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Leitliniengerechte Herzinsuffizienztherapie

D. Koudonas

herzteam wil

Herzinsuffizienz

- Epidemiologie-Einteilung der Herzinsuffizienz
- Aktuelle Pharmakotherapie/ESC Leitlinien 2021
- Neue Konzepte in der Therapie-wann und wie behandeln
- Was kommt nach der medikamentösen Therapie?

Herzinsuffizienz

- Komplexes klinisches Syndrom mit hoher Mortalität und Morbidität



Herzinsuffizienz in der Schweiz

ca.
200 000
HI-Patienten in der Schweiz ²

Jährlich **sterben** in der Schweiz ca.
18 000
Patienten an HI ¹



Mortalität

5 Jahre
nach Erstdiagnose ^{3,4}

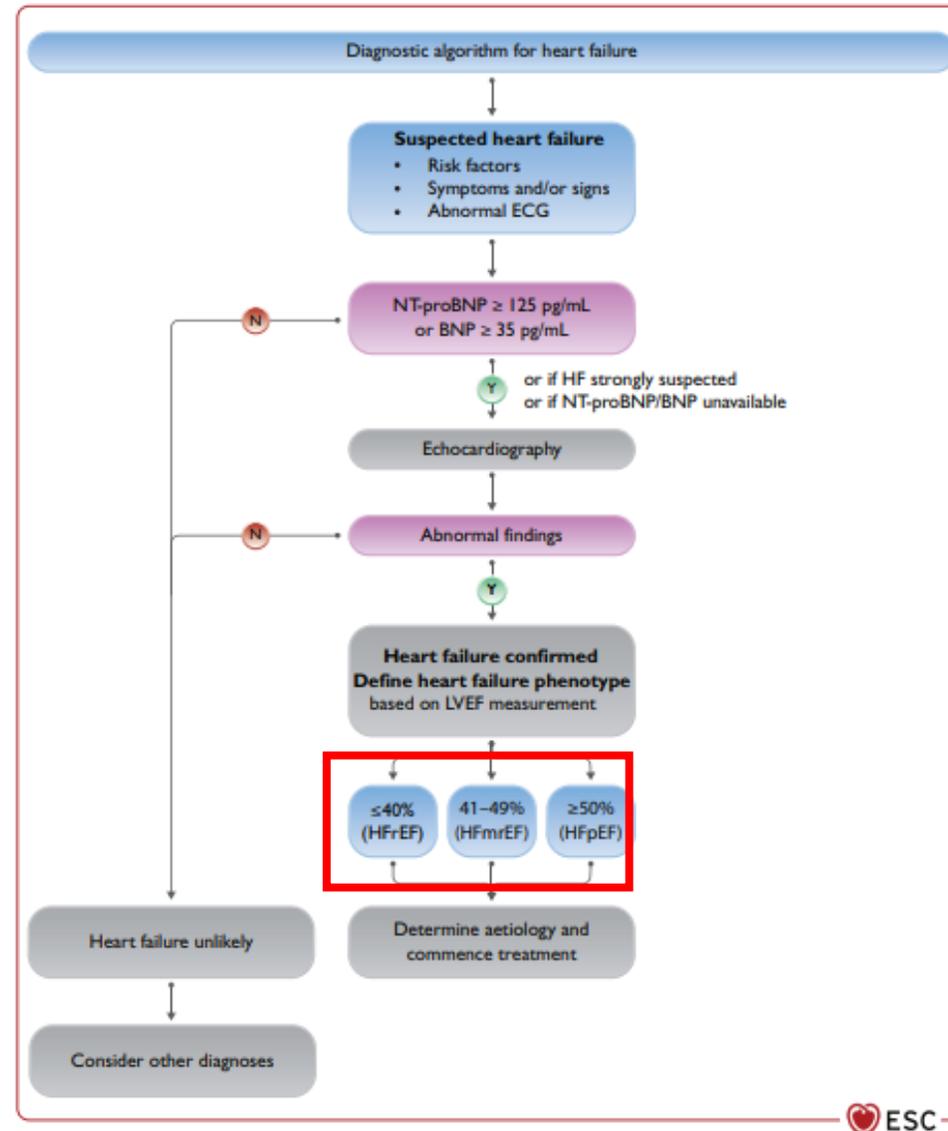


Jeder zweite HI-Patient verstirbt ^{3,4}

- Überlebensrate schlechter als bei vielen Krebserkrankungen

1.Szucs, T.D., Gesundheitsökonomische Aspekte der chronischen Herzinsuffizienz, S. Ärztezeitung, Editor. 2003.
2.Mohacsi, P., et al., Ein Curriculum für Herzinsuffizienz ist als Grundlage für die Entwicklung erforderlicher nationaler Strukturen unumgänglich: Positionspapier «Herzinsuffizienz-Curriculum» der Arbeitsgruppe Herzinsuffizienz der SGK. Cardiovascular Medicine, 2018. 21(01): p. 26-32.
3.Loehr, L.R., et al., Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study). Am J Cardiol, 2008. 101(7): p. 1016-22.
4.Roger, V.L., et al., Heart disease and stroke statistics--2012 update: a report from the American Heart Association. Circulation, 2012. 125(1): p. e2-e220.

