

PLACE

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

ROMA

Centro Congressi
di Confindustria

**Auditorium
della Tecnica**

9ª Edizione

30 Settembre

1 Ottobre

2022

CARDIOMIOPATIA DILATATIVA NON ISCHEMICA

L'ECOCARDIOGRAFIA NELLA CMPD NON ISCHEMICA: OLTRE LA FE

Dr Bruno Pinamonti Trieste





Ruoli Ecocardiografia nelle DCM

- Caratterizzazione morfo-funzionale DCM
- Indizi diagnosi specifica sottotipo DCM
- Caratteristiche ecocardiografiche
- Informazioni su severità della malattia, stratificazione prognostica, gestione terapeutica

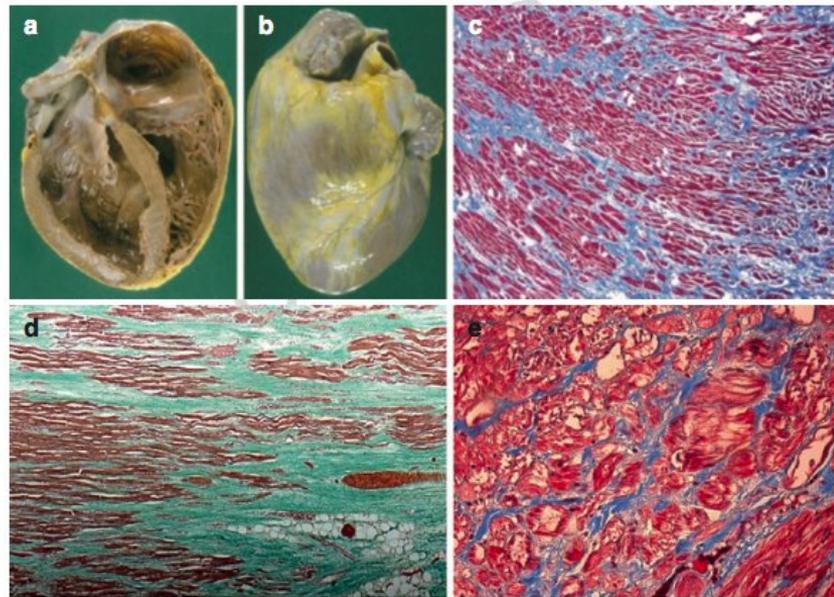


Fig. 1.3 Gross anatomy and histological specimen representative of DCM. (a, b) Gross anatomy of an explanted heart from a 26-year-old patient with DCM. (c) Azan-Mallory staining of a female patient with DCM and severe LV dysfunction; (d) histology from a patient with Duchenne's dystrophy; (e) Azan-Mallory staining from an explanted heart from a patient affected by genetically determined DCM (double mutation in desmin and potassium channels). Courtesy of Prof. Bussani, University of Trieste



Cardiac Imaging Diagnostic Criteria for DCM

- The main echocardiographic features of DCM are **LV dilatation and systolic dysfunction**
- Diagnostic criteria for DCM are **LVEF <45-50%** and **LVEDD/LVEDV > 117%** predicted value corrected for age and BSA
- The condition of MDCM (**Mildly dilated cardiomyopathy**) was defined by LVEF <45% and a normal or mildly dilated left ventricle.



DCM ECHOCARDIOGRAPHIC FEATURES

- LV DILATATION
- DIFFUSE LV HYPOKINESIS
- GLOBAL LV SYSTOLIC DYSFUNCTION (EF < 45%)
- COMMON LV DIASTOLIC DYSFUNCTION
- LEFT-RIGHT ATRIAL DILATATION
- FUNCTIONAL MITRAL REGURGITATION
- ENDOVENTRICULAR THROMBOSIS
- RV DYSFUNCTION
- PULMONARY HYPERTENSION
- VENTRICULAR DYSSINCHRONY



ESC

European Society
of Cardiology

European Heart Journal - Cardiovascular Imaging (2019) 20, 1075–1093

doi:10.1093/ehjci/jez178

EACVI CONSENSUS DOCUMENT

Multimodality imaging in the diagnosis, risk stratification, and management of patients with dilated cardiomyopathies: an expert consensus document from the European Association of Cardiovascular Imaging

Erwan Donal^{1,2*}, Victoria Delgado³, Chiara Bucciarelli-Ducci⁴, Elena Galli^{1,2}, Kristina H. Haugaa⁵, Philippe Charron^{6,7†}, Jens-Uwe Voigt⁸, Nuno Cardim⁹, P.G. Masci¹⁰, Maurizio Galderisi¹¹, Oliver Gaemperli¹², Alessia Gimelli¹³, Yigal M. Pinto^{14†}, Patrizio Lancellotti¹⁵, Gilbert Habib^{16,17}, Perry Elliott^{18,19†}, Thor Edvardsen⁵, Bernard Cosyns^{20†‡}, and Bogdan A. Popescu^{21‡}

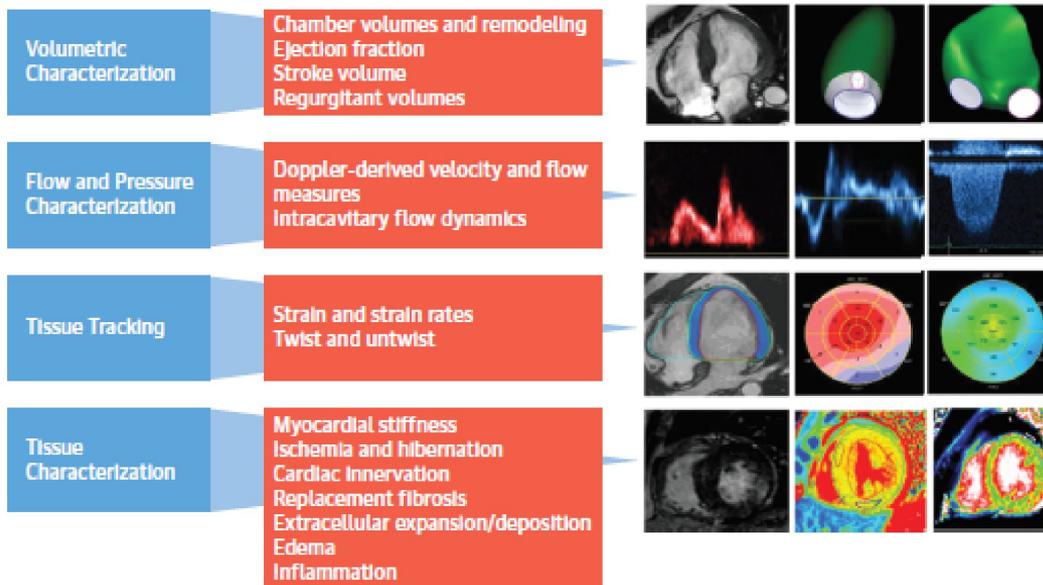
Advanced Cardiovascular Imaging in Clinical Heart Failure

Edgar Argulian, MD, MPH, Jagat Nanula, MD, PhD

JACC: HEART FAILURE
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CENTRAL ILLUSTRATION The New Framework for Application of Cardiac Imaging to Patients With Heart Failure



Argulian, E. et al. J Am Coll Cardiol HF. 2021; 3(1): 1-11.

The expansion of cardiac imaging techniques allows detailed functional assessment and tissue characterization.

