PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO
ROMA, 25 - 27 Giugno 2026

CARDIOMIOPATIA ARITMOGENA: WHAT'S NEW?

Lo scompenso cardiaco nei pazienti con cardiomiopatia aritmogena: opzioni terapeutiche ed indicazioni al trapianto cardiaco

SOC Cardiologia, Azienda Sanitaria Universitaria Friuli Centrale – University hospital of Udine

Department of Medicine Clinical Science and Education, Södersjukhuset Karolinska Institutet

Davide Stolfo
MD PhD FHFA

Heart Failure management in Arrhythmogenic Cardiomyopathy according to guidelines

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

Therapeutic options

HF treatment for HFrEF (see sections 5 and 6).

Competitive sports should be avoided, limit activities to leisure-time activities.[936]

In patients with ventricular arrhythmias: beta-blockers must be titrated to the maximally tolerated dose as first-line therapy. Amiodarone can be considered in addition to beta-blockers or if beta-blockers contraindicated or not tolerated; ICD implantation is indicated if history of aborted sudden cardiac death or sustained and/or haemodynamically poorly tolerated ventricular tachycardia.[910–912]

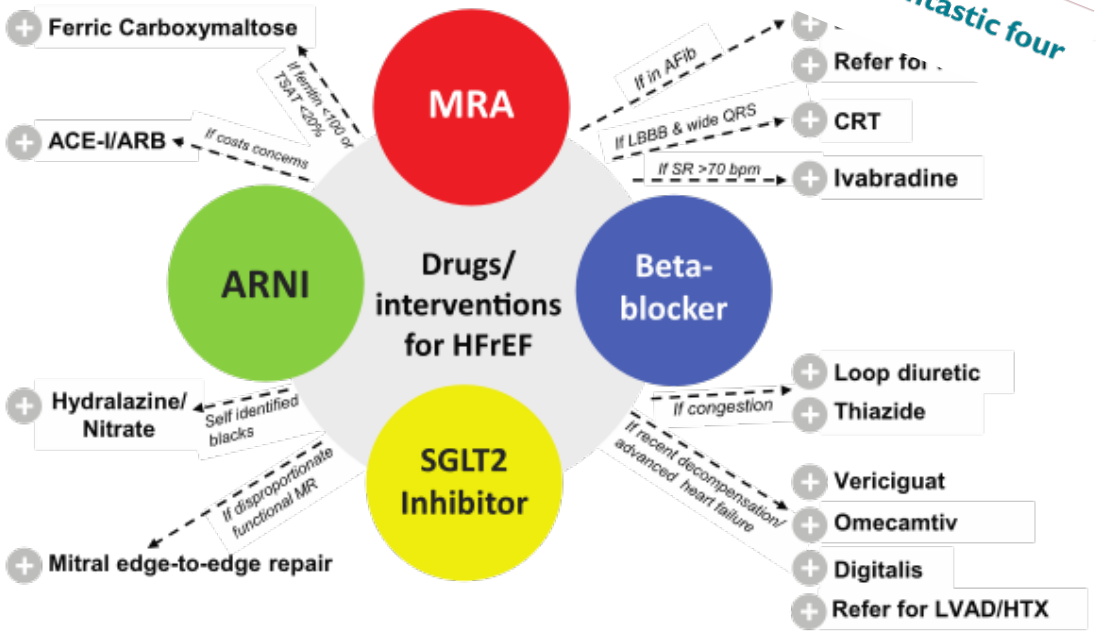
In patients with no ventricular arrhythmias: ICD can be considered (see section 6.1) even in patients with LMNA or FLNC gene mutations and LVEF <45%.[912]

ESC European Society of Cardiology
European Heart Journal (2021) **42**, 681–683
doi:10.1093/eurheartj/ehaa1012

EDITORIAL

Heart failure drug treatment: the fantastic four

Johann Bauersachs *



2023 ESC Guidelines for the management of cardiomyopathies

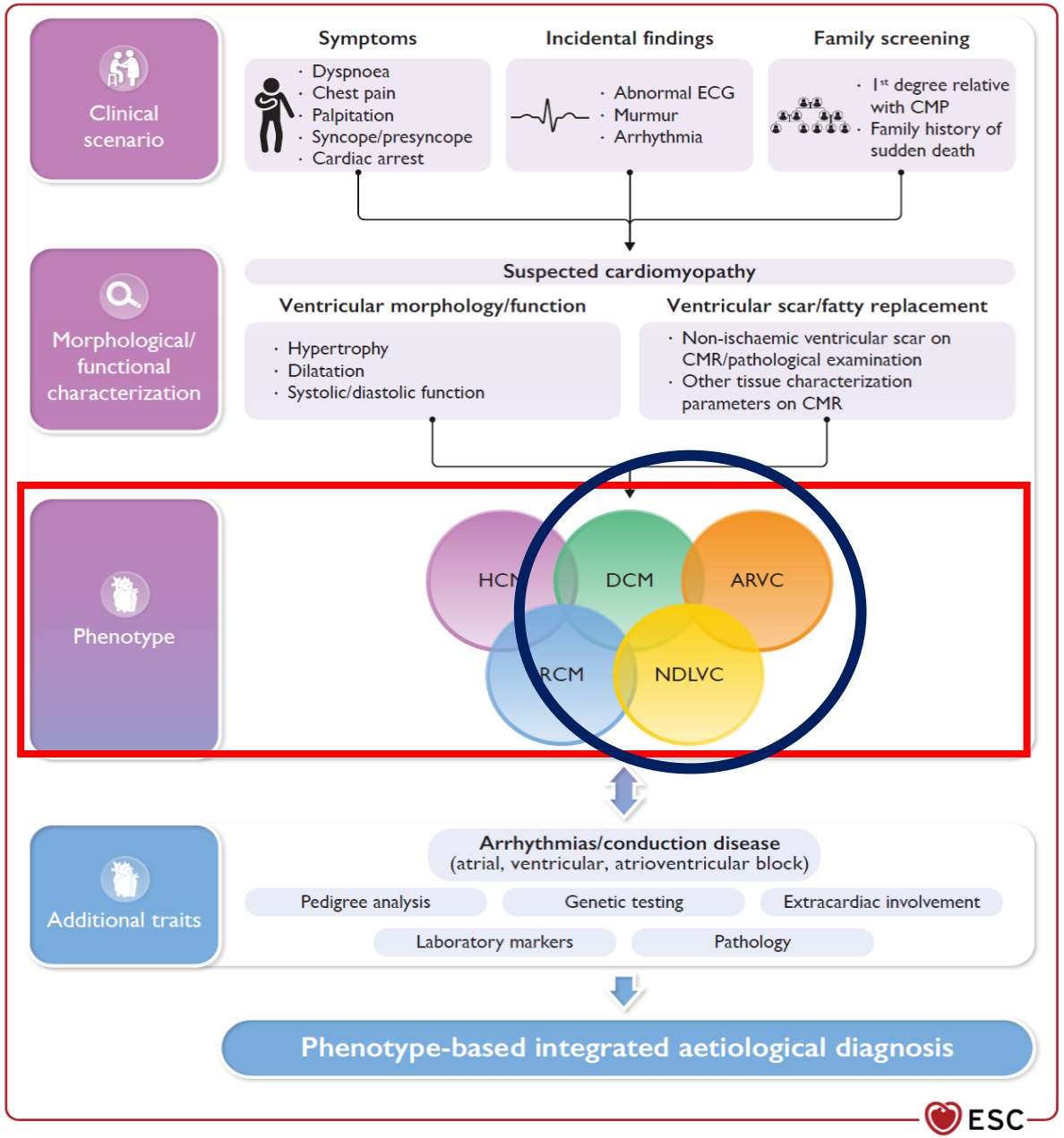
Developed by the task force on the management of cardiomyopathies of the European Society of Cardiology (ESC)

The cardiomyopathy mindset

Phenotype-centered diagnostic approach

ESC European Society of Cardiology

European Heart Journal (2023) **00**, 1–124
https://doi.org/10.1093/eurheartj/ehad194



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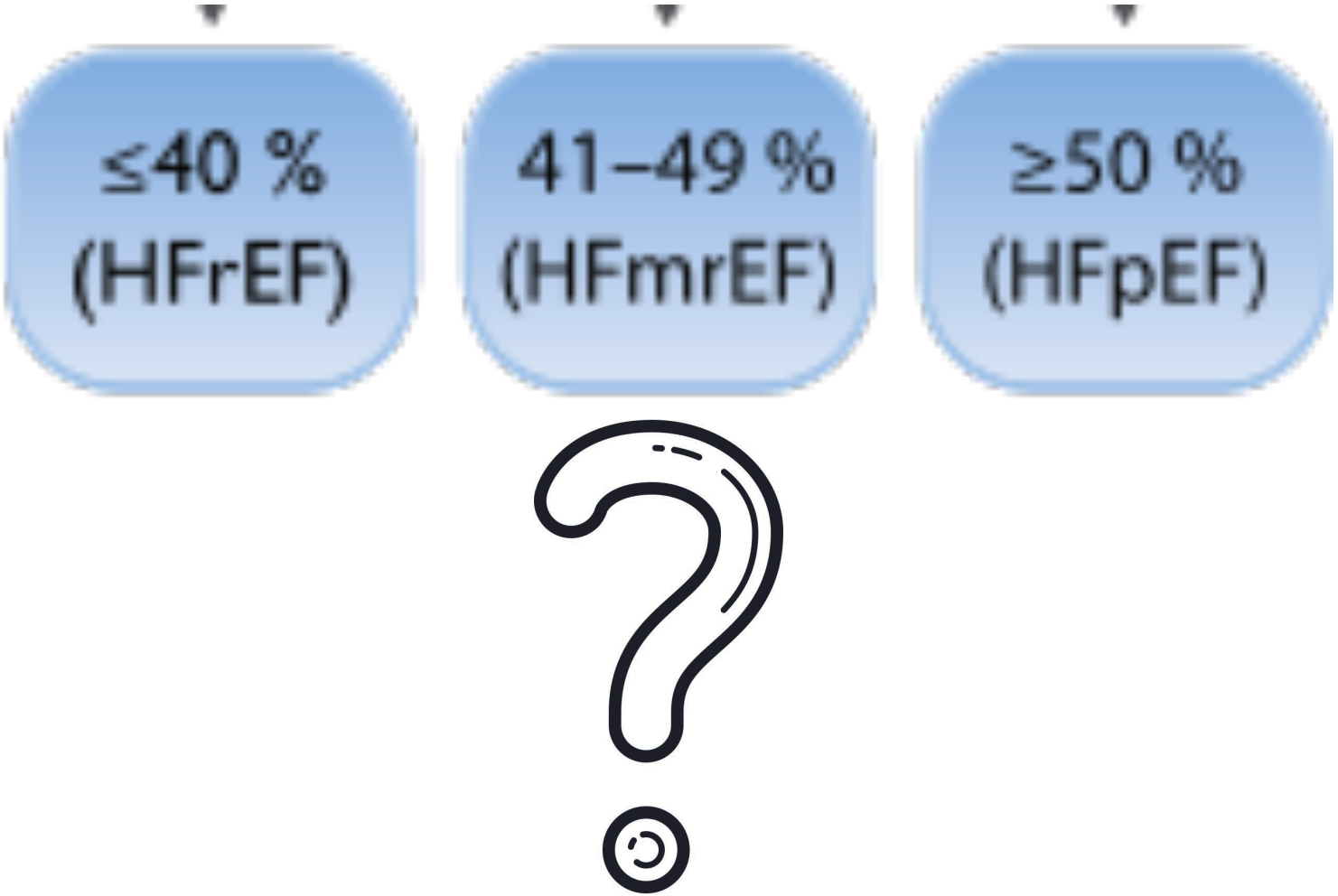
ESC European Society of Cardiology
European Heart Journal (2021) **00**, 1–128
doi:10.1093/eurheartj/ehab368