Diagnostik

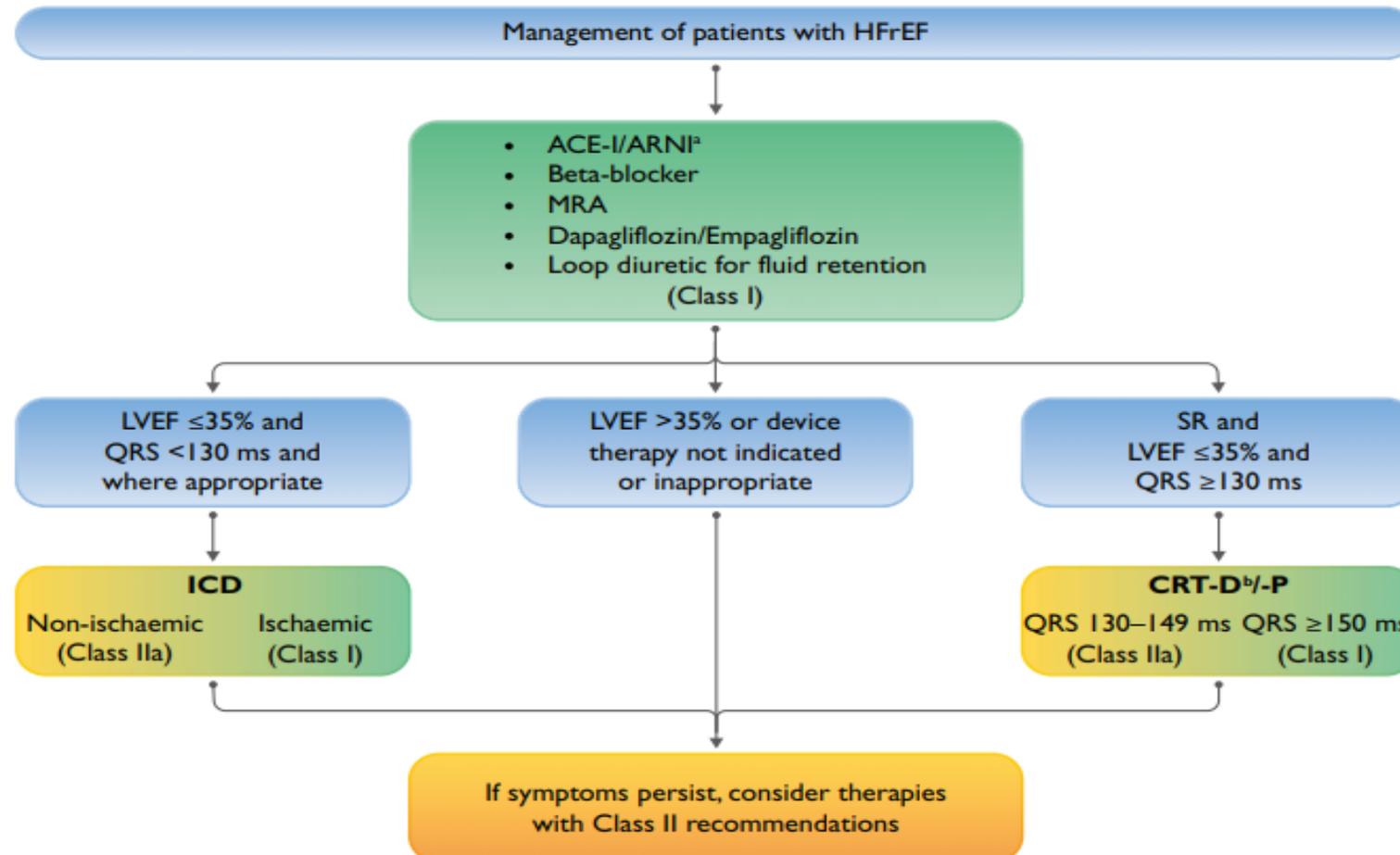


Aktuelle Klassifikation

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs ^a	Symptoms ± Signs ^a	Symptoms ± Signs ^a
	2	LVEF ≤40%	LVEF 41–49% ^b	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides ^c

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Therapie der Herzinsuffizienz (HFrEF)



Therapie der Herzinsuffizienz (HFrEF)

Management of HFrEF

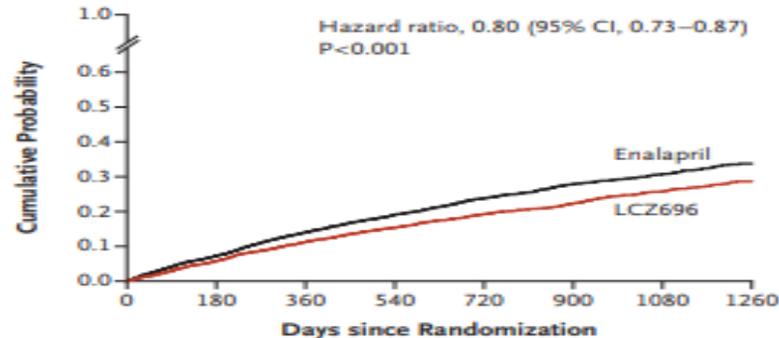


Pharmacological treatments indicated in patients with (NYHA class II–IV) heart failure with reduced ejection fraction (LVEF \leq 40%)

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

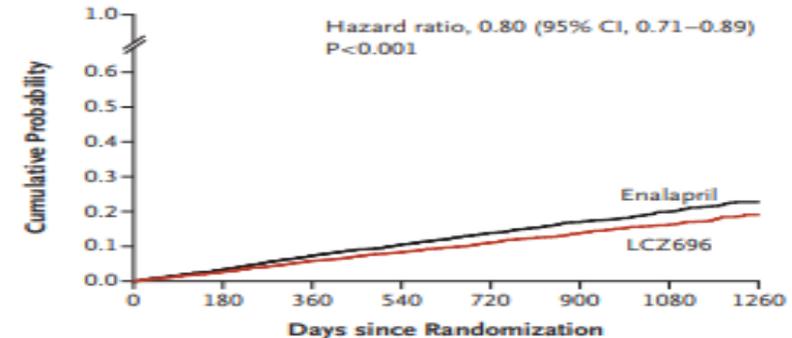
Therapie der Herzinsuffizienz (HFrEF) PARADIGM-HF

A Primary End Point



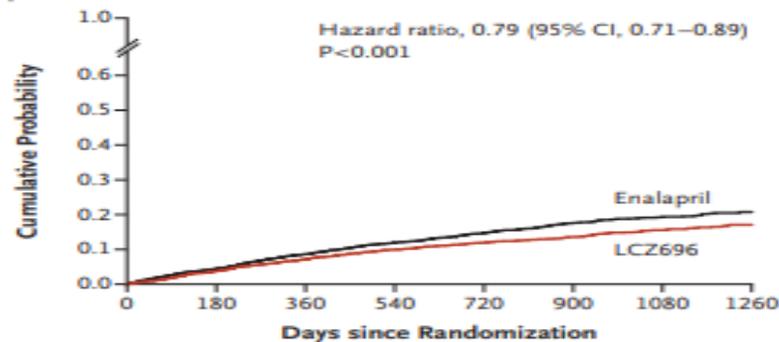
No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	4187	3922	3663	3018	2257	1544	896	249	
Enalapril	4212	3883	3579	2922	2123	1488	853	236	

B Death from Cardiovascular Causes



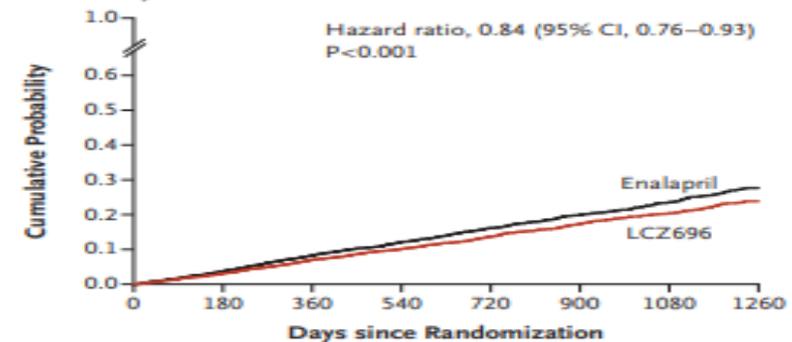
No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	4187	4056	3891	3282	2478	1716	1005	280	
Enalapril	4212	4051	3860	3231	2410	1726	994	279	

C Hospitalization for Heart Failure



No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	4187	3922	3663	3018	2257	1544	896	249	
Enalapril	4212	3883	3579	2922	2123	1488	853	236	

