

XI Reunión. Estado del Arte en
INSUFICIENCIA CARDIACA
PRÁCTICA CLÍNICA Y MODELOS ORGANIZATIVOS



Sede: **Hotel Meliá María Pita** (Av. de Pedro Barrié de la Maza, 3. A Coruña)

A CORUÑA 27-28 SEPTIEMBRE 2024



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Fotografía: Chema Ríos

XI Meeting. State of the Art in
HEART FAILURE

#ACORUÑAHF2024

CLINICAL PRACTICE AND ORGANIZATIONAL MODELS

Venue: **Hotel Meliá María Pita** (Av. de Pedro Barrié de la Maza, 3. A Coruña)



ÁREA SANITARIA
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UNIVERSIDADE DA CORUÑA



When to Refer a Patient to an Advanced HF center?

¿Cuándo derivar a un paciente para terapias avanzadas de IC?

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Madrid

Disclosure

“When to Refer a Patient to an Advanced HF center?”

Employee of: no

Stockholder in: no

Consultant for: Novartis, AstraZeneca, Rovi.

Research support from: Novartis, Astra-Zeneca, Amgen, Impulse Dynamics, Orion Pharma
Boehringer Ingelheim-Lilly.

Honoraria as speaker from: Novartis, Orion, Astra-Zeneca, Medtronic, Rovi, Impulse Dynamics y
Boehringer Ingelheim-Lilly and Abbott.

Epidemiology

- ✓ 2 % of Heart Failure population.
- ✓ Among patients with Stage C HFrEF, 4.5% progress to Stage D HF each year (Kalogeropoulos et al. JACC HF 2017).
- ✓ Standard treatment is insufficient to control patient's symptoms
- ✓ Poor QOL and prognosis
- ✓ (Advance = refractory = end-stage)

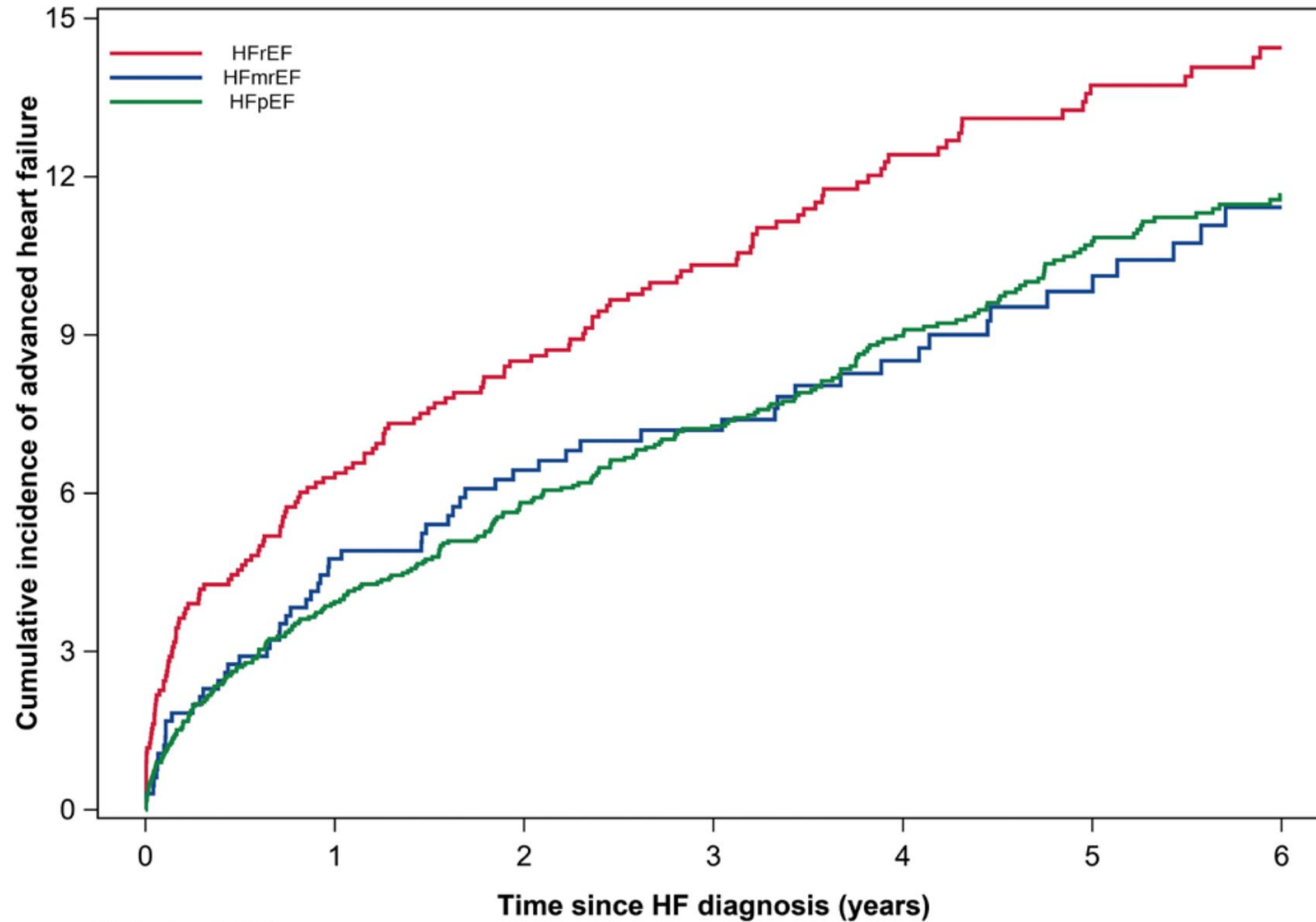
Criteria for definition of advanced heart failure

All the following criteria must be present despite OMT:

1. Severe and persistent symptoms of heart failure [NYHA class III (advanced) or IV].
2. Severe cardiac dysfunction defined by (at least one of the following):
 - LVEF ($\leq 30\%$)
 - Isolated RV failure (e.g., ARVC)
 - Non-operable severe valve abnormalities or congenital abnormalities
 - Persistently high (or increasing) BNP or NT-proBNP values and severe diastolic dysfunction or LV structural abnormalities (according to the definitions of HFpEF)
3. Episodes of pulmonary or systemic congestion requiring high-dose i.v. diuretics (or diuretic combinations) or episodes of low output requiring inotropes or vasoactive drugs or malignant arrhythmias causing >1 unplanned visit or hospitalization in the last 12 months.
4. Severe impairment of exercise capacity with inability to exercise or low 6MWT (<300 m) or $pVO_2 <12$ mL/kg/min or $<50\%$ predicted value, estimated to be of cardiac origin.

6MWT= 6-minute walk test; ARVC = arrhythmogenic right ventricular cardiomyopathy; BNP = B-type natriuretic peptide; HFpEF = heart failure with preserved ejection fraction; i.v. = intravenous; LV = left ventricular; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA =New York Heart Association; pVO_2 = peak oxygen consumption; RV = right ventricular.

Epidemiology



Olmsted County, Minnesota

	Patients-at-Risk						
	0	1	2	3	4	5	6
HFrEF	1103	848	692	558	427	329	242
HFmrEF	653	541	417	332	247	178	135
HFpEF	2438	1968	1552	1244	948	675	465

