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Clinical and echocardiographic parameters associated with outcome in secondary moderate mitral regurgitation.

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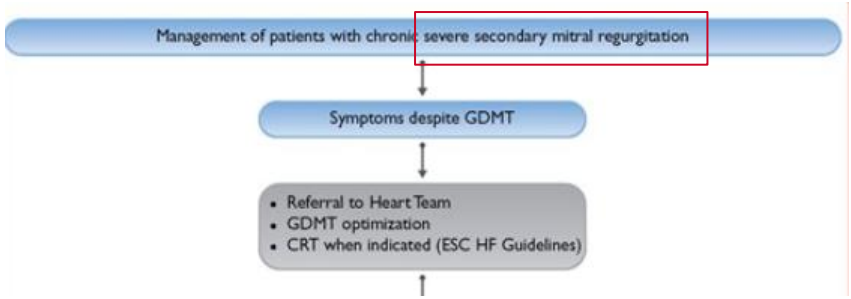
Current approach of secondary MR.



Recommendations	Class[b]	Level[c]
Valve surgery/intervention is recommended only in patients with severe SMR who remain symptomatic despite GDMT (including CRT if indicated) and has to be decided by a structured collaborative Heart Team.[247,323,336,337]	I	B

Recommendations for Intervention for Secondary MR
Referenced studies that support the recommendations are summarized in Online Data Supplement 31.

COR	LOE	Recommendations
2a	B-R	1. In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent symptoms (NYHA class II, III, or IV) while on optimal GDMT for HF (Stage D), TEER is reasonable in patients with appropriate anatomy as defined on TEE and with LVEF between 20% and 50%, LVESD ≤70 mm, and pulmonary artery systolic pressure ≤70 mm Hg.[1-8]
2a	B-NR	2. In patients with severe secondary MR (Stages C and D), mitral valve surgery is reasonable when CABG is undertaken for the treatment of myocardial ischemia.[9-15]
2b	B-NR	3. In patients with chronic severe secondary MR from atrial annular dilation with preserved LV systolic function (LVEF ≥50%) who have severe persistent symptoms (NYHA class III or IV) despite therapy for HF and therapy for associated AF or other comorbidities (Stage D), mitral valve surgery may be considered.[16-20]
2b	B-NR	4. In patients with chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) who have persistent severe symptoms (NYHA class III or IV) while on optimal GDMT for HF (Stage D), mitral valve surgery may be considered.[9,12,21-43]
2b	B-R	5. In patients with CAD and chronic severe secondary MR related to LV systolic dysfunction (LVEF <50%) (Stage D) who are undergoing mitral valve surgery because of severe symptoms (NYHA class III or IV) that persist despite GDMT for HF, chordal-sparing mitral valve replacement may be reasonable to choose over downsized annuloplasty repair.[9,12,21-32,44-47]

Vahanian, Alec, et al. "2021 ESC/EACTS Guidelines for the management of valvular heart disease: developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)." *European heart journal* 43.7 (2022): 561-632.

Otto, Catherine M., et al. "2020 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines." *Journal of the American College of Cardiology* 77.4 (2021): 450-500.

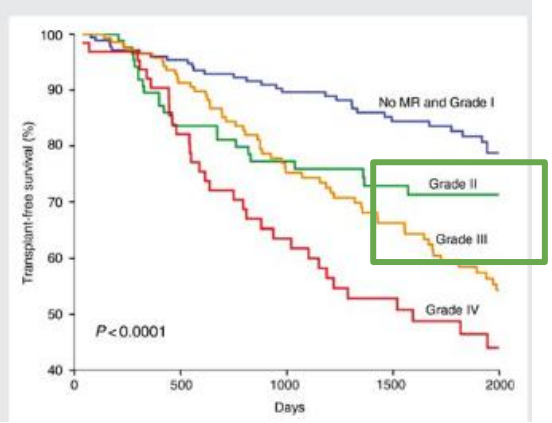
Why moderate MR?