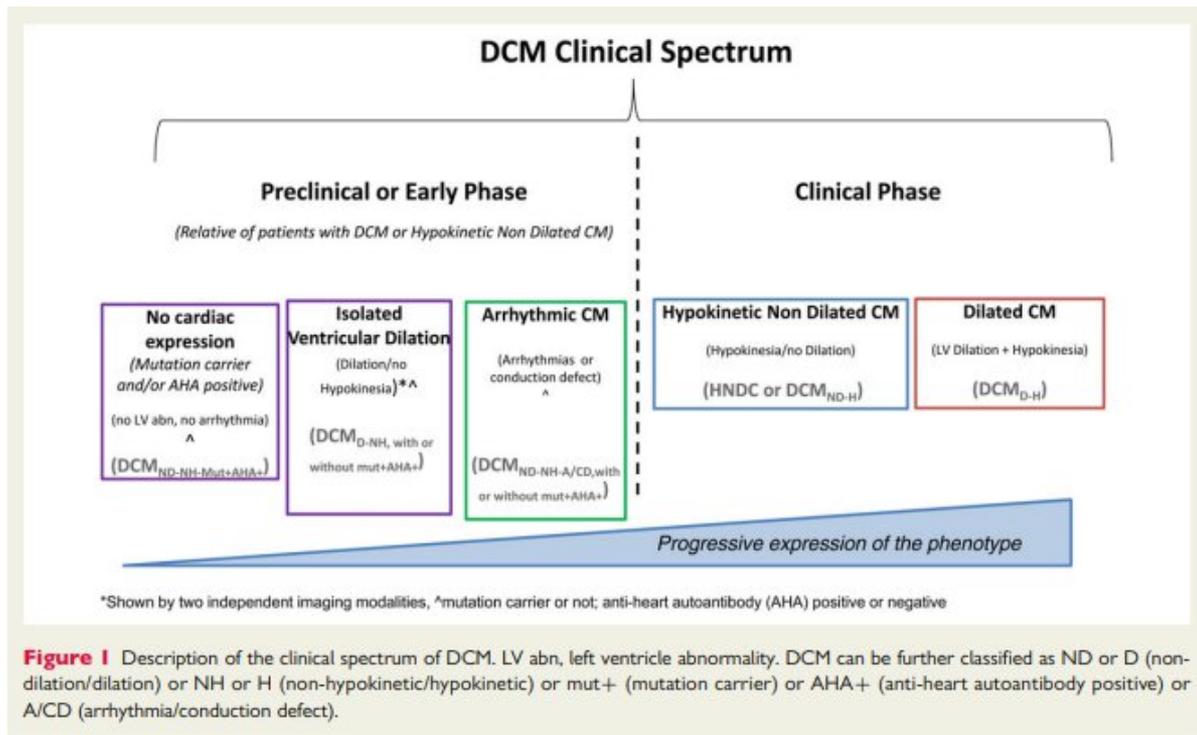


Figure 1 Description of the clinical spectrum of DCM. LV abn, left ventricle abnormality. DCM can be further classified as ND or D (non-dilation/dilation) or NH or H (non-hypokinetic/hypokinetic) or mut+ (mutation carrier) or AHA+ (anti-heart autoantibody positive) or A/CD (arrhythmia/conduction defect).

European Heart Journal, Volume 37, Issue 23, 14 June 2016,

Table 1 Recommendations for the echocardiographic assessment of LV size and function

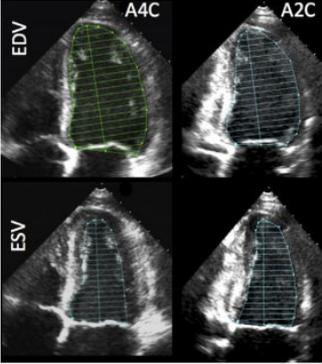
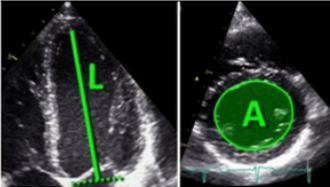
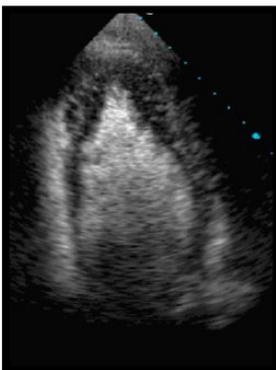
Parameter and method	Technique	Advantages	Limitations
<p>Volumes.</p> <p>Volume measurements are usually based on tracings of the blood-tissue interface in the apical four- and two-chamber views. At the mitral valve level, the contour is closed by connecting the two opposite sections of the mitral ring with a straight line. LV length is defined as the distance between the middle of this line and the most distant point of the LV contour.</p>	<p>Biplane disk summation</p> 	<ul style="list-style-type: none"> • Corrects for shape distortions • Less geometrical assumptions compared with linear dimensions 	<ul style="list-style-type: none"> • Apex frequently foreshortened • Endocardial dropout • Blind to shape distortions not visualized in the apical two- and four-chamber planes
	<p>Area-length</p> 	<ul style="list-style-type: none"> • Partial correction for shape distortion 	<ul style="list-style-type: none"> • Apex frequently foreshortened • Heavily based on geometrical assumptions • Limited published data on normal population



Table 1 Recommendations for the echocardiographic assessment of LV size and function

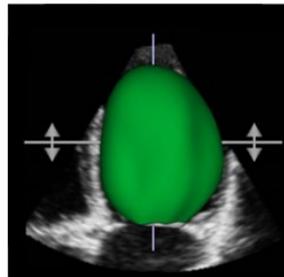


Lang et al

Endocardial border enhancement



3D data sets



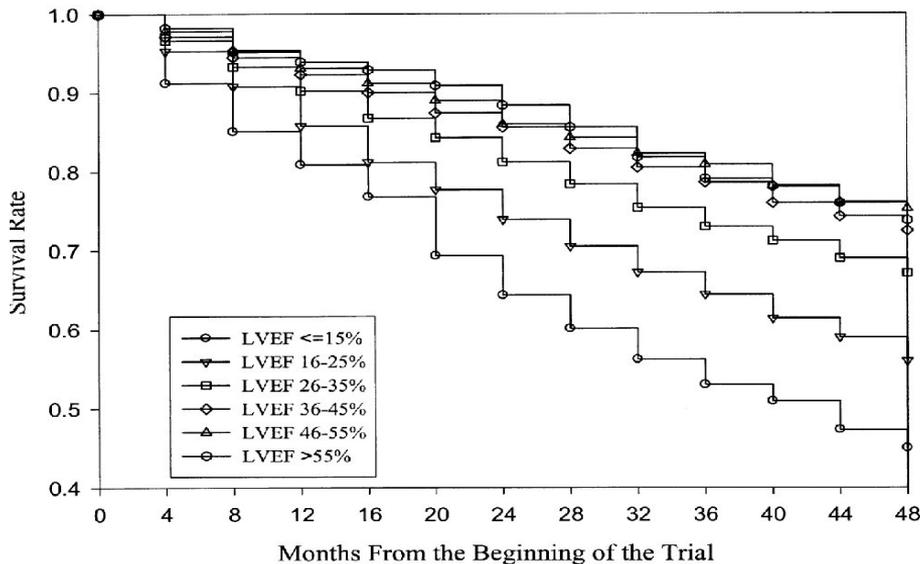
- | | |
|---|--|
| <ul style="list-style-type: none"> • Helpful in patients with suboptimal acoustic window • Provides volumes that are closer to those measured with cardiac magnetic resonance | <ul style="list-style-type: none"> • Same limitations as the above non-contrast 2D techniques • Acoustic shadowing in LV basal segments with excess contrast |
| <ul style="list-style-type: none"> • No geometrical assumption • Unaffected by foreshortening • More accurate and reproducible compared to other imaging modalities | <ul style="list-style-type: none"> • Lower temporal resolution • Less published data on normal values • Image quality dependent |



The Association of Left Ventricular Ejection Fraction, Mortality, and Cause of Death in Stable Outpatients With Heart Failure

Jepptha P. Curtis, MD,* Seth I. Sokol, MD,* Yongfei Wang, MS,* Saif S. Rathore, MPH,* Dennis T. Ko, MD,* Farid Jadbabaie, MD,* Edward L. Portnay, MD,* Stephen J. Marshallko, MD, PhD,* Martha J. Radford, MD, FACC,*§ Harlan M. Krumholz, MD, SM, FACC*†‡

New Haven, Connecticut



7,788 HF stable patients
 Mean FU: 37 mo

EF 36 - 45 %

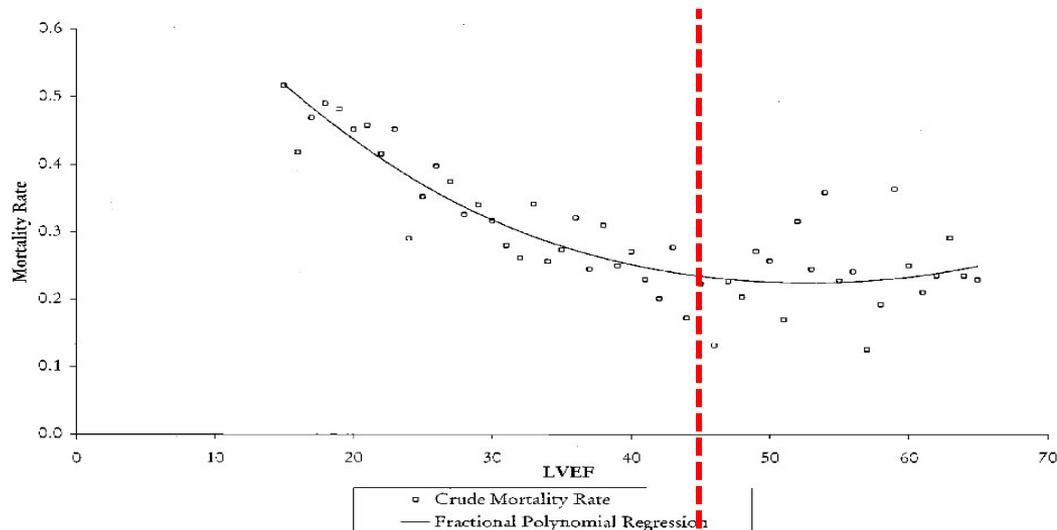




The Association of Left Ventricular Ejection Fraction, Mortality, and Cause of Death in Stable Outpatients With Heart Failure

