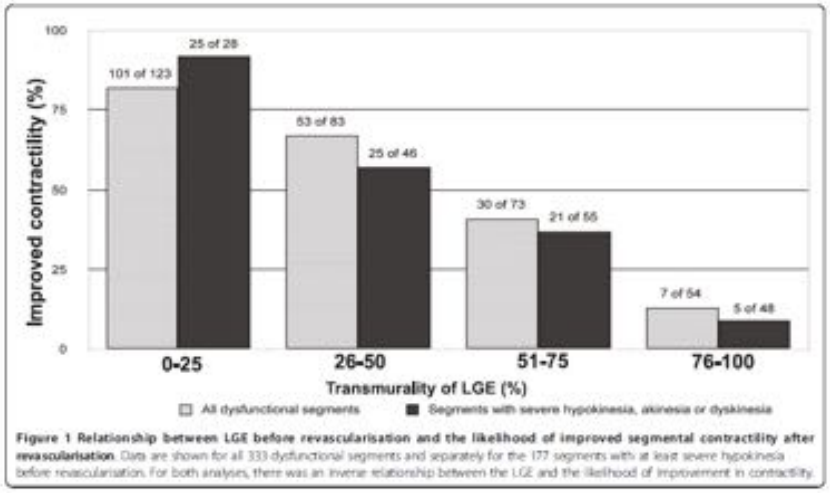

Figure 1 Relationship between LGE before revascularisation and the likelihood of improved segmental contractility after revascularisation. Data are shown for all 333 dysfunctional segments and separately for the 177 segments with at least severe hypokinesia before revascularisation. For both analyses, there was an inverse relationship between the LGE and the likelihood of improvement in contractility.

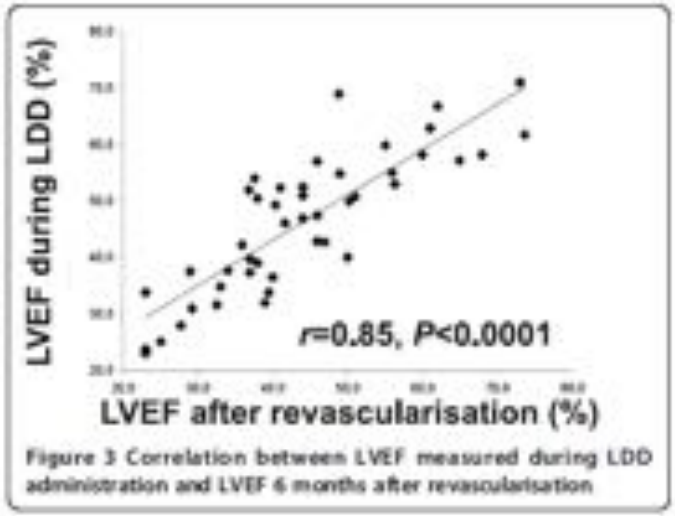

Figure 3 Correlation between LVEF measured during LDD administration and LVEF 6 months after revascularisation

Cardiac CT With Delayed Enhancement in the Characterization of Ventricular Tachycardia Structural Substrate

Relationship Between CT-Segmented Scar and Electro-Anatomic Mapping

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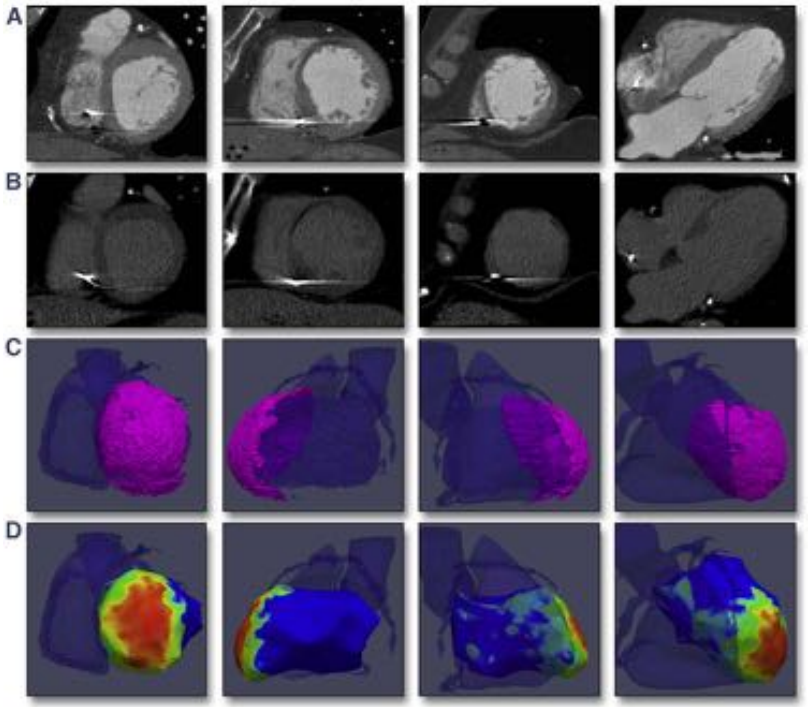
42 Patients

