#FullPhysiology

In Daily Practice

CMD assessment to predict left ventricular reverse remodelling in idiopathic DCM

MICROREV-DCM Study

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MICROREV Study – Background and Rationale

- CMD may contribute to progressive LV dysfunction and dilation in patients with DCM.
- Left ventricular reverse remodeling (LVRR) is an important marker of successful treatment, and it is associated with a lower long-term mortality.
- LVRR occurs only in about 1/3 of cases.
- Identification of predictors of LVRR is challenging but of utmost importance.
- Coronary microcirculation may represent a novel therapeutic target to promote reverse remodeling in patients with dilated cardiomyopathy.

Lima MF et al. J Am Soc Echocardiogr. 2013;26(3):278-287.
Merlo M et al. J Am Coll Cardiol. 2011;57(13):1468-1476.
Kubanek M et al. J Am Coll Cardiol. 2013; 61: 54–63.

European Heart Journal – Cardiovascular Imaging (2015) **16**, 900–909
doi:10.1093/ehjci/jev012

Quantification of coronary flow reserve in patients with ischaemic and non-ischaemic cardiomyopathy and its association with clinical outcomes

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Aims Patients with left ventricular systolic dysfunction frequently show abnormal coronary vascular function, even in the absence of overt coronary artery disease. Moreover, the severity of vascular dysfunction might be related to the aetiology of cardiomyopathy.

We sought to determine the incremental value of assessing coronary vascular dysfunction among patients with ischaemic (ICM) and non-ischaemic (NICM) cardiomyopathy at risk for adverse cardiovascular outcomes.

Methods and results Coronary flow reserve (CFR, stress/rest myocardial blood flow) was quantified in 510 consecutive patients with rest left ventricular ejection fraction (LVEF) ≤45% referred for rest/stress myocardial perfusion PET imaging. The primary end point was a composite of major adverse cardiovascular events (MACE) including cardiac death, heart failure hospitalization, late revascularization, and aborted sudden cardiac death.

Median follow-up was 8.2 months. Cox proportional hazards model was used to adjust for clinical variables. The annualized MACE rate was 26.3%. Patients in the lowest two tertiles of CFR (CFR ≤ 1.65) experienced higher MACE rates than those in the highest tertile (32.6 vs. 15.5% per year, respectively, $P = 0.004$), irrespective of aetiology of cardiomyopathy.

Conclusion Impaired coronary vascular function, as assessed by reduced CFR by PET imaging, is common in patients with both ischaemic and non-ischaemic cardiomyopathy and is associated with MACE.

Keywords coronary flow reserve • cardiomyopathy • positron emission tomography • myocardial blood flow • coronary vascular dysfunction • clinical outcomes

Prognostic Role of Myocardial Blood Flow Impairment in Idiopathic Left Ventricular Dysfunction

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Background—Depressed myocardial blood flow (MBF) has been reported in dilated cardiomyopathy. The aim of this study was to investigate whether MBF impairment is an independent predictor of prognosis in patients with idiopathic left ventricular (LV) dysfunction.

Methods and Results—Sixty-seven patients (52 male, mean age 52±12 years) with different degrees of idiopathic LV systolic dysfunction (average LV ejection fraction, 0.34±0.10; range, 0.07 to 0.49) were prospectively enrolled. Thirty-four subjects (51%) had no history of heart failure symptoms at enrollment (NYHA class I). All patients underwent clinical and functional evaluation and a PET study to measure absolute MBF at rest and after intravenous dipyridamole. During a mean follow-up of 45±37 months, 24 patients had major cardiac events, including cardiac death in 8 and development or progression of heart failure in 16 patients. Multivariate regression analysis (Cox proportional hazards model) revealed heart rate (χ^2 11.06, $P<0.001$), LV end-diastolic dimension (χ^2 11.73, $P<0.001$), and dipyridamole MBF (χ^2 11.04, $P<0.001$) as independent predictors of subsequent cardiac events. Dipyridamole MBF $\leq 1.36\ mL \cdot min^{-1} \cdot g^{-1}$ was associated with an increase in the relative risk of death, development, or progression of heart failure of 3.5 times over other more common clinical and functional variables.

Conclusions—The present study demonstrates that severely depressed MBF is a predictor of poor prognosis in patients with idiopathic LV dysfunction independently of the degree of LV functional impairment and of the presence of overt heart failure. (***Circulation*. 2002;105:186-193.**)

Regional Coronary Flow and Contractile Reserve in Patients With Idiopathic Dilated Cardiomyopathy

Emmanuel I. Skalidis, MD, Frangiskos I. Parthenakis, MD, Alexandros P. Patrianakos, MD, Michael I. Hamilos, MD, Panos E. Vardas, MD, PHD, FESC, FACC
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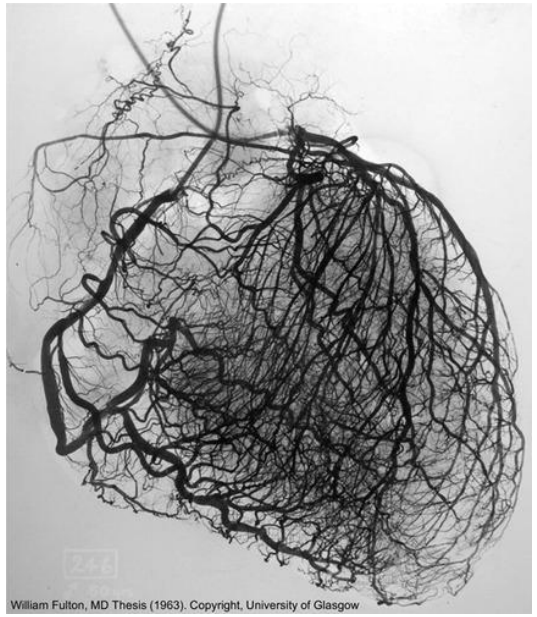
Patients with IDCM have alterations in regional coronary flow and reduced CFR. Furthermore, the correlation between regional CFR and the corresponding contractile reserve indicates that microvascular dysfunction may have a pathophysiologic role in the evolution of the disease. (J Am Coll Cardiol 2004;44:2027–32) © 2004 by the American College of Cardiology Foundation



Depressed Coronary Flow Reserve Is Associated With Decreased Myocardial Capillary Density in Patients With Heart Failure Due to Idiopathic Dilated Cardiomyopathy