Prognosis of patients with advanced HF

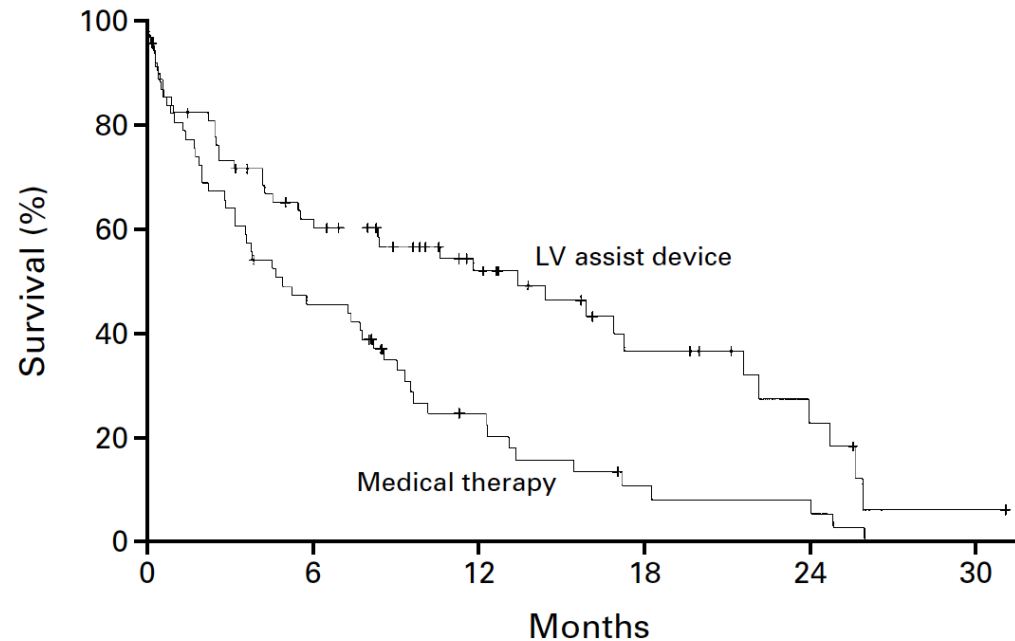
VOLUME 345

NOVEMBER 15, 2001

NUMBER 20



LONG-TERM USE OF A LEFT VENTRICULAR ASSIST DEVICE FOR END-STAGE HEART FAILURE

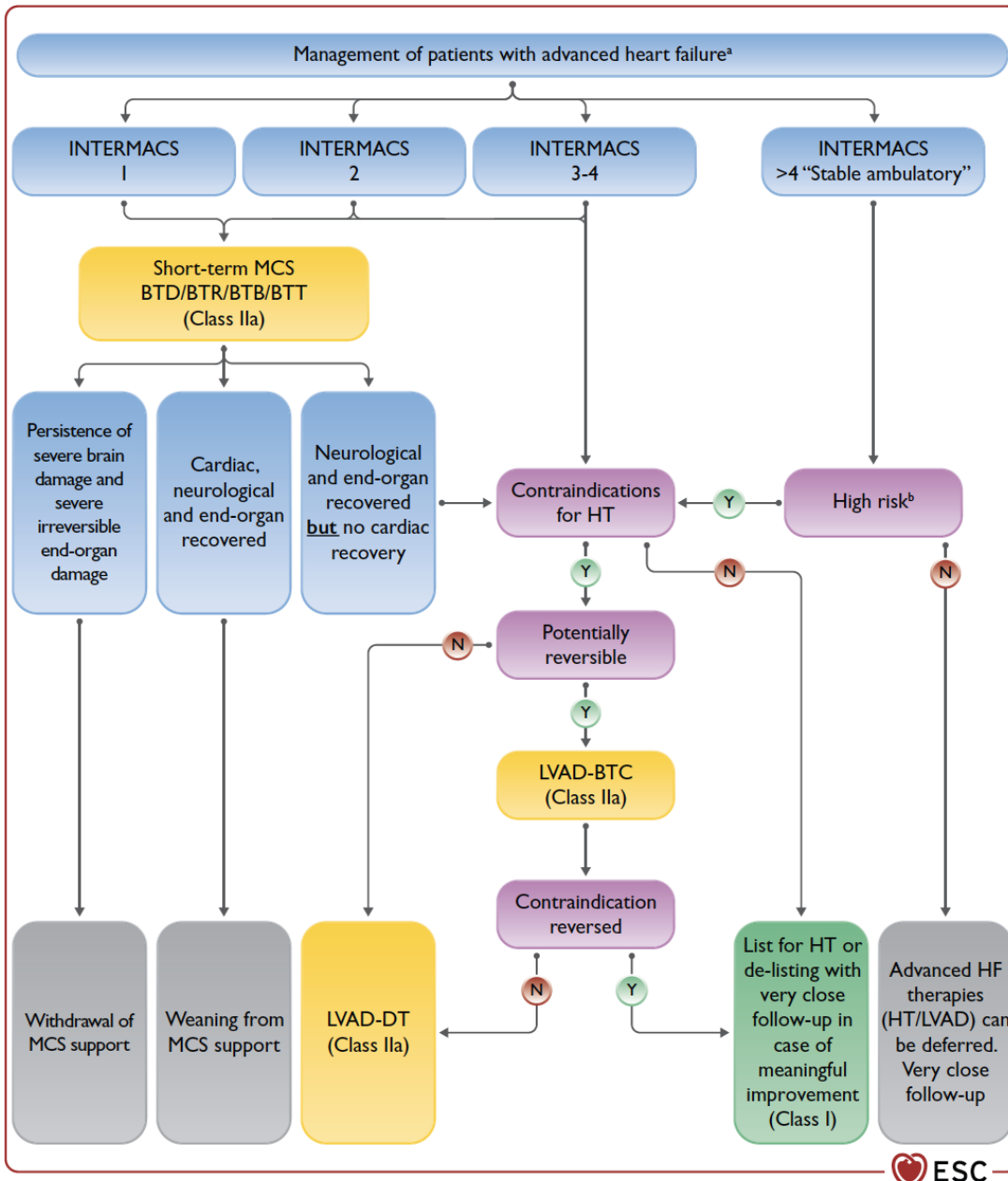


No. AT RISK

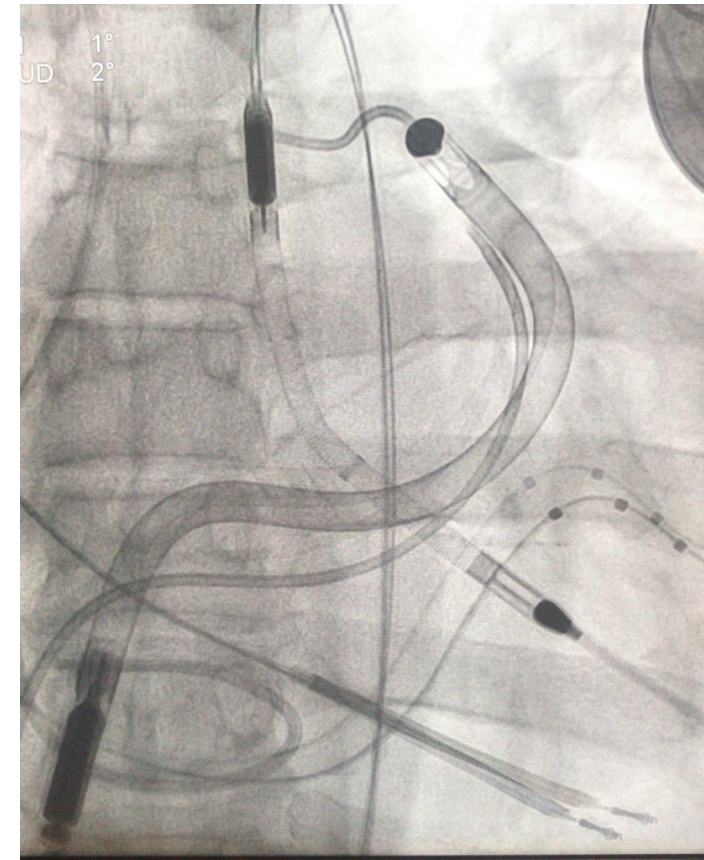
LV assist device	68	38	22	11	5	1
Medical therapy	61	27	11	4	3	0

Eligible patients

- 1.- Chronic end-stage HF
- 2.- Contraindications to HTx
- 3.- Symptoms of NYHA class IV HF for at least 90 days despite GDMT
- 4.- LVEF of 25 percent or less;
- 5.- POC < 12 ml/Kg/min or inotropic dependence.



Algorithm for the treatment of patients with advanced HF/cardiogenic shock

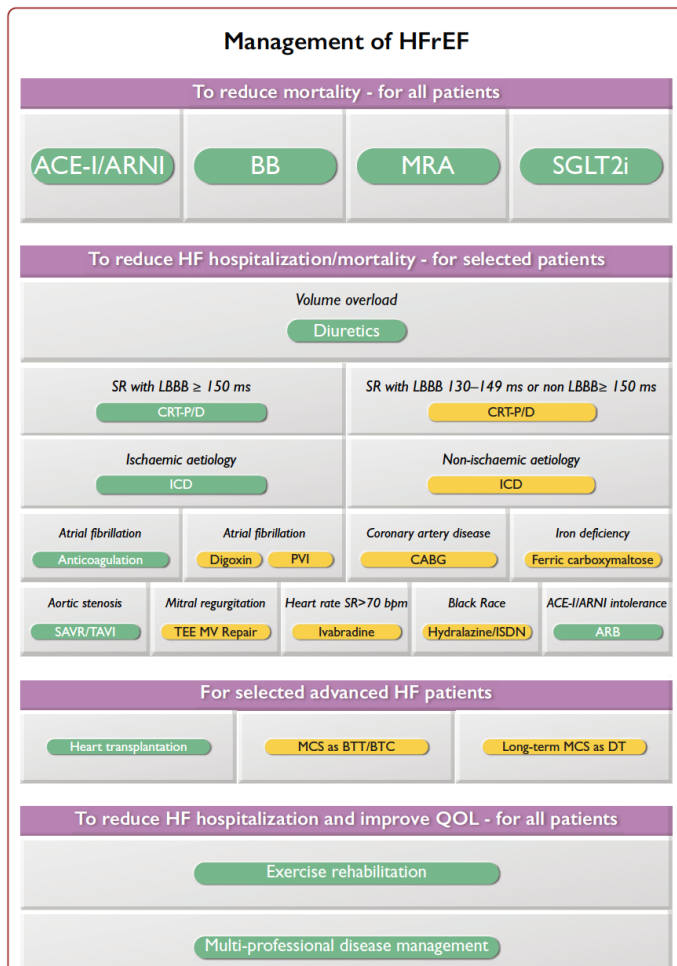


Options for patients with advanced HF


- ✓ Optimize neurohormonal inhibition and device therapy
- ✓ High risk conventional cardiac surgery
- ✓ Short term management:
 - IV drugs, management of congestion (iv diuretics, UF)
 - Mitraclip
 - Short-term MCS (IABP, Impella, CentriMag)
- ✓ Long-term management
 - Heart transplantation
 - LT-Mechanical circulatory support
 - Chronic iv inotropes, UF, peritoneal dialysis
- ✓ Palliative care

Optimize neurohormonal inhibition and device therapy

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





PARADIGM-HF

NYHA class					0.03
I or II	3178	3130			
III or IV	1002	1076			


DAPA-HF

NYHA class					
II	190/1606	289/1597			0.63 (0.52–0.75)
III or IV	196/767	213/774			0.90 (0.74–1.09)

EMPEROR Reduced

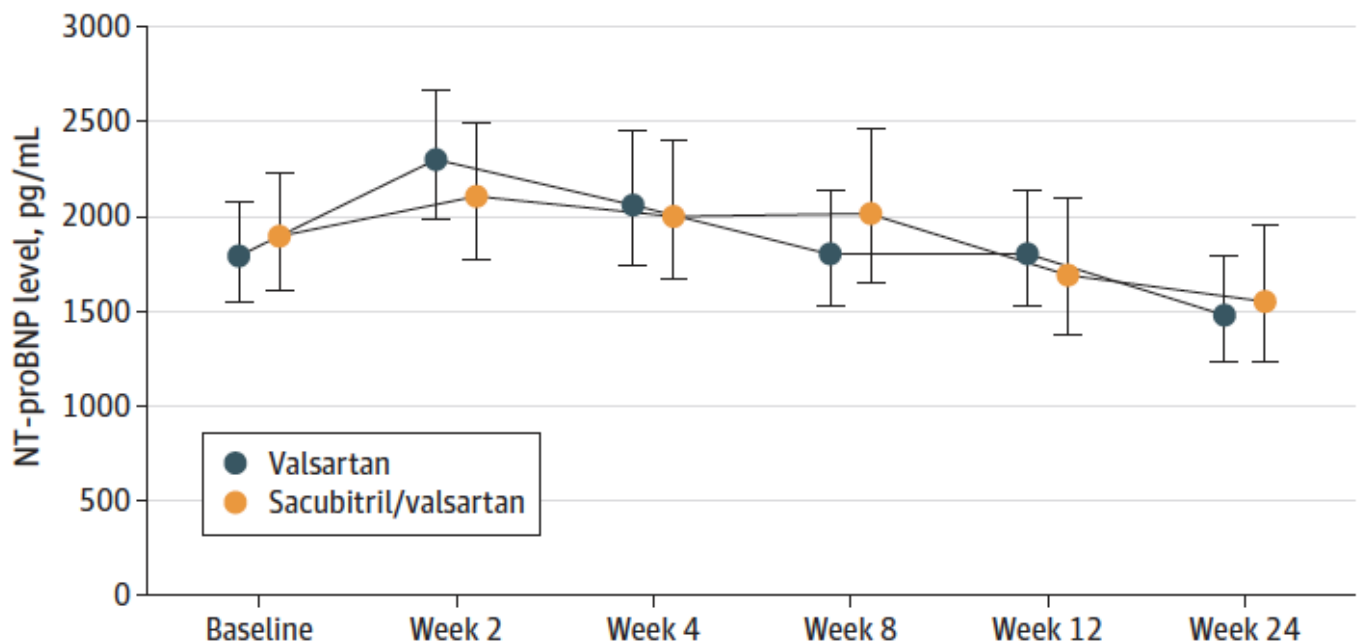
Baseline NYHA class					
II	220/1399	299/1401			0.71 (0.59–0.84)
III or IV	141/464	163/466			0.83 (0.66–1.04)

VICTORIA

NYHA class					
I or II	445	484			0.91 (0.80–1.04)
III or IV	451	487			0.87 (0.77–0.99)