Cardiac-CT: angiographic and 10-min delayed-enhancement scan

Comparison with Electro-Anatomic Mapping (EAM; low voltages, late potentials, RF ablation points)

Good concordance CT-EAM

LOW-VOLTAGES: Sn 76%, Sp 86%, NPV 95%



Short-axis (left → right – base → apex) and long-axis views of computed tomography angiography (**A**) and computed tomography delayed enhancement (**B**), showing a large anteroseptal post-ischemic scar, characterized by wall thinning, subendocardial adipose metaplasia (**A,B**), aneurismatic dilation and transmural delayed enhancement (**B**). Different projections of 3-dimensional reconstructions of computed tomography (CT) with scar segmented in **pink** are reported in **C** and corresponding projections of bipolar endocardial electroanatomic mapping (EAM) are reported in **D**, with pathological voltages represented in **green-yellow** (border zone) and **red** (dense scar) according to amplitude. ICM = ischemic dilated cardiomyopathy.

J Am Coll Cardiol Img 2016;9:822–32

Myocardial Iodine-123 *Meta*-Iodobenzylguanidine Imaging and Cardiac Events in Heart Failure

Results of the Prospective ADMIRE-HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) Study

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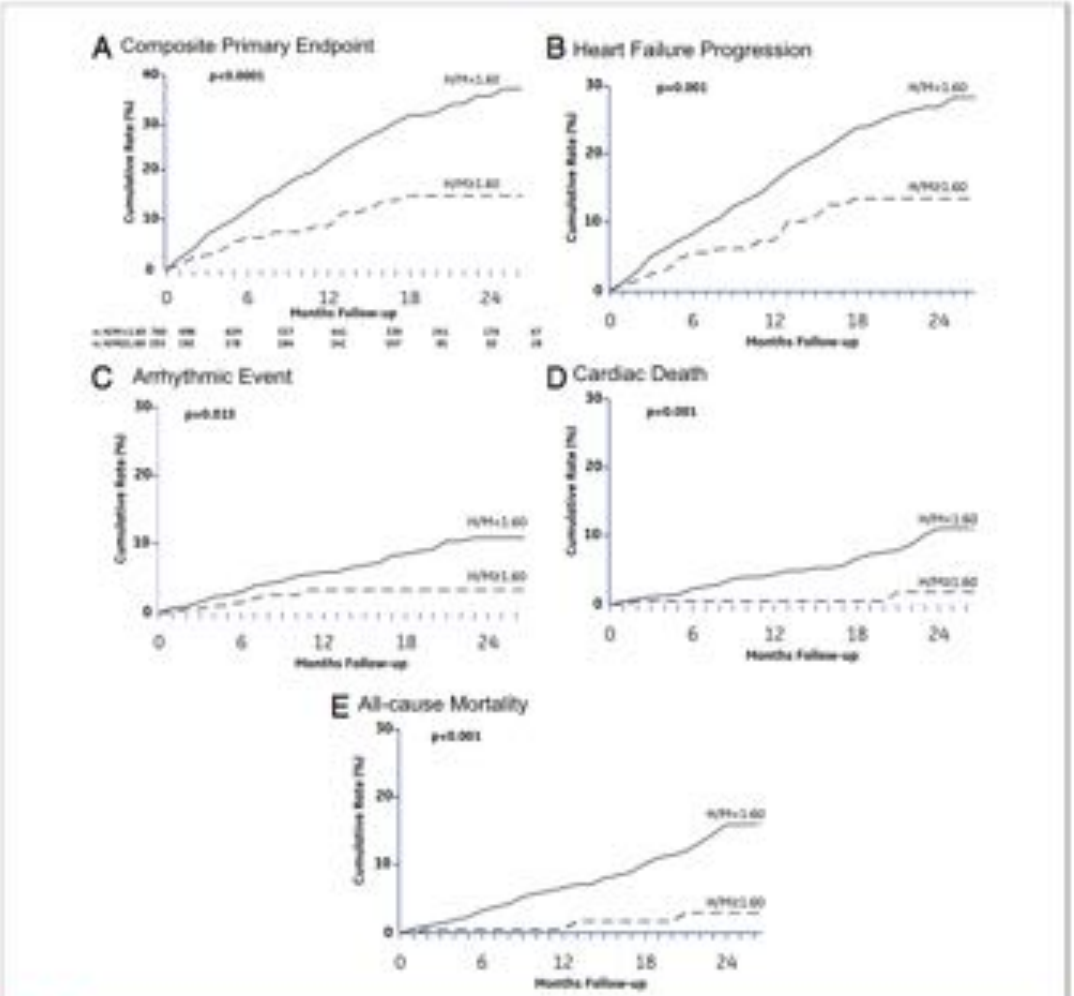