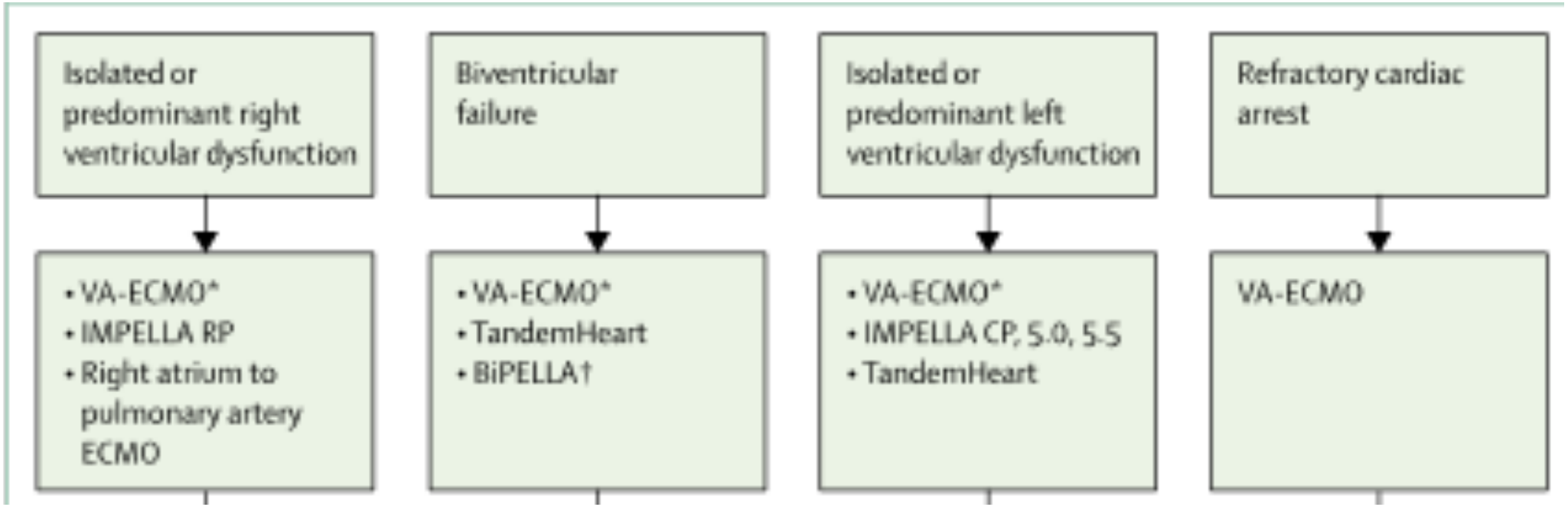
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

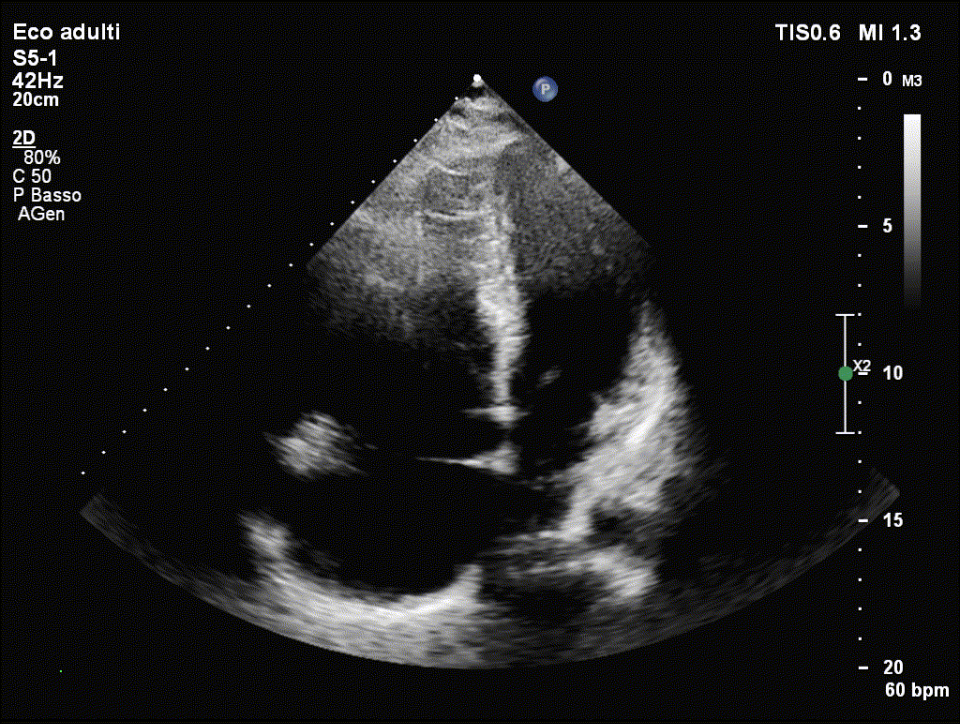
Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC



Left? Right? Both?...




Eco adulti
S5-1
42Hz
20cm
2D
80%
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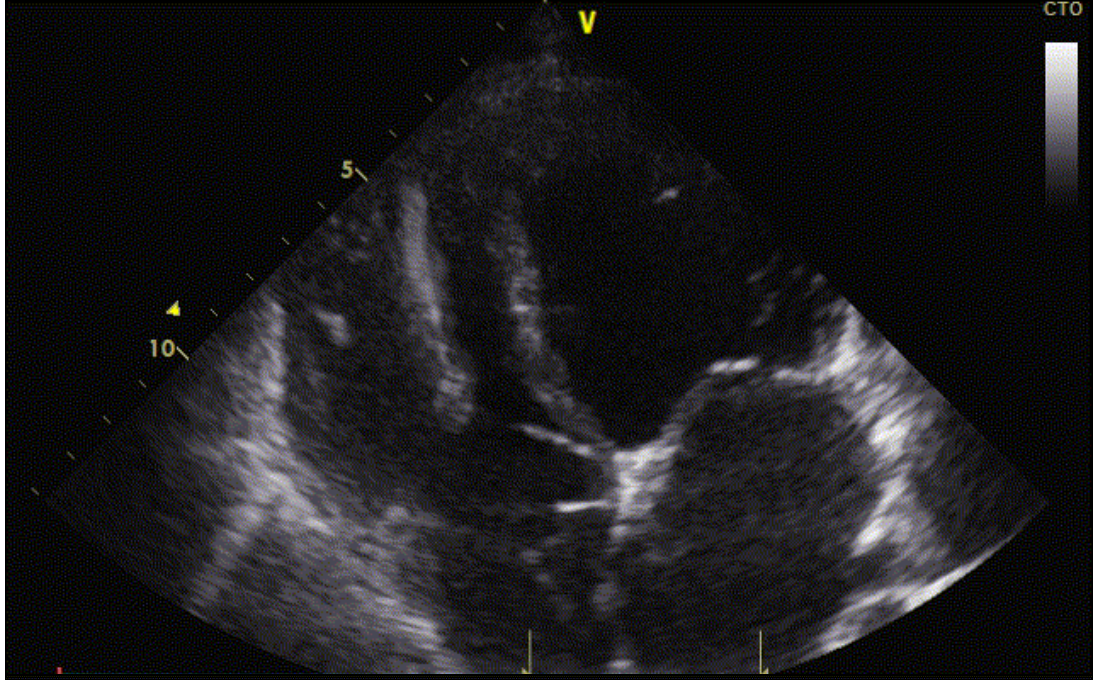
60 bpm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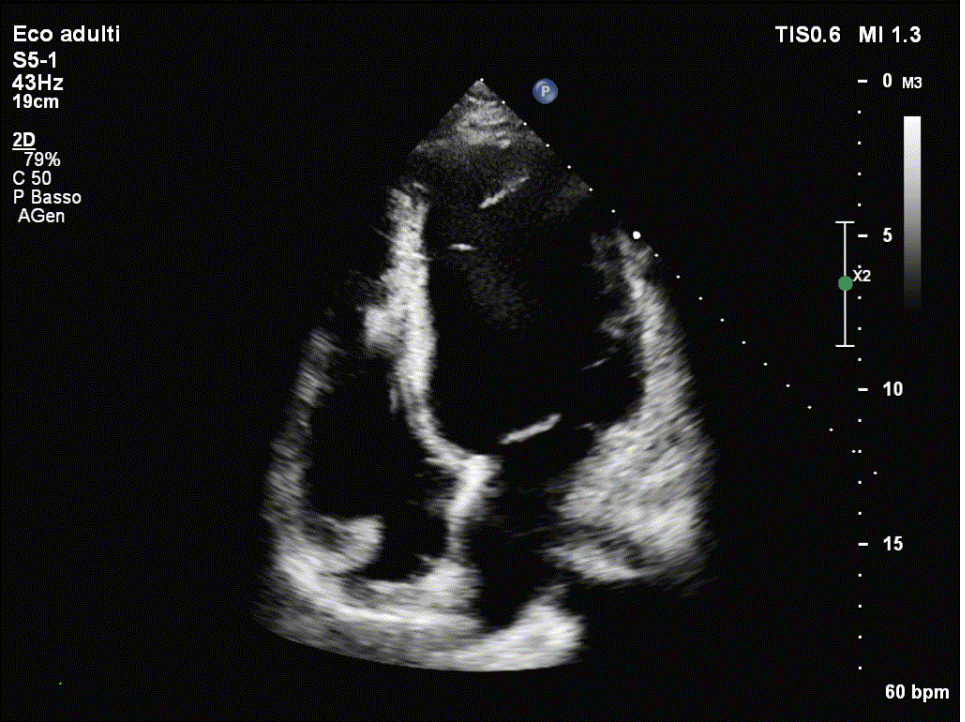
Eco adulti
S5-1
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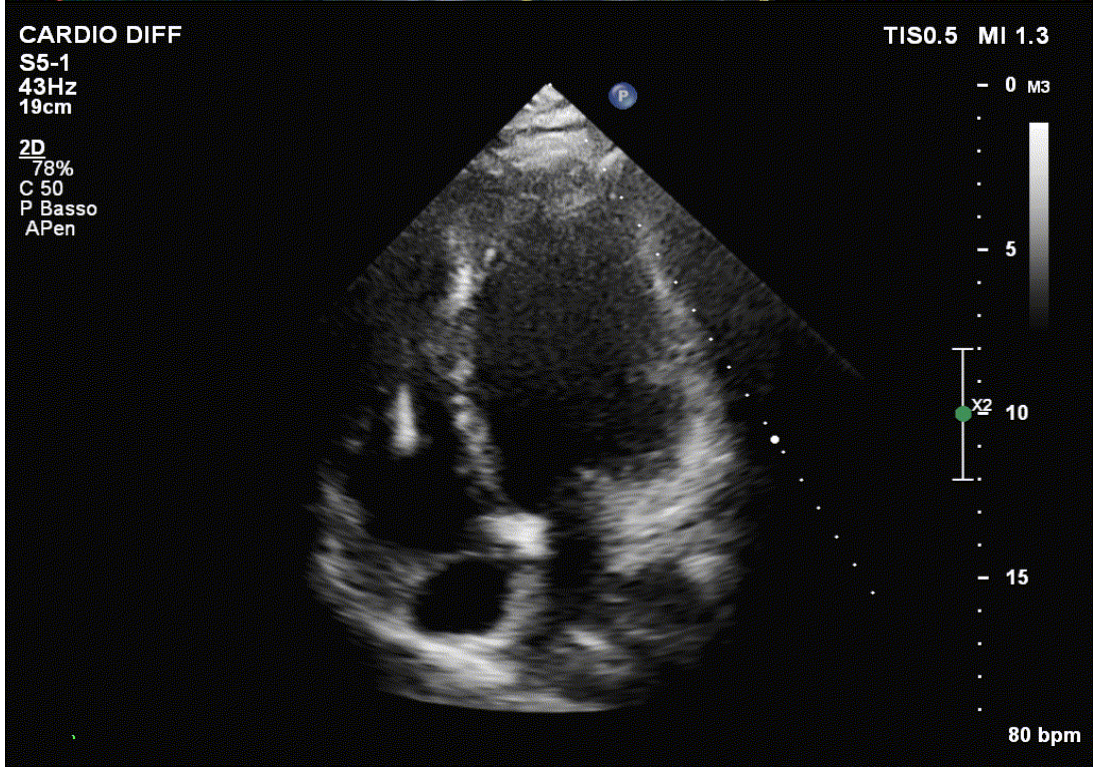
60 bpm