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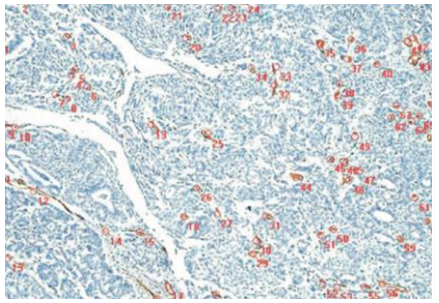

Coronary Microcirculation Remodeling in Patients with Idiopathic Dilated Cardiomyopathy

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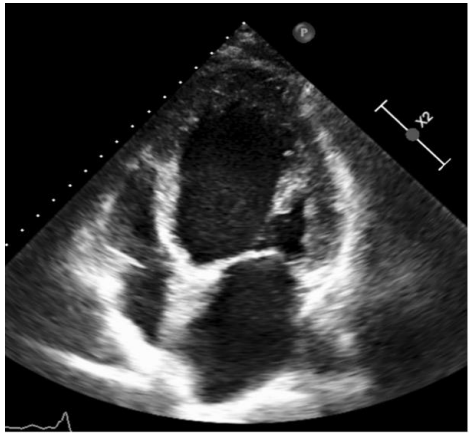

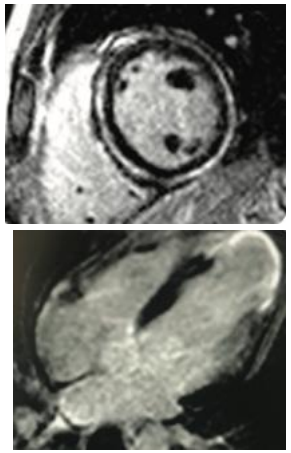

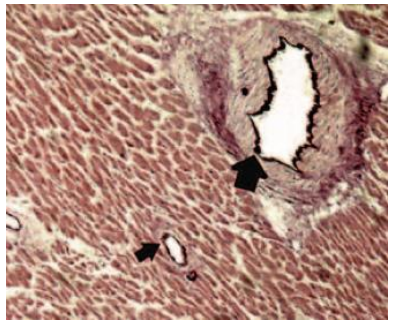

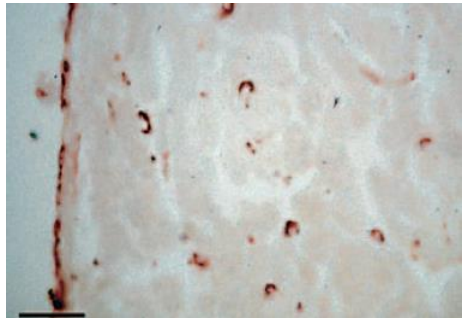

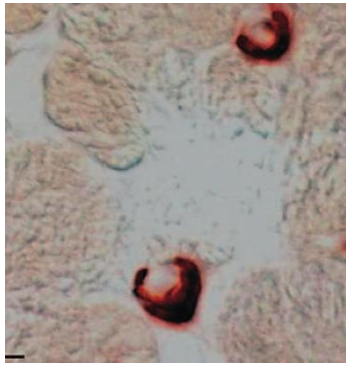

JACC: CARDIOVASCULAR IMAGING VOL. 12, NO. 8, 2019

ORIGINAL RESEARCH

Microvascular Dysfunction in Dilated Cardiomyopathy

A Quantitative Stress Perfusion Cardiovascular Magnetic Resonance Study

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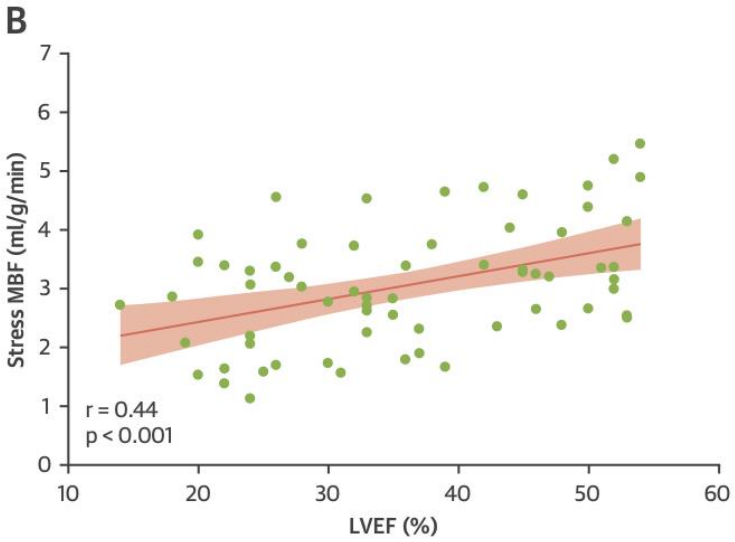