SAC/VAL in advanced HF. LIFE trial

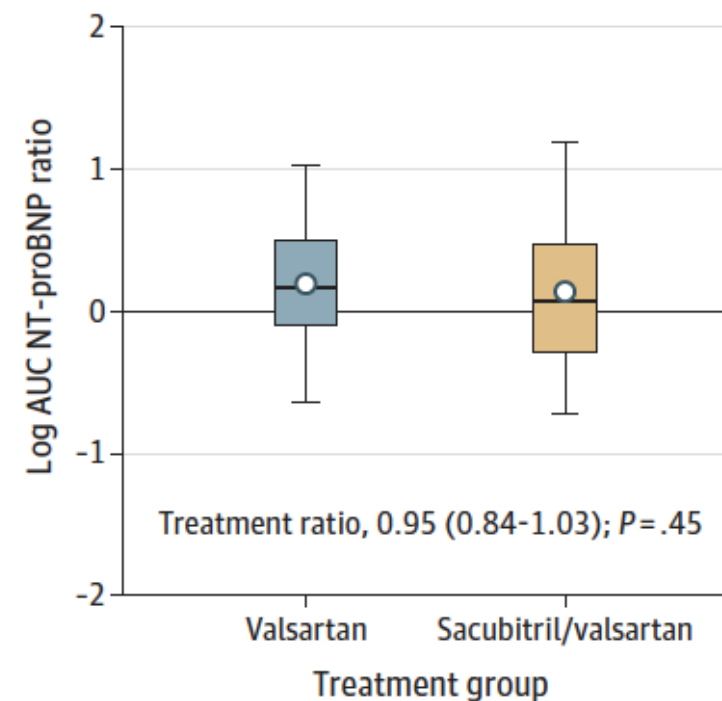
Geometric mean NT-proBNP level



No. with data

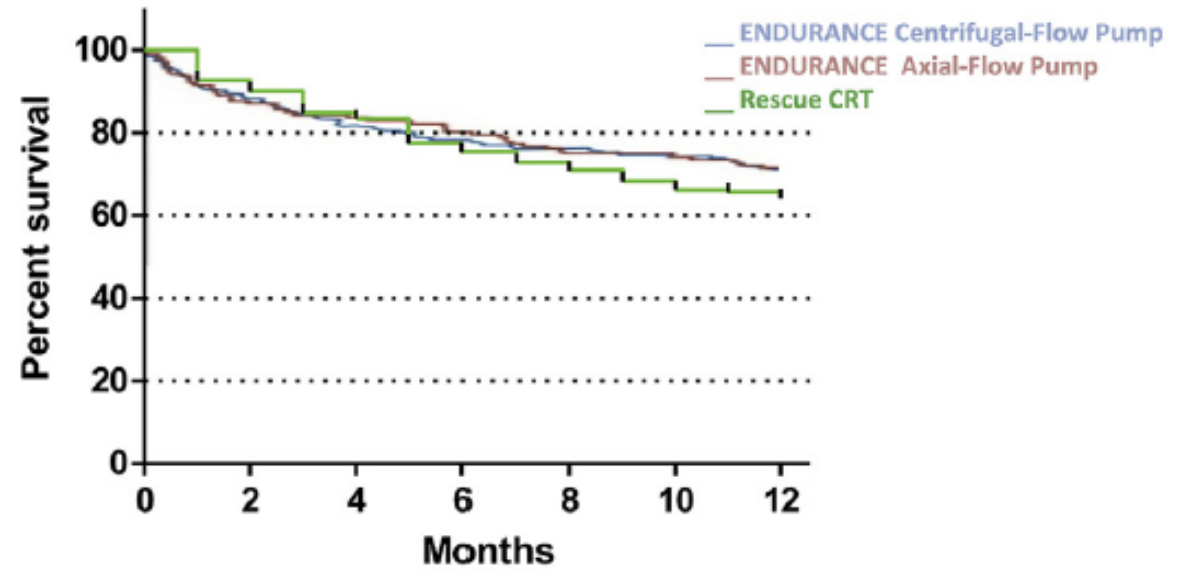
Valsartan	162	155	154	144	145	124
Sacubitril/valsartan	161	156	153	143	140	118

Log AUC NT-proBNP

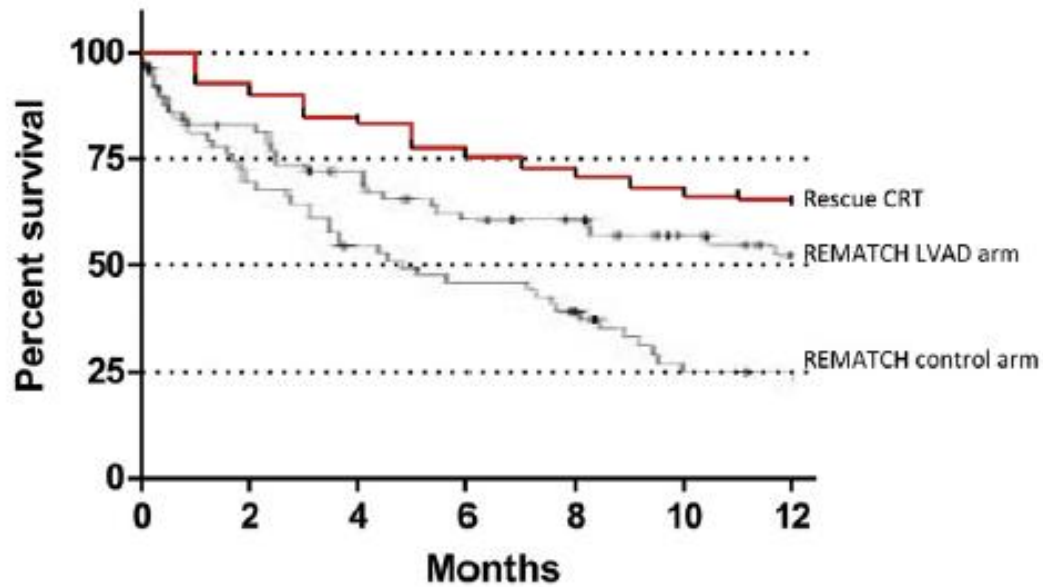


CRT in advanced HF and inotrope dependence

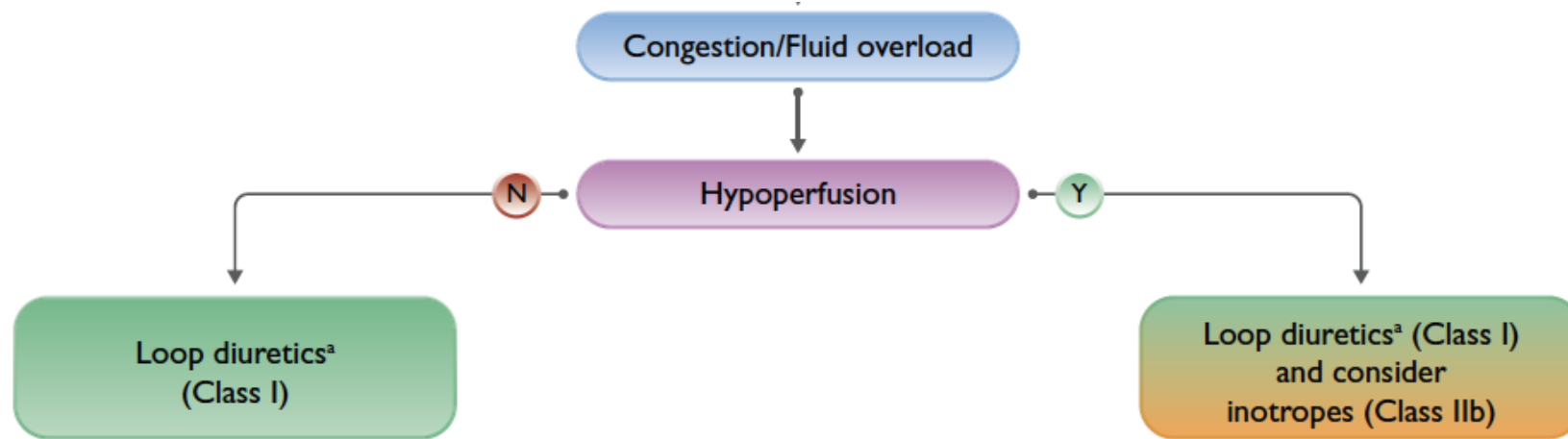
Event Free Survival ENDURANCE† vs. Survival Rescue CRT