CARDIO DIFF
S5-1
43Hz
19cm
2D
78%
C 50
P Basso
APen
TIS0.5 MI 1.3
0 M3
5
10
15
80 bpm

Where are the differences?

- Comparing the efficacy of medical interventions
- The paradox of HFmrEF
- Genotype-related differences
- Non-GDMT therapies…the future?
- End-stage disease

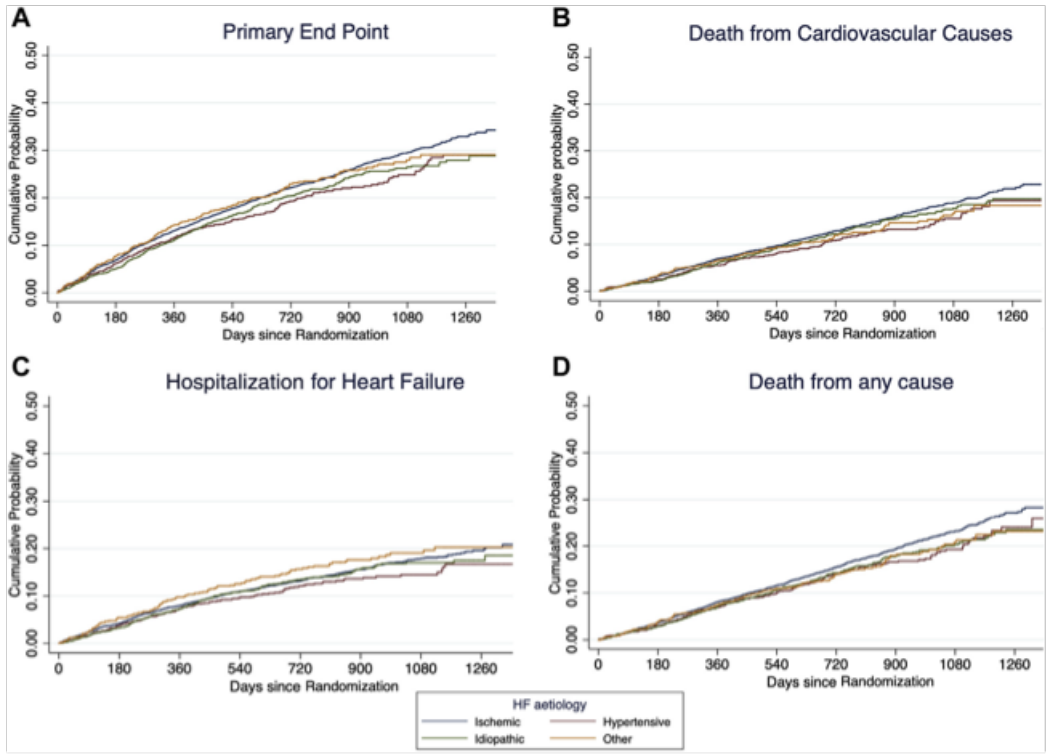
Comparing the efficacy of medical interventions

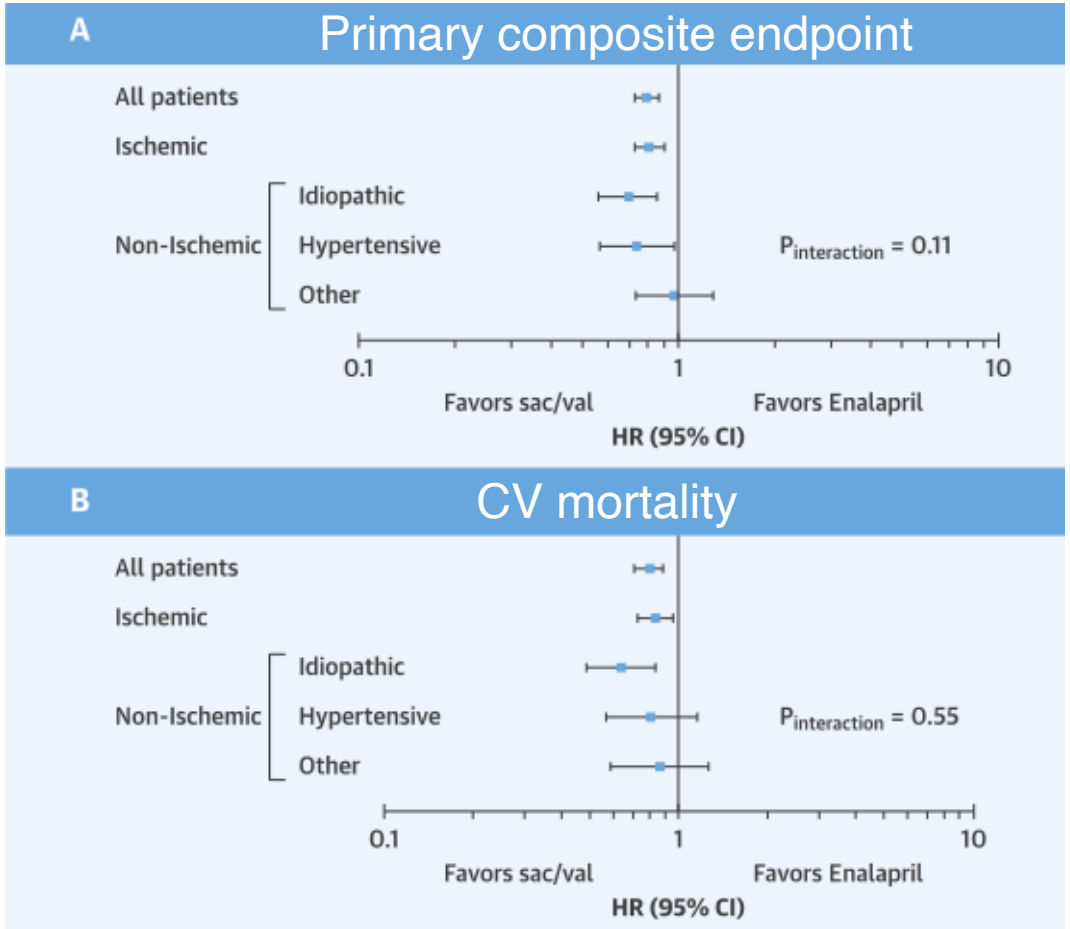
Outcomes and Effect of Treatment According to Etiology in HFrEF

An Analysis of PARADIGM-HF

ICM vs NICM

		Nonischemic (N = 3,363)			
	Ischemic (n = 5,036)	Hypertensive (n = 968)	Idiopathic (n = 1,595)	Other (n = 800)	p Value
Age, yrs	65.7 ± 10.2	64.7 ± 11.5	60.0 ± 12.3	58.3 ± 12.6	<0.001
Female	969 (19.2)	283 (29.2)	373 (29.2)	207 (25.9)	<0.001