Jeptha P. Curtis, MD,* Seth I. Sokol, MD,* Yongfei Wang, MS,* Saif S. Rathore, MPH,* Dennis T. Ko, MD,* Farid Jadbabaie, MD,* Edward L. Portnay, MD,* Stephen J. Marshallko, MD, PhD,* Martha J. Radford, MD, FACC,*§ Harlan M. Krumholz, MD, SM, FACC*†‡

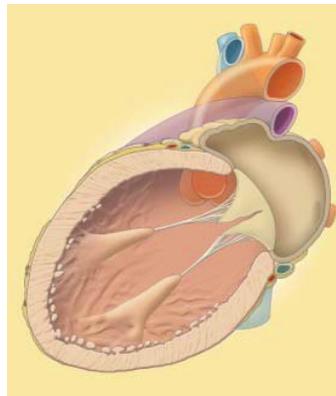
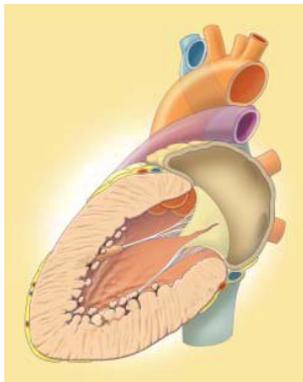
New Haven, Connecticut



45 %



CARDIAC REMODELING



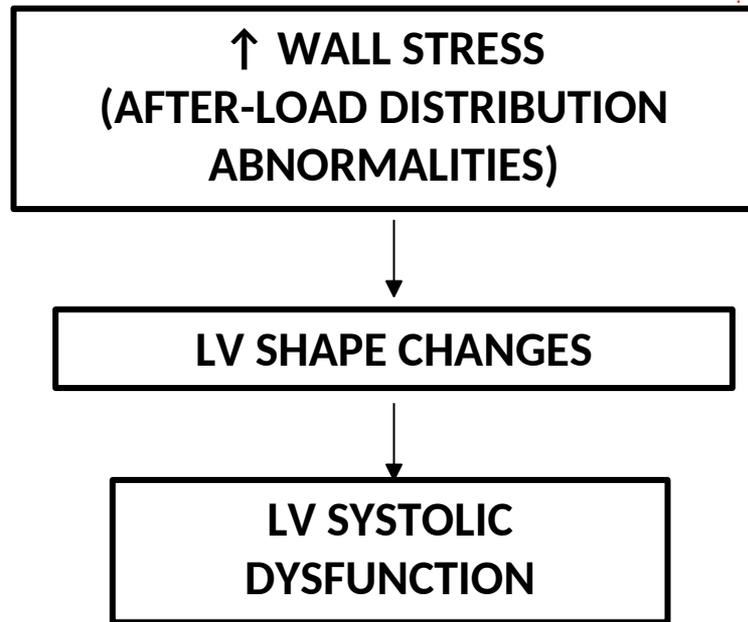
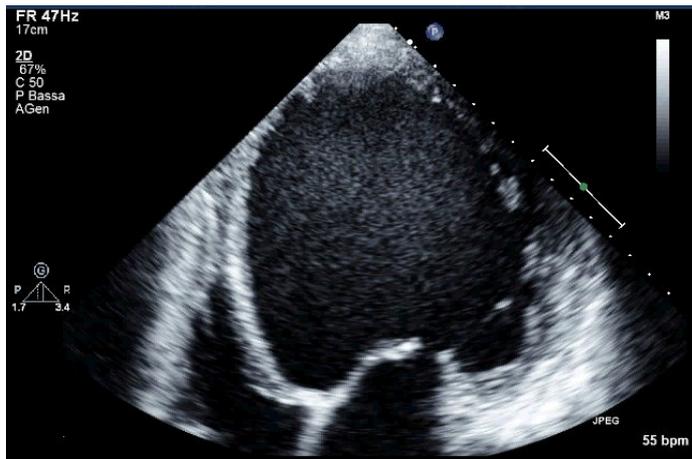
Cardiac remodelling may be defined as genome expression, molecular, cellular and interstitial changes that are manifested clinically as changes in size, shape and function of the heart after cardiac injury (Cohn et al; J. Am. Coll. Cardiol.; 2000;35;569-582)

LV progressive dilation

+

Ventricular geometry alteration

Morphology: + sphere, - ellypse



Left Ventricular Reverse Remodeling (LVRR)

Regaining of near-to-normal ventricular dimensions and form



Prevalence and Prognostic Significance of Left Ventricular Reverse Remodeling in Dilated Cardiomyopathy Receiving Tailored Medical Treatment

Marco Merlo, MD,* Stylianos A. Pyxaras, MD,* Bruno Pinamonti, MD,* Giulia Barbati, PHD,†
Andrea Di Lenarda, MD,‡ Gianfranco Sinagra, MD*

Study population: 242 DCM pts – 1988-1997 – Follow-up: 123±61 mo

LVR (evaluated at 24±7 months)

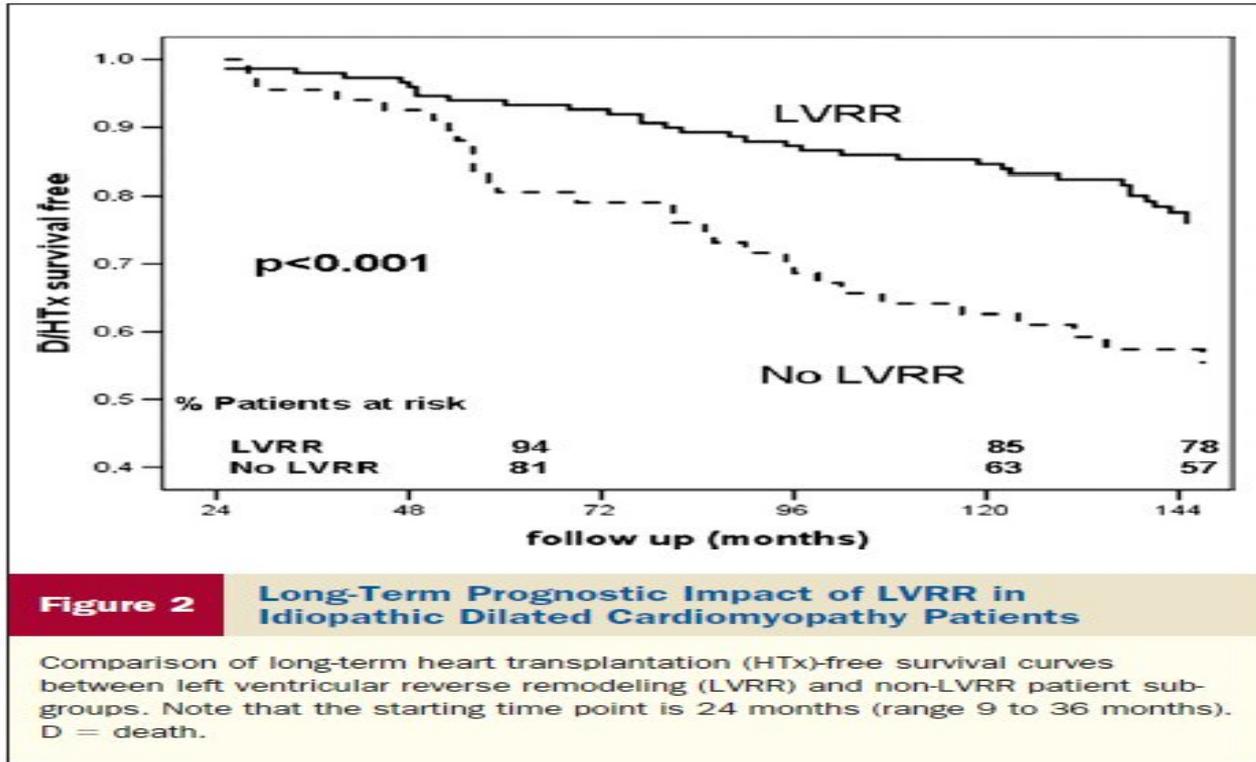
- LVEF ↑ ≥10 points % or ≥50%
- Indexed LVEDD ↓ ≥10% o ≤33 mm/m²

All patients on OPTIMAL MEDICAL TREATMENT

LVR was found in 89 of 242 patients (37%).