Figure 2 Cumulative Event Curves Comparing Subjects With H/M <1.60 Versus ≥1.60

J Am Coll Cardiol 2010;55:2212–21

European Heart Journal (2016) **37**, 2129–2200
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

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

Recommendations for implantable cardioverter-defibrillator in patients with heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
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), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:			
• IHD (unless they have had an MI in the prior 40 days – see below).	I	A	149, 156, 227
• DCM.	I	B	156, 157, 227
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A	158, 228
ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C	229–233
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B	234–238
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C	239–241

CAD = coronary artery disease; CRT = cardiac resynchronization therapy; DCM = dilated cardiomyopathy; HF = heart failure; ICD = implantable cardioverter-defibrillator; IHD = ischaemic heart disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; OMT = optimal medical therapy.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

European Heart Journal 2016;37:2129-2200

How Can Optimization of Medical Treatment Avoid Unnecessary Implantable Cardioverter-Defibrillator Implantations in Patients With Idiopathic Dilated Cardiomyopathy Presenting With "SCD-HeFT Criteria?"

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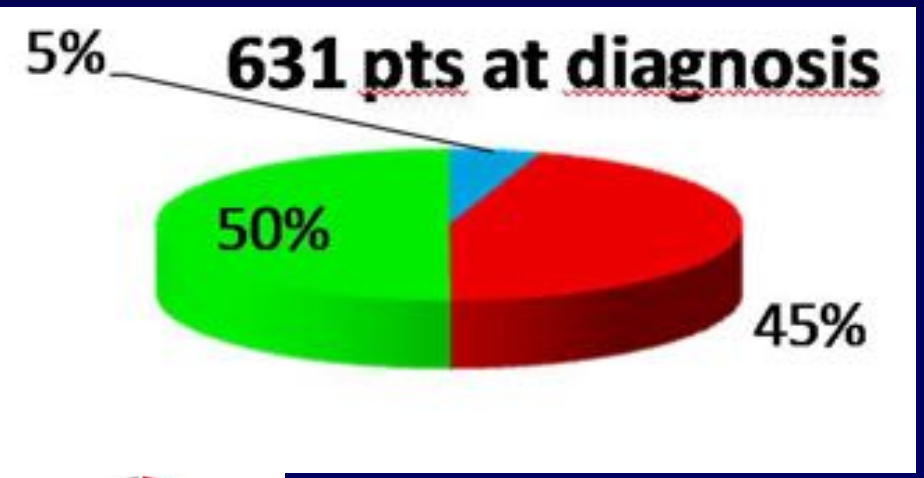
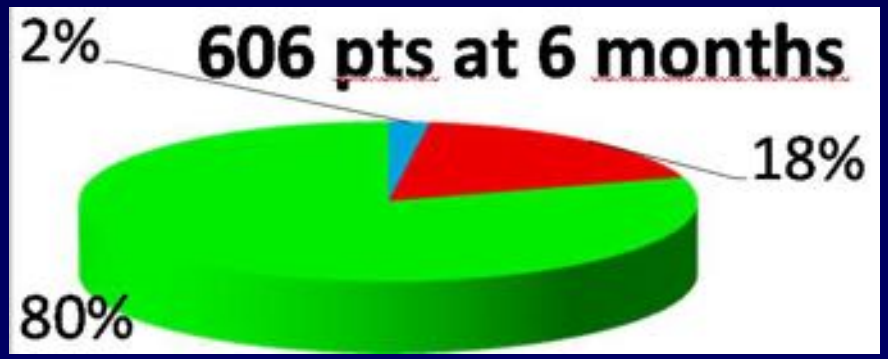
THE TRIESTE CARDIOMYOPATHIES REGISTRY 1988-2006; DCM N=631 PTS; LVEF 30±10%