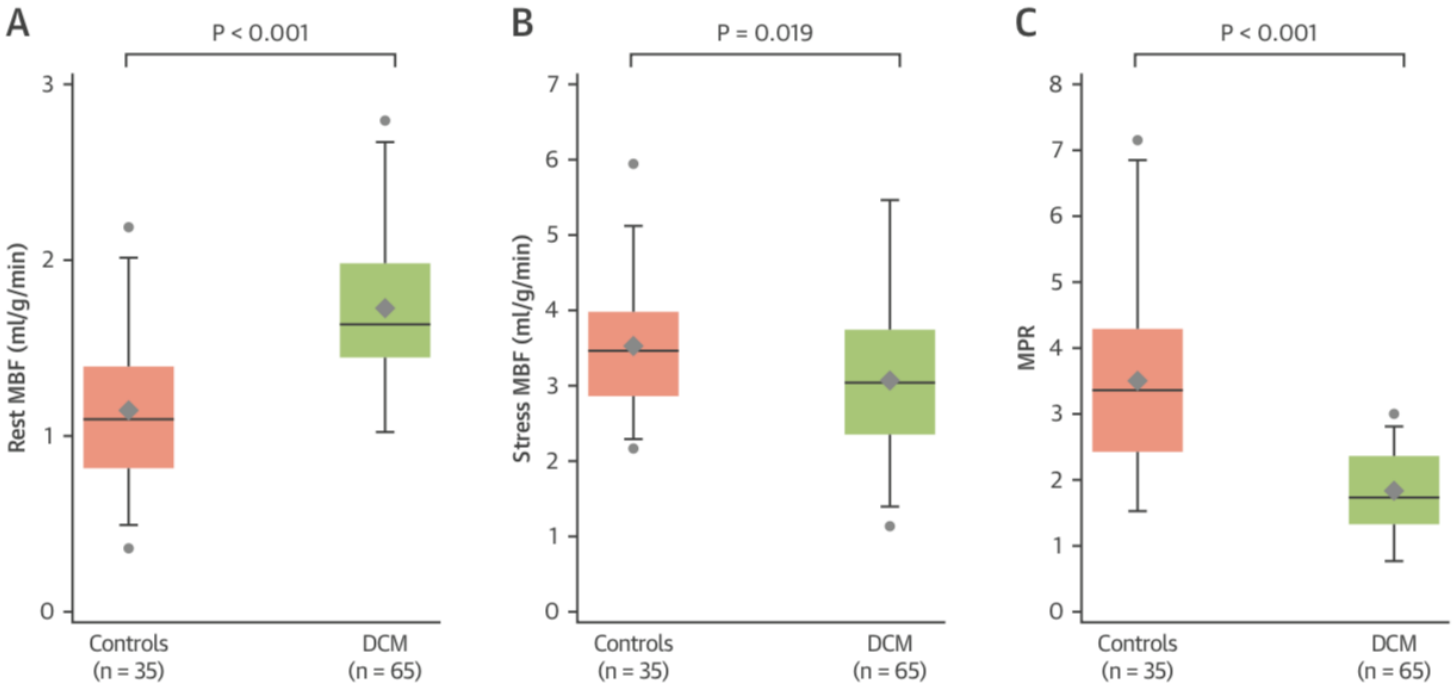

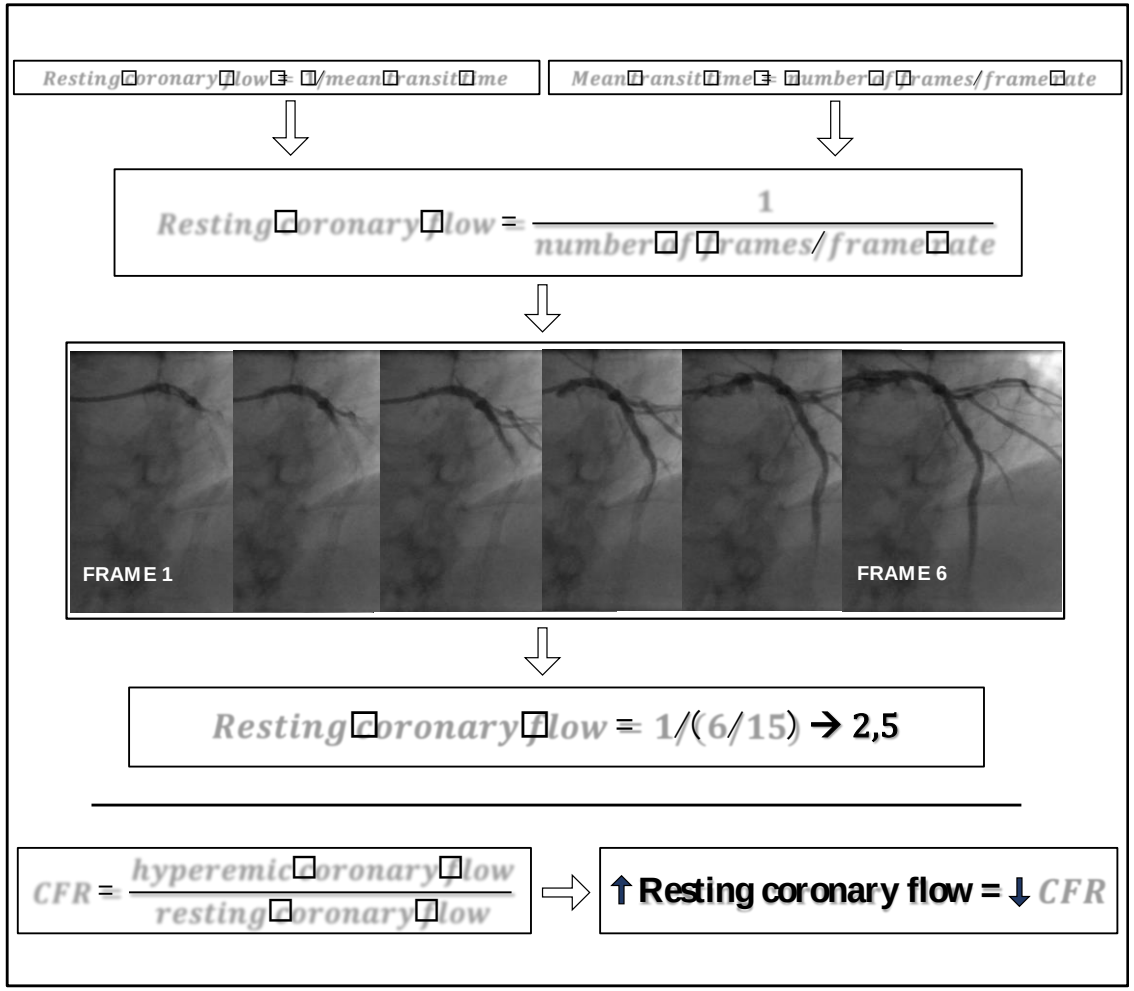

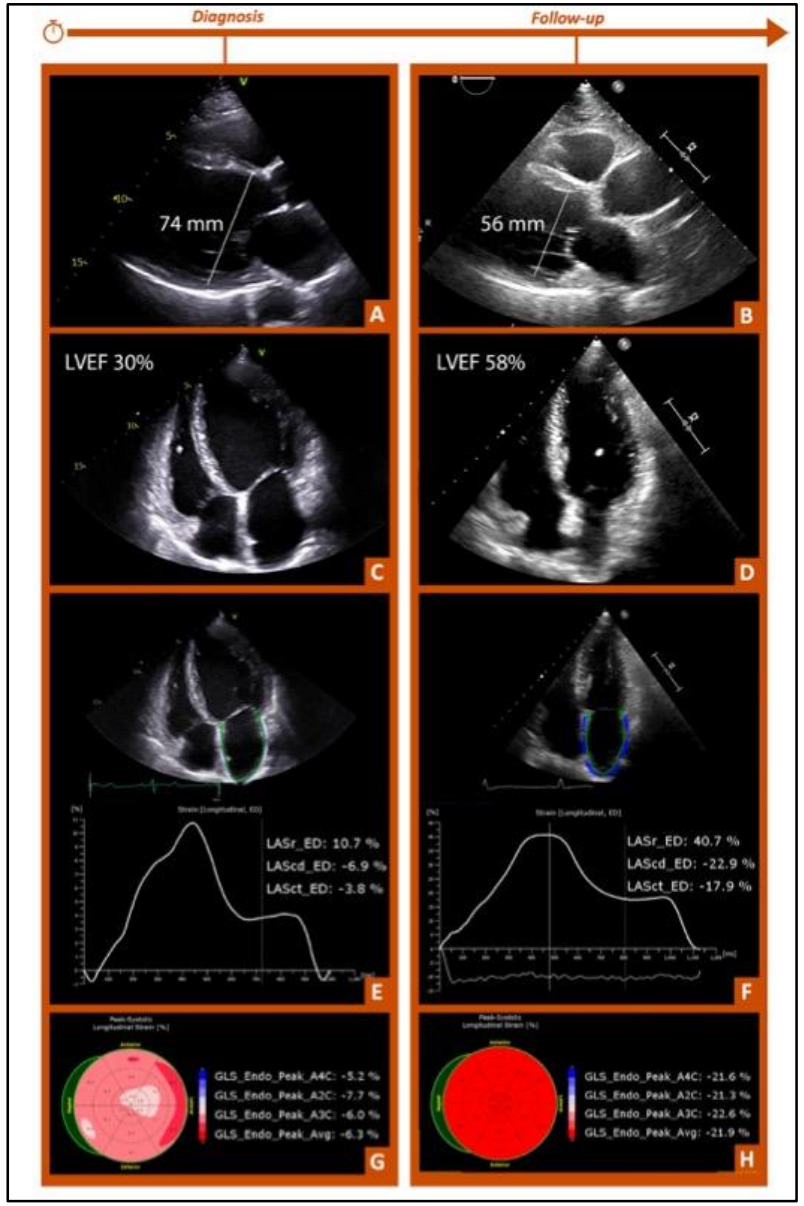

