Advanced heart failure: current situation and modern therapeutic options

Jan Krejčí

St. Anne´s University Hospital and Masaryk University, Brno, Czech Republic

Modern treatments for HF have great potential…

A Systematic Review and Network Meta-Analysis of Pharmacological Treatment of Heart Failure With Reduced Ejection Fraction

Treatment	CV Mortality	HR (95% CI)
ARNI + BB + MRA + SGLT2		0.33 (0.26-0.43)
ARNI + BB + MRA + Vericiguat		0.35 (0.26-0.47)
ARNI + BB + MRA + Omecamtiv		0.36 (0.27-0.46)
ACEI + BB + MRA + IVA		0.43 (0.35-0.54)
ACEI + BB + MRA + Vericiguat		0.44 (0.33-0.57)
ACEI + BB + MRA + Omecamtiv		0.44 (0.35-0.56)
ACEI + BB + Dig		0.65 (0.56-0.76)

Treatment	All-Cause Mortality	HR (95% CI)
ARNI + BB + MRA + SGLT2		0.39 (0.31-0.49)

Treatment	CV Mortality	HR (95% CI)
ARNI + BB + MRA + SGLT2		0.33 (0.26-0.43)

Treatment	CV Mortality or HF Hospitalization	HR (95% CI)
ARNI + BB + MRA + SGLT2		0.36 (0.29-0.46)

0.2 0.5 1 2

Tromp et al., JACC Heart Fail. 2022 Feb;10(2):73-84

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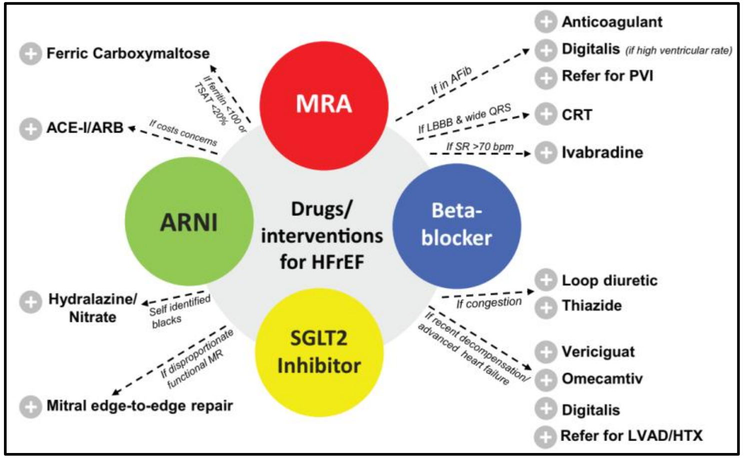
Modern treatments for HF have great potential…

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

Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

McDonagh et al. Eur Heart J. 2021;42(36):3599-3726

Heart failure drug treatment: the fantastic four



Bauersachs J. Eur Heart J. 2021 Feb 11;42(6):681-683

…if we used them correctly

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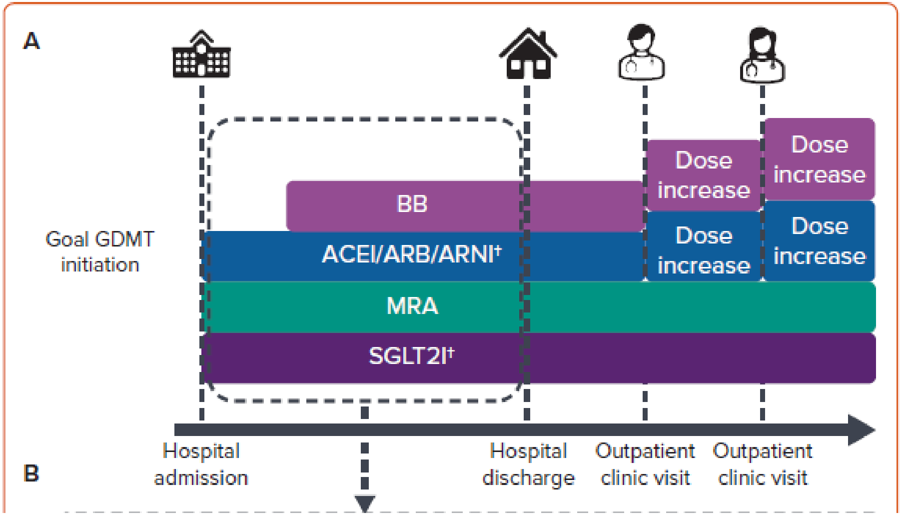
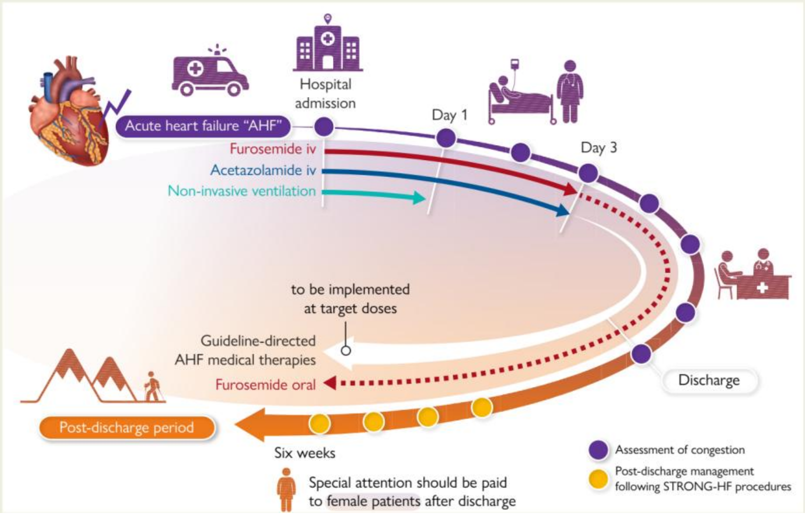
What does mean „when we use them correctly“ ?

1/ start early



Cardiac Failure Review 2022;8:e21.



European Heart Journal (2023) **44**, 4634–4649

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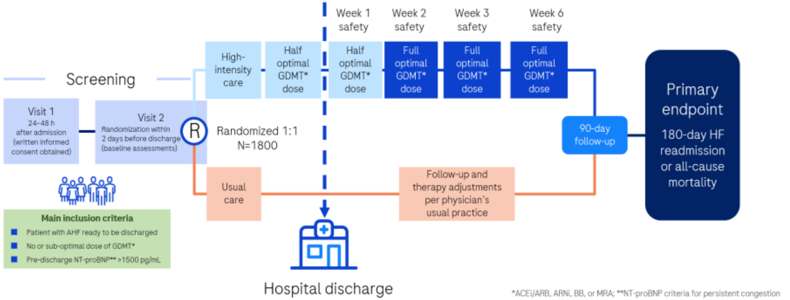
What does mean „when we use them correctly“ ?