EF<35 NYHA IV EF <35 NHYA II-III NYHA I and/or EF>35

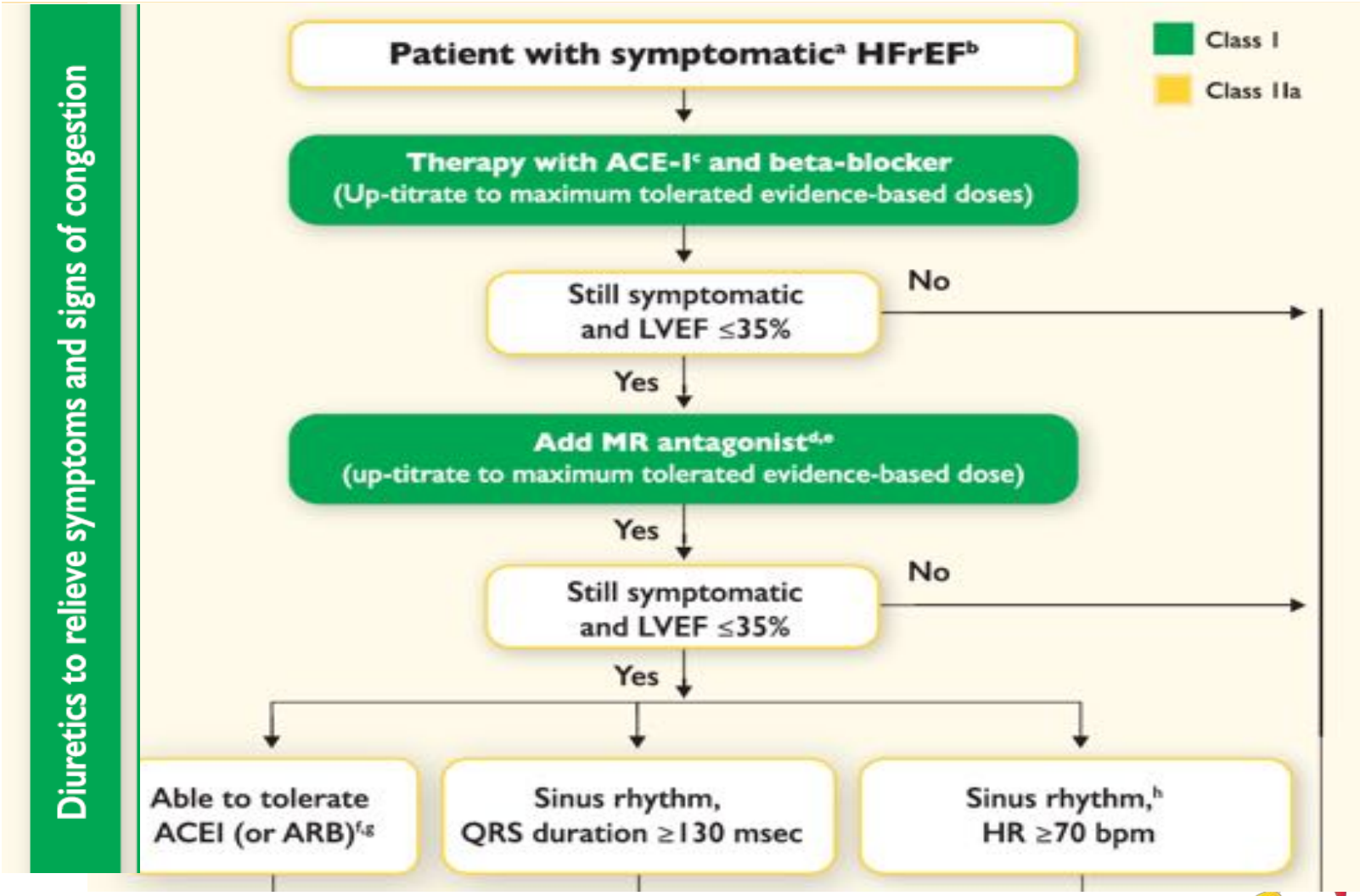




Ospedali Riuniti di Trieste

Zecchin , Sinagra et al;
Am J Cardiol 2012;109:729-35

Therapeutic algorithm for a patient with symptomatic HF with reduced ejection fraction



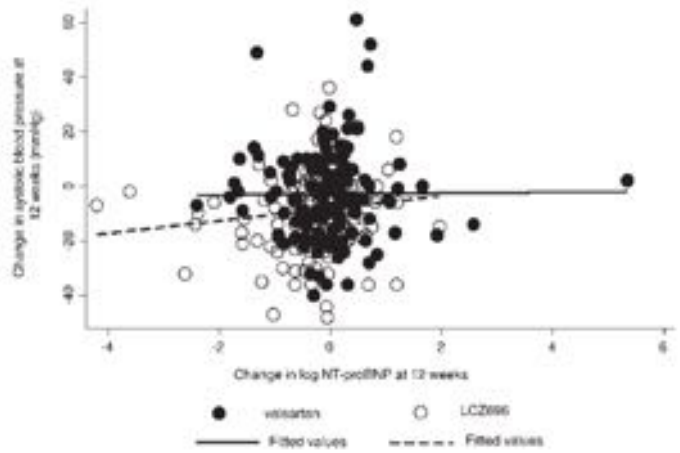
Available online on Eur J Heart Fail 2016

Independence of the blood pressure lowering effect and efficacy of the angiotensin receptor neprilysin inhibitor, LCZ696, in patients with heart failure with preserved ejection fraction: an analysis of the PARAMOUNT trial

EUROPEAN SOCIETY OF CARDIOLOGY®

Change in left atrial diameter, left atrial volume and estimated glomerular filtration rate (eGFR) according to treatment and change in systolic blood pressure at 36weeks