Portolan L, Scarsini R et al *submitted*

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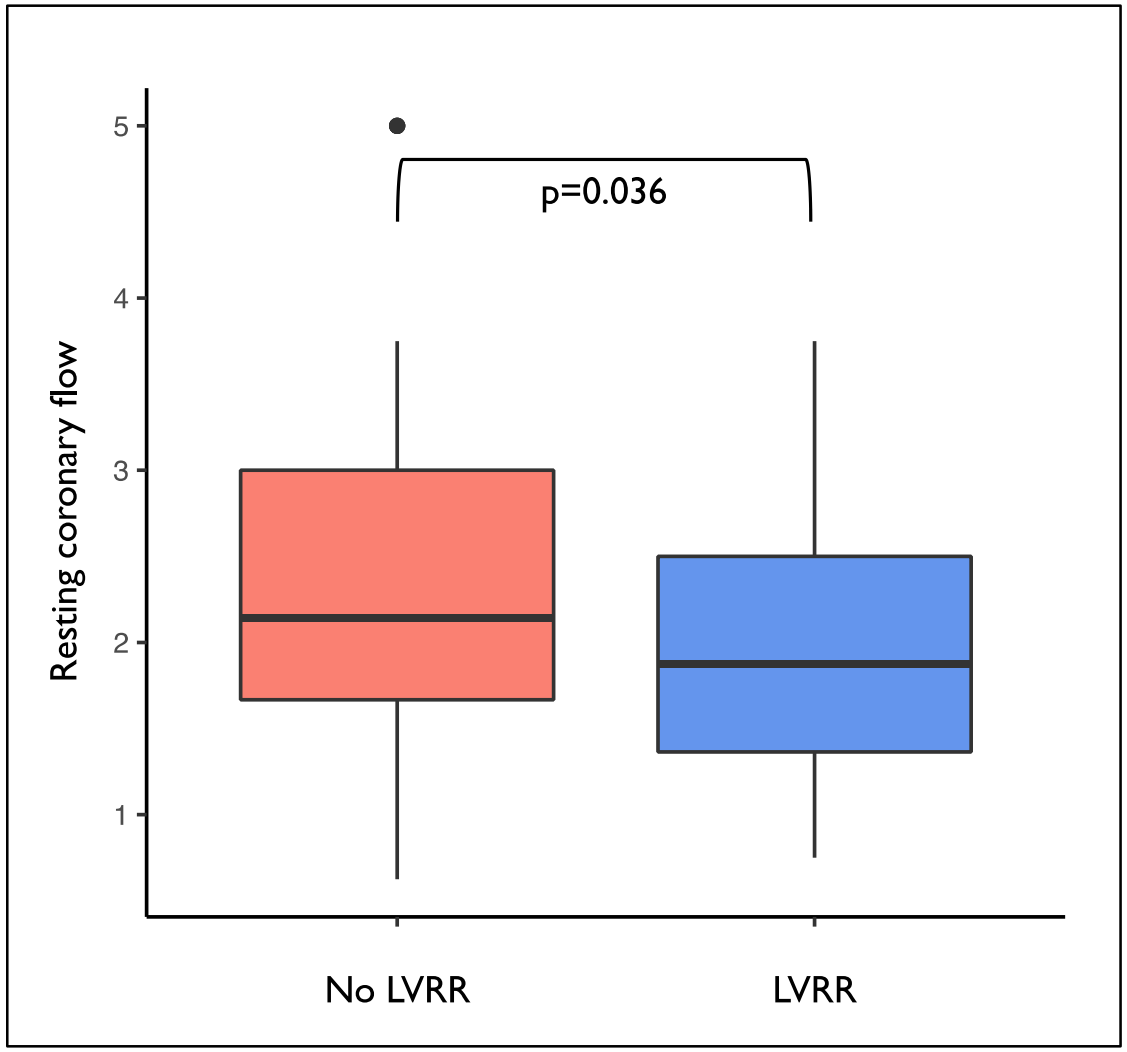