2/ up-titrate as soon as possible

STRONG-HF

STRONG-HF: Study design

Investigator-initiated trial sponsored by Roche



*ACEi/ARB, ARNi, BB, or MRA; **NT-proBNP criteria for persistent congestion

1. Kimmoun-A et al. European Journal of Heart Failure 2019: 21: **2.** 1459–1467 **2.** Gotter-G et al. Eur J Heart Fail 2021 23:1981-1982 **3.** Mebazaa-A et al. Lancet. 2022 Dec 3;400(10367):1938-1952

ACEi, angiotensin-converting enzyme inhibitors; AHF, acute heart failure; ARB, angiotensin receptor blockers; BB, beta blockers; GDMT, guideline-directed medical therapy; HF, heart failure; MRA, mineralocorticoid receptor antagonists; NT-proBNP, N-terminal pro b-type natriuretic peptide

Results

The high intensity care group: **34% relative** and **8.1% absolute risk reduction (ARR)** in the combination of death or heart failure readmission.[14]

CV (cardiovascular) death	HF readmission	All-cause death
26% lower	**44% lower**	**16% lower**

STRONG-HF study results demonstrated clear benefits for acute heart failure patients by adapting the strategy of care.

Lancet 2022; 400: 1938–52

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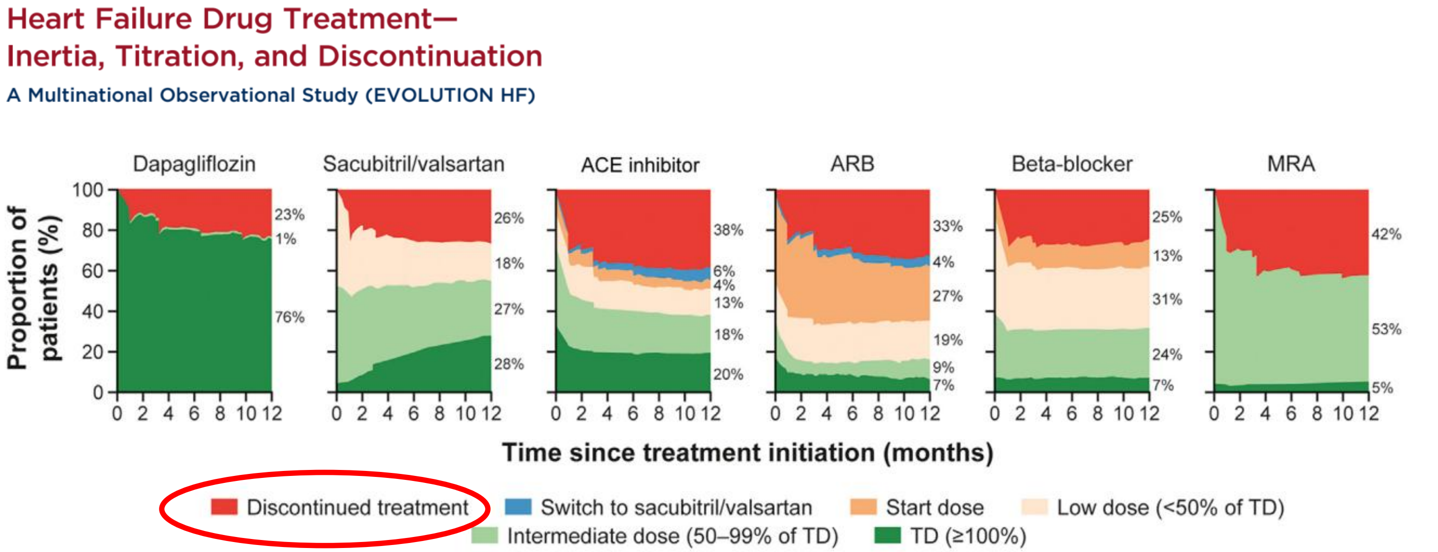
What does mean „when we use them correctly“ ?

3/ keep the patients on the medications



Savarese G, et al. J Am Coll Cardiol HF. 2023;11(1):1-14.

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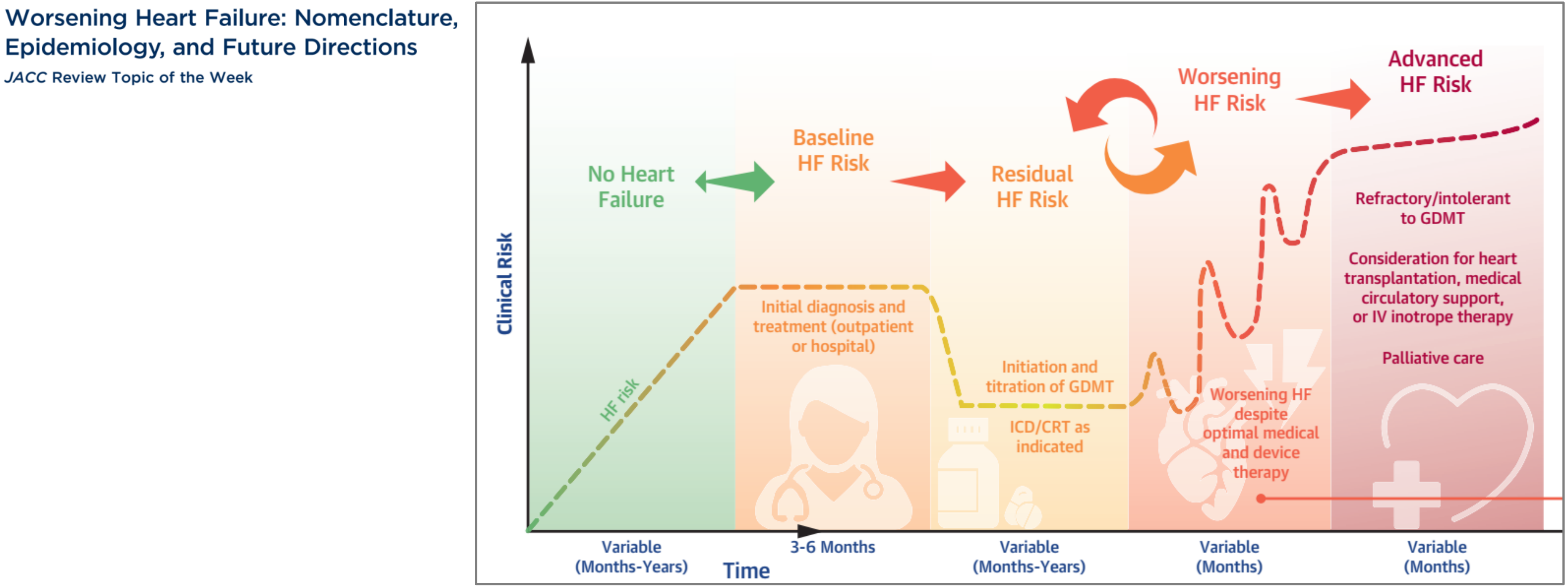
Heart failure trajectory