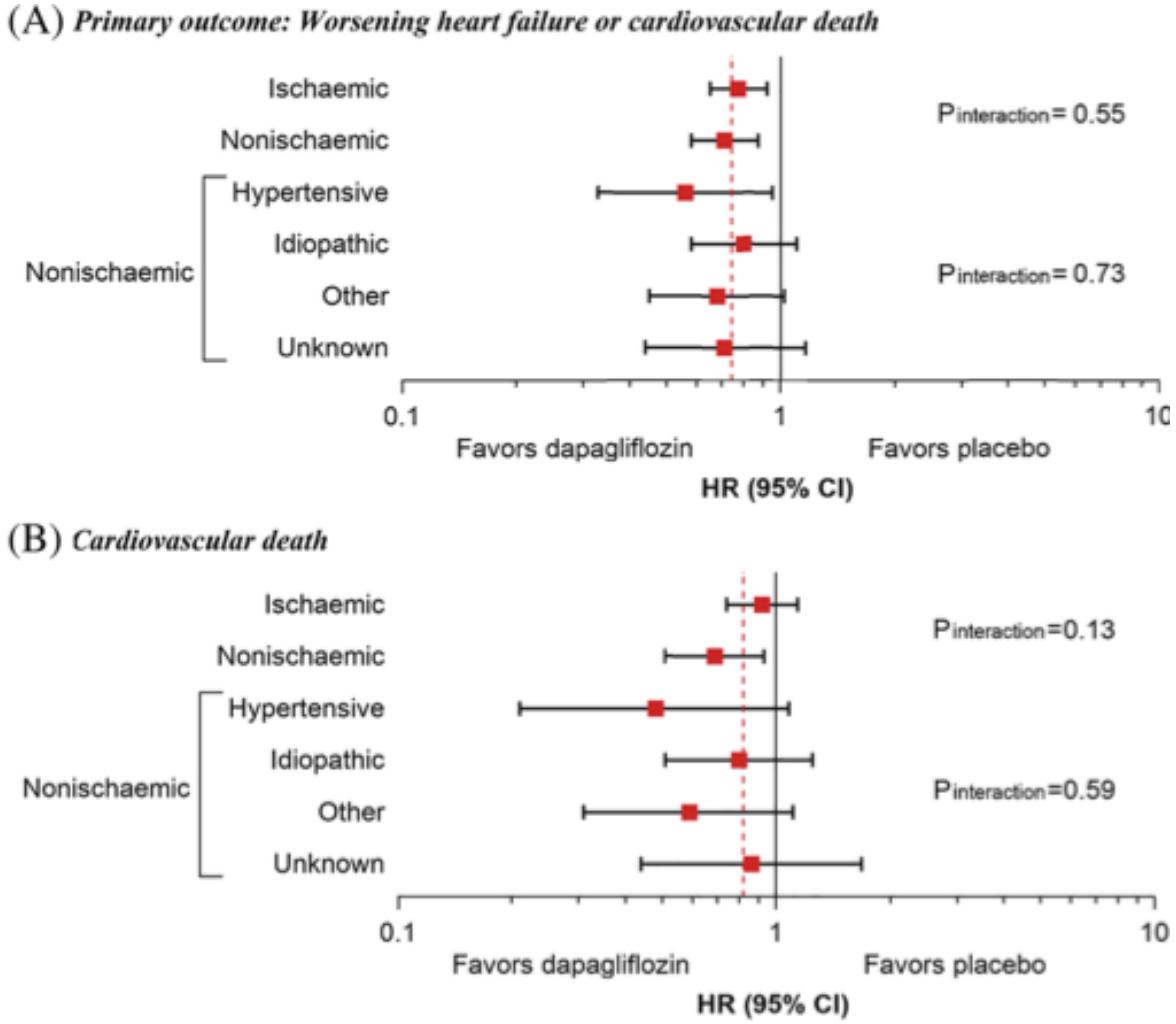




Balmforth, C. et al. J Am Coll Cardiol HF. 2019;7(6):457-65.

Efficacy and safety of dapagliflozin according to aetiology in heart failure with reduced ejection fraction: insights from the DAPA-HF trial

ICM vs NICM



Butt et al. European Journal of Heart Failure (2021) **23**, 601–613

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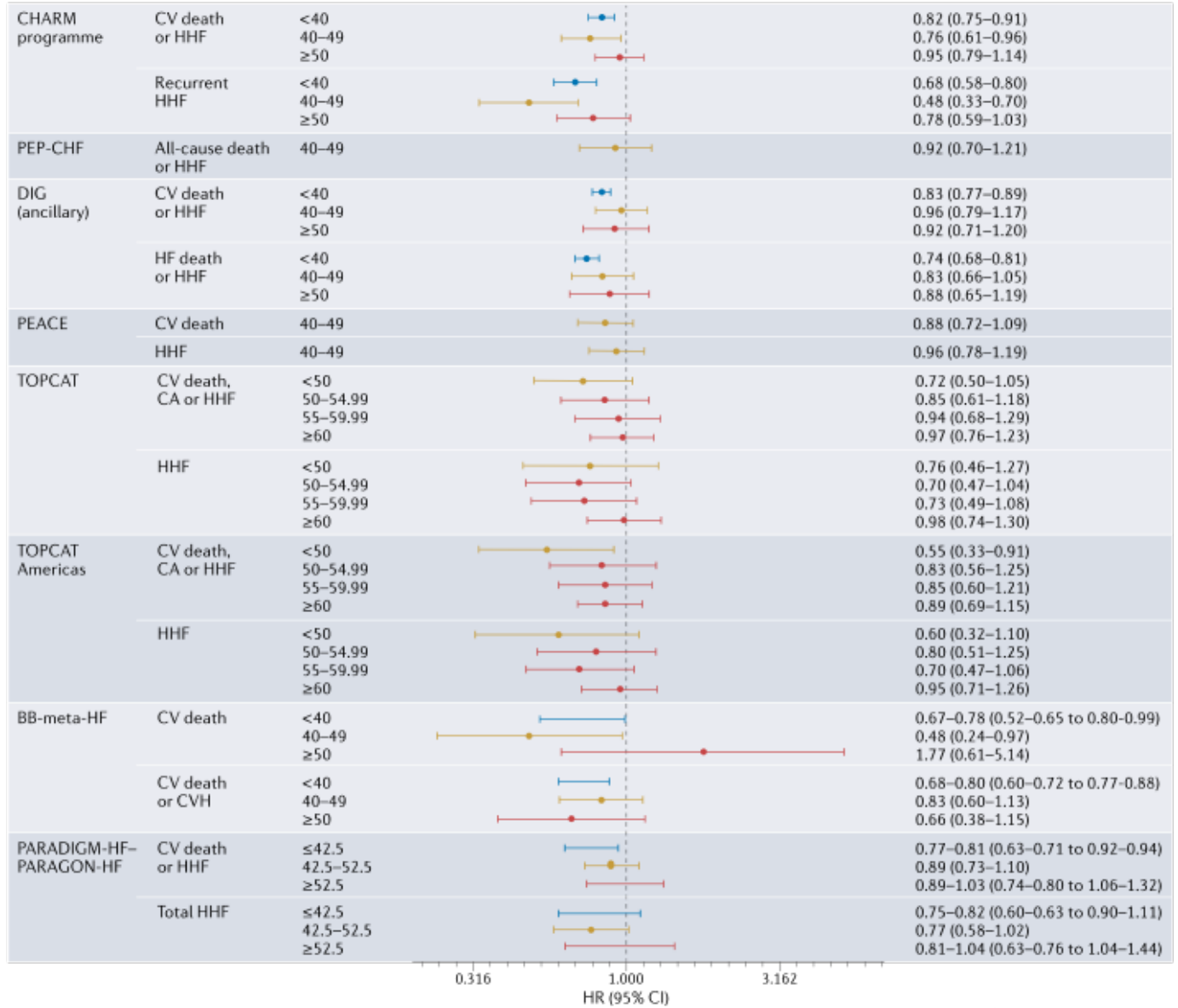
The paradox of HFmrEF

Heart failure with mid-range or mildly reduced ejection fraction

Gianluigi Savarese[1,2,4], Davide Stolfo[1,3,4], Gianfranco Sinagra[3] and Lars H. Lund[1,2]

	HFrEF	HFmrEF	HFpEF
Phenotype			
Age	↑	↑↑	↑↑↑
Women	↓↓	↓	↑
Ischaemic heart disease	↑↑↑	↑↑↑	↑
Atrial fibrillation	↑	↑↑	↑↑↑
Hypertension	↑	↑↑	↑↑↑
Chronic kidney disease	↑↑	↑↑	↑↑↑
Natriuretic peptide levels	↑↑↑	↑	↑
Prognosis			
Cardiovascular risk	↑↑↑	↑	↑
Non-cardiovascular risk	↑	↑	↑↑
Treatment			
RAS inhibitors, β-Blockers, MRA, ARNI, SGLT2i — Relative effect	+++	+++ (Ongoing trials on MRA and SGLT2i)	±
RAS inhibitors, β-Blockers, MRA, ARNI, SGLT2i — Absolute effect	+++	+ (Ongoing trials on MRA and SGLT2i)	±
ICD, CRT	+++	±	±