	Tertile 1, n = 89 (−50 to −12 mmHg) Change (95%CI)	Tertile 2, n = 83 (−11 to −2 mmHg) Change (95%CI)	Tertile 3, n = 78 (3–62 mmHg) Change (95%CI)	Overall P LCZ696 vs. valsartan (adjusted for change in SBP at 36 weeks)	P for interaction
Left atrial diameter					
LCZ696	−0.15(−0.25 to −0.06)	−0.12(−0.23 to −0.01)	−0.19(−0.32 to −0.05)	0.03	0.91
Valsartan	−0.04(−0.14 to −0.06)	−0.07(−0.16 to −0.02)	−0.11(−0.22 to −0.01)		
Left atrial indexed volume					
LCZ696	−2.65 (−4.71 to −0.59)	−1.77 (−4.87 to −1.34)	−3.74 (−7.18 to −0.29)	0.01	0.61
Valsartan	−0.28(−3.54 to −2.98)	0.22 (−2.69 to −3.14)	0.80(−2.53 to 4.13)		
eGFR					
LCZ696	−3.83(−6.99 to −0.67)	−1.28(−6.26 to −3.70)	1.86(−3.02 to −6.74)	0.002	0.69
Valsartan	−9.09(−12.78 to −5.41)	−3.03(−7.16 to −1.11)	−4.28(−7.34 to −1.23)		