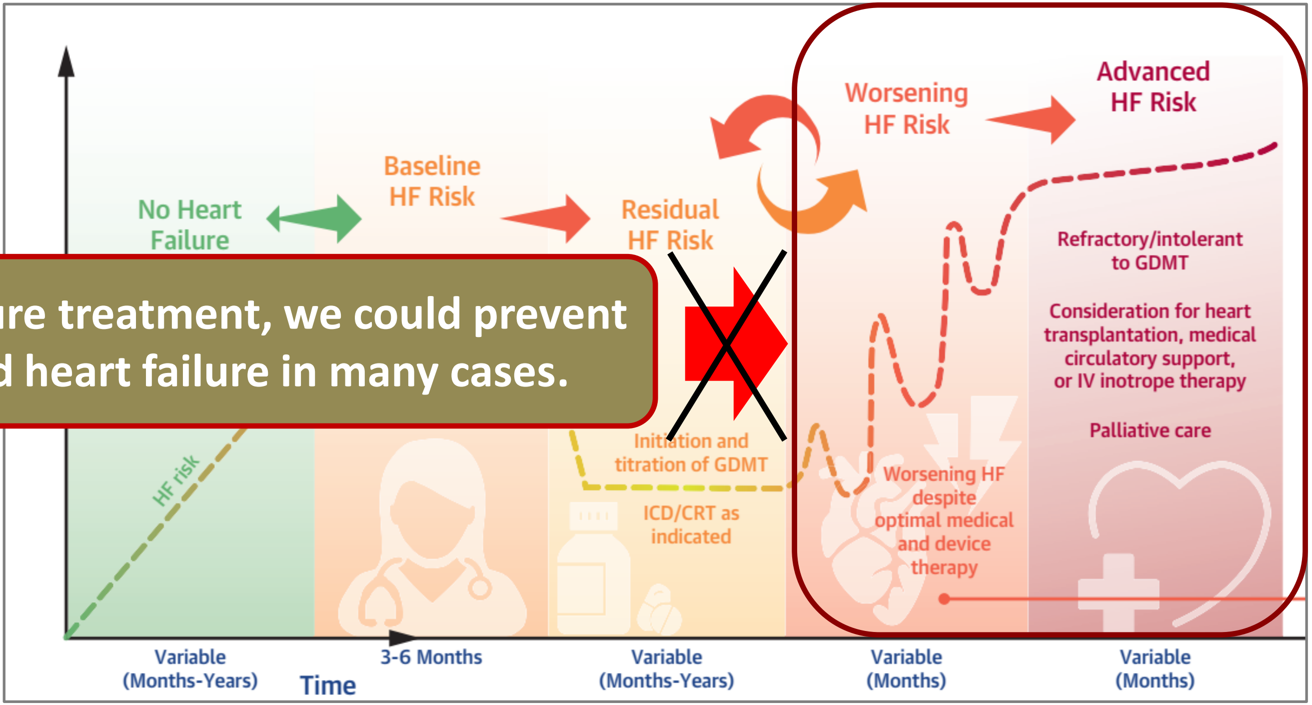


Green et al. J Am Coll Cardiol 2023;81:413-424

Heart failure trajectory - can „bad ends“ be avoided?

Worsening Heart Failure: Nomenclature, Epidemiology, and Future Directions

JACC Review Topic of the Week



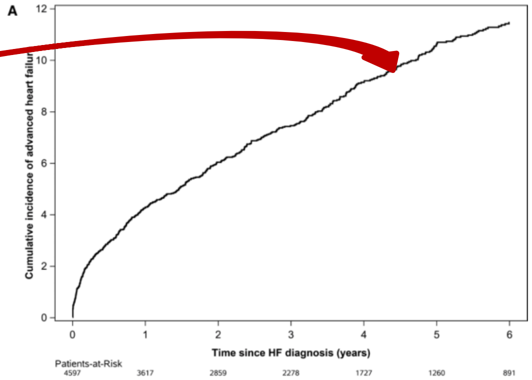
By optimizing of heart failure treatment, we could prevent progression to advanced heart failure in many cases.

Green et al. J Am Coll Cardiol 2023;81:413-424

Progression into advanced HF stage

Development of Advanced Heart Failure: A Population-Based Study

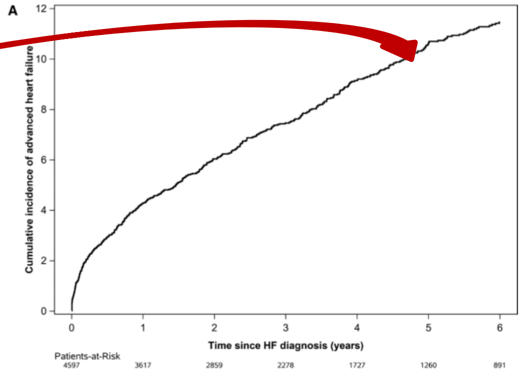
Within 5 years, approximately 10% of patients will progress to the advanced heart failure…



Subramaniam et al. Circ Heart Fail. 2022 May;15(5):e009218

Progression into advanced HF stage

Development of Advanced Heart Failure: A Population-Based Study



Within 5 years, approximately 10% of patients will progress to the advanced heart failure…

…this dramatically changes the prognosis of the disease

Table 3. **Associations of Development of Advanced Heart Failure With Risks of Death and Hospitalization**

Outcome	Unadjusted*		Adjusted*†	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
All-cause death	5.3 (4.7–5.9)	<0.001	5.0 (4.5–5.6)	<0.001
Cardiovascular death	9.0 (7.7–10.4)	<0.001	7.8 (6.7–9.1)	<0.001
All-cause hospitalization	3.2 (2.9–3.9)	<0.001	3.0 (2.7–3.4)	<0.001
HF hospitalization	11.3 (9.5–13.5)	<0.001	10.2 (8.7–12.1)	<0.001

Subramaniam et al. Circ Heart Fail. 2022 May;15(5):e009218

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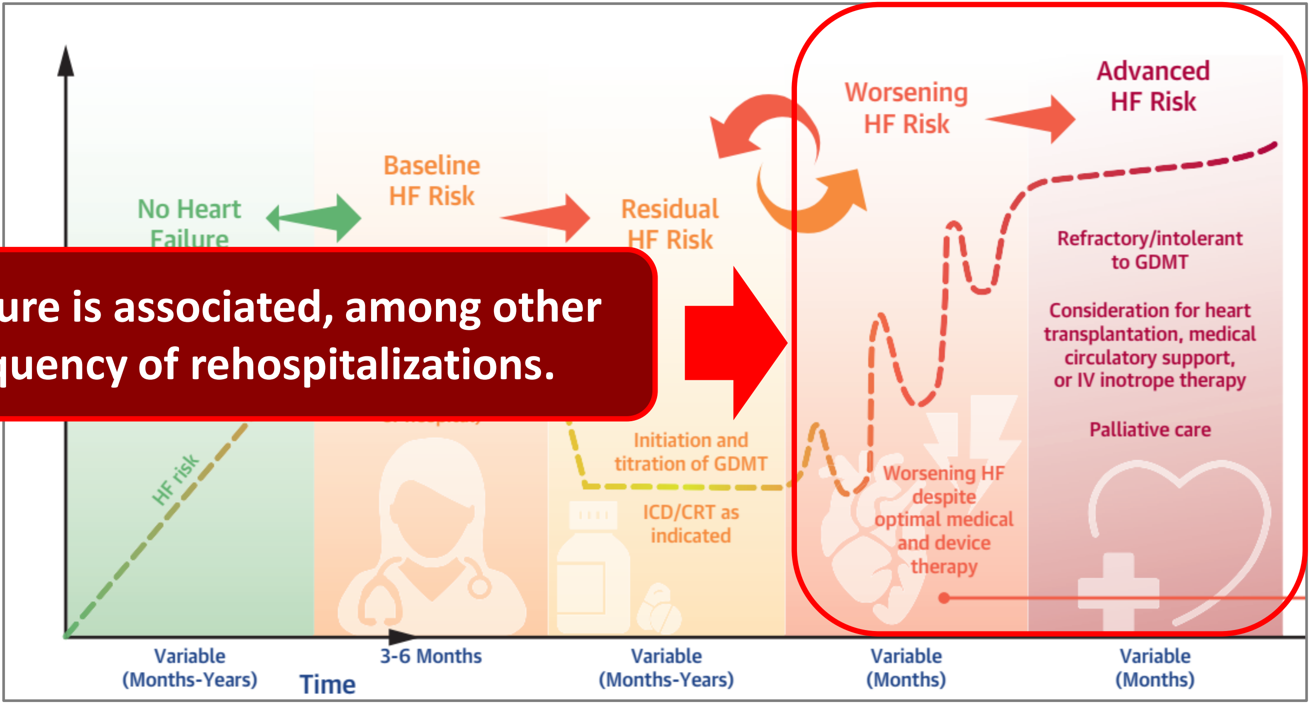
Heart failure trajectory and hospitalizations

Worsening Heart Failure: Nomenclature, Epidemiology, and Future Directions

JACC Review Topic of the Week



Worsening of heart failure is associated, among other things, with high frequency of rehospitalizations.