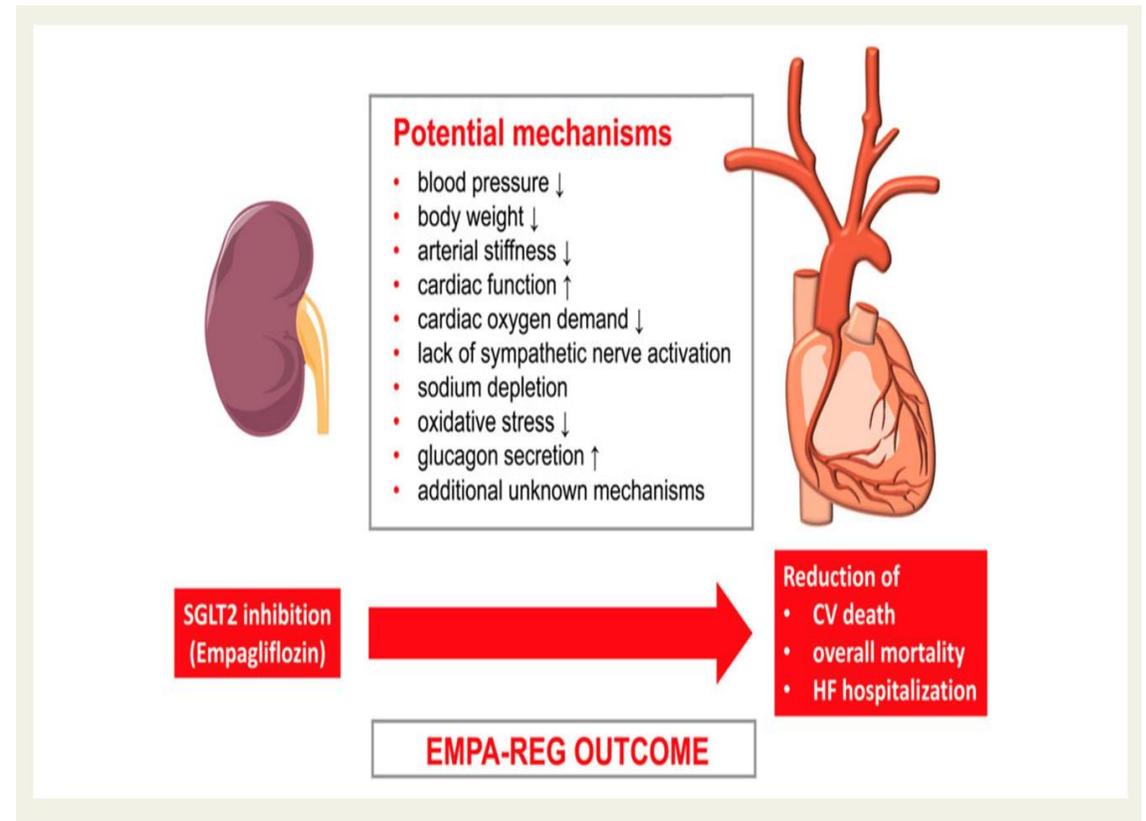
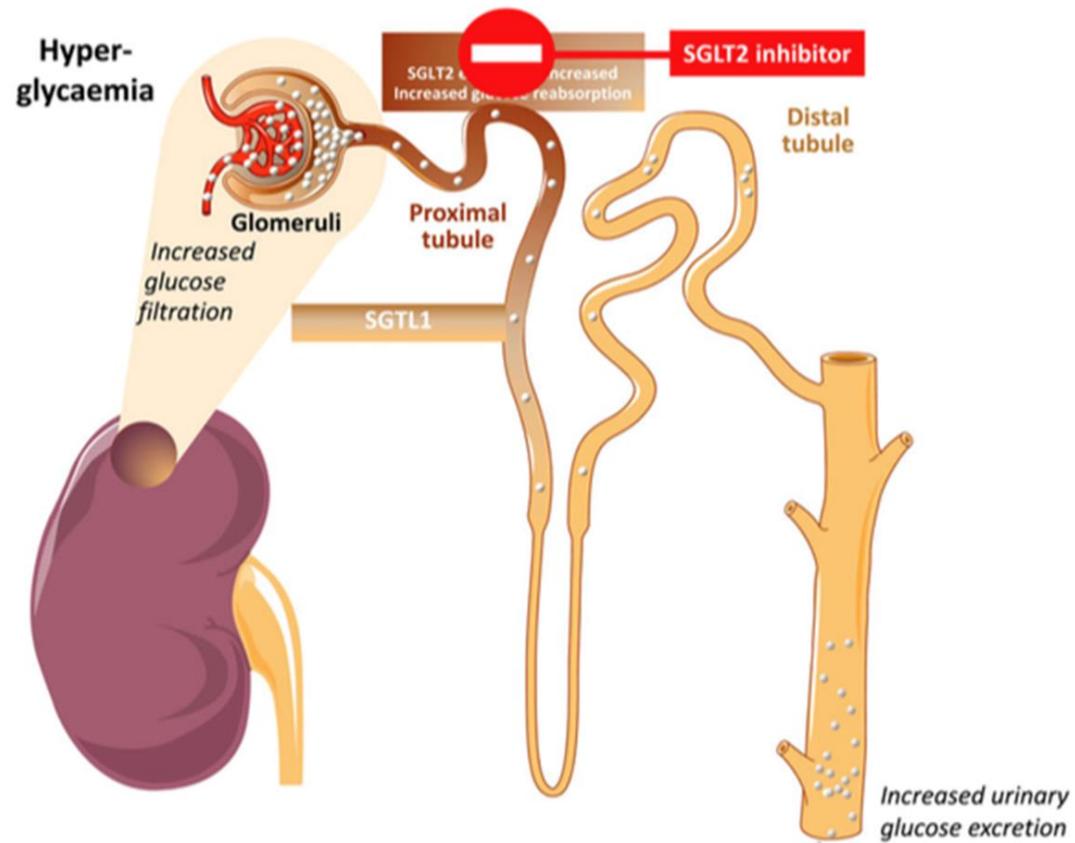
D Death from Any Cause



No. at Risk		0	180	360	540	720	900	1080	1260
LCZ696	4187	4056	3891	3282	2478	1716	1005	280	
Enalapril	4212	4051	3860	3231	2410	1726	994	279	

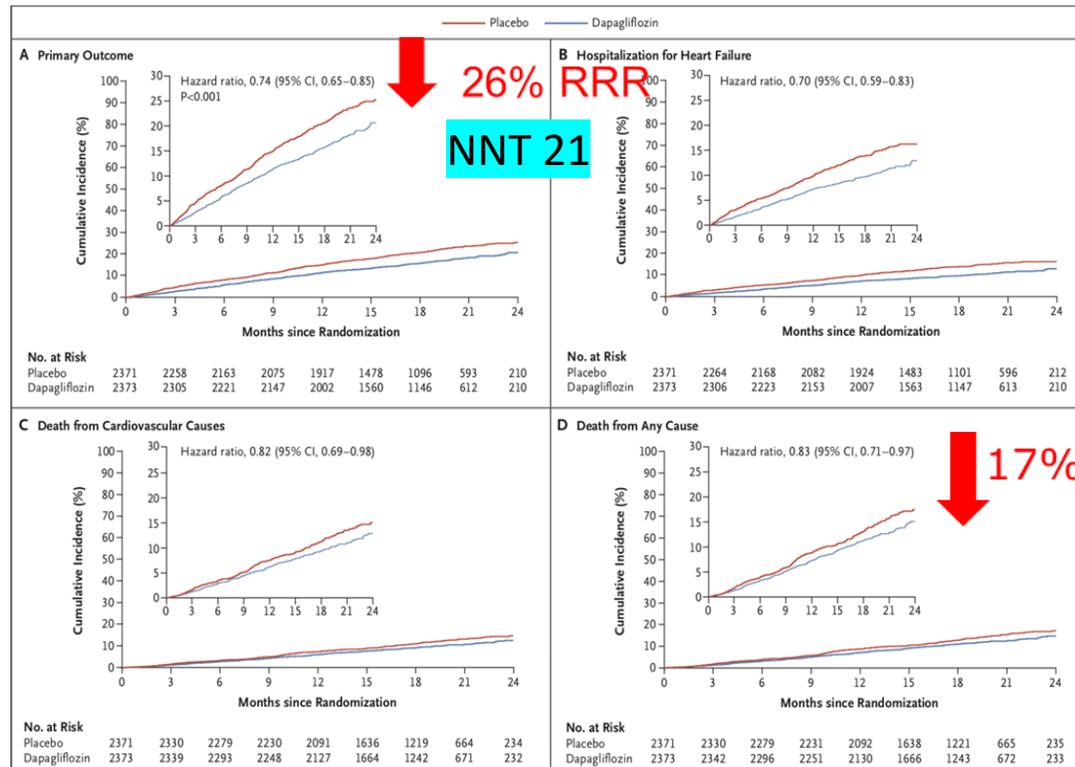
Therapie der Herzinsuffizienz (HFrEF)