PROGNOSTIC ROLE OF LV REVERSE REMODELING

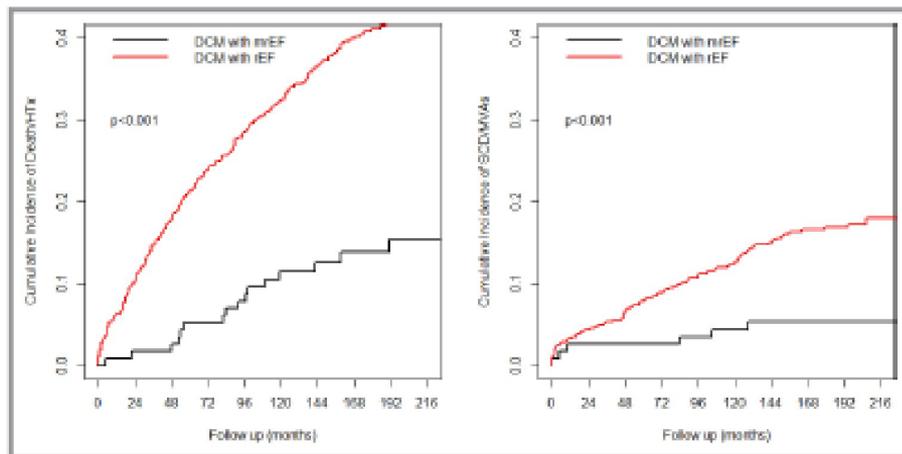




Dilated Cardiomyopathy With Mid-Range Ejection Fraction at Diagnosis: Characterization and Natural History

Piero Gentile, MD; Marco Merlo, MD; Antonio Cannatà, MD; Marco Gobbo, MD; Jessica Artico, MD; Davide Stolfo, MD; Marta Gigli, MD; Federica Ramani; Giulia Barbati, PhD; Bruno Pinamonti, MD; Gianfranco Sinagra, MD

Conclusions—mrEF identified a consistent subgroup of dilated cardiomyopathy patients diagnosed in an earlier stage with subsequent apparent better long-term evolution. However, 17% of these patients evolved into rEF despite the use of medical therapy. A baseline restrictive LV filling pattern was independently associated with subsequent evolution to rEF. (*J Am Heart Assoc.* 2019;8:e010705. DOI: 10.1161/JAHA.118.010705.)



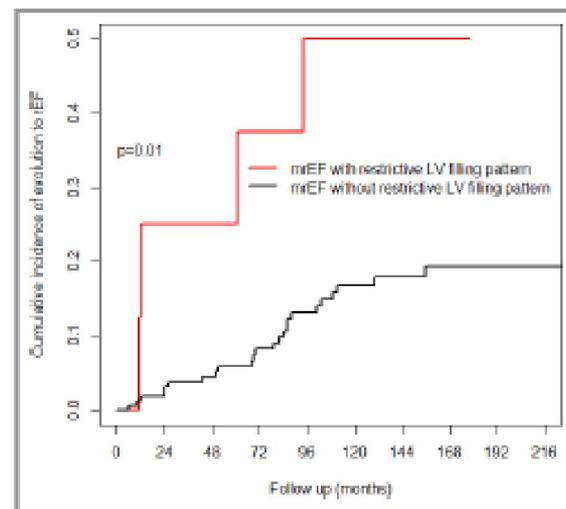
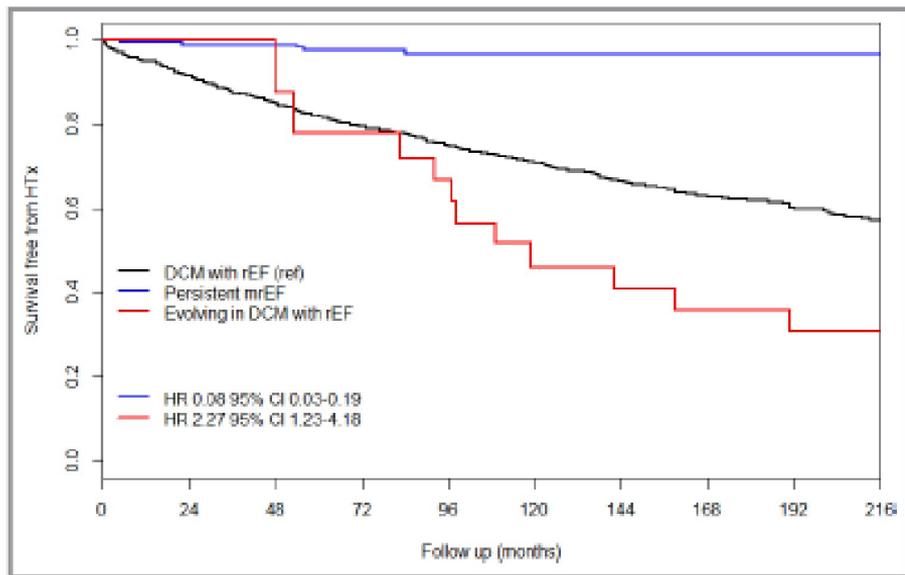



Table 1 Recommendations for the echocardiographic assessment of LV size and function

Parameter and method	Technique	Advantages	Limitations
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Global Longitudinal Strain.

Peak value of 2D longitudinal speckle tracking derived strain (%).



- Angle independent
- Established prognostic value
- Vendor dependent

Table 2 Normal values for 2D echocardiographic parameters of LV size and function according to gender

Parameter	Male		Female	
	Mean \pm SD	2-SD range	Mean \pm SD	2-SD range
LV internal dimension				
Diastolic dimension (mm)	50.2 \pm 4.1	42.0–58.4	45.0 \pm 3.6	37.8–52.2
Systolic dimension (mm)	32.4 \pm 3.7	25.0–39.8	28.2 \pm 3.3	21.6–34.8
LV volumes (biplane)				
LV EDV (mL)	106 \pm 22	62–150	76 \pm 15	46–106
LV ESV (mL)	41 \pm 10	21–61	28 \pm 7	14–42
LV volumes normalized by BSA				
LV EDV (mL/m ²)	54 \pm 10	34–74	45 \pm 8	29–61
LV ESV (mL/m ²)	21 \pm 5	11–31	16 \pm 4	8–24
LV EF (biplane)	62 \pm 5	52–72	64 \pm 5	54–74

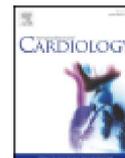


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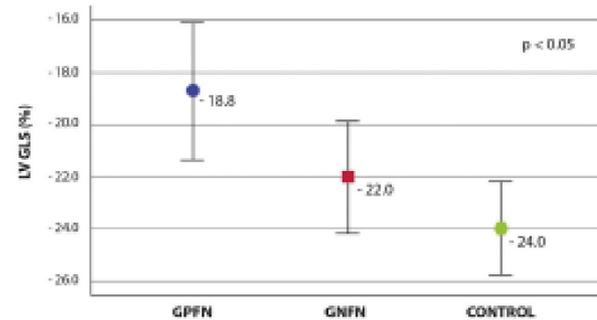
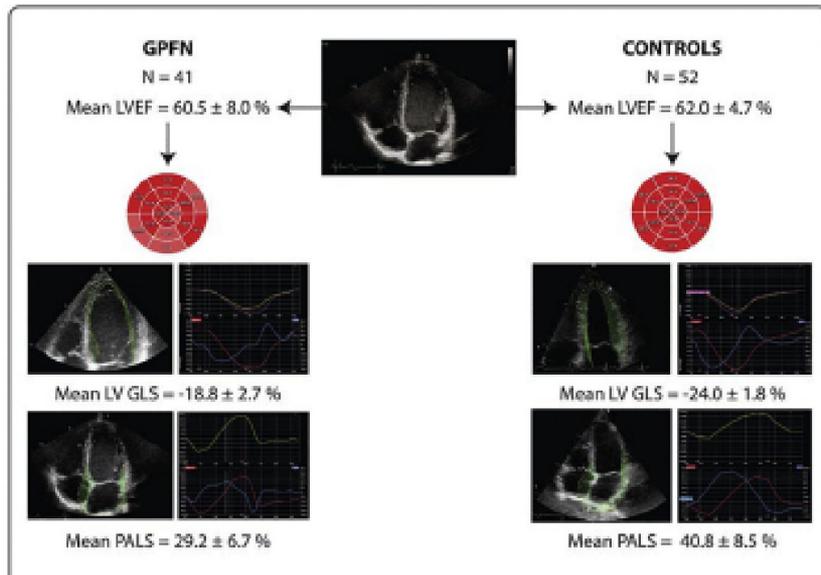
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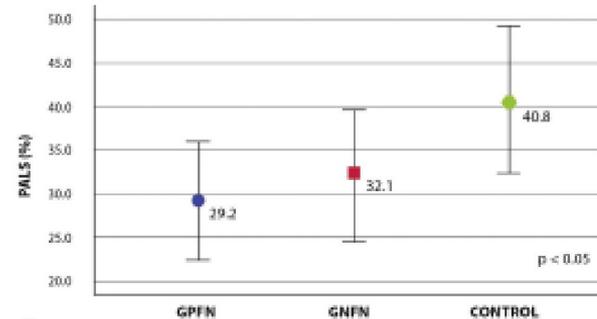
High prevalence of subtle systolic and diastolic dysfunction in genotype-positive phenotype-negative relatives of dilated cardiomyopathy patients