HFrEF characteristics | HFpEF characteristics | Intermediate characteristics



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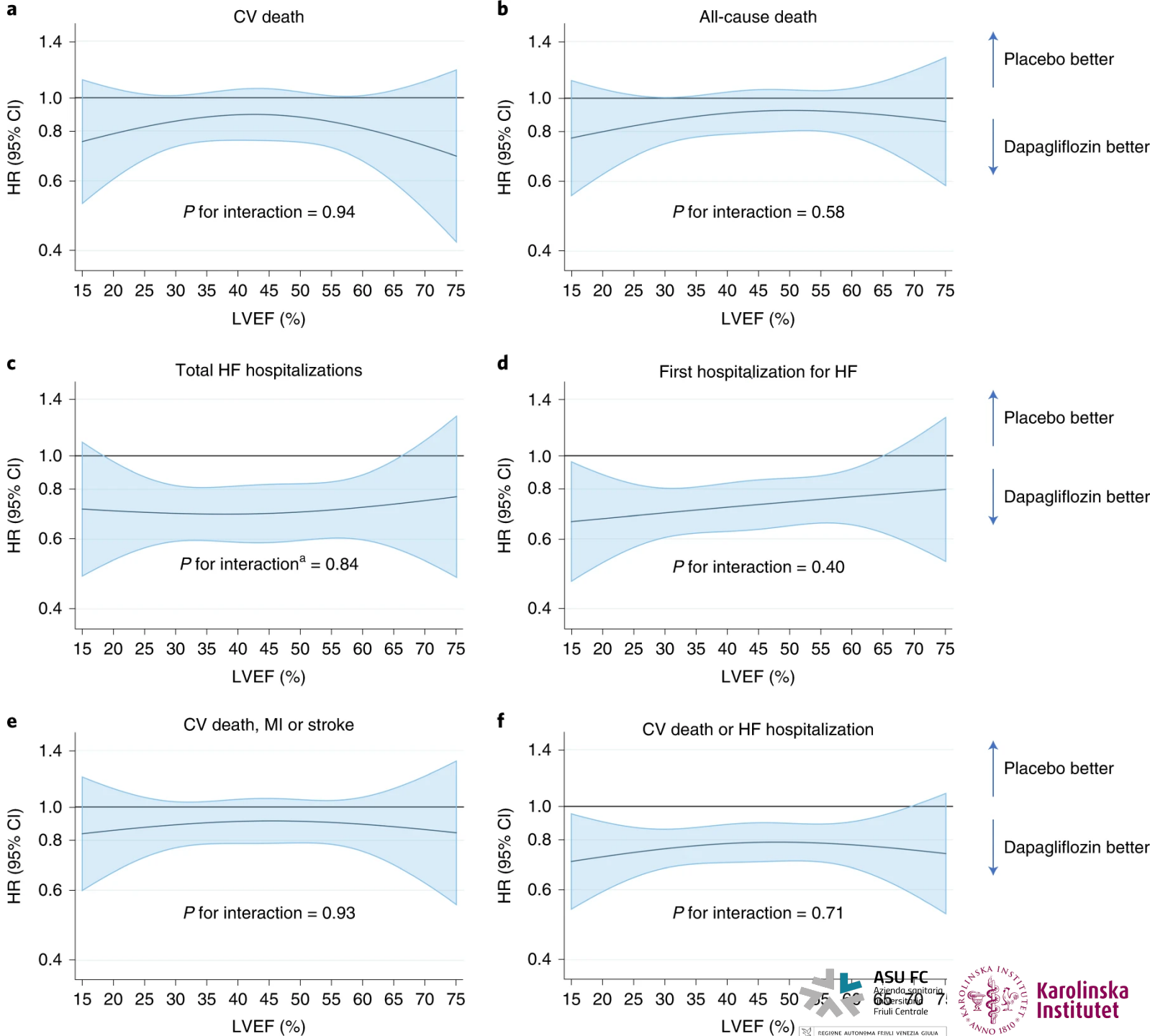
Dapagliflozin across the EF spectrum



Jhund PS et al. Nat Med. 2022;28(9):1956-1964

Genotype-related differences

Mora-Ayestarán et al. European Heart Journal 2025

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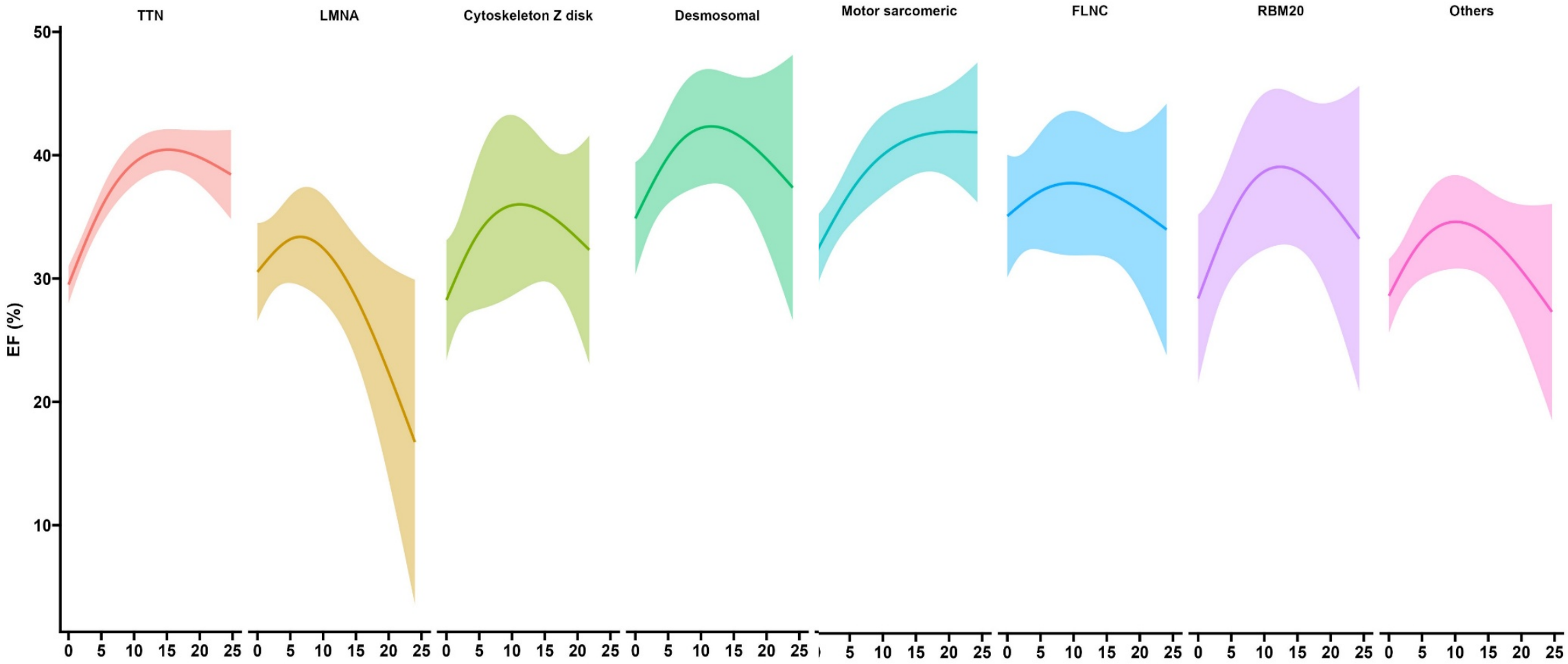
Gene-specific LVEF trajectory



Manca P, Stolfo D, Gigli M, et al. unpublished

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ESC European Heart Journal (2026) 00, 1–14
https://doi.org/10.1093/eurheartj/ehag104

Laminopathies: natural history and risk prediction of heart failure

LMNA risk score for prediction of 5-year risk of major heart failure events

Analysis of registry data

Exclusion of patients with LVEF <30% at baseline

Derivation cohort
OPALE: nationwide registry on laminopathies
470 patients

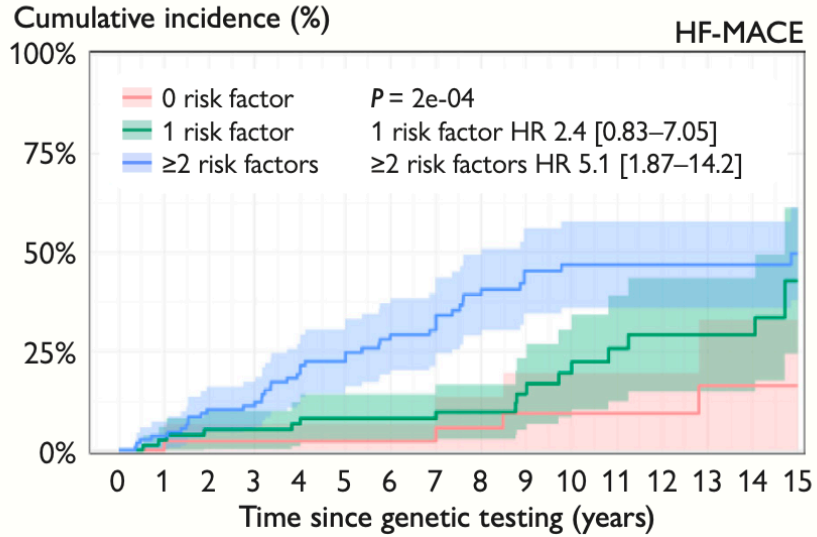
Validation cohort
Tertiary cardiology referral centres
245 patients

Five independent risk factors

	Adjusted HR
Male sex	1.86
LVEF <50%	2.18
Missense variants in head and rod domains	2.91
Complete left bundle branch block	2.99

Good discrimination of the model with C-index of 0.750 and 0.758 in the derivation and validation cohorts

An additive effect of risk factors



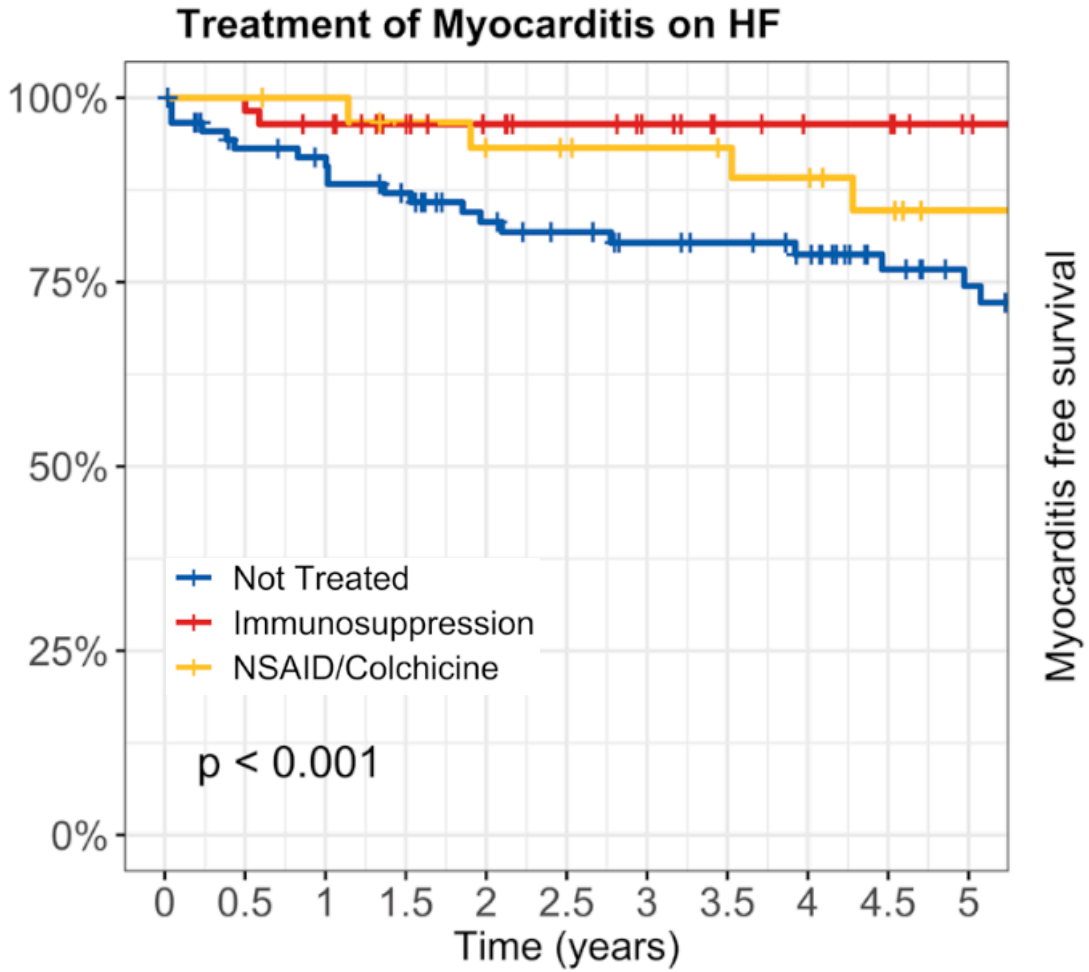
HF-MACE, heart failure-major adverse cardiac event; HR, hazard ratio; **LMNA**, lamin A/C gene; **LVEF**, left ventricular ejection fraction

Charron P, *et al. European Heart Journal.*

Non-GDMT therapies…the future?