Prognostic implications of functional mitral regurgitation according to the severity of the underlying chronic heart failure: a long-term outcome study

European Journal of Heart Failure (2010) **12**, 382–388
doi:10.1093/eurjhf/hfq014

Francesca Bursi[1]*, Andrea Barbieri[1], Francesco Grigioni[2], Letizia Reggianini[1], Vera Zanasi[1], Chiara Leuzzi[1], Caterina Ricci[1], Giulia Piovaccari[2], Angelo Branzi[2], and Maria Grazia Modena[1]

Italy, Bologna



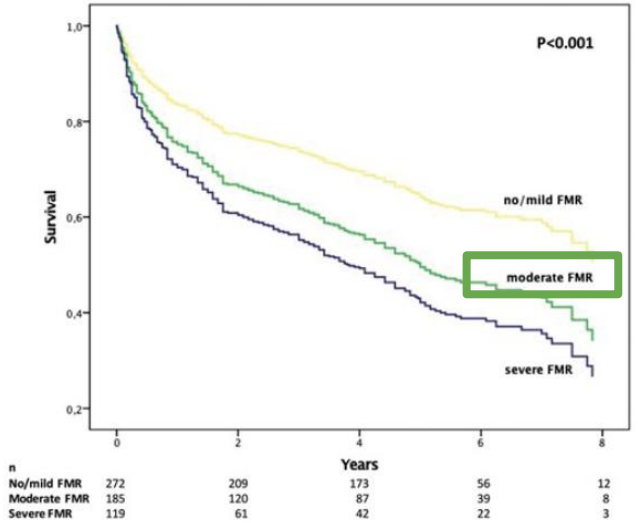
	Adjusted HR	95% CI	P
No FMR or Grade I (referent group)	1		
FMR Grade II	1.32	0.82–2.13	0.247
FMR Grade III	2.02	1.36–3.01	0.0005
FMR Grade IV	2.58	1.57–4.16	0.0001
Age	1.02	1.00–1.03	0.019
Men	1.52	1.07–2.15	0.019
NYHA class	1.42	1.12–1.79	0.003
Ischaemic aetiology	1.10	0.80–1.51	0.571
Atrial fibrillation	1.38	0.96–1.98	0.079
Chronic kidney disease	1.32	0.84–2.07	0.229
COPD	0.80	0.51–1.26	0.341
ACE inhibitors/ARBs	0.91	0.57–1.44	0.683
Beta-blockers	0.84	0.62–1.14	0.262
ICD	0.66	0.38–1.15	0.140
Cardiac resynchronization therapy	0.31	0.14–0.67	0.003
LV ejection fraction (per 10% increase)	0.74	0.60–0.91	0.003

Refining the prognostic impact of functional mitral regurgitation in chronic heart failure FREE

Georg Goliasch ✉, Philipp E Bartko, Noemi Pavo, Stephanie Neuhold, Raphael Wurm, Julia Mascherbauer, Irene M Lang, Guido Strunk, Martin Hülsmann

European Heart Journal, Volume 39, Issue 1, 01 January 2018, Pages 39–46,

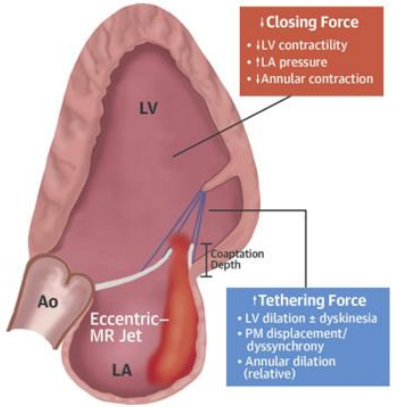
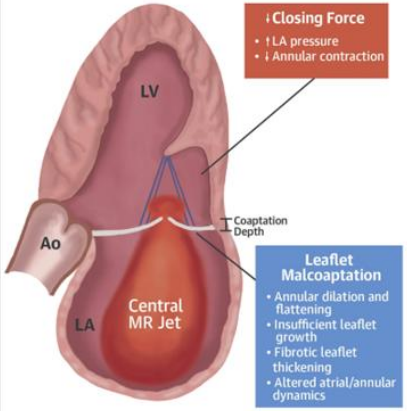
Vienna General Hospital,



Adjusted for: age, sex, ischaemic aetiology of heart failure, serum creatinine and NT-proBNP.

Etiology of MR

CENTRAL ILLUSTRATION: Secondary Mitral Regurgitation Versus Atrial Functional Mitral Regurgitation

Secondary Mitral Regurgitation	Atrial Functional Mitral Regurgitation
	
Etiology and Prevalence	
• 11%-59% post myocardial infarction • >50% in dilated cardiomyopathy	• 6%-7% in lone AF • Up to 53% in HFpEF
Diagnosis	
• Systolic LV dysfunction • Restricted leaflet motion and tethering • Eccentric jet > central jet • Relative LA dilation	• Normal systolic LV function • Normal leaflet motion • Central jet • Severe LA dilation
Management	
• Optimal HF therapy • Cardiac resynchronization therapy • Revascularization • MitraClip	• Address AF/HFpEF risk factors and lifestyle • HF therapy, diuretics as indicated • Early sinus restoration strategy • ?Intervention, annuloplasty, MitraClip

Deferm, S. et al. J Am Coll Cardiol. 2019;73(19):2465-76.