Alessia Paldino^{a,1,2}, Giulia De Angelis^{a,1,2}, Matteo Dal Ferro^{a,2}, Giorgio Faganello^{b,2}, Aldostefano Porcari^{a,2}, Giulia Barbati^{c,2}, Renata Korcova^{a,2}, Piero Gentile^{a,2}, Jessica Artico^{a,2}, Antonio Cannatà^{a,2}, Marta Gigli^{a,2}, Bruno Pinamonti^{a,2}, Marco Merlo^{a,*,2}, Gianfranco Sinagra^{a,2}

Conclusion: Despite standard echocardiographic parameters are within the normal range, LV GLS and PALS are lower in GPN relatives of DCM patients when compared to healthy individuals, suggesting a consistent proportion of subtle systolic and diastolic dysfunction in this population.



A



B



Incremental Prognostic Value of Assessing Left Ventricular Myocardial Mechanics in Patients With Chronic Systolic Heart Failure

Hirohiko Motoki, MD, PhD,* Allen G. Borowski, RDCS,* Kevin Shrestha, AB,*
 Richard W. Troughton, MB, ChB, PhD,† W. H. Wilson Tang, MD,* James D. Thomas, MD,*
 Allan L. Klein, MD*
 (J Am Coll Cardiol 2012;60:

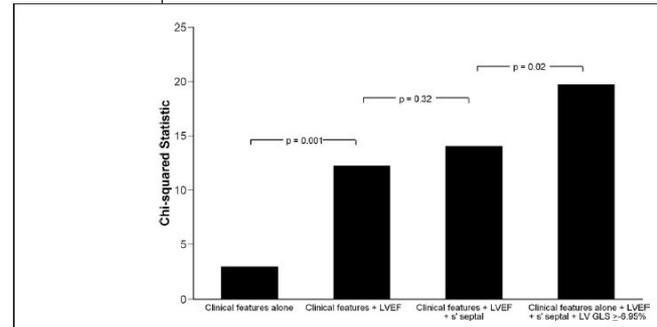
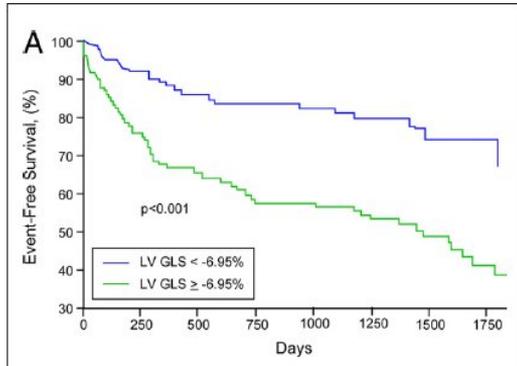
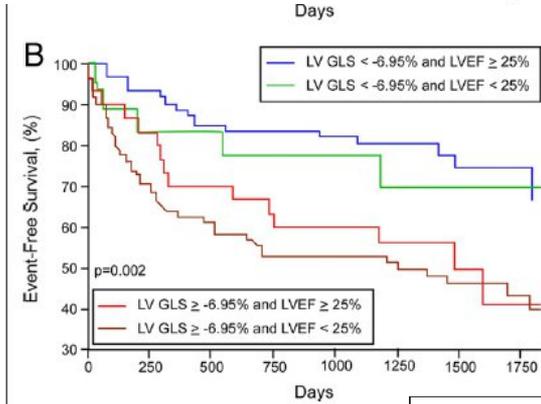
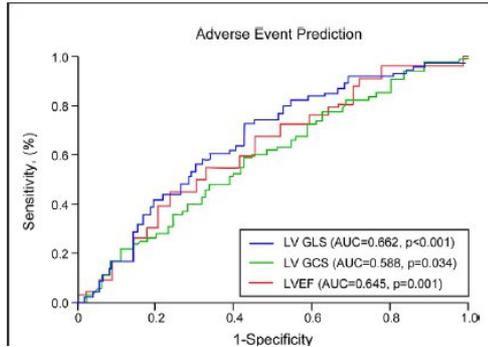
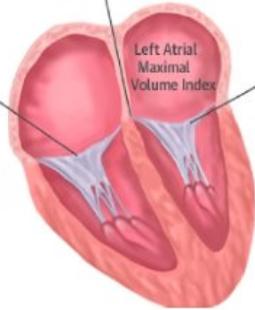
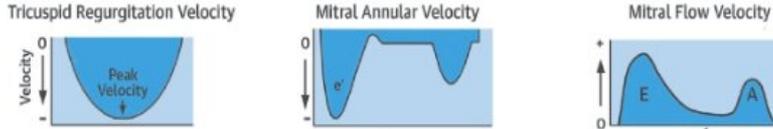


Figure 6 Incremental Value of LV GLS Over Conventional Parameters



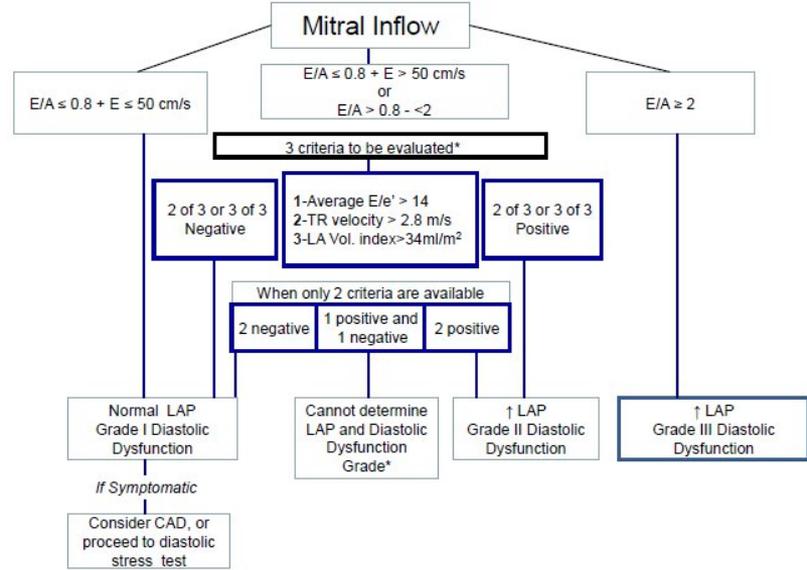
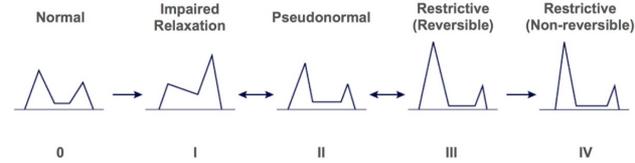
A. Echocardiography Parameters for Estimation of LV Filling Pressure



Parameter	Cutoff Value
• Peak Tricuspid Regurgitation Velocity	>2.8 m/sec
• E/e'	>14
• Left Atrial Maximal Volume Index	>34 ml/m ²