Garcia-Pavia P et al. Circ Heart Fail. 2024;17:e011548

Prognostic Role of Myocarditis-Like Episodes and Their Treatment in Patients With Pathogenic Desmoplakin Variants



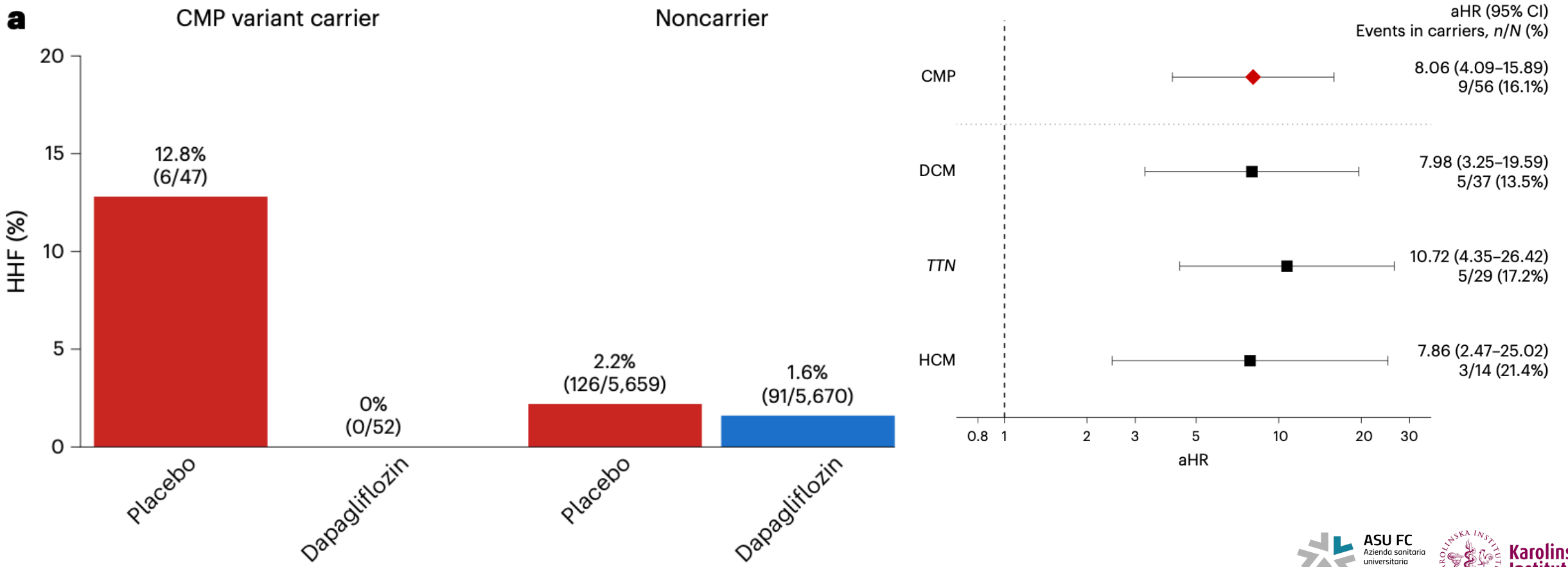
Gasperetti et al. Circulation. 2025;152:978–989.

nature medicine

Article

https://doi.org/10.1038/s41591-026-04439-x

Effects of SGLT2 inhibition on incident heart failure in carriers of cardiomyopathy-associated genetic variants



End-stage disease?

Are we ok with this?

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Are we ok with this?

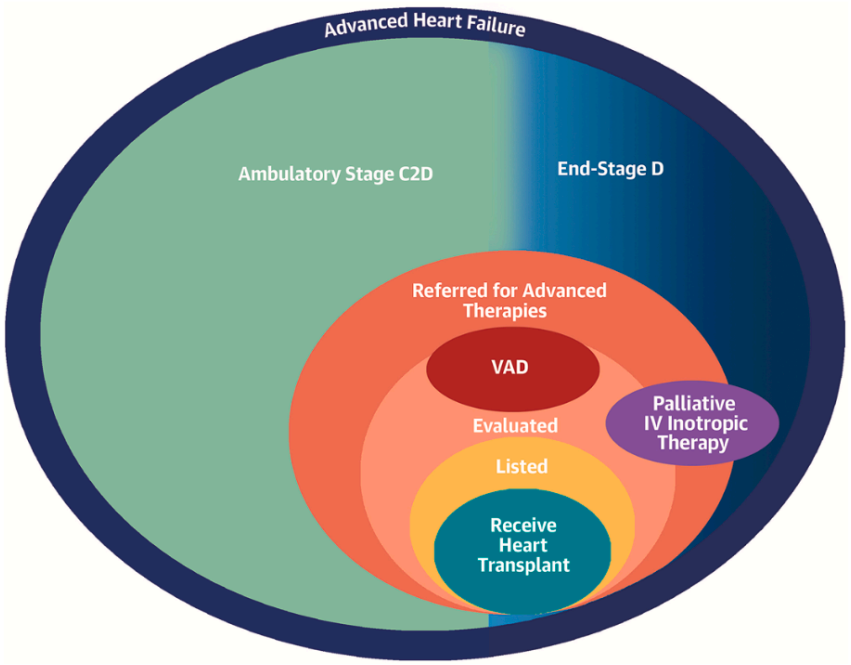
Need to Define Severe Heart Failure

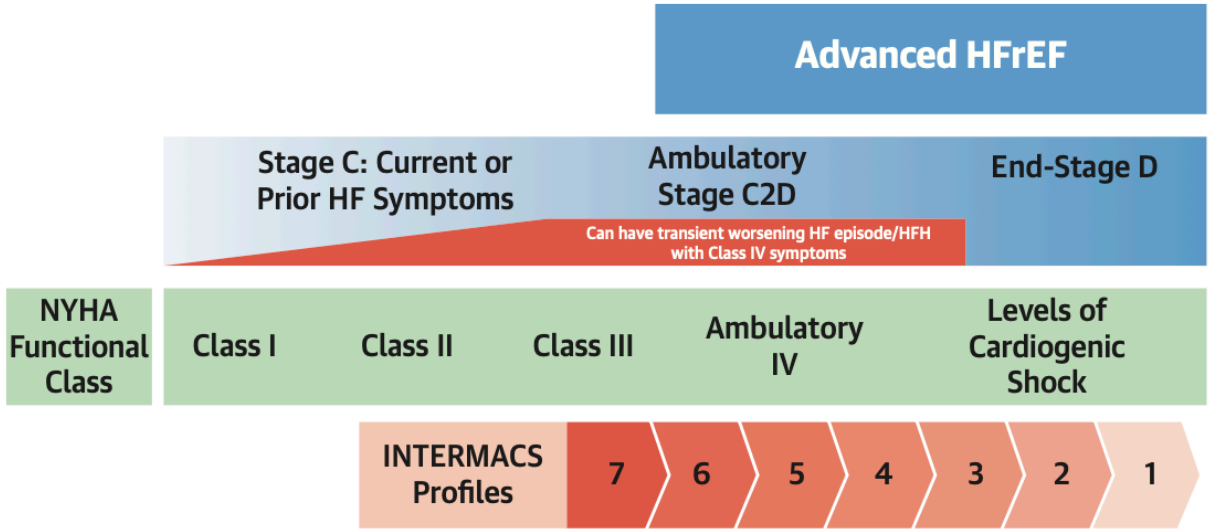
A Subgroup of Stage C Heart Failure

Biykem Bozkurt, MD, PhD, *Editor-in-Chief, JACC: Hart Failure*

Ambulatory Stage C2D Heart Failure Definitions and Current Therapeutic Approaches

JACC: Heart Failure Position Statement





Stage C2D

Recognition

All 3 Core Features Present:

- Persistent NYHA functional class III/ambulatory IV symptoms despite stage C therapies
- Ambulatory out of hospital without IV inotropic therapy
- Objective exercise limitation (6MW <300 m-350 m; $PkVO_2$ 11-15 mL/kg/min, <55%-60% predicted)

Optimization and Escalation

- Review and optimize first line-stage C therapies (eg, Class I pillars, CRT)
- Refer for MCS, transplant in highly selected patients
- Consider adding stage C Class II medications (eg, digoxin, hyd/nit, vericiguat, ivabradine), remote monitoring, and/or device therapies
- Enroll in clinical trials of new therapies
- Align strategies with patient preferences to enhance quality of life ± survival

Future Directions

- Curate C2D cohorts (leverage AI)
- Refine C2D definitions and phenotypes
- Investigate adaptation of current stage C therapies for C2D phenotypes
- Develop novel C2D options (eg, gene-based, antifibrotics, micro-circulatory devices, oral inotropes)

Dunlay SM, et al. JACC Heart Fail. 2026;14(6):103101.

You are a Cardiologist…
Do not Disregard the Phenotype

ACM?