Survival REMATCH† vs. Survival Rescue CRT

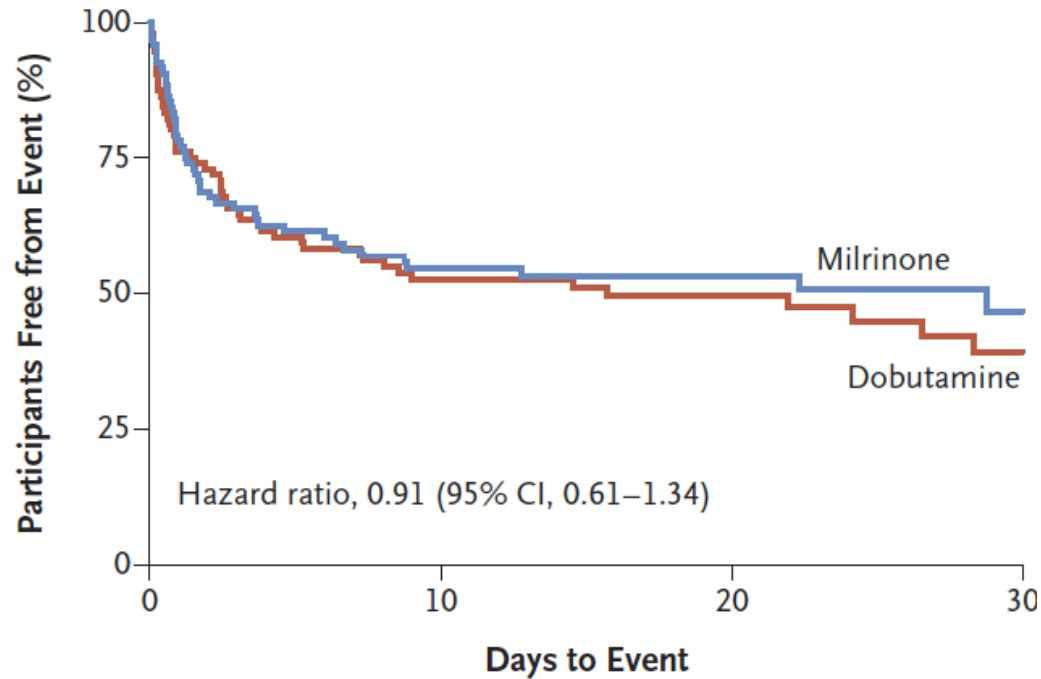


Management of patients with acute decompensated



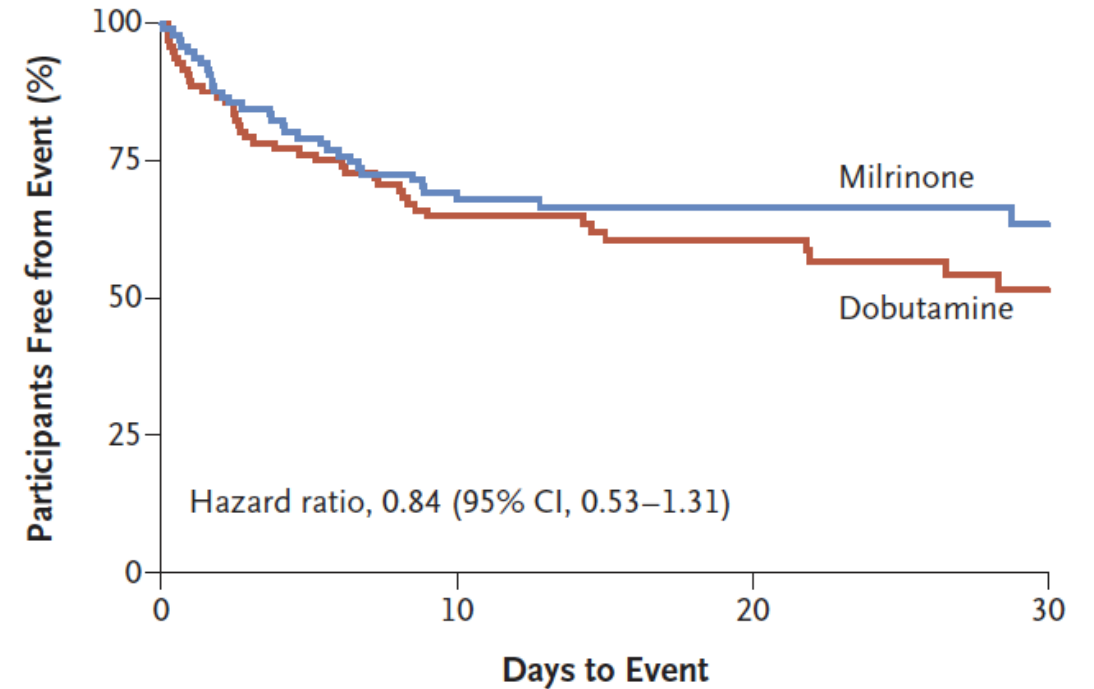
Recommendations	Class	Level
Renal replacement therapy should be considered in patients with refractory volume overload and end-stage kidney failure	IIa	C
Continuous inotropes and/or vasopressors may be considered in patients with low cardiac output and evidence of organ hypoperfusion as bridge to MCS or heart transplantation.	IIb	C
Ultrafiltration may be considered in refractory volume overload unresponsive to diuretic treatment.	IIb	C

Milrinona vs dobutamine in patients with cardiogenic shock DOREMI-Trial



No. at Risk				No. at Risk	
Milrinone	96	42	26	7	
Dobutamine	96	43	25	13	

Primary composite outcome: death from any cause, resuscitated cardiac arrest, receipt of a HTx or MCS, nonfatal MI, TIA or stroke, or initiation of renal replacement therapy



No. at Risk				No. at Risk	
Milrinone	96	55	34	15	
Dobutamine	96	55	33	19	

Death from any cause

Eff cacy and safety of intermittent intravenous outpatient administration of levosimendan in patients with advanced heart failure: the LION-HEART multicentre randomised trial

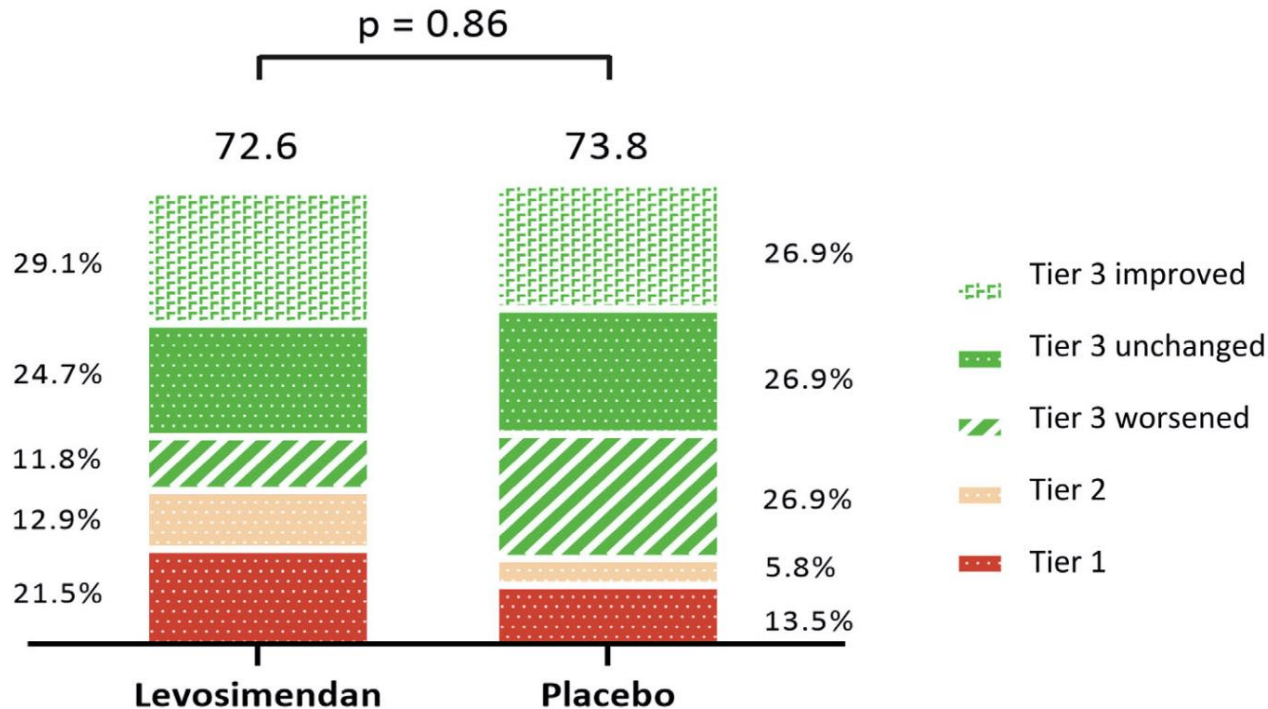
Intermittent intravenous outpatient administration of levosimendan

José Comín-Colet^{1,2*}, Nicolás Manito², Javier Segovia-Cubero³, Juan Delgado⁴, José Manuel García Pinilla⁵, Luis Almenar⁶, María G. Crespo-Leiro⁷, Alessandro Sionis⁸, Teresa Blasco⁹, Domingo Pascual-Figal¹⁰, Francisco Gonzalez-Vilchez¹¹, José Luis Lambert-Rodríguez¹², María Grau¹³, and Jordi Bruguera¹, on behalf of the LION-HEART Study Investigators

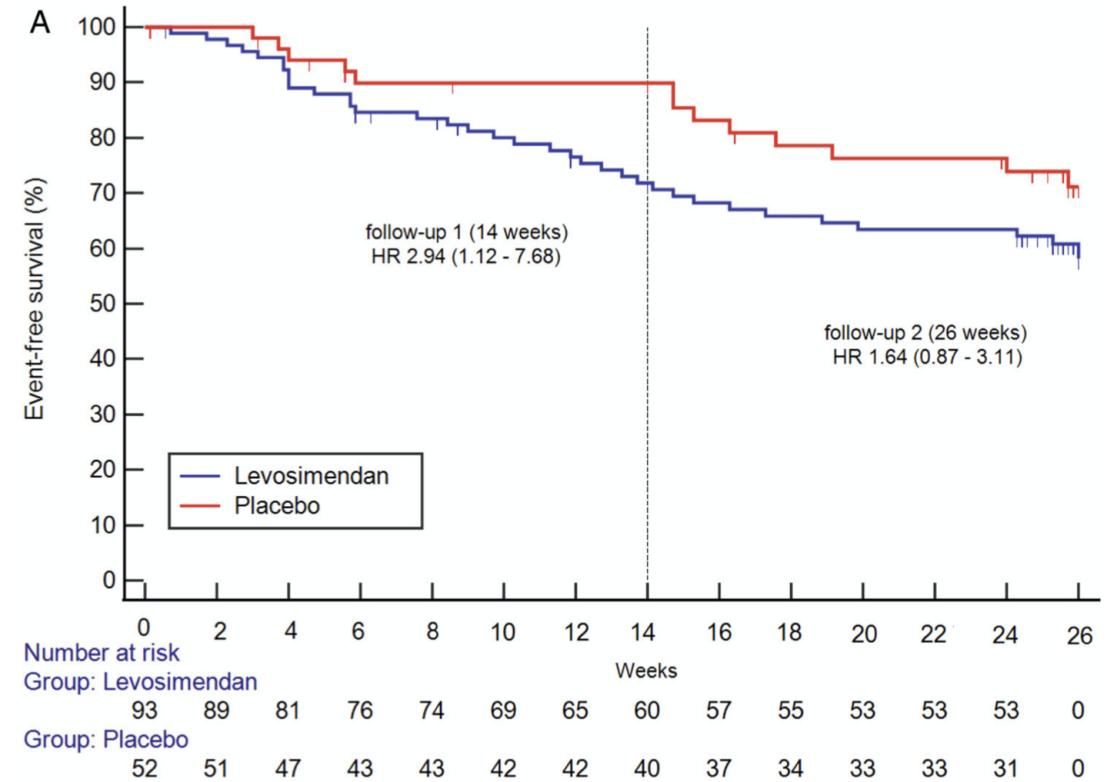
	Levosimendan (n=48)				Placebo (n=21)				p-value	Hazard ratio (95% CI)	p-value
	Total Events	Patients with Event	Rate (%)	Incidence per 100 patient-years at risk	Total Events	Patients with Event	Rate (%)	Incidence per 100 patient-years at risk			
Death or other terminal events											
All-cause death	15	15	31.2	31.3	8	8	38.1	38.1	0.781	0.80 [0.34-1.90]	0.620
Heart Transplant	0	0	0	0.0	2	2	9.5	9.5	0.090	-	-
LVAD implant	0	0	0	0.0	1	1	4.8	4.8	0.304	-	-
Hospitalization											
HF hospitalization	19	11	22.9	22.9	18	14	66.7	66.7	0.001	0.25 [0.11-0.56]	0.001
CV hospitalization	21	12	25.0	25.0	23	14	66.7	66.7	0.003	0.27 [0.12-0.59]	0.001
Non-CV hospitalization	15	9	18.8	18.8	5	4	19.0	19.0	0.999	1.01 [0.31-3.27]	0.990
All-cause hospitalization	36	17	35.4	35.4	28	15	71.4	71.4	0.012	0.37 [0.19-0.75]	0.006
Composite End-points											
HF hospitalization or all-cause death	34	22	45.8	29.2	26	17	81.0	66.7	0.015	0.33 [0.16-0.70]	0.004
CV hospitalization or all-cause death	36	22	45.8	39.6	31	17	81.0	81.0	0.015	0.32 [0.16-0.61]	0.001
All-cause hospitalization or all-cause death	51	25	52.1	45.8	36	18	85.7	85.7	0.017	0.38 [0.20-0.71]	0.003
Heart transplant or LVAD implant	0	0	0.0	0.0	3	3	14.3	14.3	0.025	-	-
HTx or LVAD or death	15	15	31.2	31.3	11	10	47.6	47.6	0.303	0.55 [0.25-1.22]	0.143
HF hospitalization or HTx or LVAD	19	11	22.9	22.9	21	14	66.7	66.7	0.001	0.25 [0.11-0.55]	0.001
HF hospitalization or HTx or LVAD or death	34	22	45.8	41.7	29	17	81.0	81.0	0.015	0.34 [0.17-0.65]	0.001
CV hospitalization or HTx or LVAD	21	12	25.0	25.0	25	14	66.7	66.7	0.003	0.27 [0.12-0.58]	0.001
CV hospitalization or HTx or LVAD or death	36	22	45.8	41.7	33	17	81.0	81.0	0.015	0.33 [0.17-0.63]	0.001