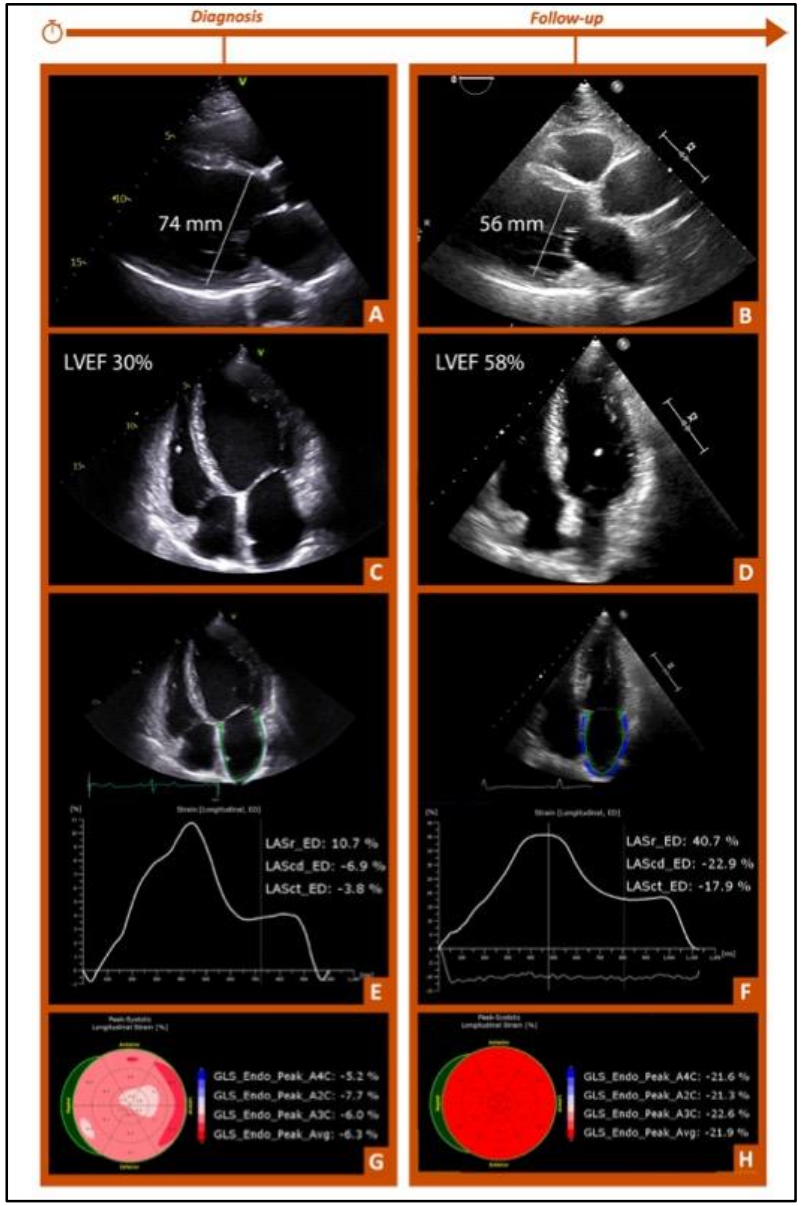

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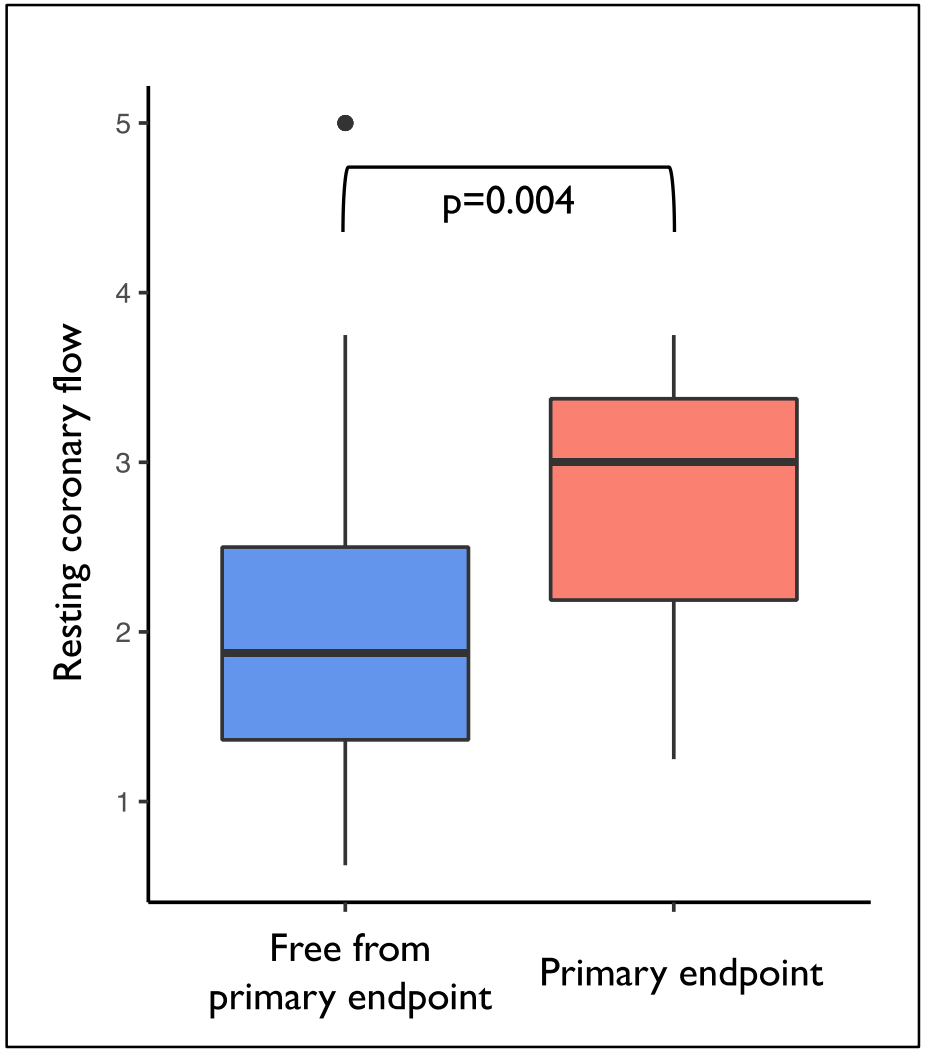