SGLT2 Inhibition



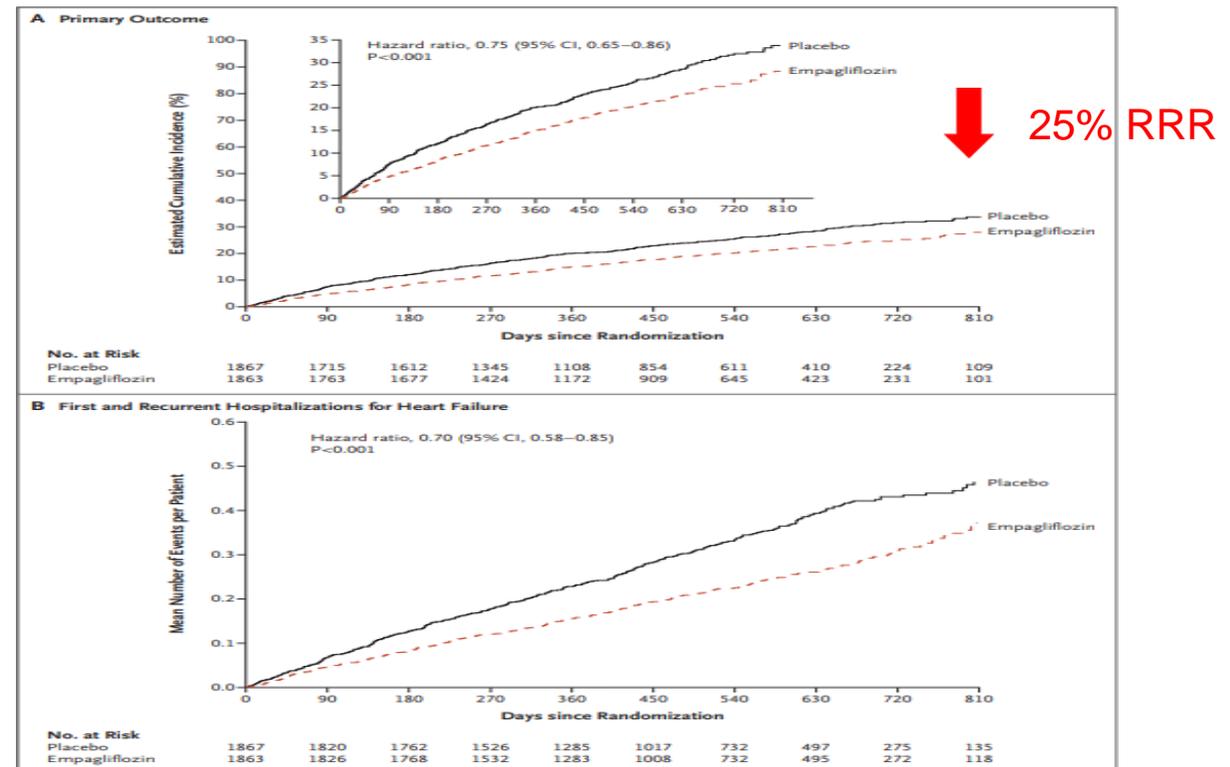
Therapie der Herzinsuffizienz (HFrEF) SGLT2 Inhibition

Dapagliflozin in Patients with Heart Failure und Reduced Ejection Fraction



McMurray et al., NEJM 2019

Cardiovascular und Renal Outcomes with Empagliflozin in Heart failure

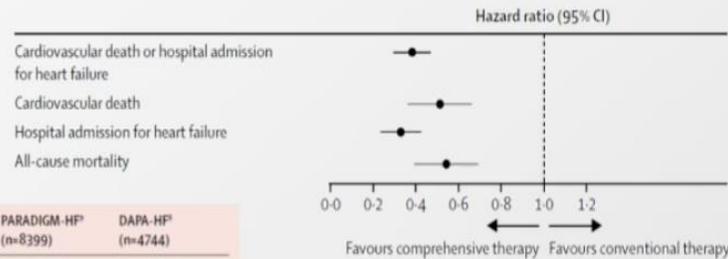


M. Packer et al., NEJM 2020

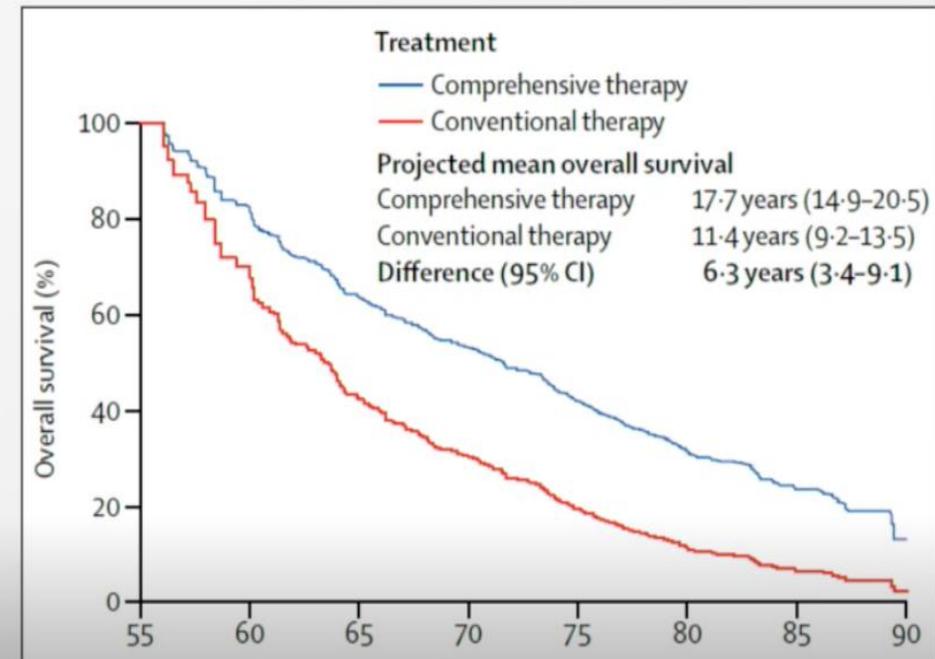
Moderne Therapie vs. Standard bei HFrEF

„Moderne Therapie“ vs. Standard (ACEi und BB) bei HFrEF

	EMPHASIS-HF ^a (n=2737)	PARADIGM-HF ^b (n=8399)	DAPA-HF ^c (n=4744)
Comparison	Eplerenone vs placebo	Sacubitril-valsartan vs enalapril	Dapagliflozin vs placebo
Enrolment period	2006-10	2009-12	2017-18
Median follow-up, months	21 (10-33)	27 (19-36)	18 (13-21)
Age, years	69 (8)	64 (11)	66 (11)
Sex			
Men	2127 (78%)	6567 (78%)	3635 (77%)
Women	610 (22%)	1832 (22%)	1109 (23%)
Systolic blood pressure, mm Hg	124 (17)	121 (15)	122 (16)
Heart rate, beats per min	72 (13)	72 (12)	72 (12)
Left ventricular ejection fraction, %	26 (5)	30 (6)	31 (7)
New York Heart Association class			
1	0	389 (5%)	0
2	2737 (100%)	5919 (70%)	3203 (68%)
3	0	2018 (24%)	1498 (32%)
4	0	60 (1%)	43 (1%)
Atrial fibrillation	844 (31%)	3091 (37%)	1818 (38%)
Diabetes	859 (31%)	2907 (35%)	1983 (42%)