Severe Atrial Functional Mitral Regurgitation

Clinical and Echocardiographic Characteristics, Management and Outcomes

Oltion Mesi, MD,[a] Mohamed M. Gad, MD,[a] Alejandro D. Crane, MD,[a] Jay Ramchand, MBBS,[b] Rishi Puri, MD, PhD,[b] Habib Layoun, MD,[b] Rhonda Miyasaka, MD,[b] Marc A. Gillinov, MD,[c] Per Wierup, MD, PhD,[c] Brian P. Griffin, MD,[b] Samir R. Kapadia, MD,[b] Serge C. Harb, MD[b]

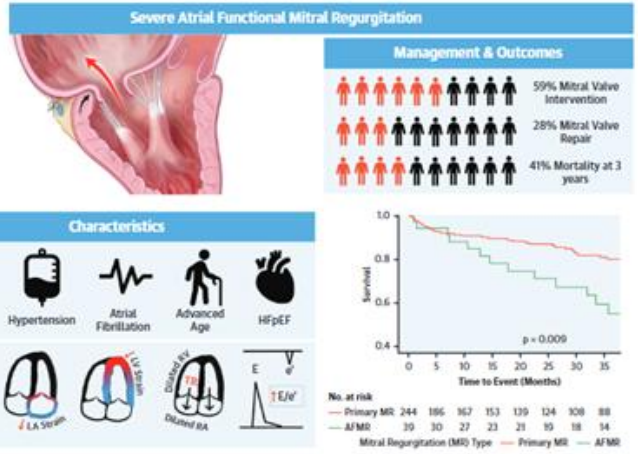
JACC imaging 2021

Severe MR, normal EF

- AFMR
  - N=39
  - Divided in 2 groups
    - Central jet , 30pt
    - Posterior jet , 9pt

      No significant difference in death
- Primary MR
  - N=244

- => significant difference in survival, HF hospitalisation between both groups
- Worse outcome for aFMR



Mesi, O. et al. J Am Coll Cardiol Img. 2021;14(4):797-808.

Clinical and echocardiographic parameters associated with outcome in secondary moderate mitral regurgitation.

Population	Intervention	Outcome
n= 1061, all moderate MR Euvolemic and haemodynamic stable condition =3 months after ACS or heart failure hospitalization =6 months after CRT implantation	Retrospective Clinical and echocardiographic risk factors	Primary: All-cause mortality Secondary: composite: all-cause mortality and heart failure * *increase of loop diuretics or heart failure hospitalization