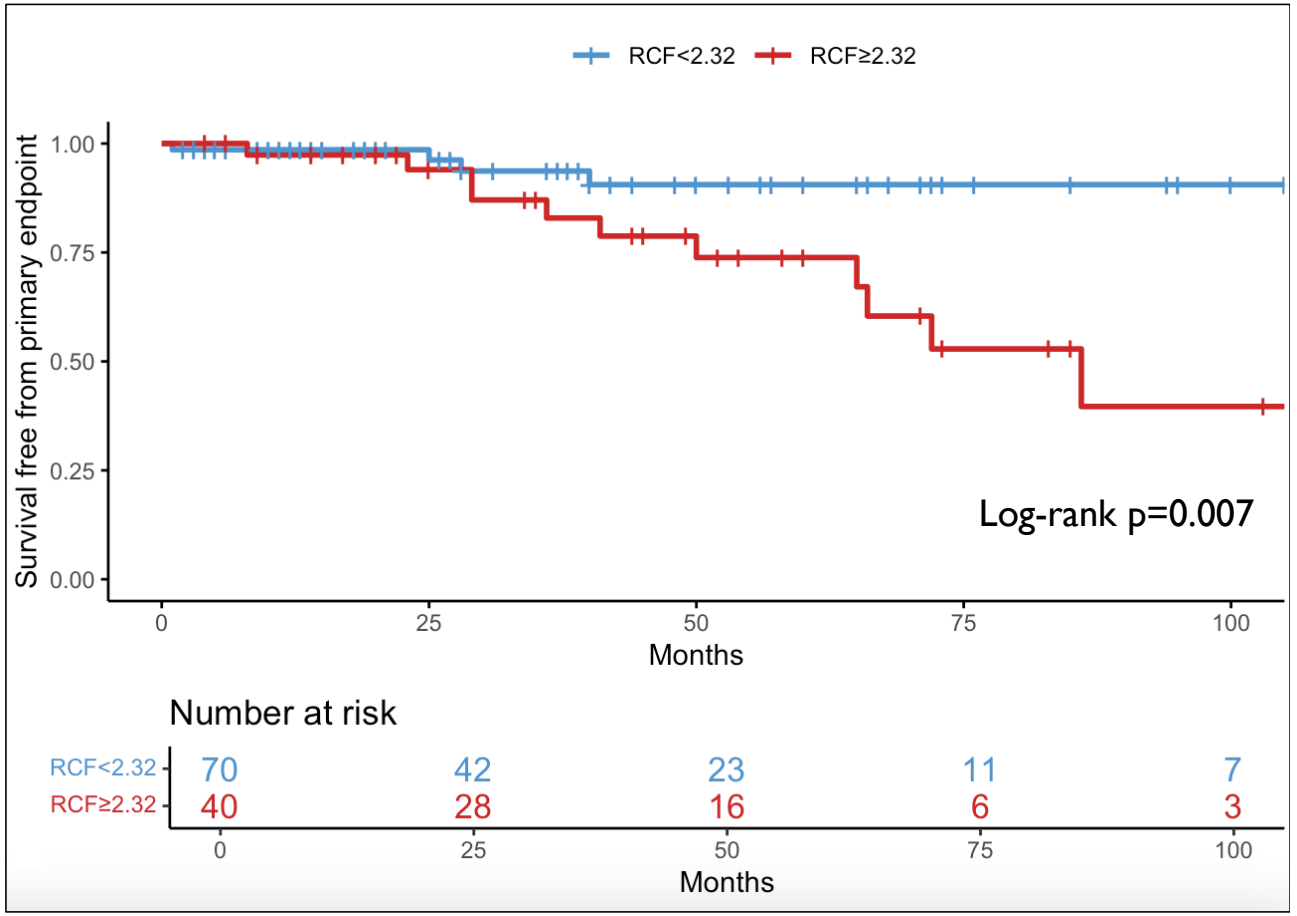

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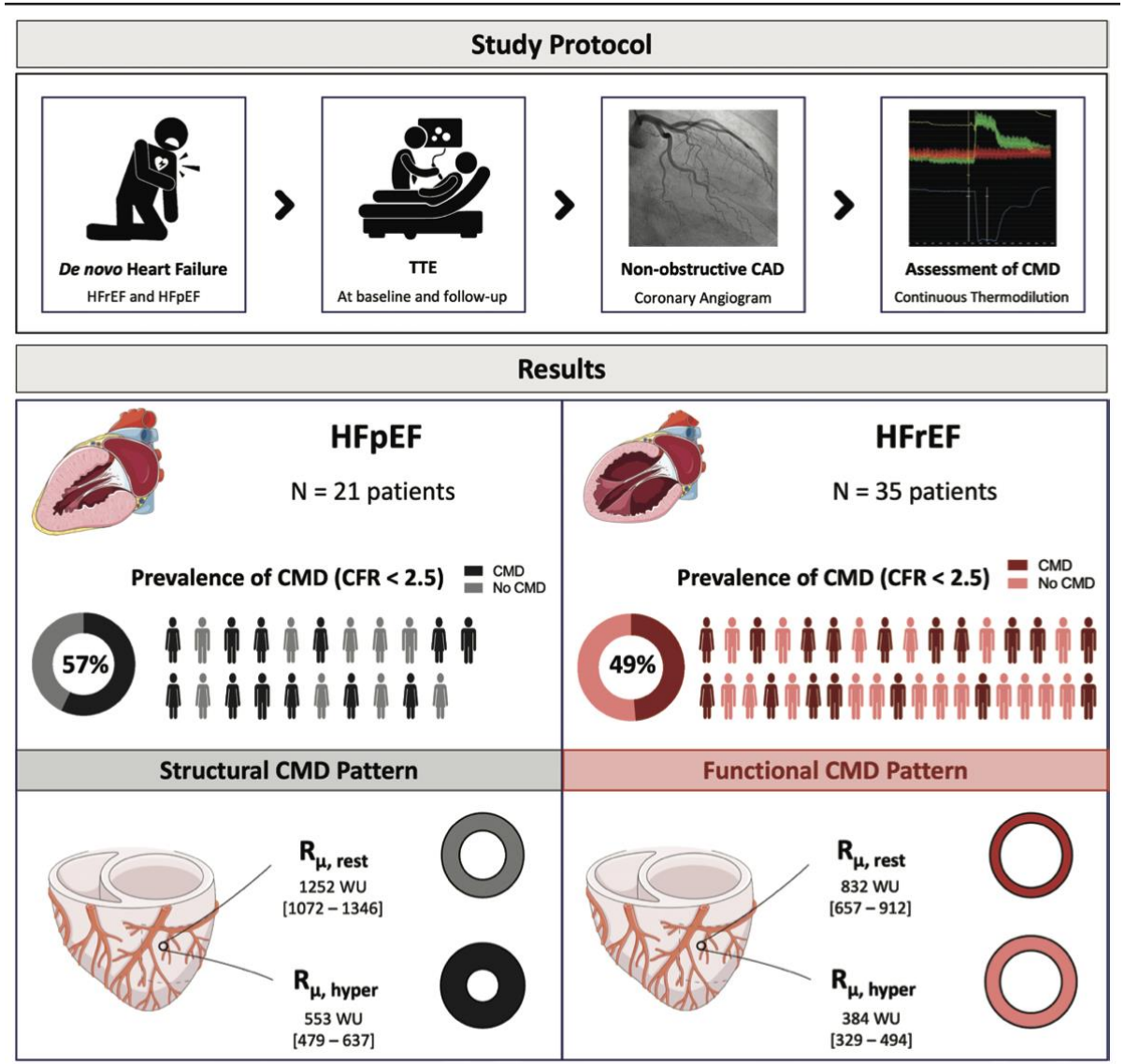