Repetitive levosimendan infusions for patients with advanced chronic heart failure in the vulnerable post-discharge period: The multinational randomized LeoDOR trial

Gerhard Pözl^{1*}, Johann Altenberger², Josep Comín-Colet³, Juan F. Delgado⁴, Francesco Fedele⁵, Martín Jesús García-González⁶, Finn Gustafsson⁷, Josep Masip⁸, Zoltán Papp⁹, Stefan Störk¹⁰, Hanno Ulmer¹¹, Sarah Maier¹¹, Bojan Vrtovec¹², Gerhard Wikström¹³, Endre Zima¹⁴, and Axel Bauer¹, for the LeoDOR Investigators



Tier 1 = time to death or urgent heart transplantation or implantation of a ventricular assist device



Mitraclip in advanced HF and cardiogenic shock

YES

COAPT criteria

Indication CoR IIa LoE B for M-TEER in SMR

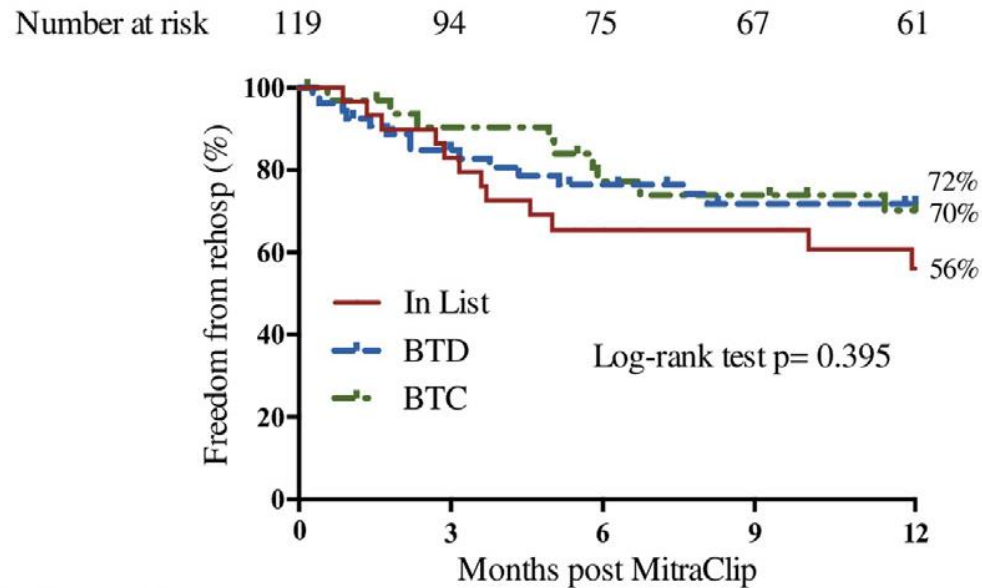
NO

- Severe SMR
- Optimised HF treatments according to 2021 ESC guidelines
- NYHA Class II, III or ambulatory IV
- LVEF 20-50%
- LV end-systolic diameter ≤ 70 mm
- At least one HF hospitalisation within the previous year or increased NP levels^a
- Anatomy judged suitable for M-TEER^b

- Haemodynamic instability^c
- Stage D HF^d
- Moderate or severe RV dysfunction
- Systolic pulmonary pressure >70 mmHg
- COPD requiring oxygen or steroid
- Coronary, aortic or tricuspid valve disease requiring surgery
- Hypertrophic, restrictive or infiltrative cardiomyopathy

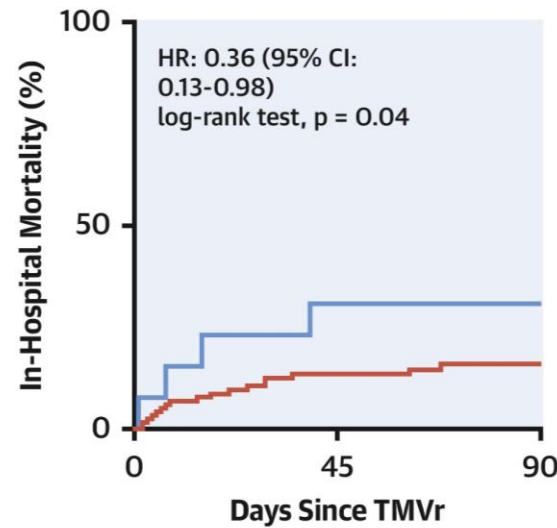
Mitraclip in advanced HF and cardiogenic shock

International MitraBridge Registry

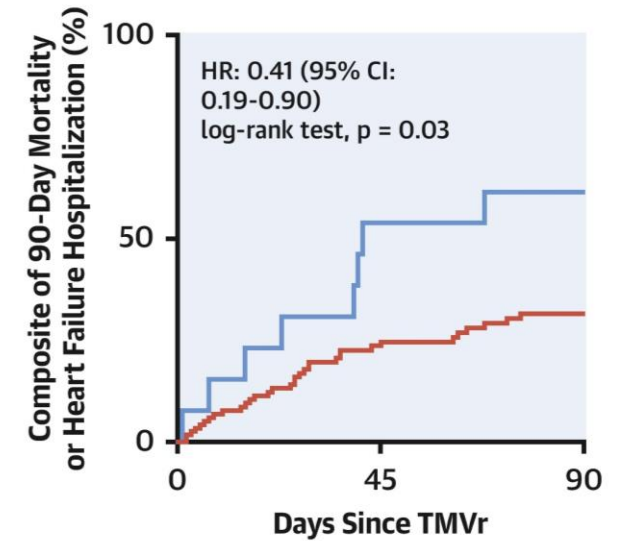


Number at risk	0	3	6	9	12
In List	31	24	17	15	13
BTD	54	42	35	30	29
BTC	34	28	23	22	19

Systematic review of TMVr in CS



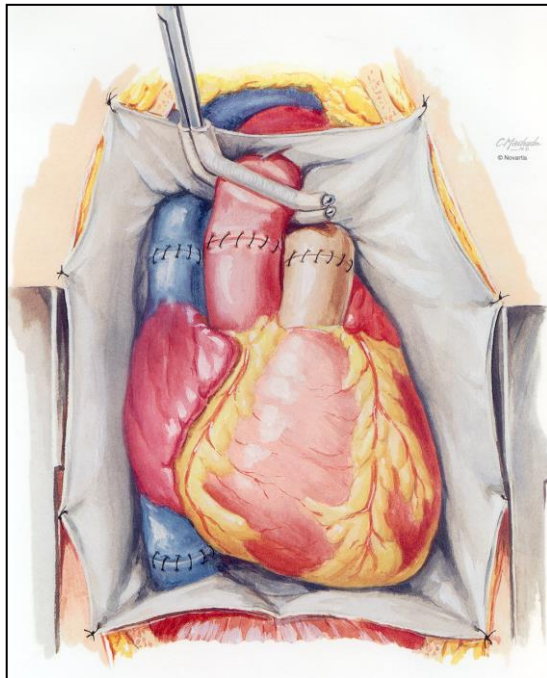
No. at Risk	0	45	90
Failure	14	8	5
Success	119	77	61



No. at Risk	0	45	90
Failure	14	6	3
Success	119	71	57

Advanced HF therapies (approaching near 90% 1-y survival and 70% 5-y survival)