„Moderne“ 4-fach Therapie bei HFrEF vs. Standardtherapie (ACEI, BB)



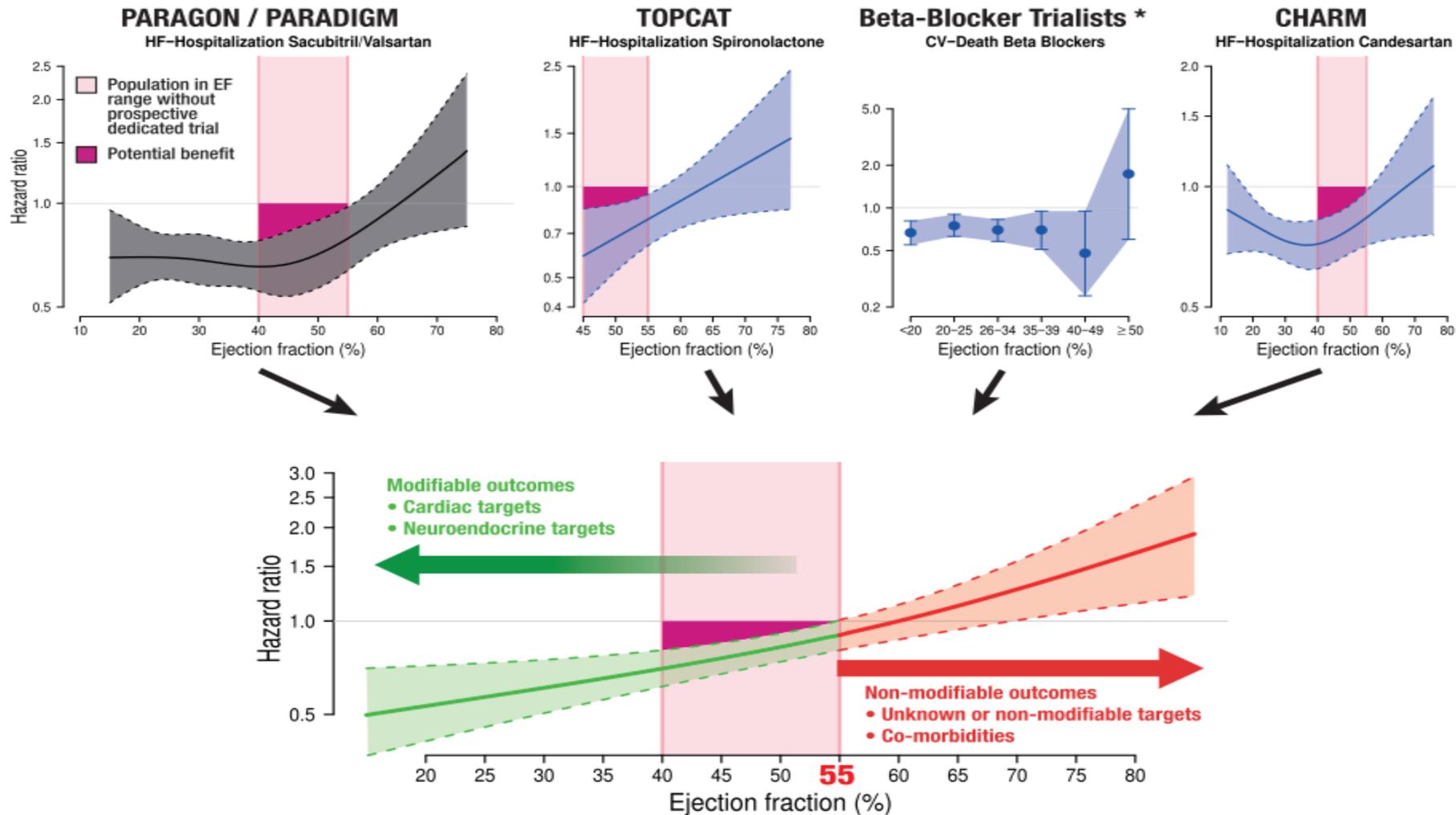
Therapie der Herzinsuffizienz (HFmrEF)

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs ^a	Symptoms ± Signs ^a	Symptoms ± Signs ^a
	2	LVEF ≤40%	LVEF 41–49% ^b	LVEF ≥50%
	3	–	–	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides ^c

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Mc Donagh et al. European Heart Journal (2021)

Therapie der Herzinsuffizienz (HFmrEF)



Therapie der Herzinsuffizienz (HFmrEF)

Recommendations	Class ^a	Level ^b
Diuretics are recommended in patients with congestion and HFmrEF in order to alleviate symptoms and signs. ¹³⁷	I	C
An ACE-I may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. ¹¹	IIb	C
An ARB may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. ²⁴⁵	IIb	C
A beta-blocker may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. ^{12,119}	IIb	C
An MRA may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. ²⁴⁶	IIb	C
Sacubitril/valsartan may be considered for patients with HFmrEF to reduce the risk of HF hospitalization and death. ^{13,247}	IIb	C

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Therapie der Herzinsuffizienz (HFpEF)

Type of HF	HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs ^a	Symptoms ± Signs ^a
	2	LVEF ≤40%	LVEF ≥50%
	3	–	–
			Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides