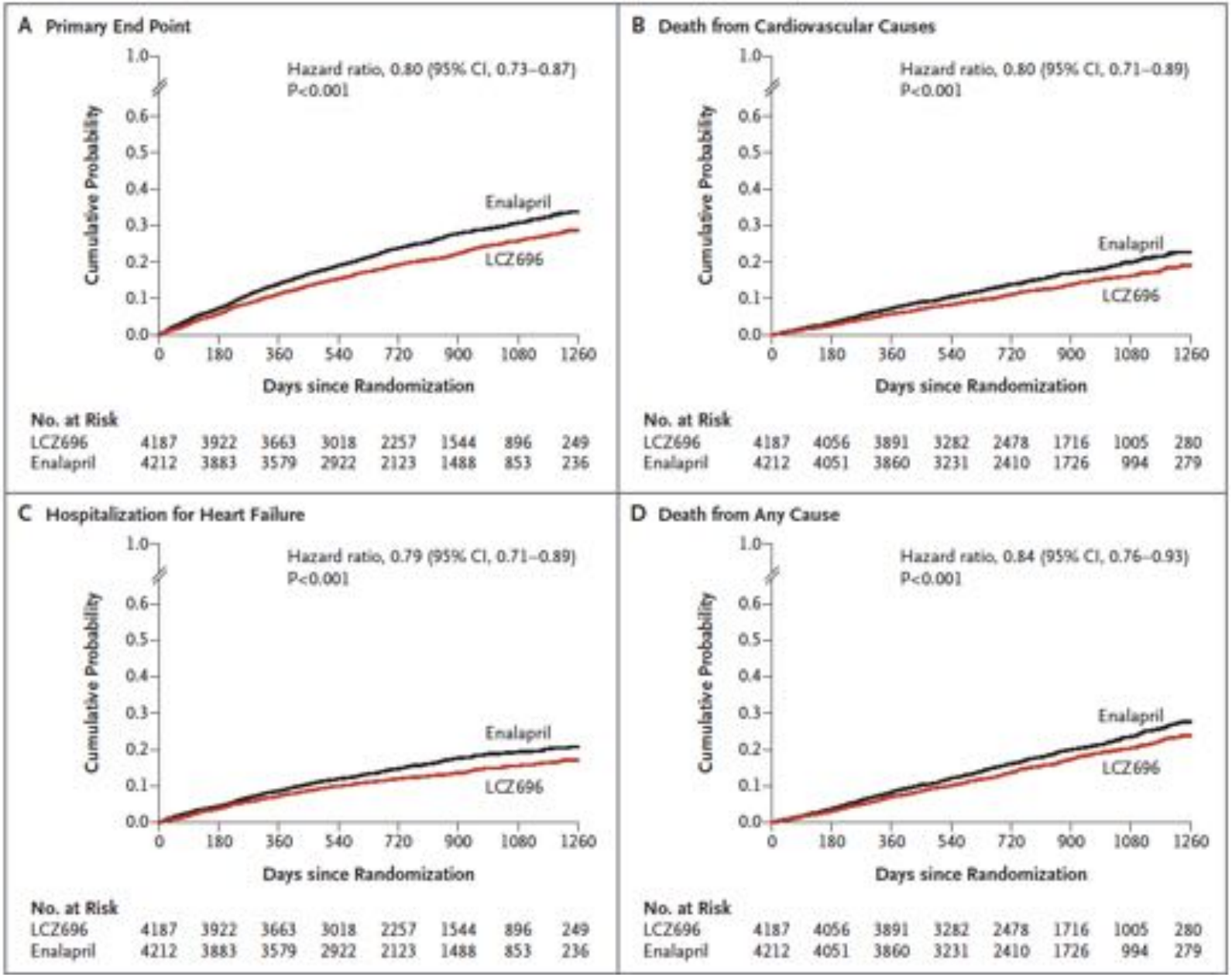


Correlation between change in systolic blood pressure at 12weeks and change in *N*-terminal pro-brain natriuretic peptide (NT-proBNP) at 12weeks according to randomized treatment, LCZ696 (open circles, dashed line), valsartan (closed circles, solid line).