ASE/EACVI GUIDELINES AND STANDARDS

Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging

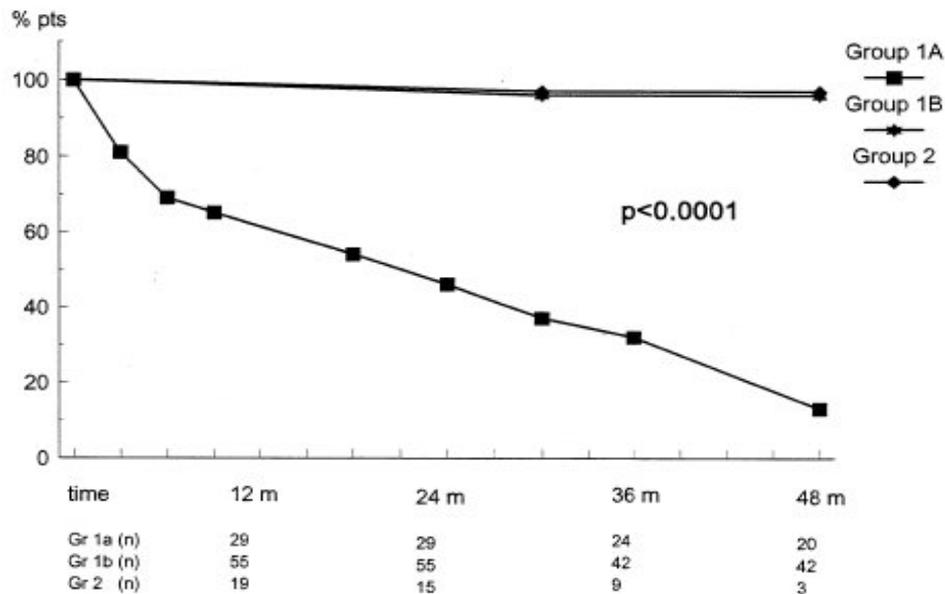


(* : LAP indeterminate if only 1 of 3 parameters available. Pulmonary vein S/D ratio <1 applicable to conclude elevated LAP in patients with depressed LV EF)

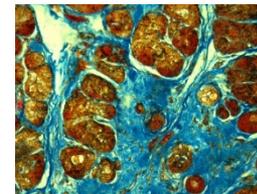


Persistence of Restrictive Left Ventricular Filling Pattern in Dilated Cardiomyopathy: An Ominous Prognostic Sign

BRUNO PINAMONTI, MD, MASSIMO ZECCHIN, MD, ANDREA Di LENARDA, MD,
 DARIO GREGORI, MA, PhD, GIANFRANCO SINAGRA, MD, FULVIO CAMERINI, MD



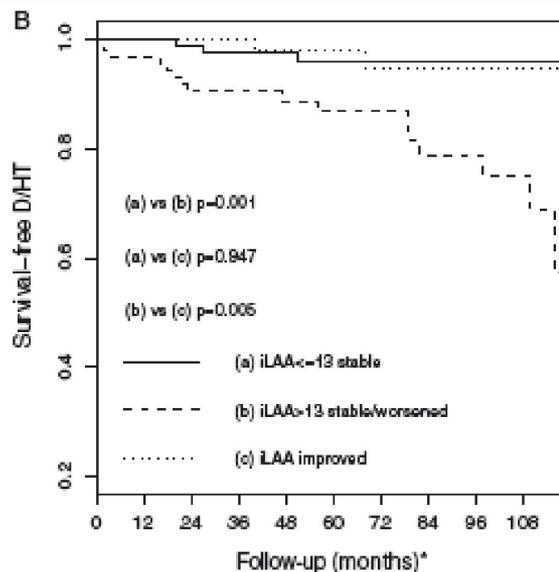
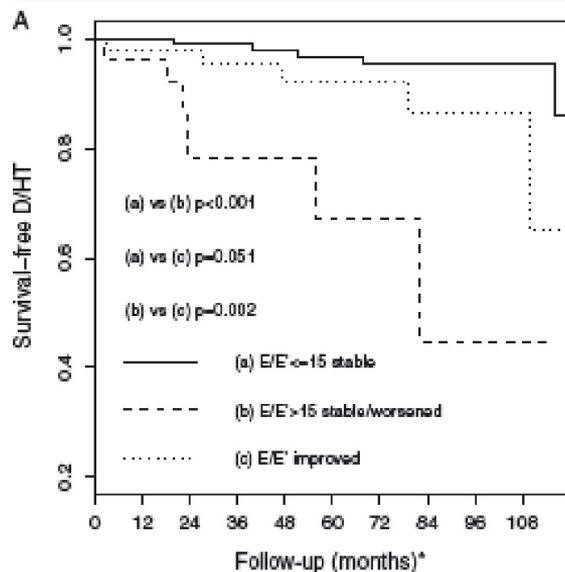
(J Am Coll Cardiol 1997;29:604-12)





Prognostic impact of short-term changes of E/E' ratio and left atrial size in dilated cardiomyopathy

Marco Merlo^{1*}, Davide Stolfo¹, Marco Gobbo¹, Giacomo Gabassi¹, Giulia Barbat², Paola Naso¹, Gabriele Secoli¹, Andrea Boscutti¹, Federica Ramani¹, Marta Gigli¹, Bruno Pinamonti¹, and Gianfranco Sinagra¹

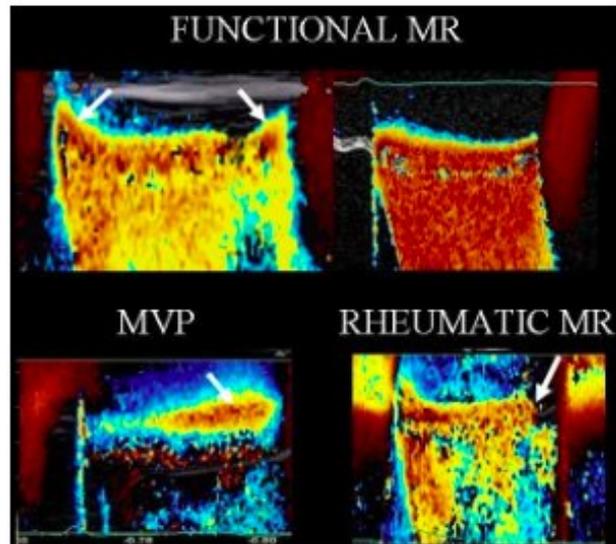
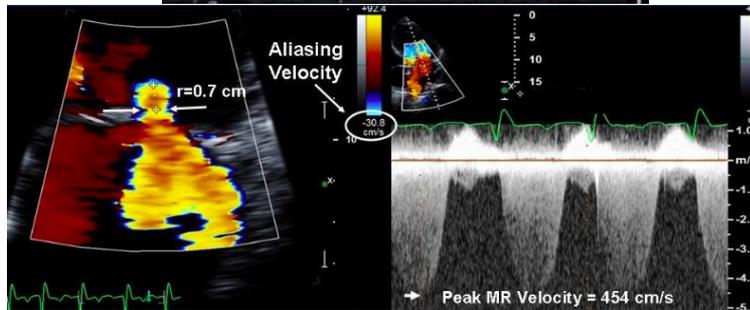
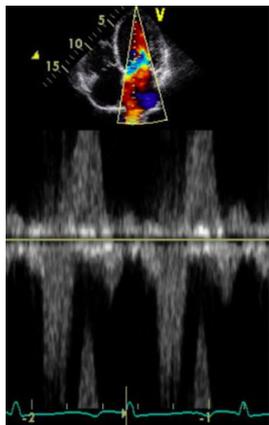
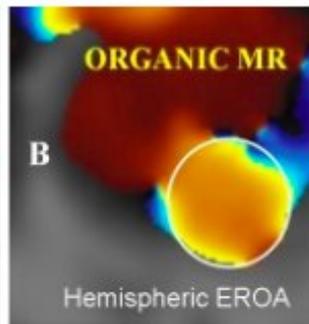
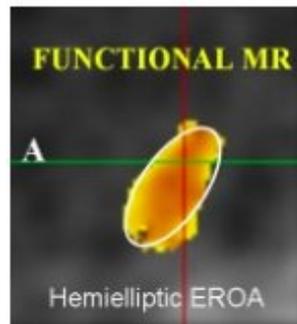
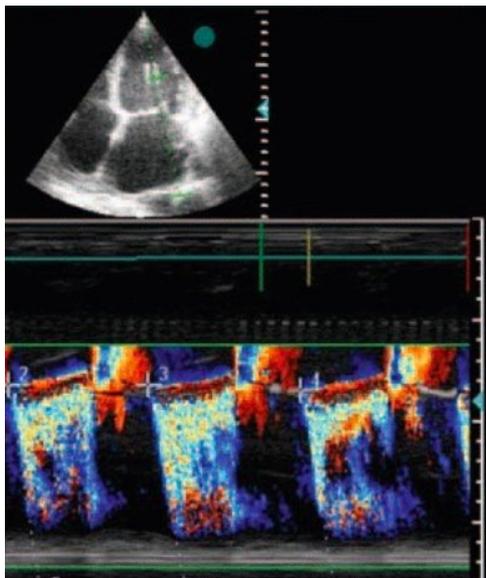
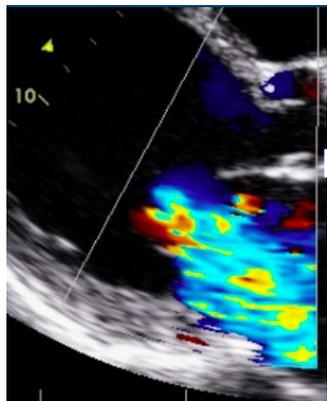