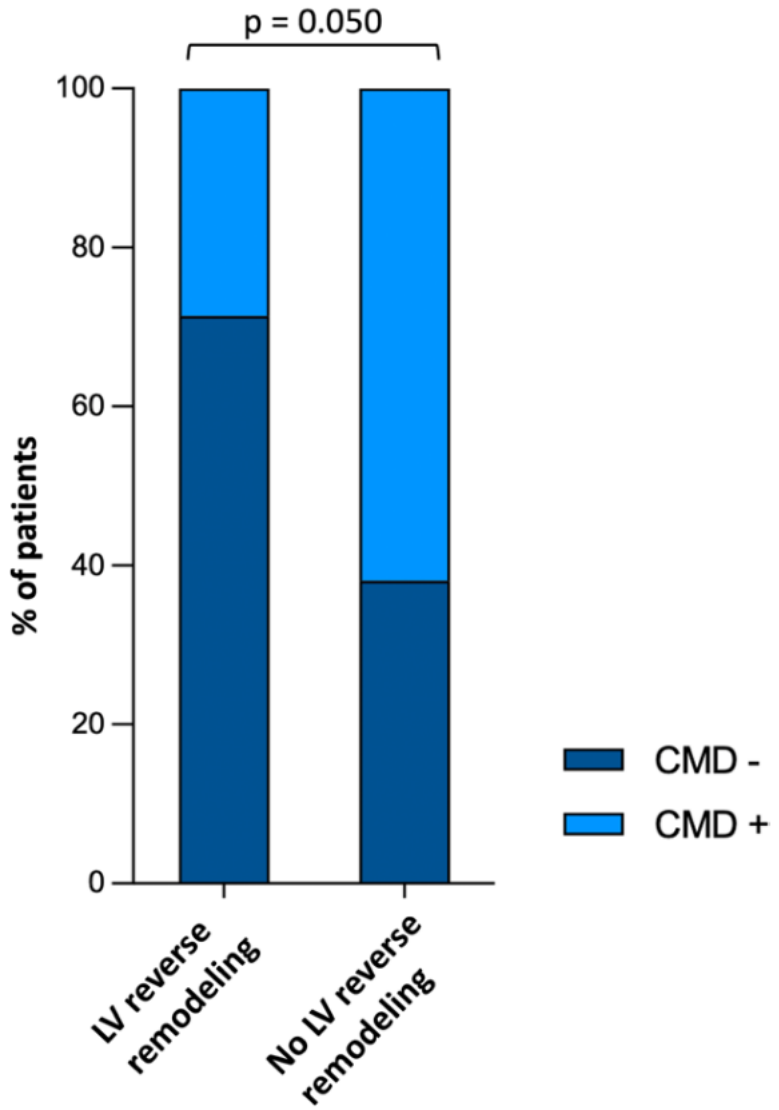

Paolisso P et al Circ Heart Failure 2024

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MICROREV-DCM Study

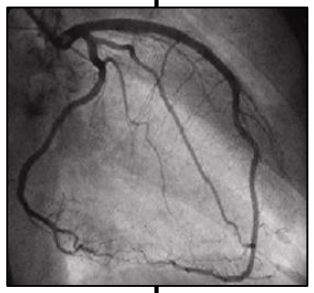
Prospective, multicenter, interventional study

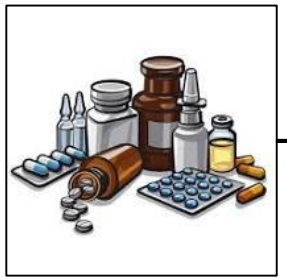
Aims:

- Assess **the impact of CMD on LV adverse and reverse remodeling** in idiopathic DCM.
- To identify different **CMD endotypes** in patients with DCM using a comprehensive #FullPhysiology approach.
- To assess the correlation between CMD and **adverse clinical outcomes** in DCM.

DCM with LVEF ≤40%
(naive of HF medical therapy)

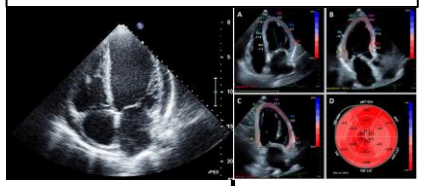
Exclusion criteria:
- obstructive CAD (DS>70% or DS 50-70% with FFR≤0.8)
- prior MI
- prior PCI or CABG
- severe valvular disease
- peripartum DCM
- acute myocarditis
- persistent tachyarrhythmias
- Excessive alcohol intake
- History of chemotherapy





OMT

12 months



LVRR

OMT titration

Follow up
HF clinic

DCM with LVEF ≤40%
(naive of HF medical therapy)

Exclusion criteria:
- obstructive CAD (DS>70% or DS 50-70% with FFR≤0.8)
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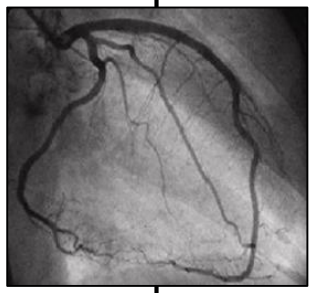
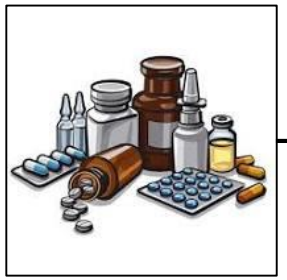
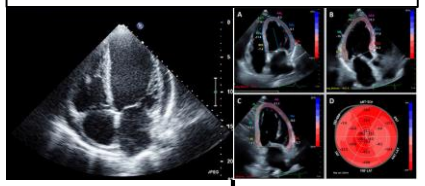