European Journal of Heart Failure (2014) **16**, 671–677

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure

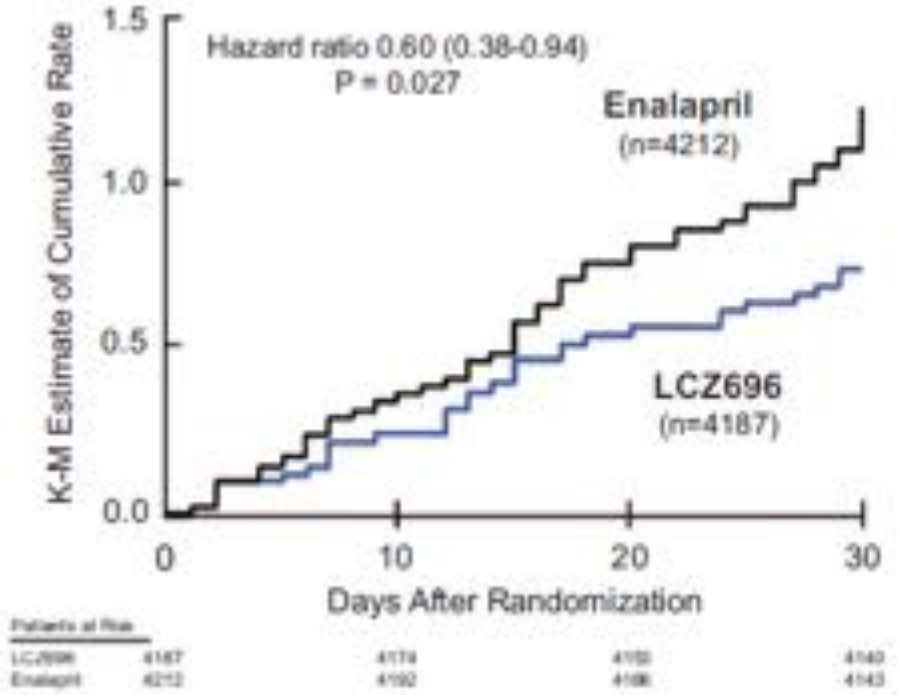
The NEW ENGLAND JOURNAL of MEDICINE



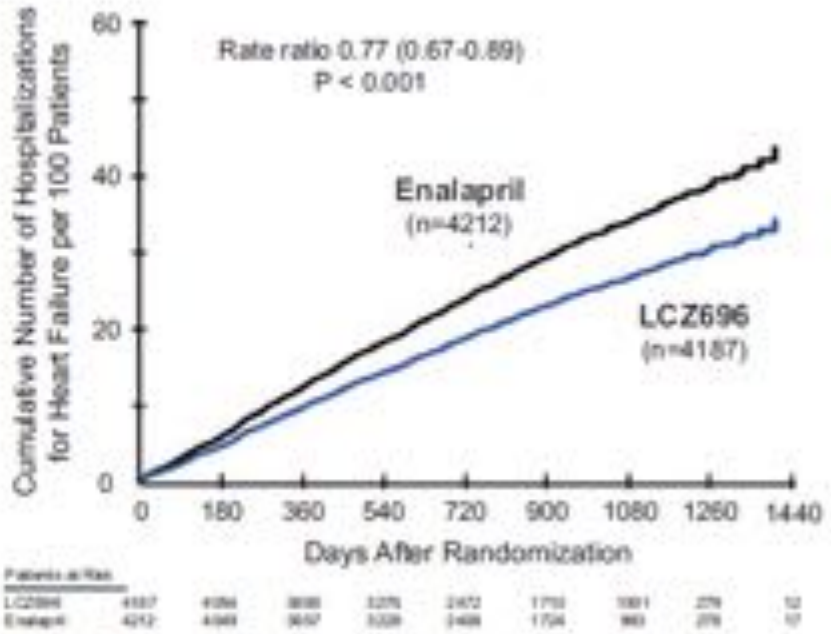
Mc Murray J. Et al N Engl J Med 2014;371:993-1004.

Angiotensin Receptor Neprilysin Inhibition Compared With Enalapril on the Risk of Clinical Progression in Surviving Patients With Heart Failure