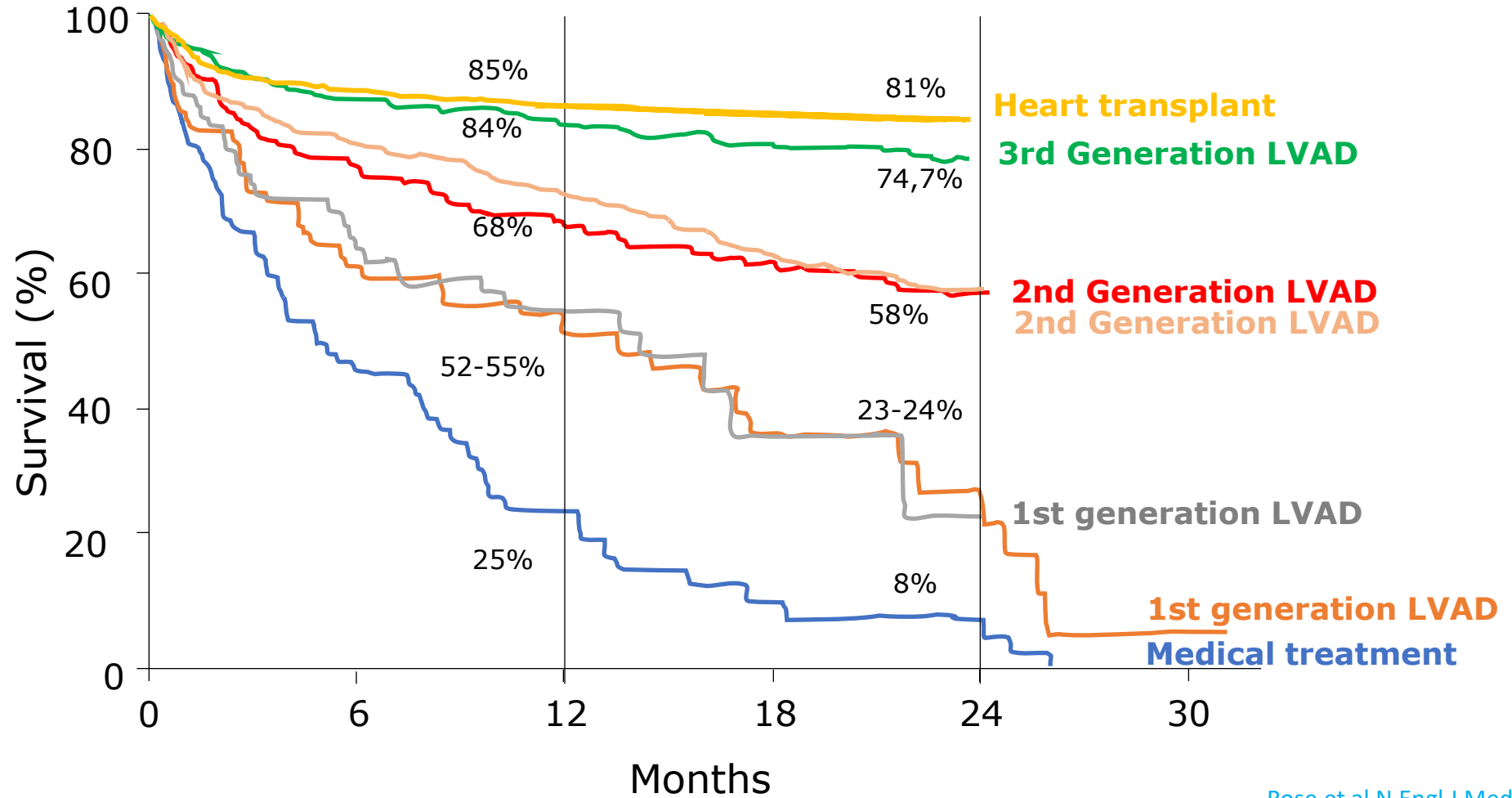
Heart transplantation



LT-MCS



Heart transplantation and Long-term MCS



Rose et al N Engl J Med 2001

Slaughter et al N Engl J Med 2009 / www.ishlt.org

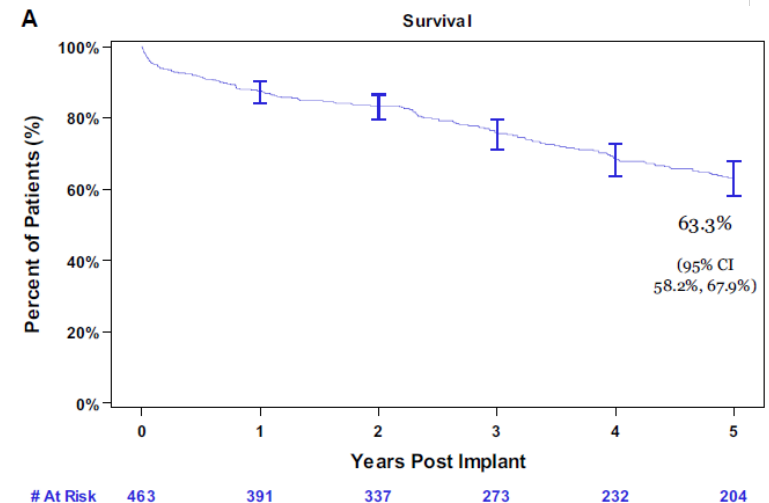
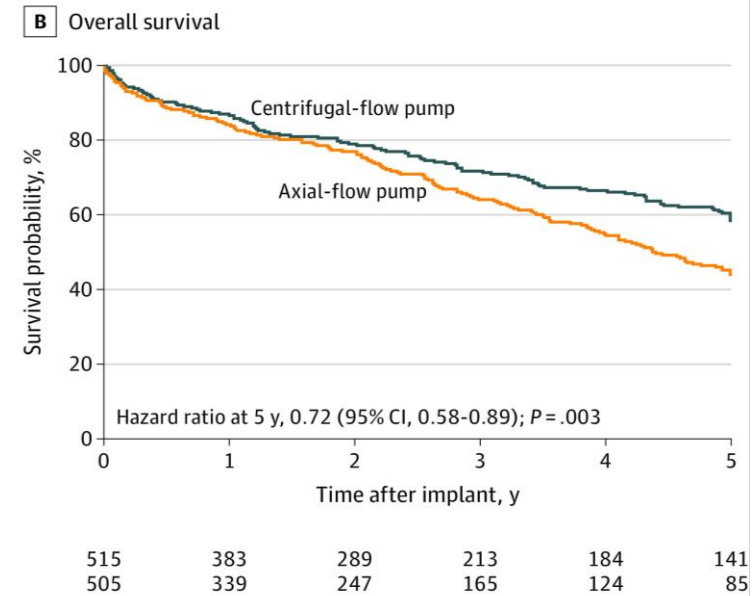
Mehra MR, et al. A fully magnetically levitated left ventricular assist device. New England Journal of Medicine. 2019 Apr 25;380(17):1618-27.

Five-Year Outcomes in Patients With Fully Magnetically Levitated Left Ventricular Assist Device

Median survival > 5 years

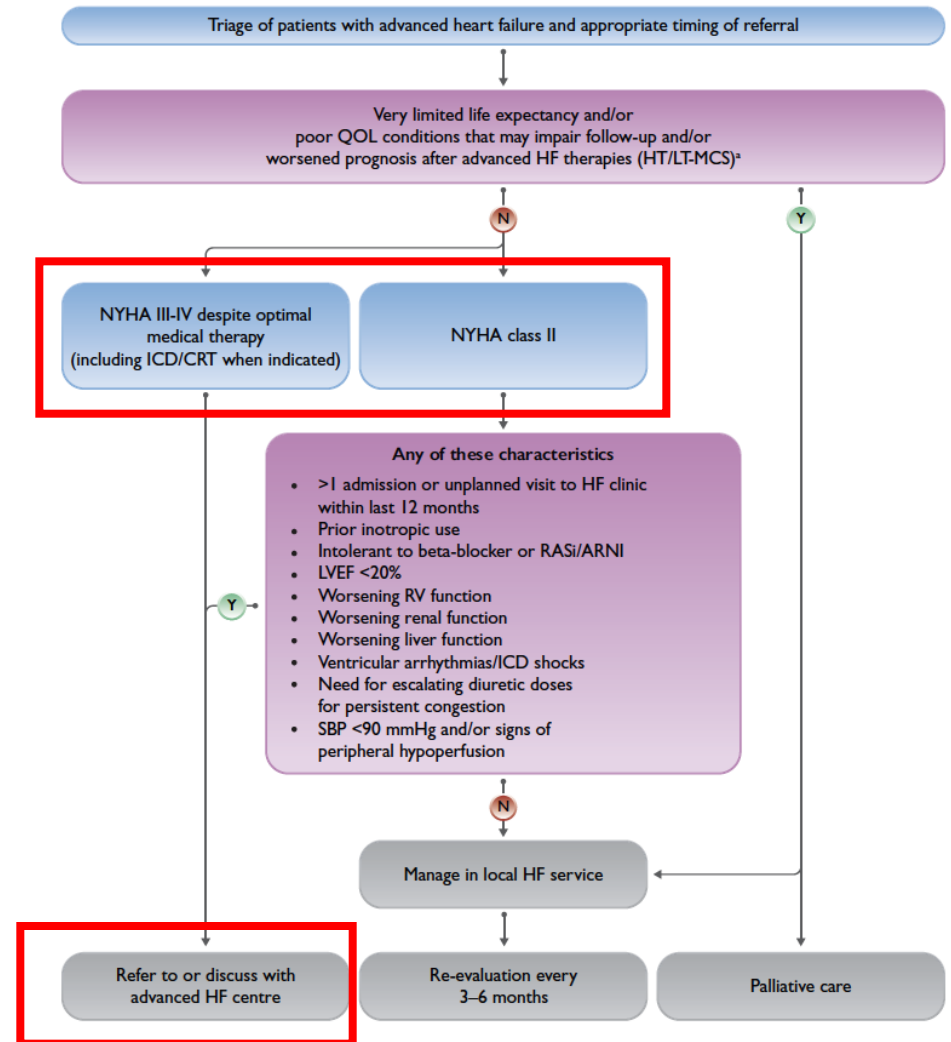
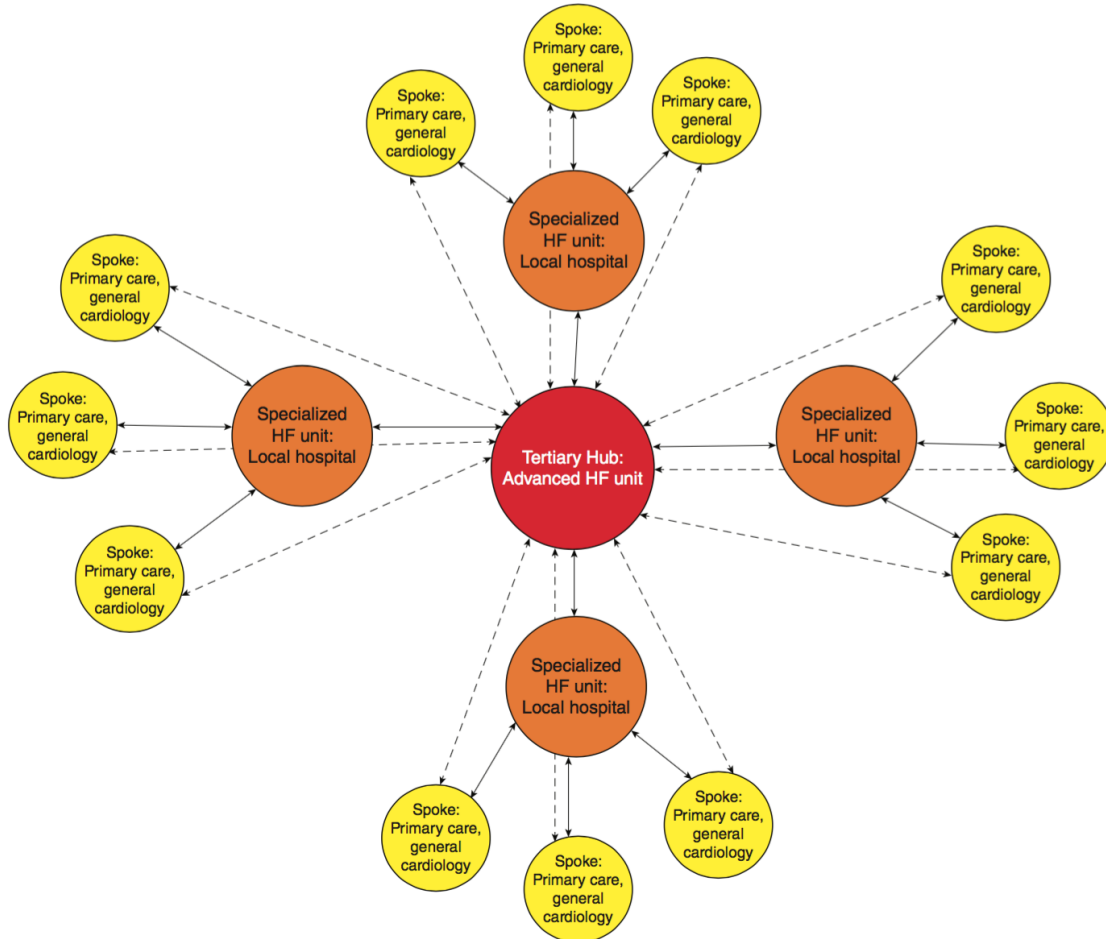
- MOMENTUM 3 Trial¹ – **58.4%**
Clinical trial data
- HM3 CE Trial² – **61%**