Green et al. J Am Coll Cardiol 2023;81:413-424

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Heart failure trajectory and hospitalizations

Global Comparison of Readmission Rates for Patients With Heart Failure

RESULTS In total, 24 papers reporting on 30-day and 23 papers on 1-year readmission were included. Of the 1.5 million individuals at risk, 13.2% (95% CI: 10.5%-16.1%) were readmitted within 30 days and 35.7% (95% CI: 27.1%-44.9%) within 1 year. A total of 33 papers reported on 30-day and 45 papers on 1-year mortality. Of the 1.5 million individuals hospitalized for HF, 7.6% (95% CI: 6.1%-9.3%) died within 30 days and 23.3% (95% CI: 20.8%-25.9%) died within 1 year. Substantial variation in risk across countries was unexplained by countries' gross domestic product, proportion of gross domestic product spent on health care, and Gini coefficient.

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Foroutan et al. J Am Coll Cardiol 2023;82:430-444.

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Hospitalization as a marker of poor prognosis

Global Comparison of Readmission Rates for Patients With Heart Failure

RESULTS In total, 24 papers reporting on 30-day and 23 papers on 1-year readmission were included. Of the 1.5 million individuals at risk, 13.2% (95% CI: 10.5%-16.1%) were readmitted within 30 days and 35.7% (95% CI: 27.1%-44.9%) within 1 year. A total of 33 papers reported on 30-day and 45 papers on 1-year mortality. Of the 1.5 million individuals hospitalized for HF, 7.6% (95% CI: 6.1%-9.3%) died within 30 days and 23.3% (95% CI: 20.8%-25.9%) died within 1 year. Substantial variation in risk across countries was unexplained by countries' gross domestic product, proportion of gross domestic product spent on health care, and Gini coefficient.

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Foroutan et al. J Am Coll Cardiol 2023;82:430-444.

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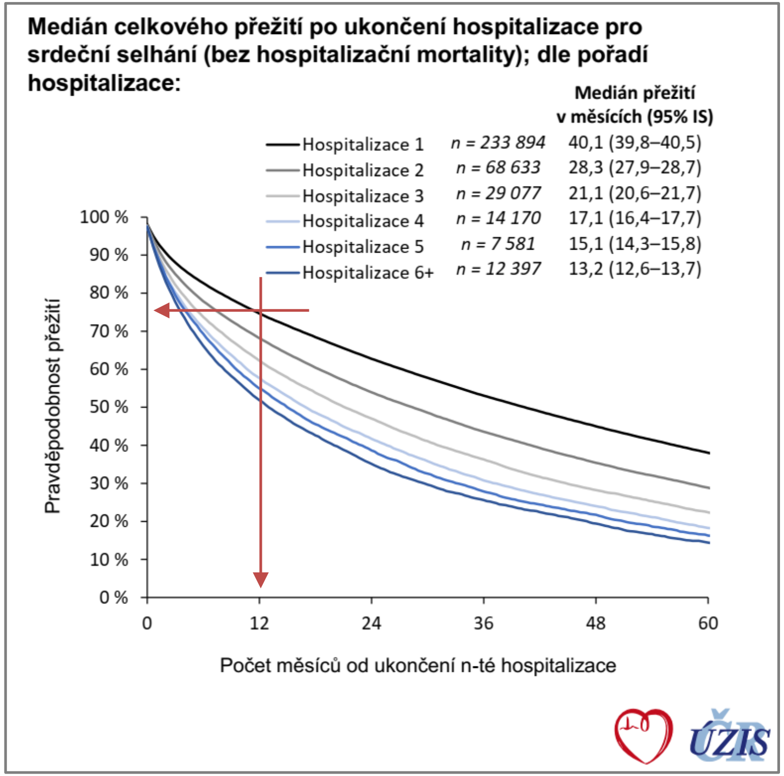
Rehospitalizations and survival: real data from Czech Republic



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NKVP ČR 2030: souhrnná analytická studie, Srdeční selhání v ČR, slide 22, dostupné na www.nzip.cz/data/nkis/nkis-srdecni-selhani/nkis-srdecni-selhani.pdf

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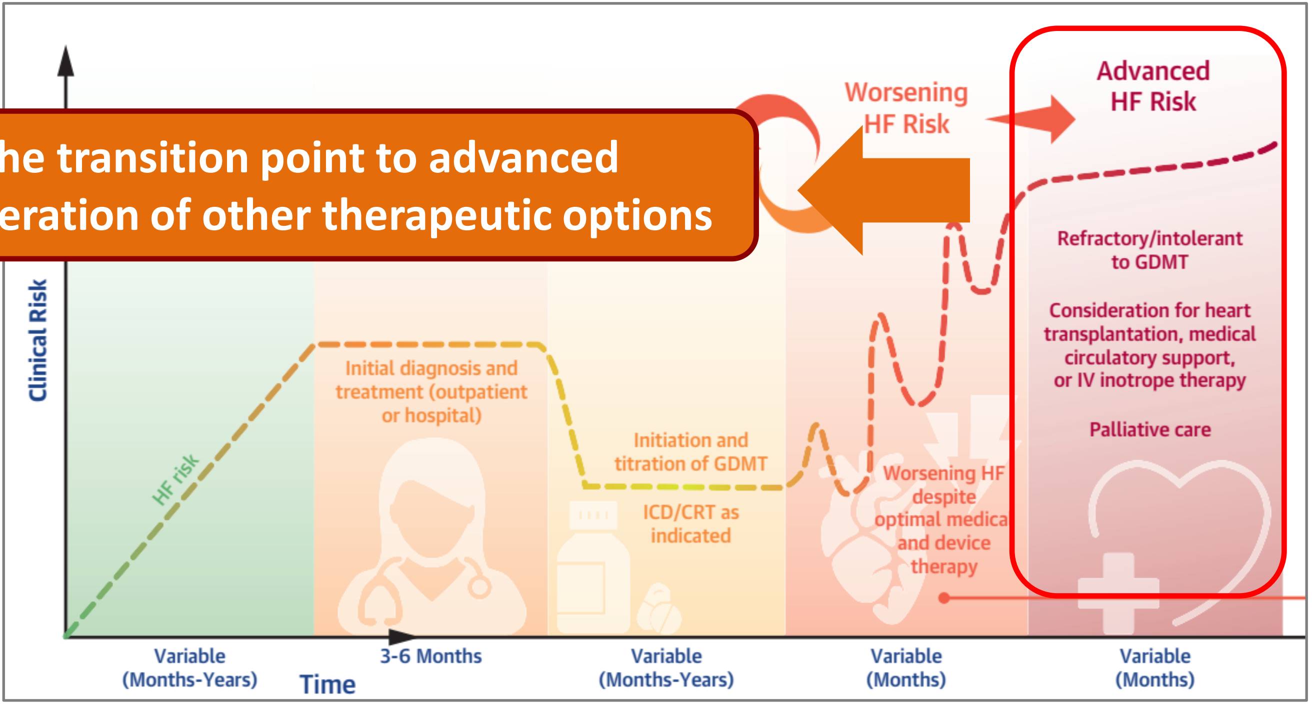
Transition to advanced heart failure: what is needed?