Time to first hospitalization for HF during the first 30 days



Cumulative number of hospitalizations for HF



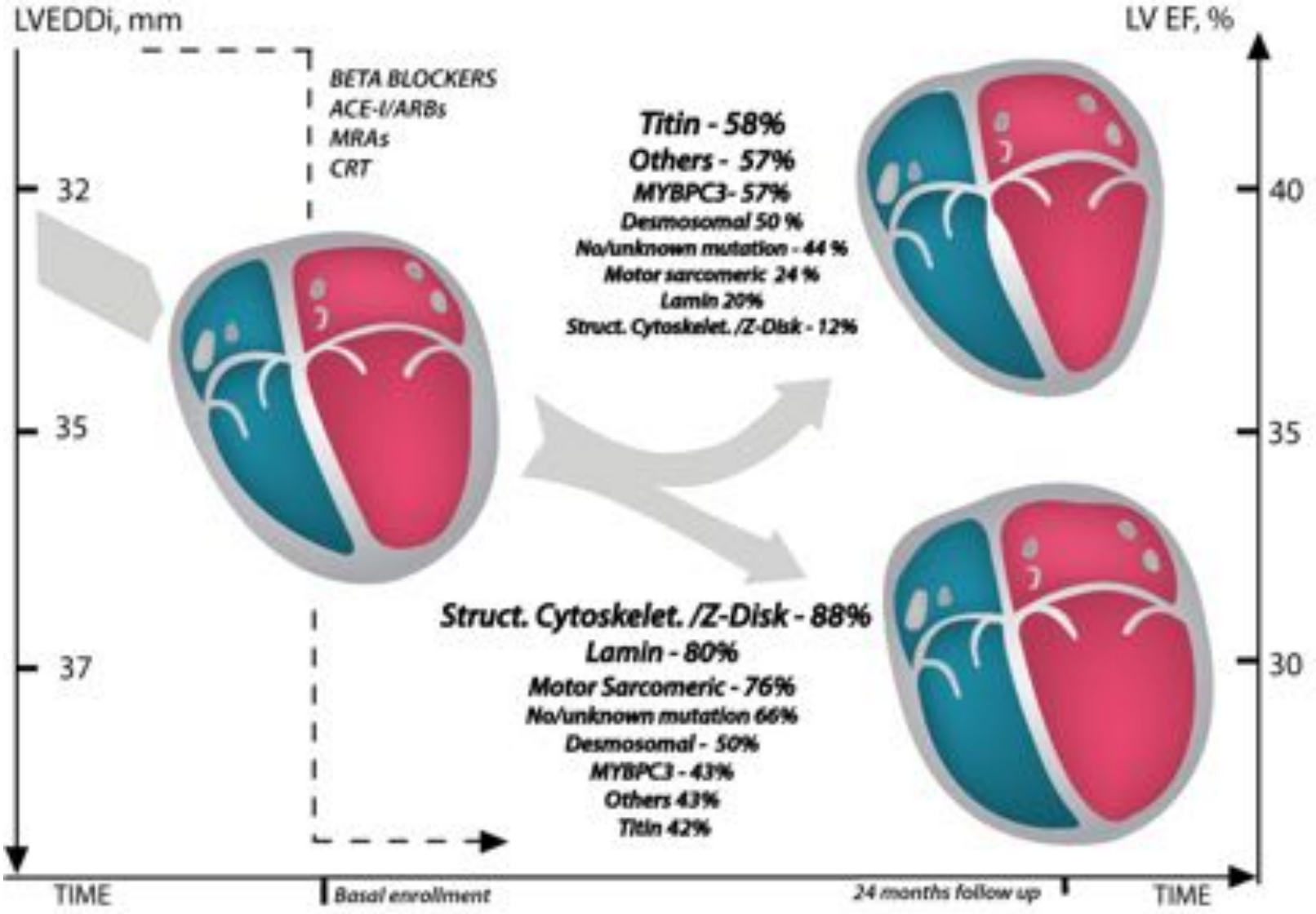
Packer M et al, Circulation 2015

Heart

Association between Mutation Status and Left Ventricular Reverse Remodeling in Dilated Cardiomyopathy

Genotype-Phenotype Correlations: Association between Mutation Status and Left Ventricular Reverse Remodeling in Idiopathic Dilated Cardiomyopathy.

Dal Ferro, Sinagra et al, Heart 2017



Take home message

- **“FE”: dato dinamico, da contestualizzare ed associare a valutazione diastole, RV e atrii;**
- **fondamentale per diagnosi, selezione/valutazione tp e prognosi;**
- **valore aggiunto del 3D echo e strain in alcuni setting;**
- **CRM per caratterizzazione tissutale, diagnosi e prognosi in vari modelli eziologici;**
- **scelta delle metodiche basata su informatività, accuratezza, accessibilità, economicità, impatto biologico;**
- **decisioni non basate sul “numero” ma sulla valutazione “multiparametrica”**