- **Cardiac MRI**
- **CPET**



OMT

12 months



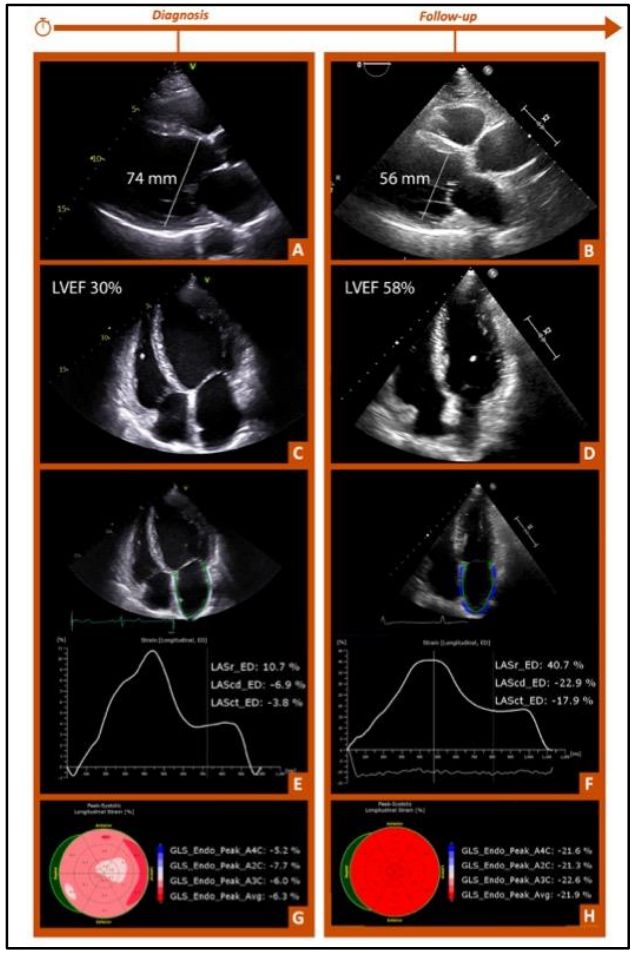
LVRR

- **Cardiac MRI**
- **CPET**

OMT titration

Follow up
HF clinic

Primary endpoint



Left ventricular reverse remodeling after 12 months of ESC guidelines directed OMT in patients with and without CMD

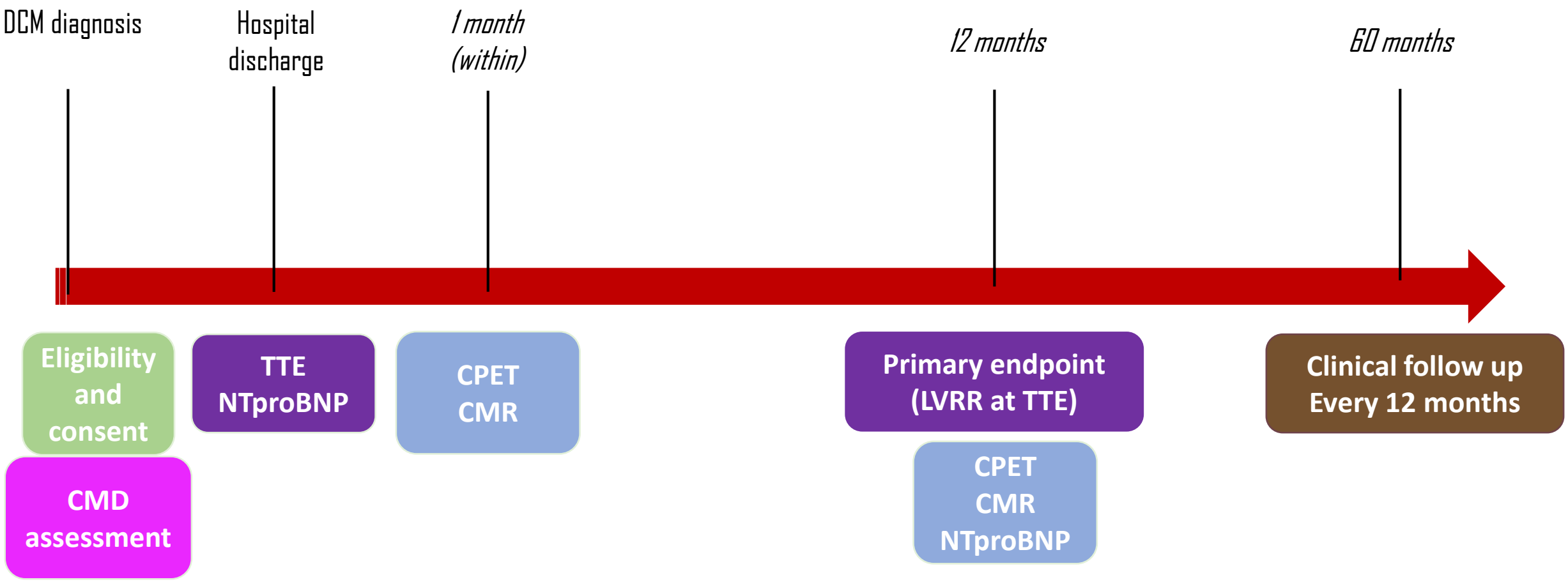
- **LVRR**: LVEF increase ≥ 10% and LVEDDi decrease ≥ 10% at TTE
- **Independent central corelab** (Verona)

Merlo M et al. J Am Coll Cardiol. 2011;57(13):1468-1476.
Kubanek M et al. J Am Coll Cardiol. 2013; 61: 54–63.

Secondary endpoints

- Composite of **cardiovascular death, new hospitalization for HF, ICD implantation, heart transplantation or ventricular mechanical assistance implantation** during follow-up in patients with and without CMD.
- **LVRR at cardiac MRI** after 12 months of guidelines directed OMT
- Correlation between CMD, fibrosis, and **adverse cardiac remodeling at cardiac MRI**.
- Changes in **functional capacity at CPET** after 12 months of guidelines-defined OMT
- **CMD endotypes** in patients affected by DCM and to correlate measures of microcirculatory function with the severity of adverse cardiac remodeling.

Study procedures



Sample size

- **Expected results:** We expect to observe that patients with idiopathic DCM and CMD will exhibit a suboptimal response to guidelines directed OMT and, consequently, a less frequent LVRR at follow up.

- **Preliminary data:** 110 patients admitted at with a new diagnosis of idiopathic DCM and followed in HF outpatient clinic AOUI Verona between 2015 and 2020. Mean indexed LVEDD was 32.4±5.8 and the mean LVEF was 29.0±6.5.

- A total sample of at least **190 patients** will be enrolled in this study in order to achieve a power of 80% and a level of significance of 5% (two sided), in detecting a true difference in means between the test and the reference group of 3.2 mm of indexed LVEDD and 2.9% LVEF at 12 months of follow up.

MICROREV team

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Flavio Ribichini

Core-lab:
Giovanni Benfari

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#Grazi

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