Worsening Heart Failure: Nomenclature, Epidemiology, and Future Directions

JACC Review Topic of the Week

1/ Early recognition of the transition point to advanced heart failure and consideration of other therapeutic options



Green et al. J Am Coll Cardiol 2023;81:413-424

Recognition of advanced HF: „ I NEED HELP “

Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology

1/ Early recognition of the transition point to advanced heart failure and consideration of other therapeutic options

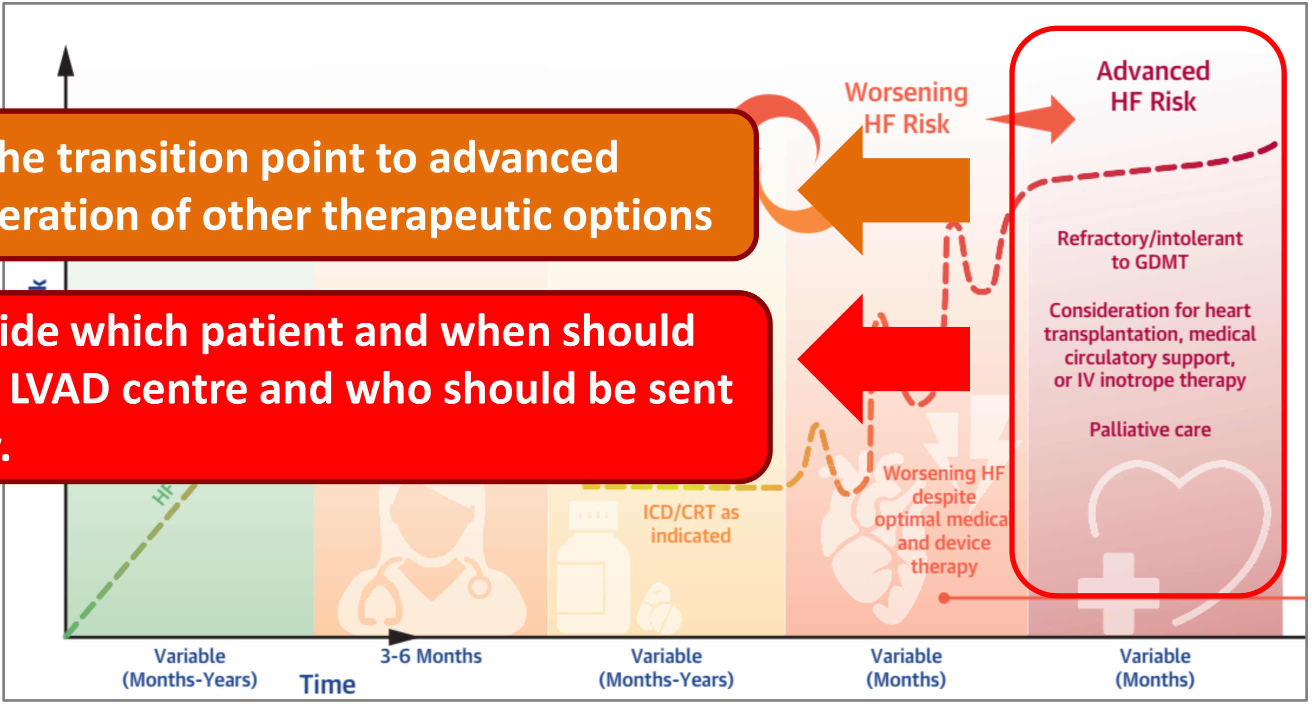
I	**I**notropes	Previous or ongoing requirement for dobutamine, milrinone, dopamine, or levosimendan
N	**N**YHA class/ natriuretic peptide	Persisting NYHA class III or IV and/or persistently high BNP or NT-proBNP
E	**E**nd-organ dysfunction	Worsening renal or liver dysfunction in the setting of heart failure
E	**E**jection fraction	Very low ejection fraction <20%
D	**D**efibrillator shocks	Recurrent appropriate defibrillator shocks
H	**H**ospitalizations	More than 1 hospitalization with heart failure in the last 12 months
E	**E**dema/escalating diuretics	Persisting fluid overload and/or increasing diuretic requirement
L	**L**ow blood pressure	Consistently low BP with systolic <90 to 100 mmHg
P	**P**rognostic medication	Inability to up-titrate (or need to decrease/cease) ACEI, beta-blockers, ARNIs, or MRAs

Crespo-Leiro et al. Eur J Heart Fail. 2018 Nov;20(11):1505-1535.

Transition to advanced heart failure: what is needed?

Worsening Heart Failure: Nomenclature, Epidemiology, and Future Directions

JACC Review Topic of the Week



1/ Early recognition of the transition point to advanced heart failure and consideration of other therapeutic options

2/ The right time to decide which patient and when should be referred to the HTx / LVAD centre and who should be sent to palliative care facility.

Green et al. J Am Coll Cardiol 2023;81:413-424

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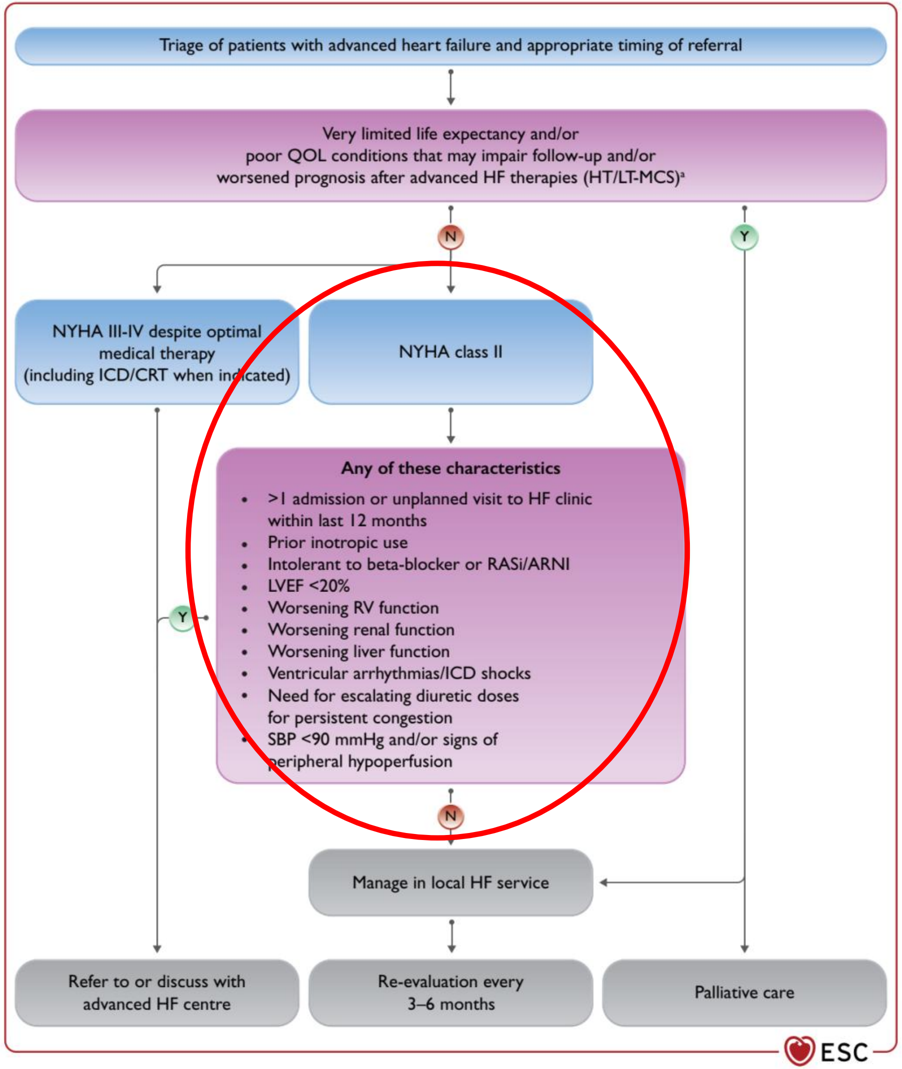
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