- ELEVATE Register³ - **63,3%**
Real world data
- 2023 INTERMACS Report⁴ - **63,7%**



1. M Mehra, et al. JAMA. 2022 Sep 27; 328(12): 1233–1242; 2. Netuka I, et al., The Journal of Heart and Lung Transplantation 2021; 40(4): 247-250; 3. Sami F, et al., Journal of Cardiac Failure 2022; 28(12): 1683-1691; 4. Schmitto et al., European Heart Journal 2023 published online Nov 2023; 5. Jorde et al., Annals of thoracic surgery 2024; 117(1): 33-44

Hub and spoke model for Heart Failure



Triggers for Referral of HF Patient for Advanced Therapies Evaluation (I need help acronym)

Inotropes

NYHA or NT-proBNP

End-organ dysfunction (liver/kidney)

Ejection Fraction (LVEF < 20%)

Defibrillator shocks (appropriate)

Hospitalizations (≥ 1 last year)

Edema/escalating diuretics

Low systolic blood pressure < 90-100

Prognostic medication

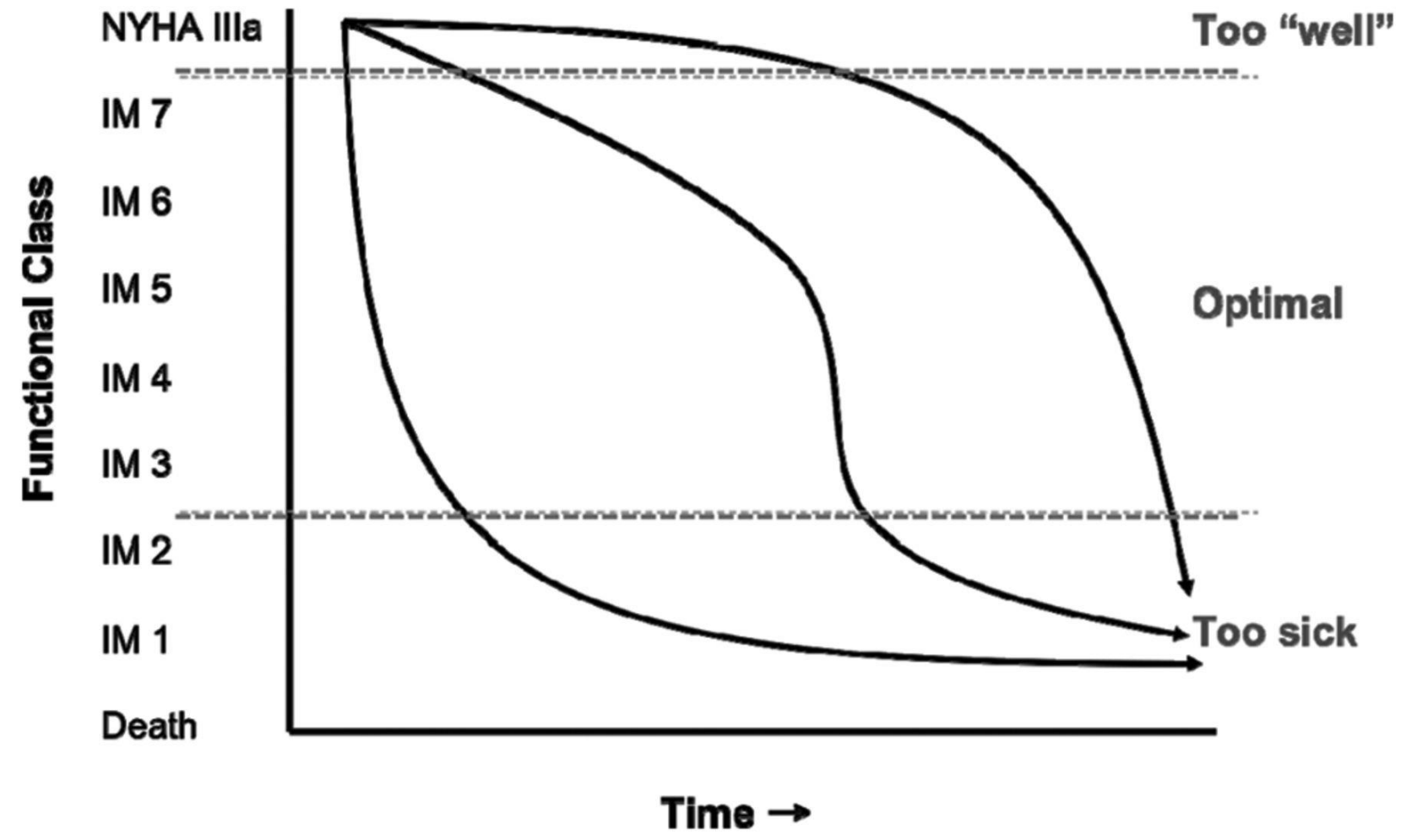
Triage of patients with advanced HF

When is the perfect time to refer?

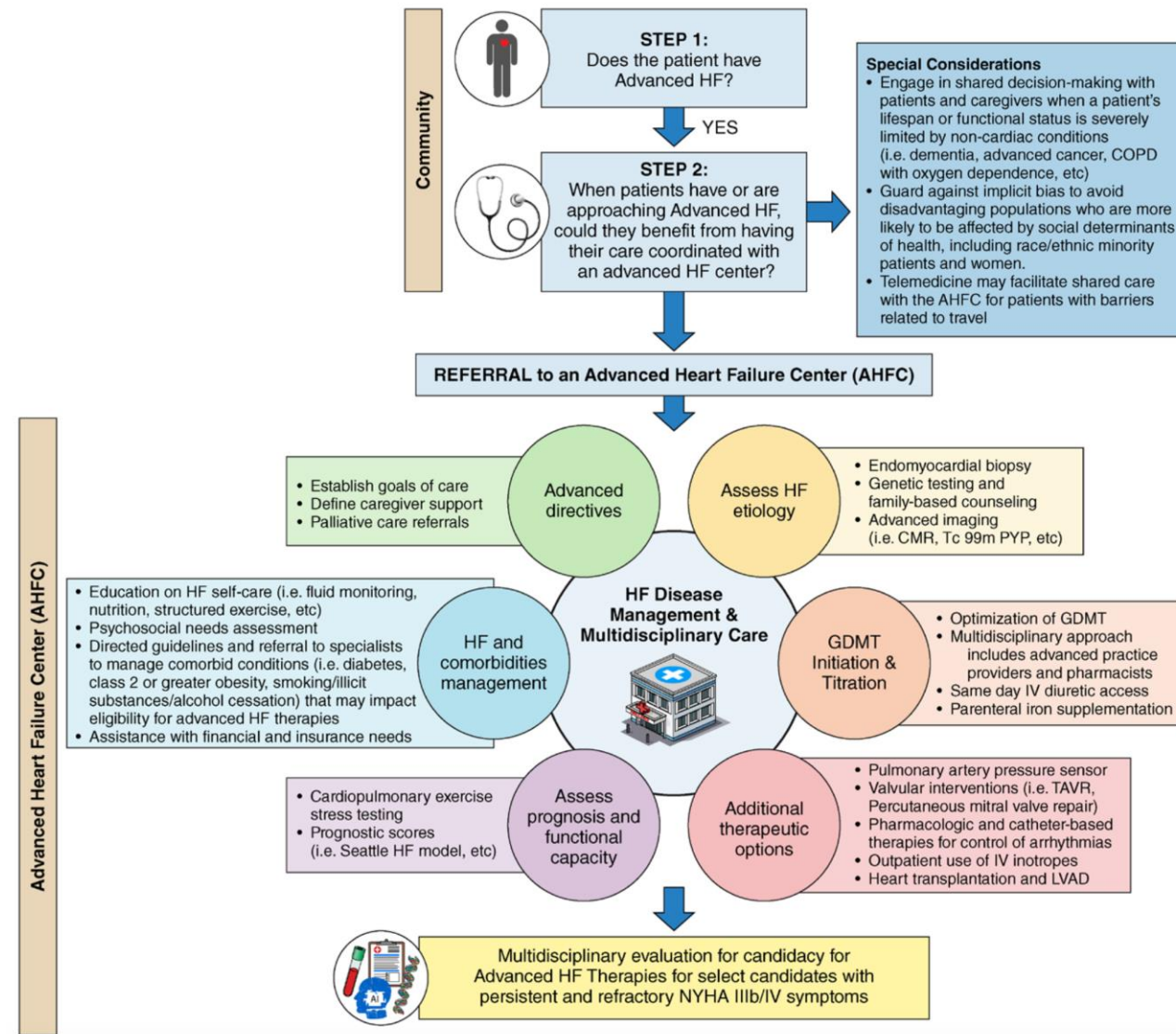


Triage of patients with advanced HF

When is the perfect time to refer?