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1846 patients moderate FMR

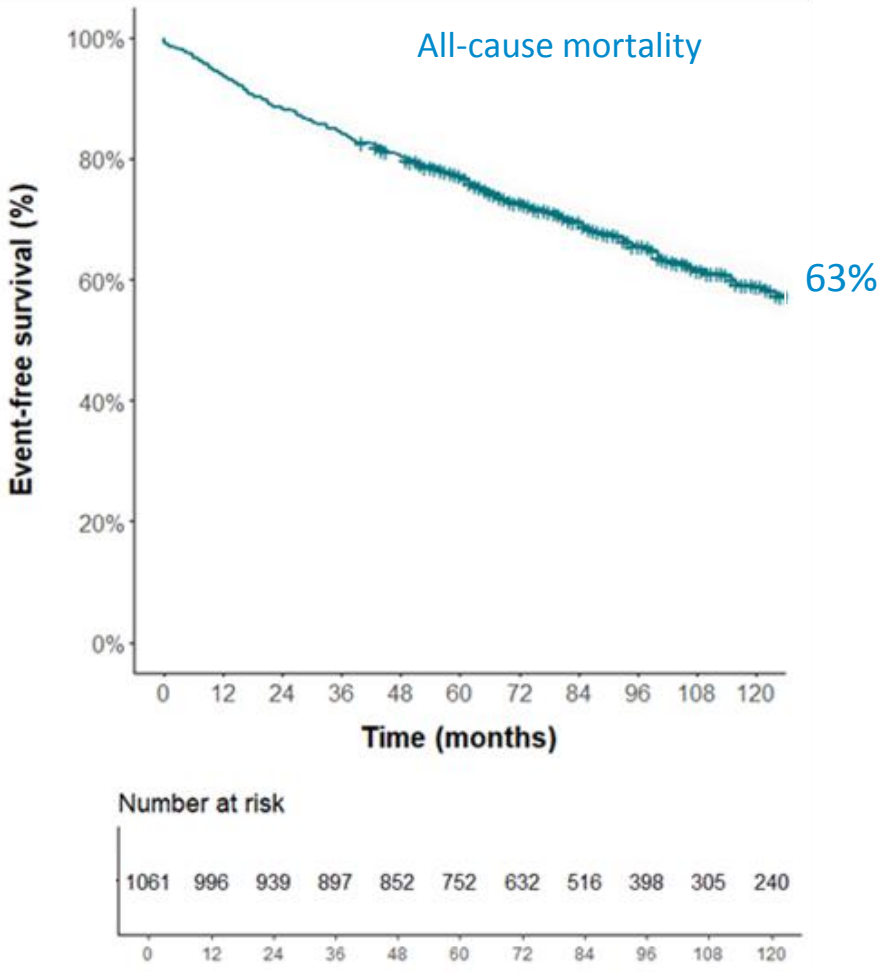
Time range: 2008-2018

Excluded patients:
- Congenital cardiomyopathy, n= 36
- Hypertrophic obstructive cardiomyopathy, n= 28
- Mild regurgitation aortic regurgitation or > mild stenosis of left-sided valves, n= 236
- Previous left-sided valve surgery, n= 128
- Echo only during congestion or acute coronary syndrome without follow-up echo, n= 270
- Poor image quality or no patient files, n= 87