2/ The right time to decide when and which patient should be referred to the HTx / LVAD centre.

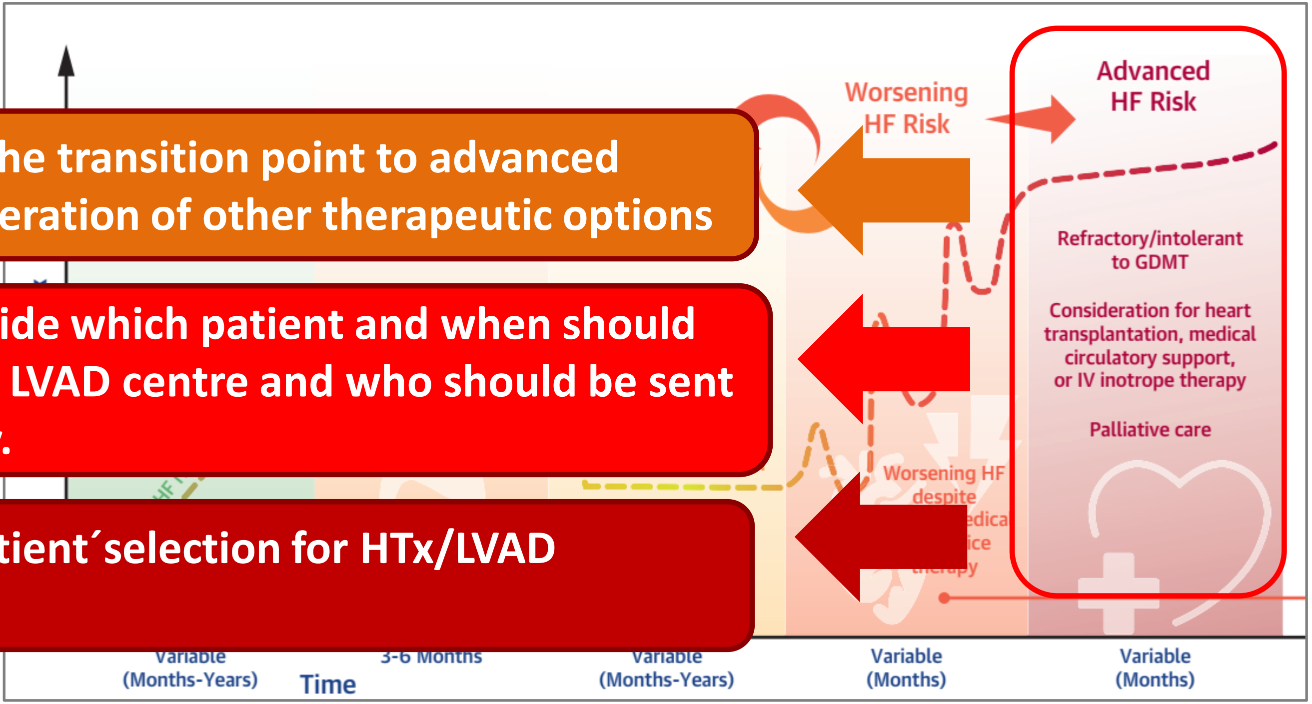


McDonagh et al. Eur Heart J. 2021;42(36):3599-3726

Transition to advanced heart failure: what is needed?

Worsening Heart Failure: Nomenclature, Epidemiology, and Future Directions

JACC Review Topic of the Week



1/ Early recognition of the transition point to advanced heart failure and consideration of other therapeutic options

2/ The right time to decide which patient and when should be referred to the HTx / LVAD centre and who should be sent to palliative care facility.

3/ Optimal timing of patient´selection for HTx/LVAD implantation

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Green et al. J Am Coll Cardiol 2023;81:413-424

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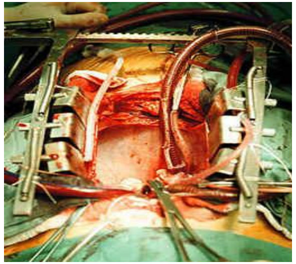
3/ Optimal timing of patient´ selection for HTx/LVAD implantation