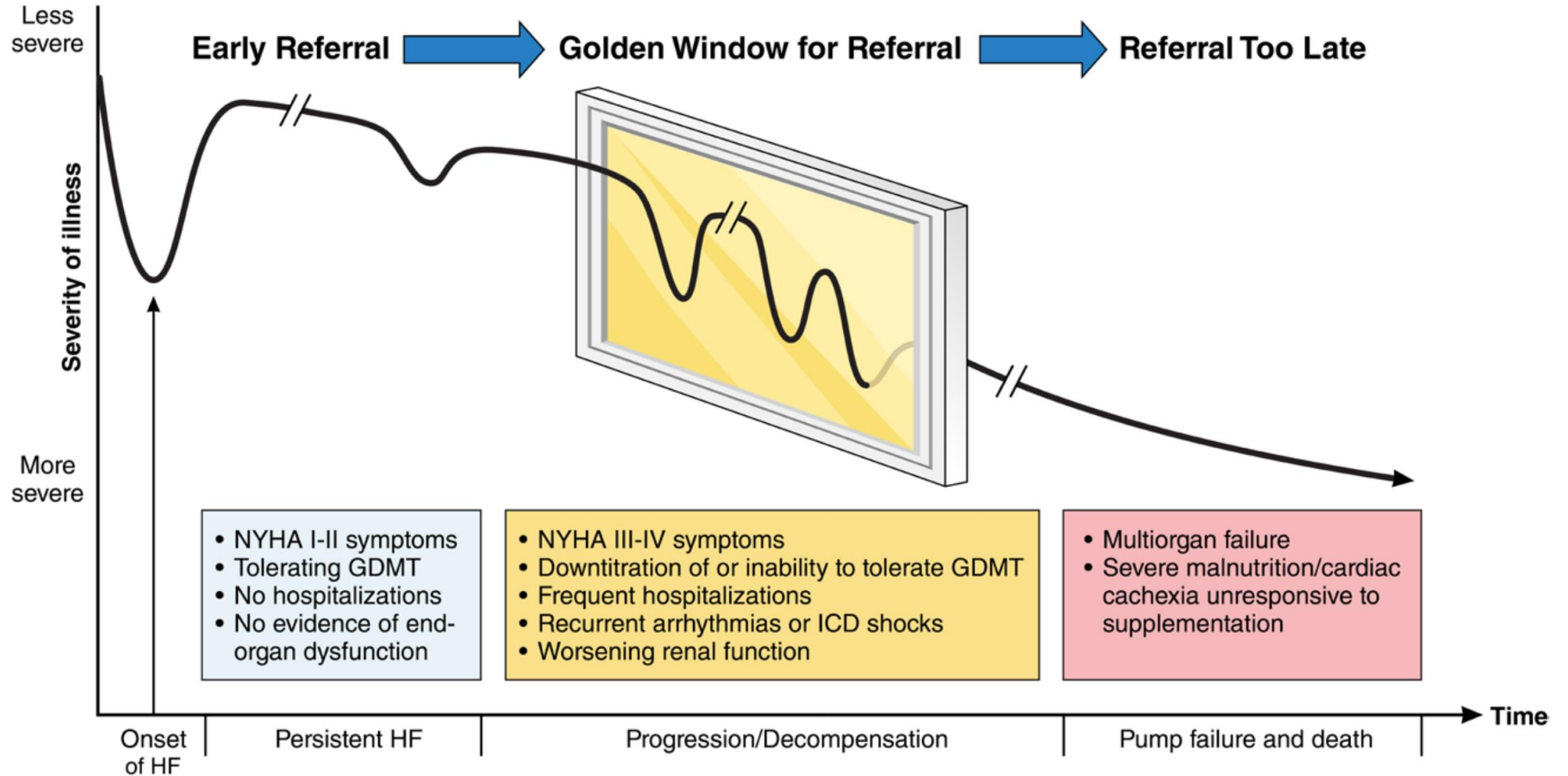


Practices of Referring Patients to Advanced HF Centers



Practices of Referring Patients to Advanced HF Centers

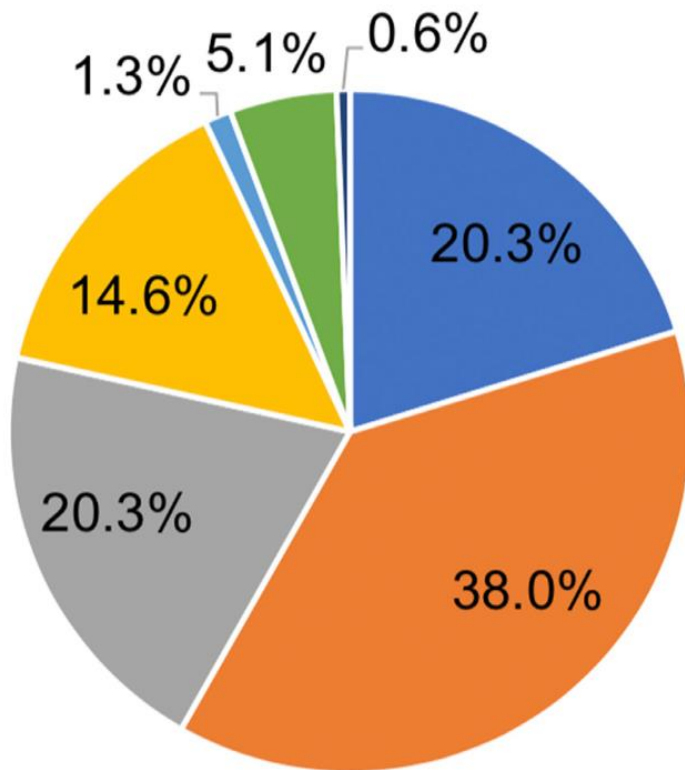
Golden window for referral for consideration of advanced HF therapies



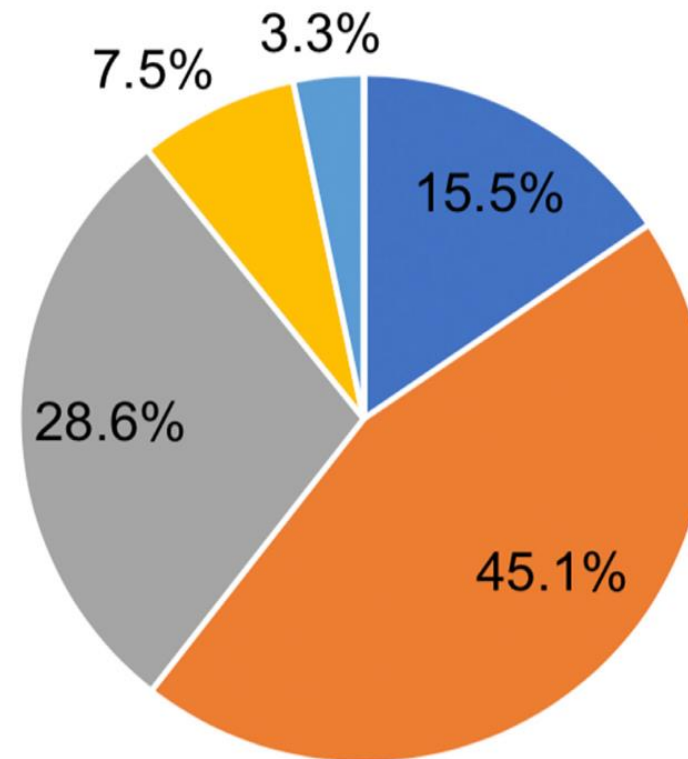
Practices of Referring Patients to Advanced HF Centers

Primary reason cited to not offer advanced HF therapies

**Mechanical Circulatory Support
(N=158)**



**Heart Transplant
(N=213)**

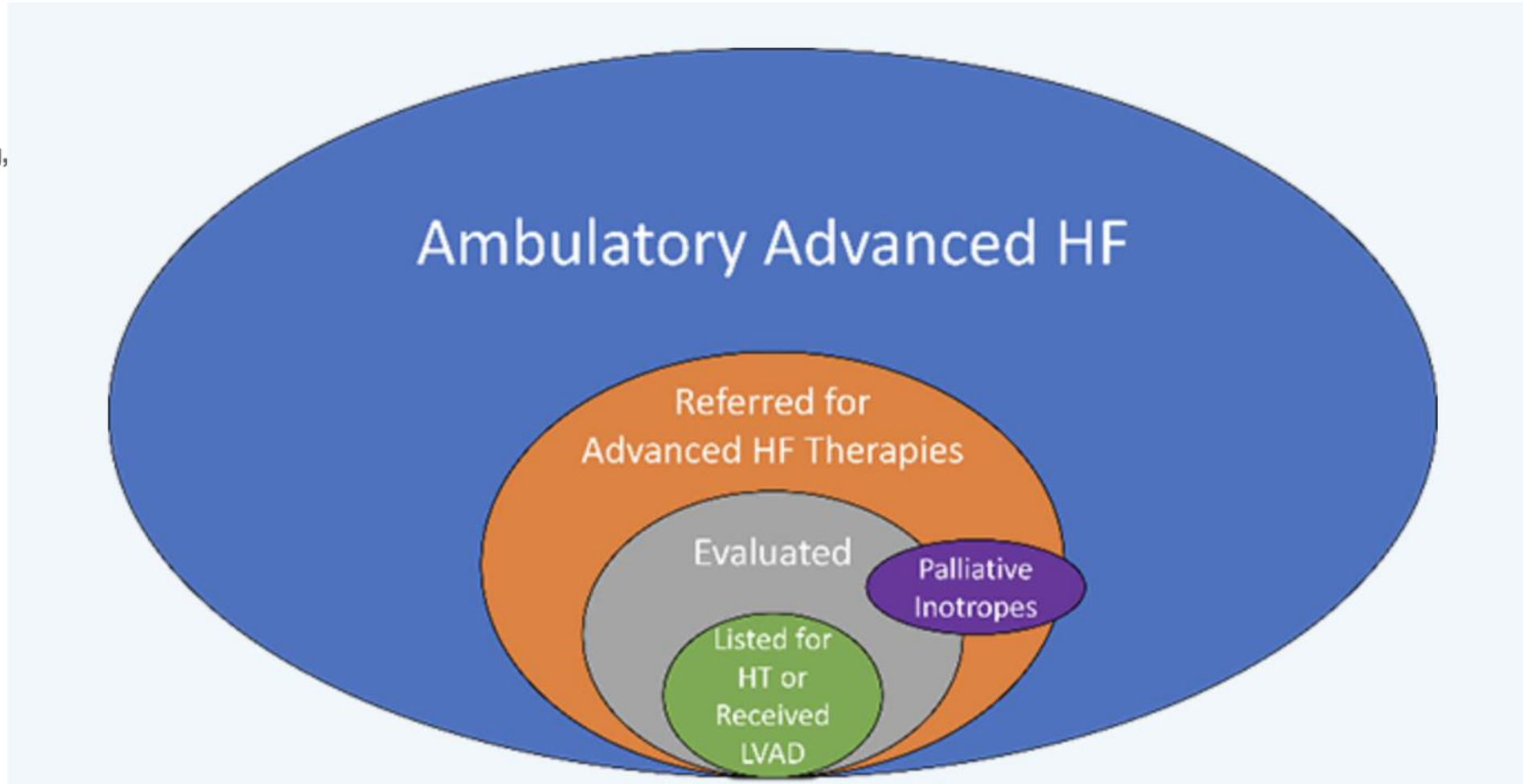


- Too Well
- Too Sick
- Psychsocial
- Patient Dec
- Malignancy
- RV Failure
- Infection

Advanced Heart Failure Workshop: Trajectories and Triage for Ambulatory Stage Pre-D and D



National Heart, Lung,
and Blood Institute



Advanced Heart Failure Workshop: Trajectories and Triage for Ambulatory Stage Pre-D and D

- Identify patients who may be **disadvantaged** by the current allocation system when therapy based on physiological need confers lower priority.
- Improve DMCS use as a **complement or alternative** therapy to HT.
- Direct patients to advanced HF centers through **earlier referrals**.
- **Synergize LVAD and HT** in the same patient to maximize QOL and survival benefit
 - Bridge-to-myocardial recovery for increased GDMT (for GDMT-naïve patients).
 - Extended BTT to delay HT and extend the overall survival benefit of combined therapies (particularly attractive for younger patients).
 - Identify higher risk patients who may benefit from DMCS rather than HT to permit heart allocation to those with HT as the only option (e.g., pediatric patients) or when HT provides greater survival benefit.

Take home messages

- ✓ Advanced HF is a major sanitary problem with high rates of hospitalizations, mortality, important impact on quality of life and elevated costs.
- ✓ The 2018 HFA-ESC updated definition of advanced HF describes new diagnostic criteria and treatment options for these patients.
- ✓ Recognizing the patient with advanced HF is critical to facilitate timely referral to advanced HF centers. Organization: Hub & Spoke Model of Care.
- ✓ Early referral is key to avoid debilitation and end organ dysfunction that may preclude candidacy for advanced HF therapy.
- ✓ HTx remains the best strategy to improve survival and quality of life.
- ✓ LT MCS are rapidly improving clinical outcomes either as BTT or DT. Synergize LVAD and HT in the same patient to maximize QOL and survival benefit.