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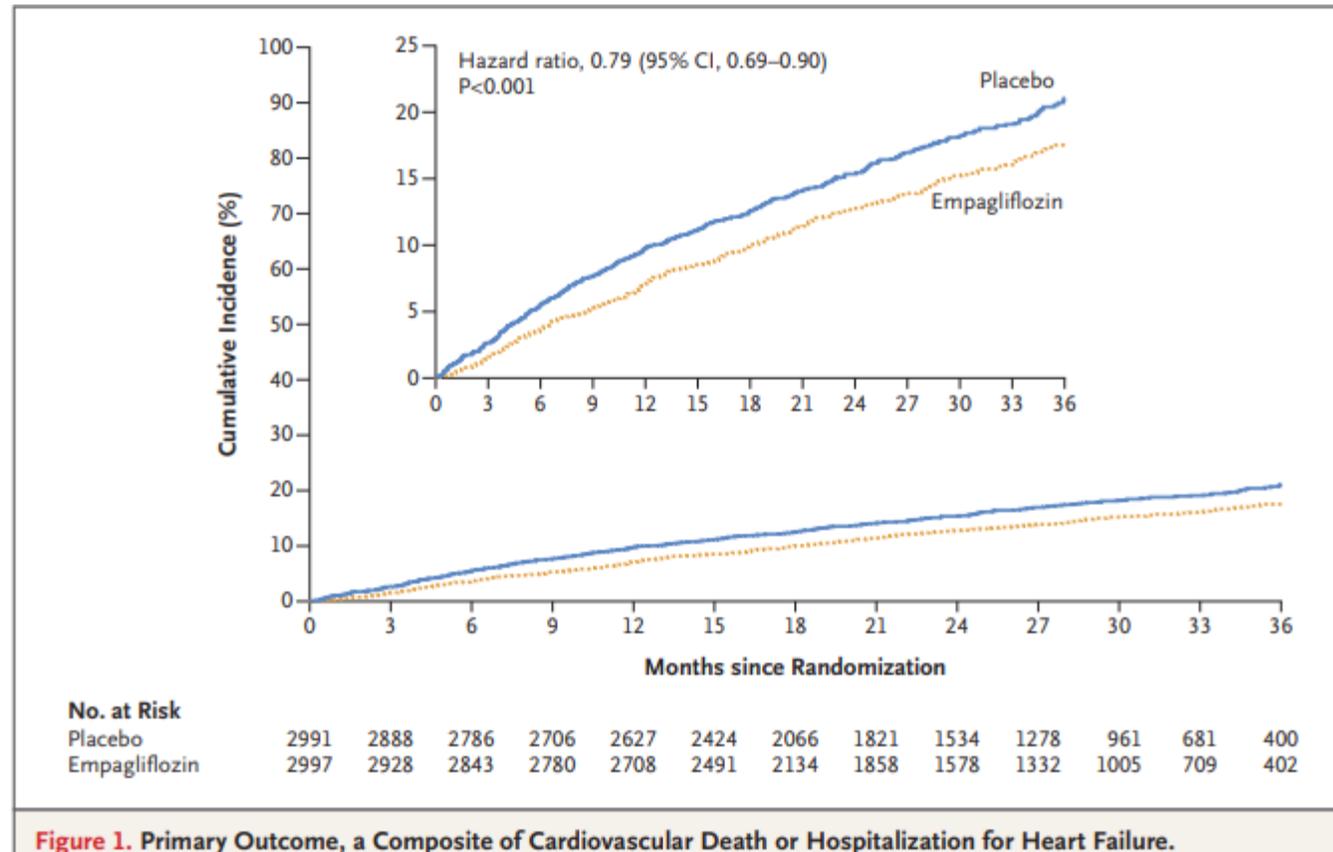
Therapie der Herzinsuffizienz (HFpEF)

Recommendations for the treatment of patients with heart failure with preserved ejection fraction

Recommendations	Class ^a	Level ^b
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	I	C
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs. ¹³⁷	I	C

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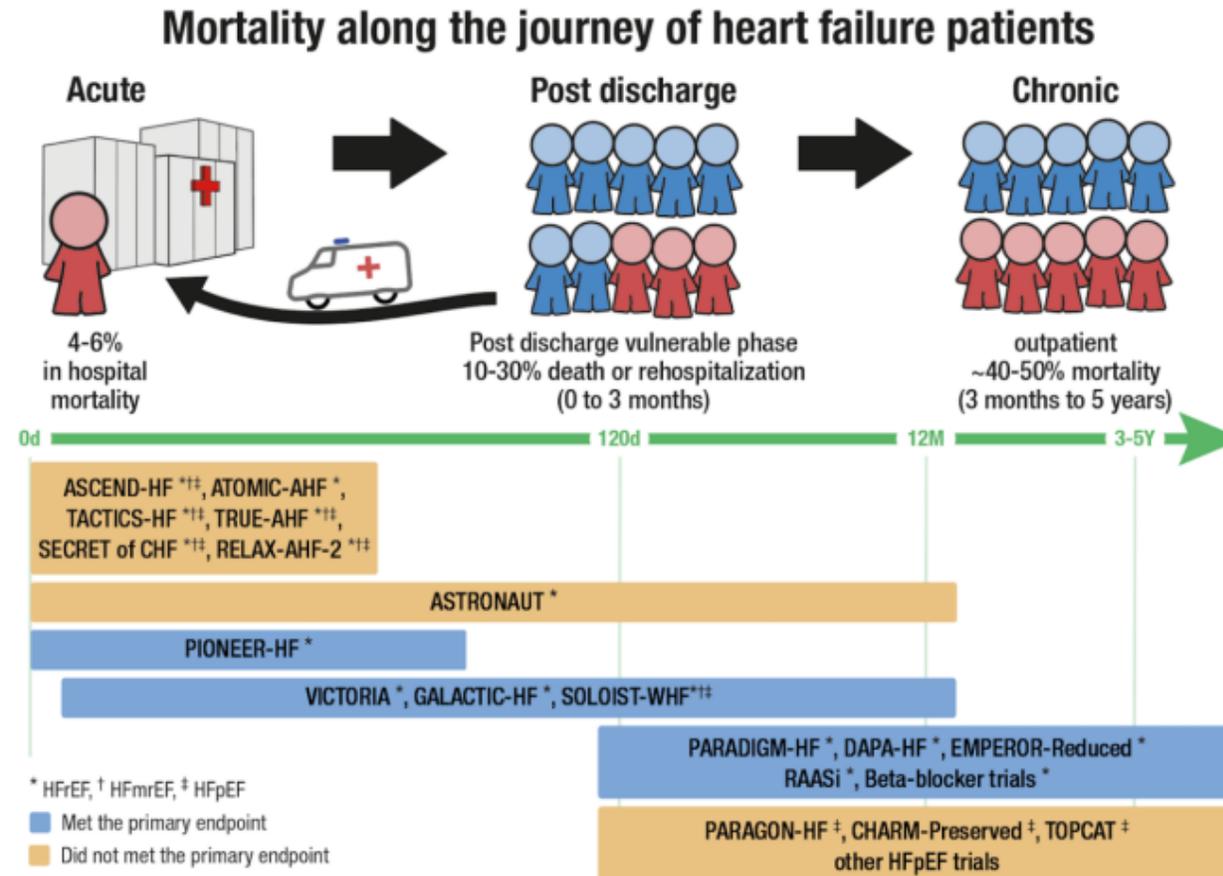
EMPEROR-PRESERVED SGLT2-Hemmer bei HFpEF