Recommendations for the treatment of patients with advanced heart failure

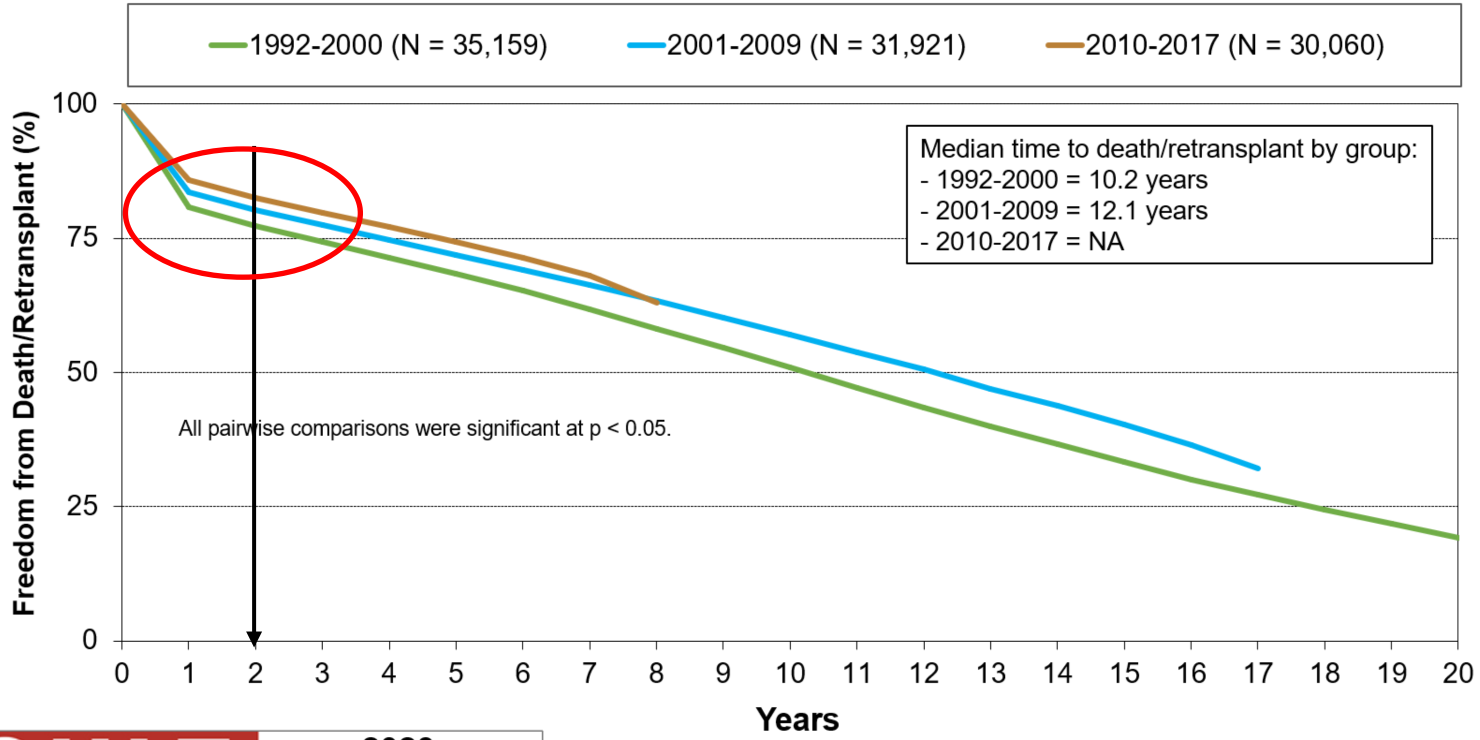
Recommendations	Class[a]	Level[b]
Patients being considered for long-term MCS must have good compliance, appropriate capacity for device handling and psychosocial support.[414–416]	I	C
Heart transplantation is recommended for patients with advanced HF, refractory to medical/device therapy and who do not have absolute contraindications.	I	C
Long-term MCS should be considered in patients with advanced HFrEF despite optimal medical and device therapy, not eligible for heart transplantation or other surgical options, and without severe right ventricular dysfunction, to reduce the risk of death and improve symptoms.[378,396,397,401,402,404,417]	IIa	A
Long-term MCS should be considered in patients with advanced HFrEF refractory to optimal medical and device therapy as a bridge to cardiac transplantation in order to improve symptoms, reduce the risk of HF hospitalization and the risk of premature death.[398–400,402,404]	IIa	B

McDonagh et al. Eur Heart J. 2021;42(36):3599-3726



Kaplan-Meier Freedom from Death/Retransplant for Adult Heart Recipients by Transplant Era

(Deceased Donor Heart Transplants: January 1992 – June 2017)



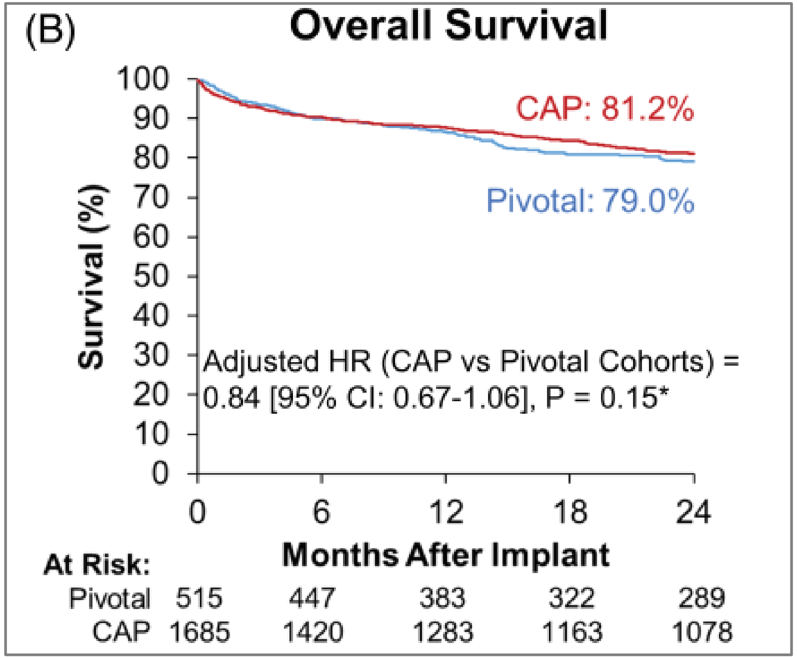
ISHLT • INTERNATIONAL SOCIETY FOR HEART AND LUNG TRANSPLANTATION
2023
JHLT. 2023 Oct; 42(10): 1321-1333

Primary results of long-term outcomes in the MOMENTUM 3 pivotal trial and continued access protocol study phase: a study of 2200 HeartMate 3 left ventricular assist device implants

Table 1 **Comparison of baseline characteristics between the pivotal and continued access protocol cohorts**

Baseline variable	Pivotal cohort (*n* = 515)	CAP cohort (*n* = 1685)	*P*-value*
Age, years	59.2 ± 12.4	59.9 ± 12.2	0.22
BSA, m^2	2.07 ± 0.27	2.08 ± 0.29	0.86
BMI, kg/m^2	29.2 ± 6.3	29.1 ± 6.7	0.84
Male sex	410 (79.6%)	1342 (79.6%)	0.99
Caucasian	341 (66.2%)	1135 (67.4%)	0.60
Ischaemic aetiology of heart failure	216 (41.9%)	760 (45.1%)	0.21
Intended use			
Destination therapy	317 (61.6%)	1274 (75.6%)	<0.001
Bridge to transplant	112 (21.7%)	173 (10.3%)	<0.001
Bridge to candidacy	86 (16.7%)	233 (13.8%)	0.11
Bridge to recovery	0 (0%)	4 (0.2%)	0.58
Rescue therapy	0 (0%)	1 (0.1%)	1.00
IABP	64 (12.4%)	282 (16.7%)	0.019
INTERMACS profile			
1	11 (2.1%)	69 (4.1%)	0.036
2	156 (30.4%)	517 (31.0%)	0.79
3	272 (52.9%)	843 (50.5%)	0.33
4–7	75 (14.6%)	241 (14.3%)	0.88
Diabetes	233 (45.2%)	690 (40.9%)	0.08
Prior stroke	50 (9.7%)	128 (7.6%)	0.12
ACE inhibitor or ARB	158 (30.7%)	338 (20.1%)	<0.001
Beta-blocker	284 (55.1%)	668 (39.6%)	<0.001
Inotropes	444 (86.2%)	1474 (87.5%)	0.45

2-year survival after LVAD implantation is similar to HTx survival



European Journal of Heart Failure (2021) **23**, 1392–1400

How successful are we at this?

Progression into advHF stage and the need advTx

HFSTATS
EPIDEMIOLOGY AND OUTCOMES

Heart Failure Epidemiology and Outcomes Statistics:
A Report of the Heart Failure Society of America

- The U.S. National Institutes of Health estimates that of the approximately 400.000 - 600,000 patients with advanced HF in the U.S., 50.000 to 100.000 patients per year could be indicated for LVAD or TAH implantation.