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Insufficienza Mitralica





Functional Mitral Regurgitation Outcome and Grading in Heart Failure With Reduced Ejection Fraction

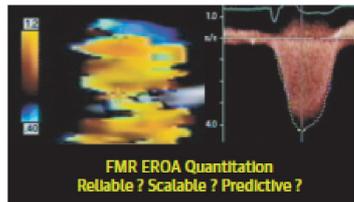


Giovanni Benfari, MD, Clémence Antoine, MD, Benjamin Essayagh, MD, Roberta Batista, MD, Joseph Maalouf, MD, Andrea Rossi, MD, Francesco Grigioni, MD, Prabin Thapa, MS, Hector I. Michelena, MD, Maurice Enriquez-Sarano, MD

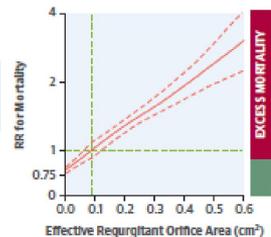
CONCLUSIONS In HF_{rEF}, FMR is skewed towards smaller EROA. Nevertheless, when measured in routine practice, EROA is the strongest independent FMR determinant of survival after diagnosis. Excess mortality increases exponentially above the threshold of 0.10 cm², with a much steeper slope than in DMR, for any EROA increment. An expanded EROA-based stratification, superior to existing grading schemes in determining survival, should allow guideline harmonization. (J Am Coll Cardiol Img 2021;14:2303-2315) © 2021 by the American College of Cardiology Foundation.



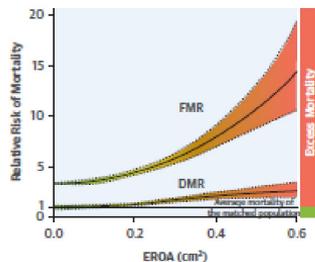
CENTRAL ILLUSTRATION Outcome and Harmonized Grading of Functional Mitral Regurgitation Effective Regurgitation Orifice Area in Heart Failure With Reduced Ejection Fraction



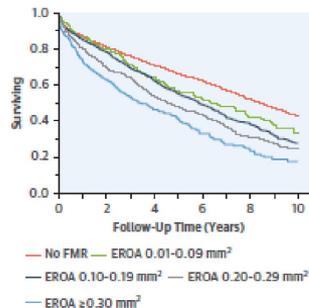
Quantified FMR cohort:
 N = 6,381
 Average EF 36%
 In routine practice



Much steeper excess mortality vs. general population than DMR



EROA skewed towards low values but independently determines survival EROA 0.10 cm² threshold of excess mortality



An expanded scale of FMR grading based on EROA to harmonize guidelines

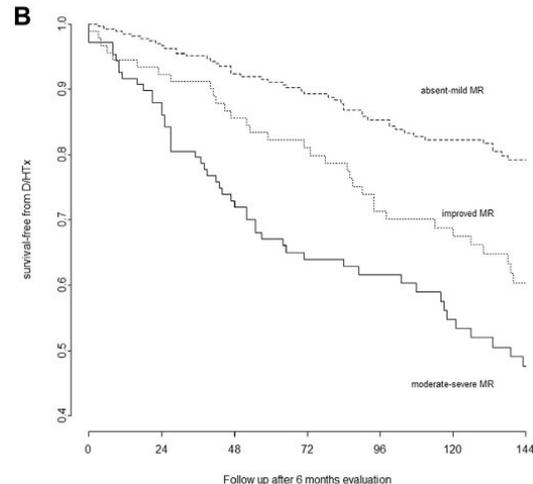
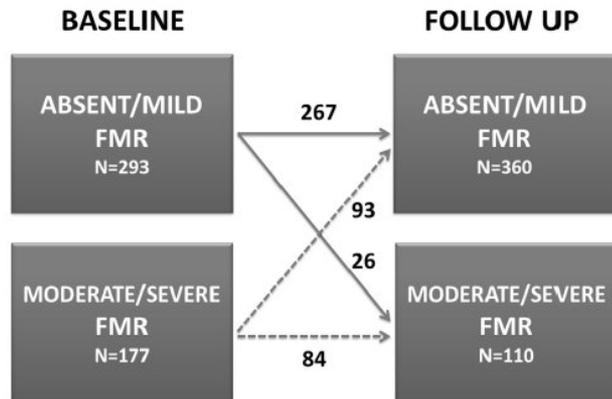
Benfari, G. et al. J Am Coll Cardiol Img. 2021;14(12):2303-2315.

(Top left) Example of effective regurgitant orifice area (EROA) measurement. (Top right) Spline curve of mortality under medical management within the heart failure with reduced ejection fraction cohort. Excess mortality (HR >1.00) appears for low EROA ~0.10 cm², then increases steadily with increasing EROA values without plateau. (Lower right) Survival under medical management stratified by expanded strata of EROA in functional mitral regurgitation (FMR). (Lower left) Spline curves representing excess mortality risk (vs. expected mortality of the Minnesota general population specific for each cohort) according to EROA values for FMR and degenerative mitral regurgitation (DMR). A risk ratio of 1 represents mortality equivalent to that expected in Minnesota. FMR curve displays earlier rise with sustained and exponentially steeper increase in risk with even modest increases in EROA versus linear and slower pace in DMR.



Early Improvement of Functional Mitral Regurgitation in Patients With Idiopathic Dilated Cardiomyopathy

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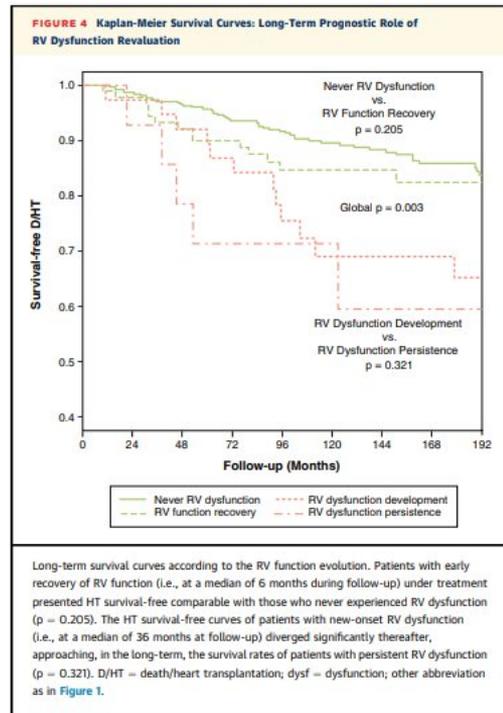
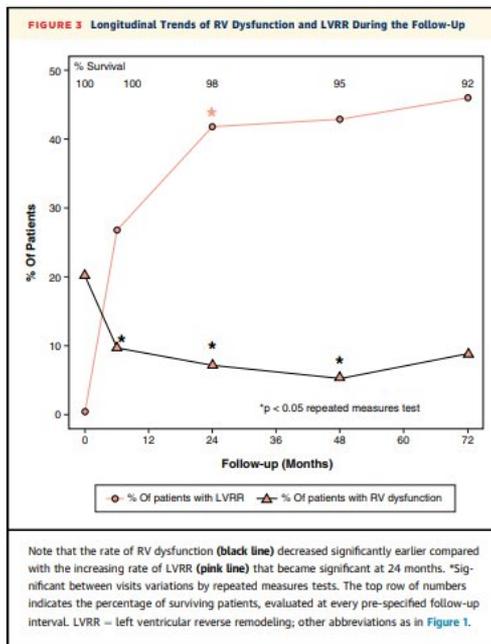