DCM

CM/HCM

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Do not Disregard the Phenotype

Arrhythmias +
++

48 yrs
NYHA III
1 HF hospitalization <12 months
sPAP 61 mmHg
PVR 2.8 UW
TPG 14 mmHg

Extensive RV
LGE

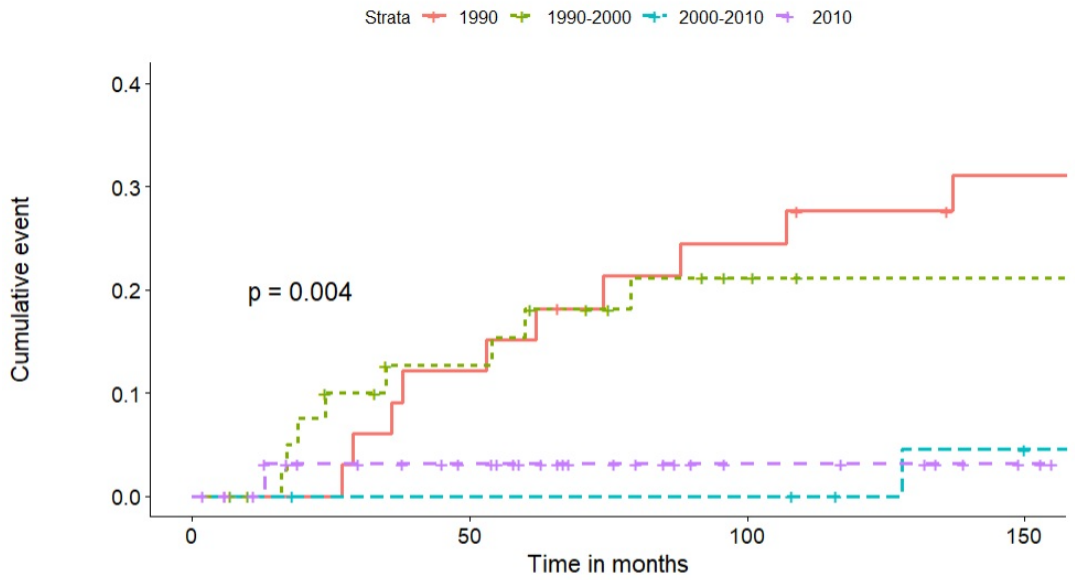
48 yrs
NYHA III
1 HF hospitalization <12 months
sPAP 45 mmHg
PCWP 19
RAP 15
Moderate TR

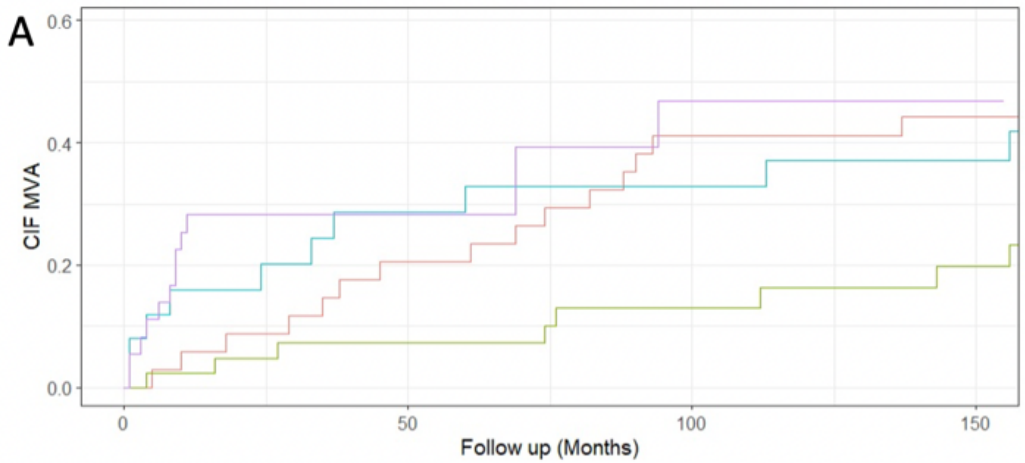
DCM

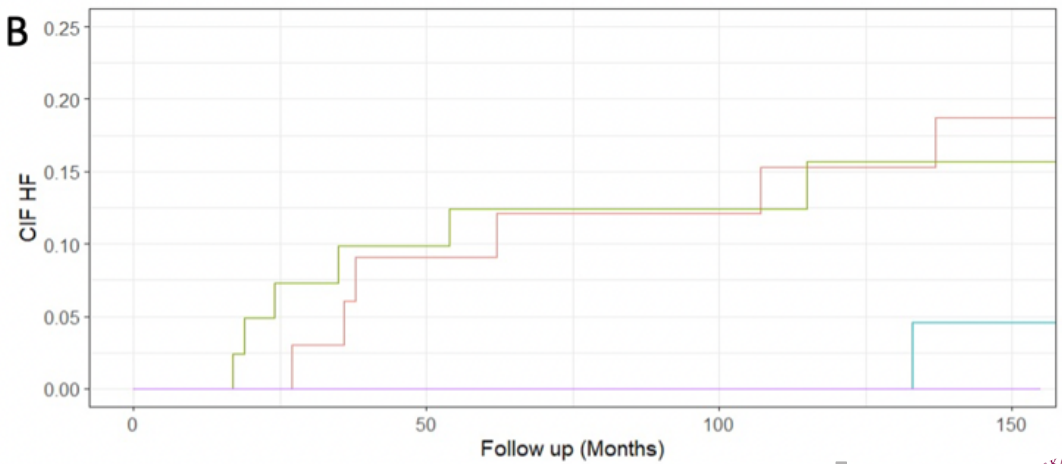
RCM/HCM

ACM

ARVC outcomes – decades of enrollment







Cappelletto, Stolfo et al. Unpublished

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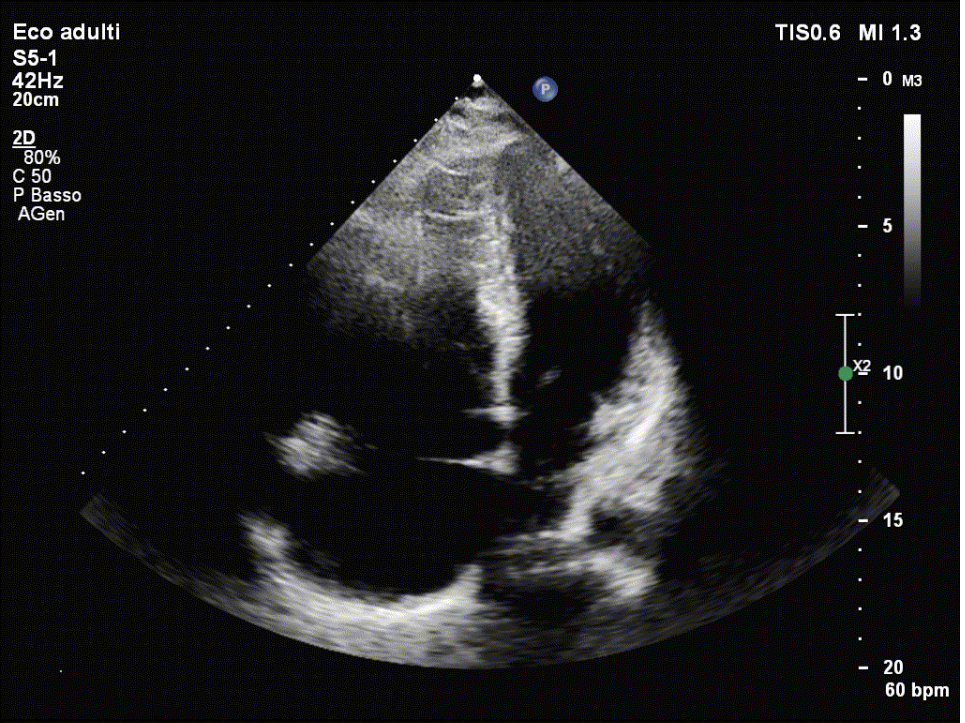
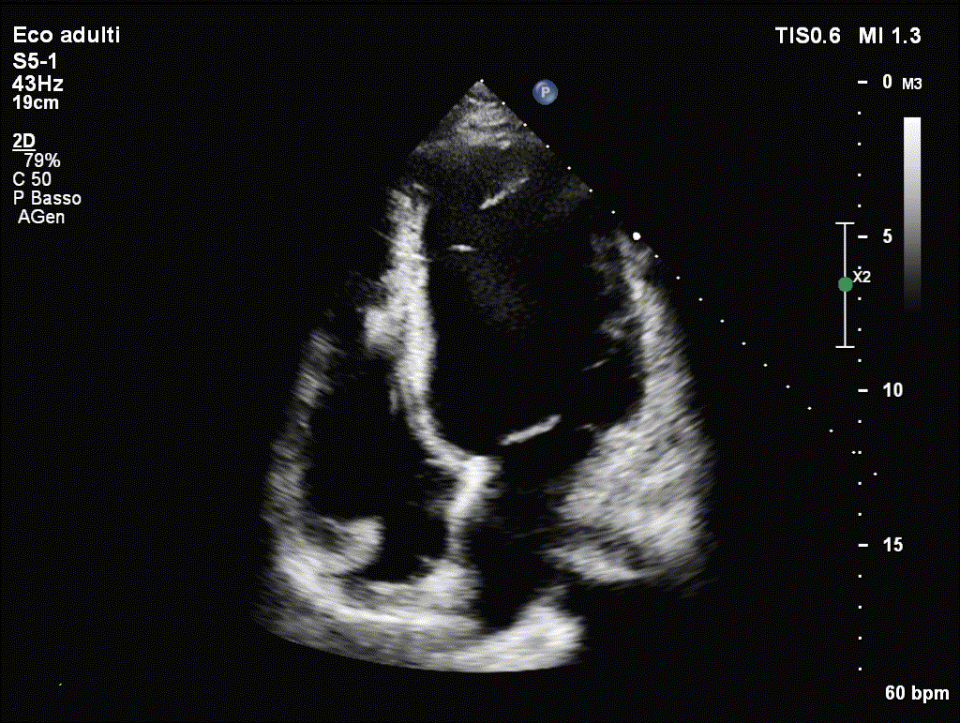