- Reality: approximately 3,000-4,000 HTx are performed annually, and 2,000-3,000 LVADs are implanted in the US (this represents 7-14%)

Bozkurt et al. J Card Fail. 2023; 29(10): 1412-1451

What it means for Czech Republic?

- There should be 20.000-45.000 patients with advanced HF in the Czech Republic - estimated 2.500-5.000 patients could be implanted per year

- Reality in CZ: 75-90 HTx per year, about 50 LVADs per year (2.5-5%)

- *HF death in 2023 in Czech Republic:*
  - *110 patients (age 40-49 years)*
  - *262 pts (age 50-59 years)*
  - *681 pts (age 60-69 years)*

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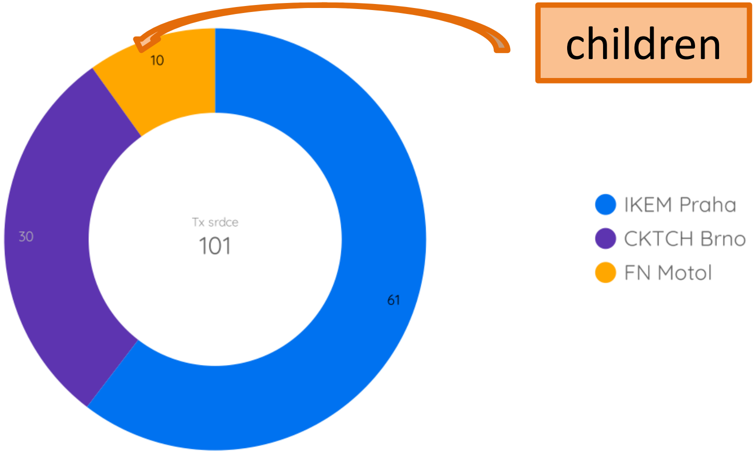
HTx situation in Czech Republic

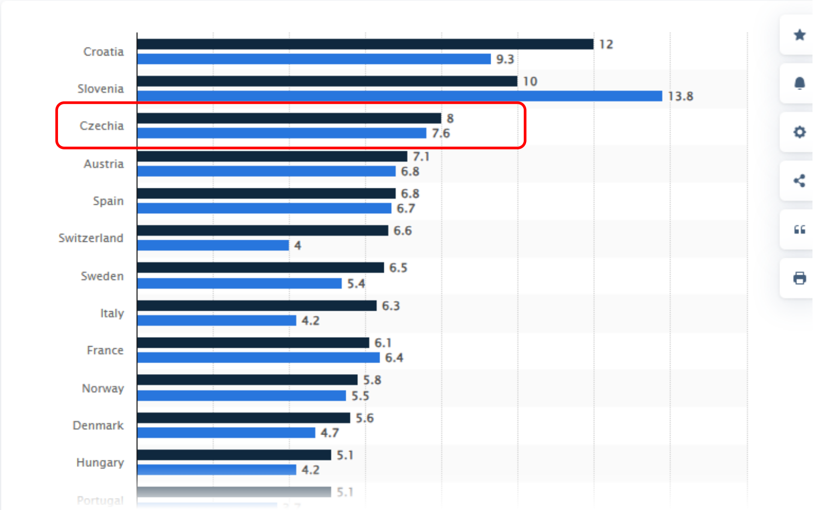
Počet transplantací srdce podle zařízení [1]

rok 2024 / celkový počet transplantací srdce v České republice



Zdroj: Domácí statistiky. Koordinační středisko transplantací [online]. Dostupné z: https://kst.cz/statistiky/

Rate of heart transplant procedures per million population country



https://www.statista.com/statistics/537910/heart-transplant-rate-in-europe/

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…and what is the LVAD reality?

Multicenter exploration of specialist palliative care in patients with left ventricular assist devices – a retrospective study

Theresa Tenge[1,2], Shaylin Shahinzad[2], Stefan Meier[1], Manuela Schallenburger[2], Yann-Nicolas Batzler[2], Jacqueline Schwartz[2*], Anja Coym[3], Johannes Rosenbruch[4], Mitra Tewes[5], Steffen T. Simon[6], Carmen Roch[7], Ute Hiby[8], Christian Jung[9], Udo Boeken[10], Jan Gaertner[11,12] and Martin Neukirchen[1,2]

According to the German heart surgery report, a total of 9,503 ventricular assist devices were implanted between 2012 and 2022 [15]. Based on information from the

Germany: 11 LVAD implants / million

Czech republic: 5 LVAD implants / million

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Tenge et al. BMC Palliat Care 23, 229 (2024).

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Main tasks in advanced HF

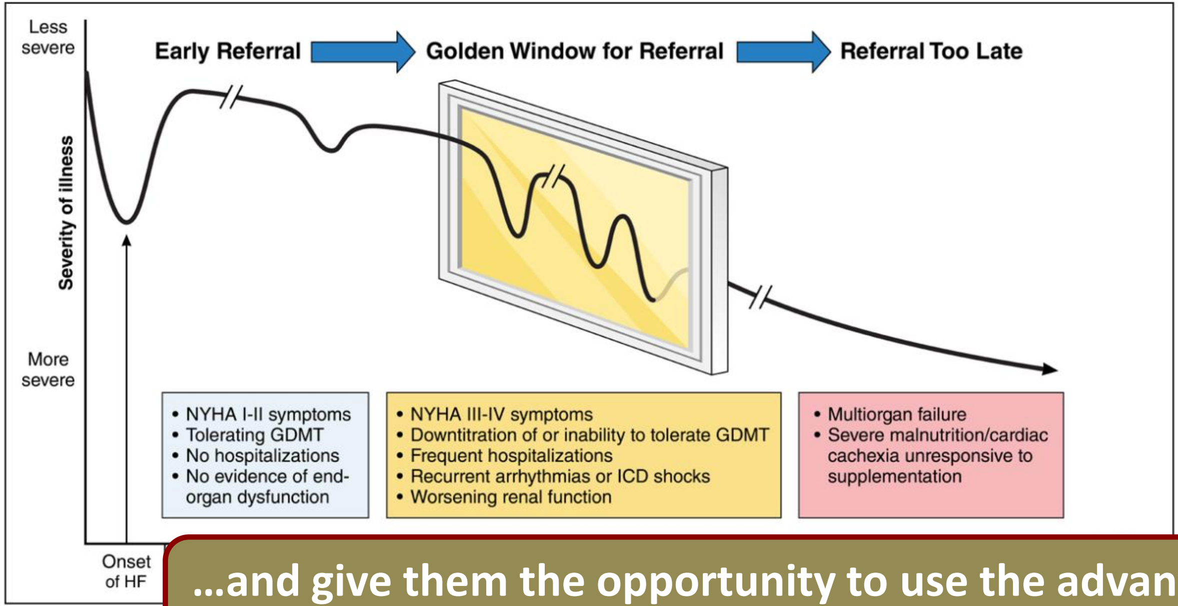
1/ treat the patients with HF in a way to avoid progression to advanced HF

2/ identify patients with advanced heart failure early and decide on further treatment options

3/ ensure quality palliative care for the majority of patients who cannot be candidates for advanced treatment

4/ select suitable candidates for HTx / LVAD implantation and refer them to centres in a timely manner

Identify and refer suitable candidates to HTx / LVAD centers



…and give them the opportunity to use the advantage of modern advanced treatments and change their fate

Morris et al. Circulation 2021;144:e238-250.

Thanks for your attention!

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