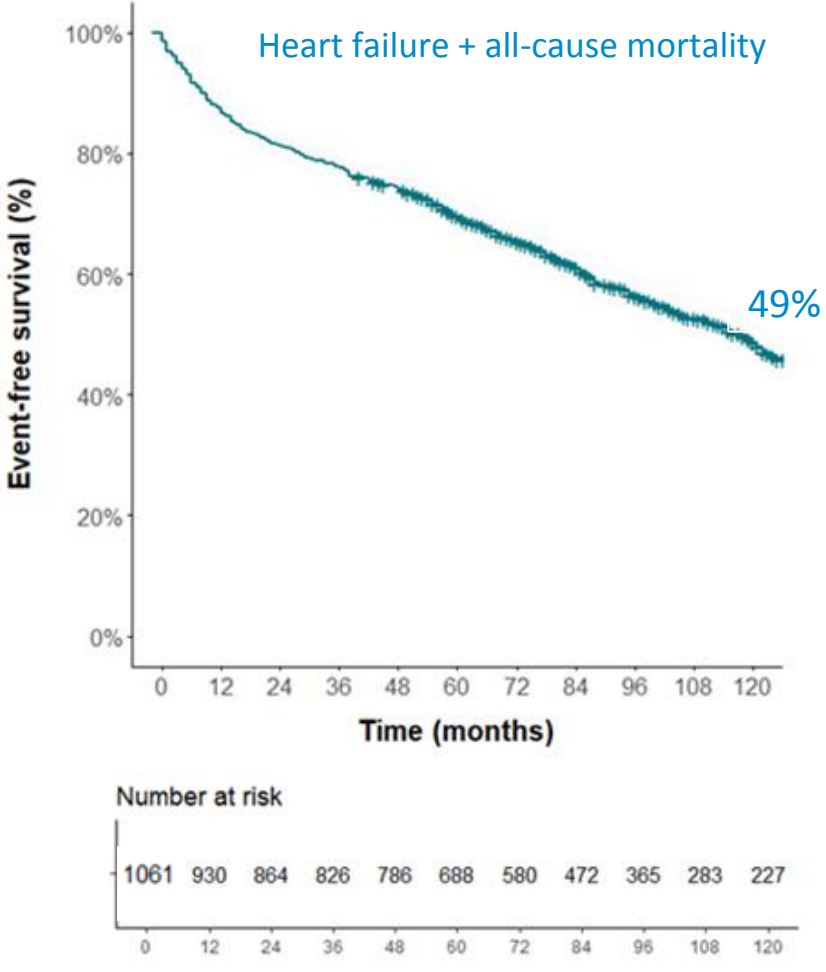
1061 patients moderate FMR

Clinical characteristics	Total population n = 1061	Echo characteristics	Total population n = 1061
Age, years	69 (±11)	**EF, %**	45 (±14)
Sex, male	624 (59)	**FMR Etiology** **aFMR** **vFMR LV EF ≥40%** **vFMR LV EF<40%**	 325 (33) 329 (31) 380 (36)
Arterial hypertension	617 (58)	**LV end- diastolic volume index mL/m²**	74 (72 -76)
Diabetes Mellitus	179 (17)	**LV end-systolic volume index, mL/m²**	44 (42 - 46)
COPD	142 (13)	**Vena Contracta, mm**	4 (±1)
eGFR, mL/min/1,73m2	65 (± 23)	**EROA, mm2**	24 (±7)
History of heart failure hospital admission	412 (39)	**Regurgitation Volume, mL**	38 (±12)
Coronary artery disease	483 (46)	**Regurgitation Fraction, %**	31 (16)
Atrial fibrillation	556 (52)	**LAVI, mL/m2**	38 (29 - 49)
NYHA class III-IV	207 (19)	**E/E'**	14 (13 - 14)
History of stroke	133 (13)	**Severe TR**	158 (15)
Beta blockers	766 (72)	**TR gradient, mmHg**	27 (20 - 34)
ACEi/ARB/ARNI	720 (68)	**RV-PA coupling index, mm/mmHg**	0.80 (±0.6)

All-cause mortality



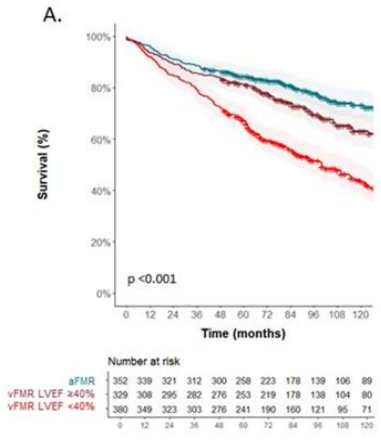
Heart failure + all-cause mortality



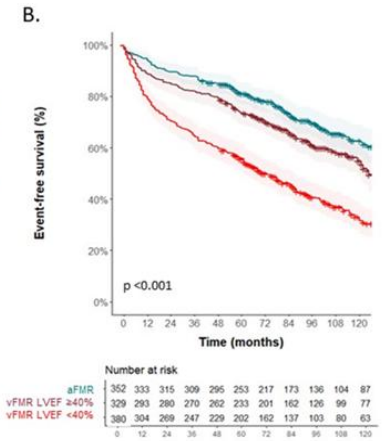
Multivariable Cox regression analysis.	Outcome: all cause mortality.		Outcome: heart failure and all -cause mortality.	
Variable	HR (CI)	p-value	HR (CI)	p-value
Age, years	**1.034 (1.023 - 1.045))**	**<0.001**	**1.022 (1.013 - 1.031)**	**<0.001**
Sex, male	**1.698 (1.351 - 2.134)**	**<0.001**	**1.489 (1.230 - 1.802)**	**<0.001**
Diabetes	**1.406 (1.097 - 1.804)**	**0.007**	**1.491 (1.205 - 1.845)**	**<0.001**
COPD	**1.362 (1.055 - 1.758)**	**0.018**	**1.261 (1.486 - 2.290)**	**0.049**
Coronary artery disease	**0.970 (0.770 - 1.223)**	0.797	0.981 (0.804 - 1.196)	0.848
eGFR	**0.999 (0.998 - 1.000)**	**0.042**	**0.999 (0.998 - 1.000)**	**0.003**
Atrial fibrillation	**N/A**	N/A	1.121 (0.918 - 1.367)	0.262
NYHA class III - IV	**1.578 (1.244 - 2.002)**	**<0.001**	**1.365 (1.104 - 1.687)**	**0.004**
aFMR **vFMR, LV EF ≥40%** **vFMR, LV EF <40%**	**ref.** **1.528 (1.108 - 2.106)** **1.960 (1.434 - 2.679)**	**<0.001** **0.010** **<0.001**	**ref.** **1.583 (1.198 - 2.093)** **1.956 (1.498 - 2.553)**	**<0.001** **0.001** **<0.001**
LAVI, mL/m²	**1.007 (1.001 - 1.012)**	**0.013**	**1.008 (1.003 - 1.012)**	**0.001**
Severe TR	**1.181 (0.896 - 1.557)**	**0.003**	1.176 (0.925 - 1.495)	0.186
RV - PA coupling index	**0.797 (0.642 - 0.990)**	**0.041**	**0.762 (0.631 - 0.920)**	**0.005**
MVI (time - dependent)	**1.359 (1.026 - 1.800)**	**0.032**	**1.302 (1.017 - 1.668)**	**0.037**
CRT (time - dependent)	**1.389 (1.023 - 1.886)**	**0.036**	**1.328 (1.010 - 1.744)**	**0.042**