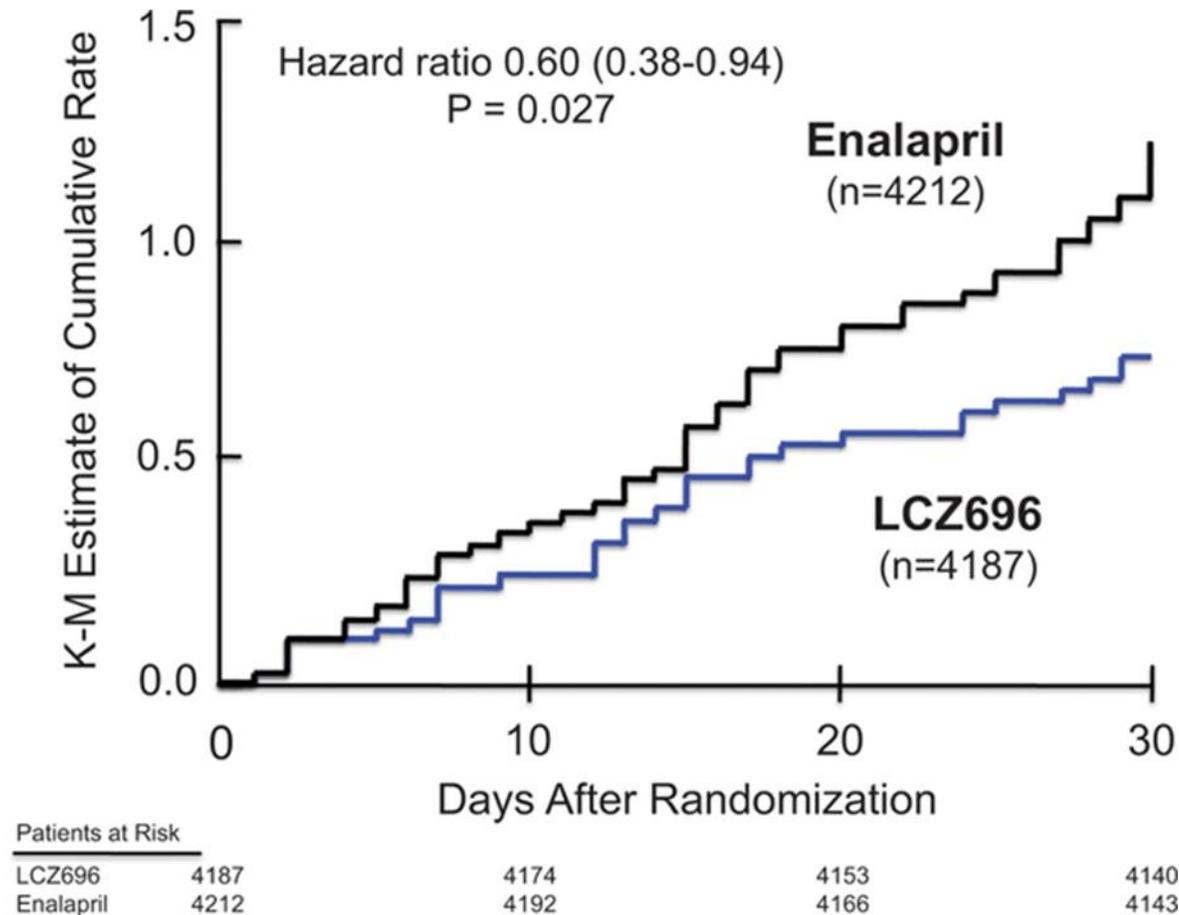
Einteilung

- Epidemiologie-Typen der Herzinsuffizienz
- Aktuelle Pharmakotherapie/ESC Leitlinien 2021
- Neue Konzepte in der Therapie-wann und wie behandeln
- Was kommt nach der medikamentösen Therapie?