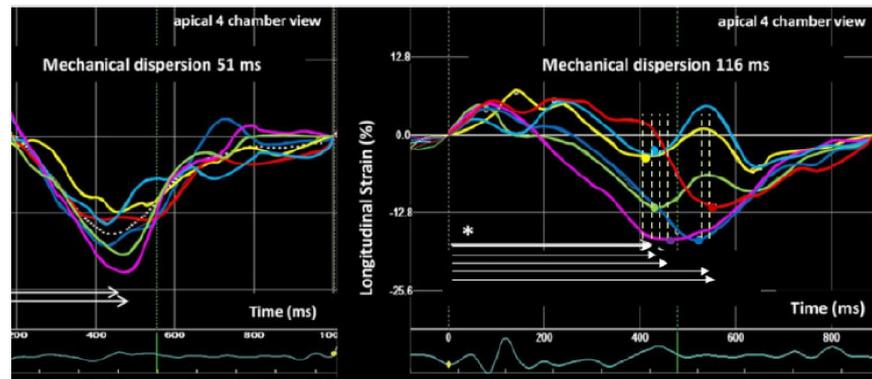
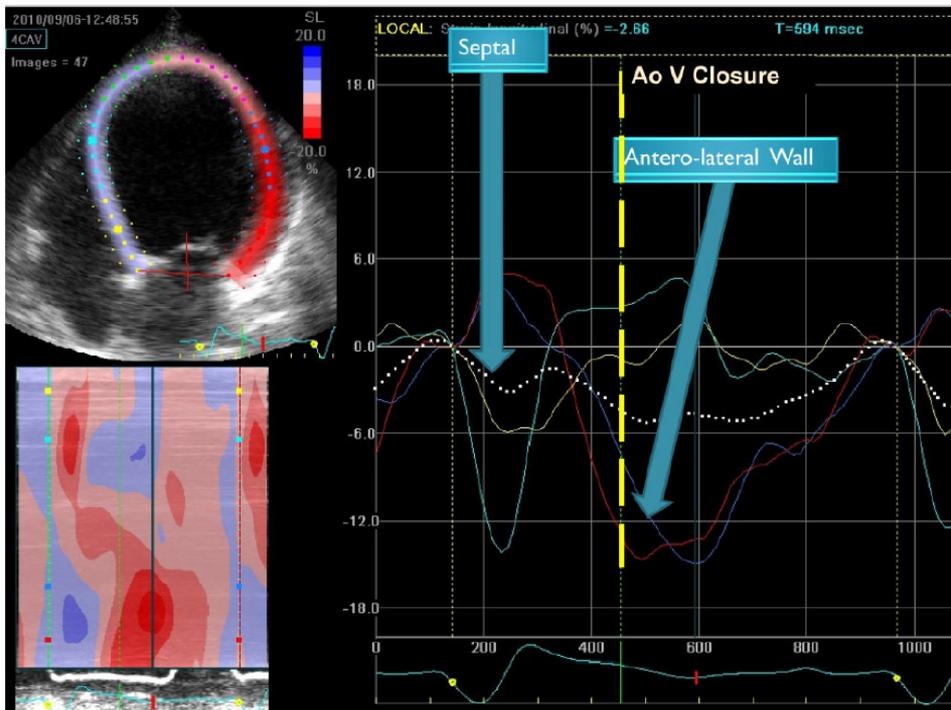
In conclusion, in a large cohort of patients with IDC receiving optimal medical treatment, early improvement of FMR was frequent (53%) and emerged as a favorable independent prognostic factor with an incremental short- and long-term power compared with the baseline evaluation. © 2015 Elsevier Inc. All rights reserved. (Am J Cardiol 2015;■:■—■)



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

Marco Merlo, MD,¹ Marco Gobbo, MD,² Davide Stolfo, MD,³ Pasquale Losurdo, MD,³ Federica Ramani, PhD,⁴ Giulia Barbati, PhD,^{5,6} Alberto Pivetta, MD,⁵ Andrea Di Lenarda, MD,⁵ Marco Anzini, MD,⁵ Marta Gigli, MD,³ Bruno Pinamonti, MD,³ Gianfranco Sinagra, MD³





Normal

Abnormal



Results of the Predictors of Response to CRT (PROSPECT) Trial

Eugene S. Chung, MD; Angel R. Leon, MD; Luigi Tavazzi, MD; Jing-Ping Sun, MD; Petros Nihoyannopoulos, MD; John Merlino, MD; William T. Abraham, MD; Stefano Ghio, MD; Christophe Leclercq, MD; Jeroen J. Bax, MD; Cheuk-Man Yu, MD, FRCP; John Goresan III, MD; Martin St John Sutton, FRCP; Johan De Sutter, MD, PhD; Jaime Murillo, MD

Circulation

Chung et al Echocardiographic Predictors of Response to CRT

Conclusion—Given the modest sensitivity and specificity in this multicenter setting despite training and central analysis, no single echocardiographic measure of dyssynchrony may be recommended to improve patient selection for CRT beyond current guidelines. Efforts aimed at reducing variability arising from technical and interpretative factors may improve the predictive power of these echocardiographic parameters in a broad clinical setting. (*Circulation*. 2008;117:2608-2616.)

characteristics fulfill the current indications for CRT and whose clinical response rates are comparable to other trials of CRT,¹ the findings of PROSPECT suggest that various echocardiographic measures of ventricular dyssynchrony as applied in this study were unable to distinguish responders from nonresponders to a degree that should affect clinical decision making. Thus, current clinical criteria, including the ECG, remain the standard for CRT patient selection.

Given the background of numerous smaller, single-center studies demonstrating a strong correlation between echocardiographic measures of mechanical dyssynchrony and clinical response to CRT,¹¹⁻¹⁸ the results of PROSPECT are somewhat surprising. There may be several explanations for this discrepancy.

Echocardiography, dyssynchrony, and the response to cardiac resynchronization therapy

Cheuk-Man Yu^{1*}, John E. Sanderson¹, and John Gorcsan III²

Prospect trial

In retrospect, this study was blighted with major problems ranging from patient selection, methodology, technical expertise, ageing echocardiographic equipment from three different vendors, which were not standardized for frame rates with three different software programmes for offline analysis. In addition, three different core laboratories were used for echocardiography dyssynchrony analyses that were not calibrated for dyssynchrony analysis, which introduced the possibility of variability in analysis. These limitations have been highlighted elsewhere but are serious enough to undermine the conclusions.^{5,6,32} For example, 20.2% of patients had a LVEF more than 35% suggesting inclusion of less severe heart failure patients who did not meet the entry criteria or guideline recommendations for CRT. Furthermore, 37.8% had an LV end-diastolic dimension <65 mm, which raises the question how reverse remodelling, which was one of the primary endpoints, can be expected to occur in a non-dilated ventricle. In addition, interobserver variability was high. The study used a reduction of LV end-systolic volume >15% to define volumetric responders, although interobserver variability for this parameter was 14.5%, which was unacceptably high and may not be reliable to detect true responders.³ The mediocre image quality acquired from ageing echocardiographic machines also preclude competent off-line analysis of colour-coded TDI images, and in fact only 39% of enrolled patients had dyssynchrony analysis from the 12 LV segments. Proficiency with any new technology takes time to acquire.

The PROSPECT trial was started in 2003 when the implantation technique of CRT devices was already mature, it was still the beginning of dyssynchrony analysis, in which technical training and knowledge transfer had yet to develop. With the recent advancement of echocardiographic technologies for dyssynchrony assessment and importantly mastering of skills for dyssynchrony assessment in many echocardiographic centres worldwide, now will be good time to conduct another multicentre trial to address whether baseline dyssynchrony can predict favourable response and clinical outcome to CRT. Therefore, the PROSPECT trial should not be a reason for discarding the whole concept of mechanical dyssynchrony, which is still the most likely target of CRT or the need for identifying non-responders to save them the hazards of a treatment that has risks and will provide them with no benefit and possibly worsen their condition.





ECOCARDIOGRAFIA NELLA CMPD: OLTRE LA FE? CONCLUSIONI (I)

- Il calcolo dei volumi e della FE del ventricolo sinistro è ancora un dato fondamentale nella CMPD: importanza diagnostica e prognostica; guida alla terapia e nel follow-up
- Necessario calcolo accurato, riproducibilità accettabile da verificare, ev. uso del contrasto, eco 3D se buona esperienza del Centro
- Tuttavia da ricordare i limiti della FE: dipendente dal carico, scarsa correlazione coi sintomi...



ECOCARDIOGRAFIA NELLA CMPD: OLTRE LA FE? CONCLUSIONI (II)

- L'analisi dello strain (GLS) con la metodica dello speckle tracking è potenzialmente utile nella CMPD anche se ancora non rientra nelle linee guida gestionali della malattia
- Utili per caratterizzare la CMPD specie nella stratificazione prognostica e nel follow-up sono parametri di funzione diastolica, l'IM, il Vd_x