Focus on ETIOLOGY

All-cause mortality

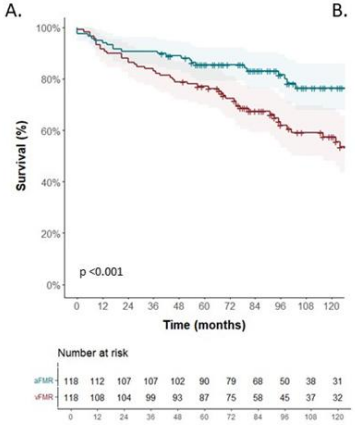


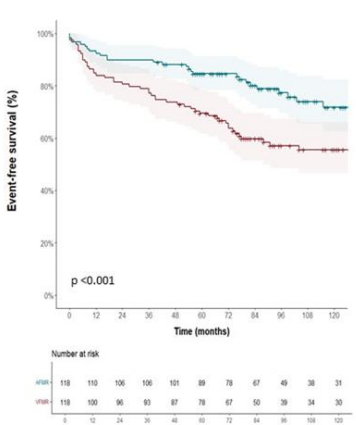
Heart failure + all-cause mortality



Total population

aFMR
vFMR



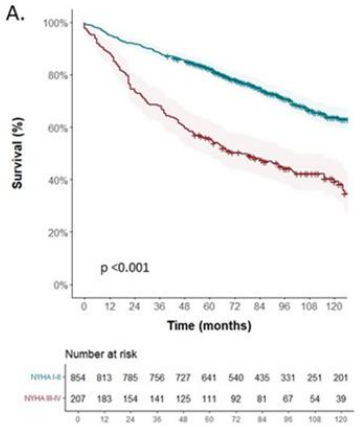


Matched groups

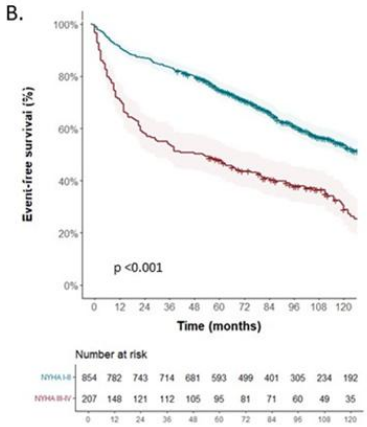
Groups are matched for:
age, sex, diabetes, COPD, eGFR, NYHA class, LV EF, LAVI, TR, RV-PA coupling index

Focus on NYHA

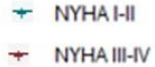
All-cause mortality

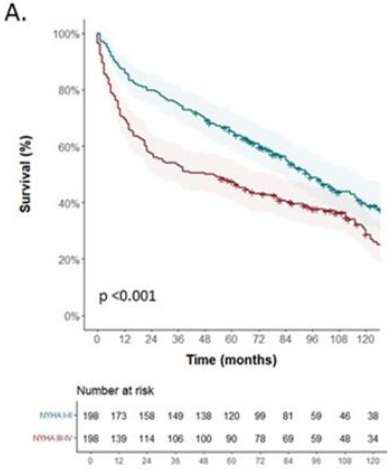


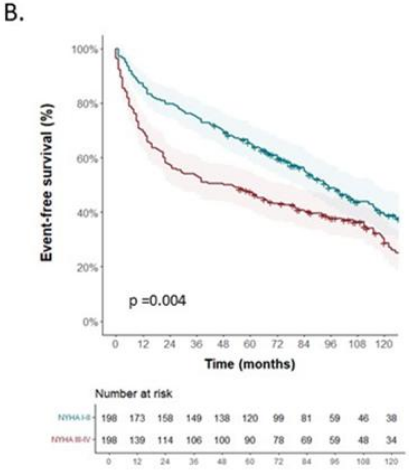
Heart failure + all-cause mortality



Total population







Matched groups

Groups are matched for:
age, sex, diabetes, COPD, eGFR, FMR etiology+LV EF, LVEF, LAVI, TR, RV-PA coupling index

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Conclusion:

In moderate MR, symptoms and FMR etiology have a significant association with outcome.

Early recognition of etiology implies a better risk stratification and may be helpful in management.

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