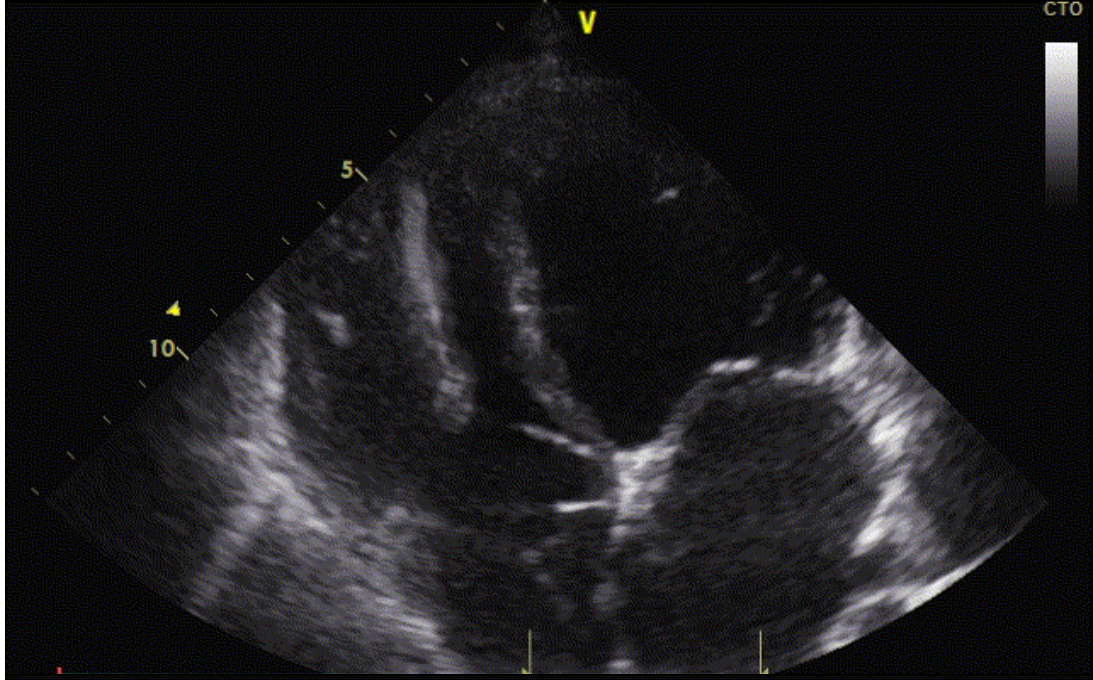


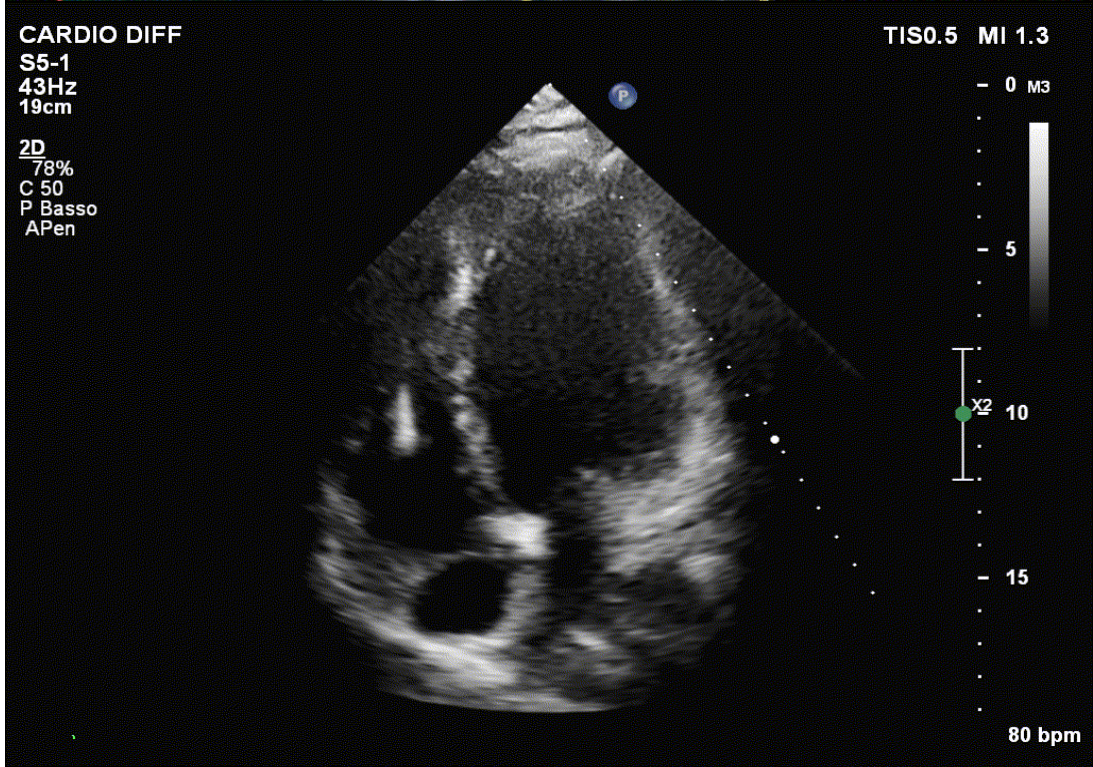
Mean Age

32 yrs

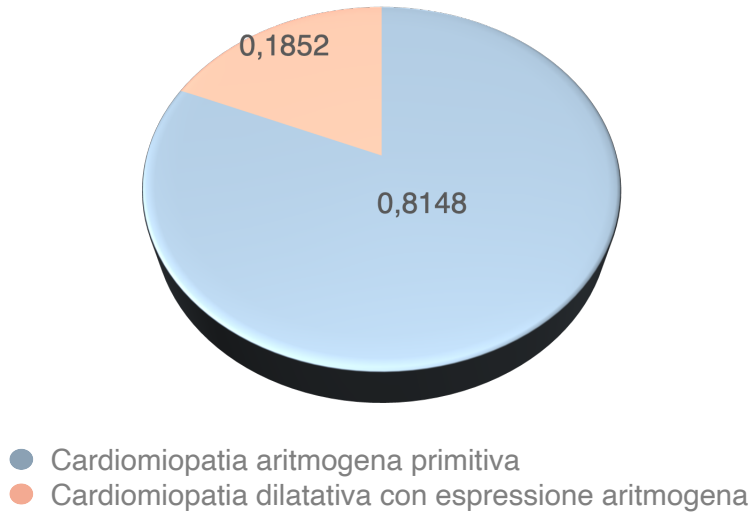
4 arrhyhtmic storms

3 Stage C2 HF





ACM – Transplant activity and outcomes



Male (n, %)	19 (70)
Age (median, SD)	40 (13)
Age > 65y (n, %)	2 (7.4)
Redo Surgery (n, %)	2 (7.4)
Diabetes (n, %)	0 (0)
Hypertension (n, %)	2 (7.4)
COPD (n, %)	2 (7.4)
AF (n, %)	4 (15)
CKD (n, %)	5 (10)
PM/ICD (n, %)	12 (44)
MCS (n, %) - ECMO	2 (7.4)
- IABP	1 (3.7)

Courtesy of Prof. Vendramin – Cardiothoracovascular Department – ASUFC (Udine)

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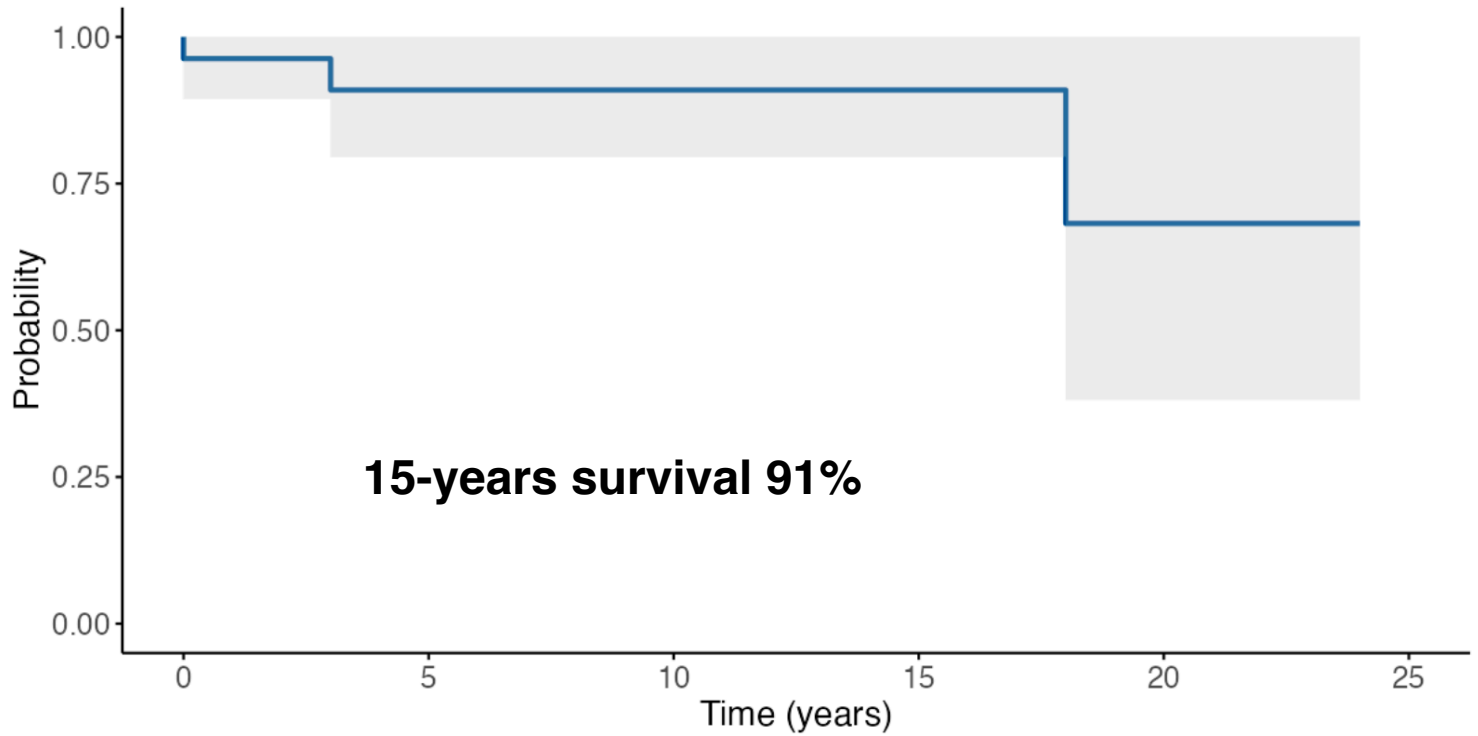
ACM – Transplant activity and outcomes



Courtesy of Prof. Vendramin – Cardiothoracovascular Department – ASUFC (Udine)

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