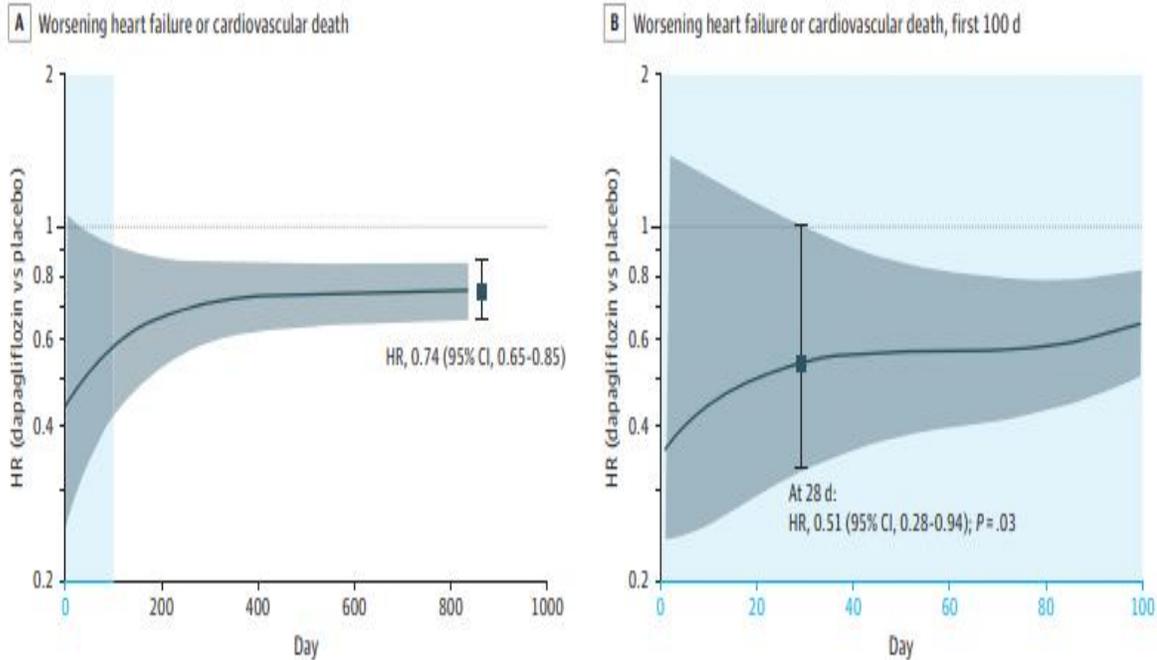
'Time is prognosis' in heart failure



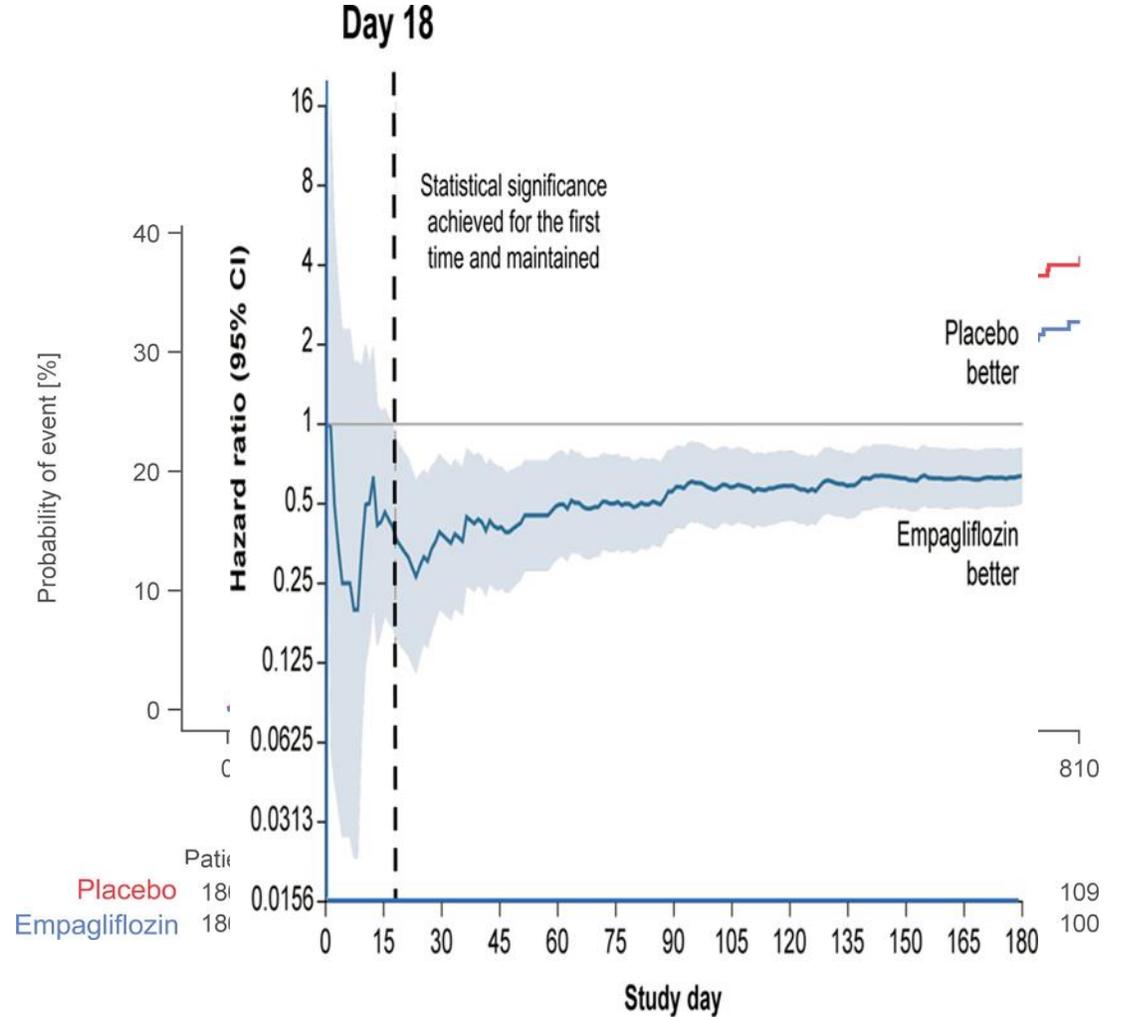
Früher Nutzen von Sacubitril/Valsartan



Früher Nutzen von SGLT2-Hemmern



Berg et al. JAMA Cardiology 2021; 6 (5):499-507



Packer et al. Circulation October 2021 144, 1284-1294

Frühe Therapieinitiierung

Therapie der Herzinsuffizienz mit reduzierter Pumpfunktion (LVEF \leq 40%)

alt

Herkömmliches Therapieschema

- Titration bei zur Zieldosis bei jedem Schritt
- Übliche Zeitdauer > 6 Monate



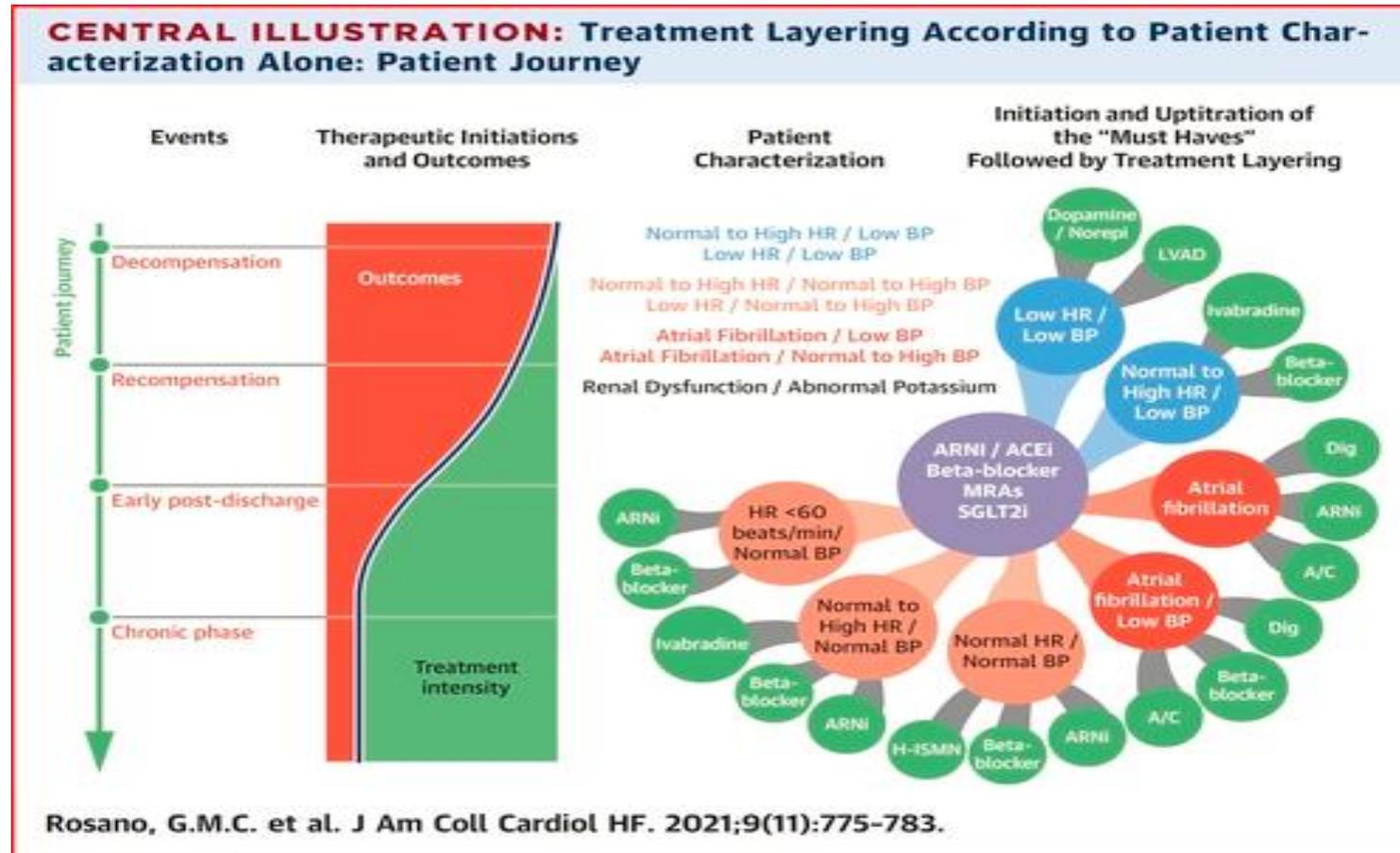
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Rasche Therapieeinleitung

- Alle drei Schritte innerhalb von 4 Wochen empfohlen
- Titration zur Zieldosis erst nach Initiierung aller Medikationen
- Nicht die exakte Sequenz ist wichtig, sondern in kurzer Zeit alle 4 Therapien zu implementieren



Medikamentöse Therapieeinleitung nach klinischem Phänotyp



Weitere Substanzen

I_f-channel inhibitor			Soluble guanylate cyclase stimulator		
Ivabradine should be considered in symptomatic patients with LVEF ≤35%, in SR and a resting heart rate ≥70 b.p.m. despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I/(or ARNI), and an MRA, to reduce the risk of HF hospitalization and CV death. ¹³⁹	IIa	B	Vericiguat may be considered in patients in NYHA class II–IV who have had worsening HF despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA to reduce the risk of CV mortality or HF hospitalization. ¹⁴¹	IIb	B
Ivabradine should be considered in symptomatic patients with LVEF ≤35%, in SR and a resting heart rate ≥70 b.p.m. who are unable to tolerate or have contraindications for a beta-blocker to reduce the risk of HF hospitalization and CV death. Patients should also receive an ACE-I (or ARNI) and an MRA. ¹⁴⁰	IIa	C	Hydralazine and isosorbide dinitrate		
			Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with LVEF ≤35% or with an LVEF <45% combined with a dilated left ventricle in NYHA class III–IV despite treatment with an ACE-I (or ARNI), a beta-blocker and an MRA to reduce the risk of HF hospitalization and death. ¹⁴²	IIa	B

NEU

VICTORIA - Vericiguat

Inclusion Criteria

“Chronic HF”

- NYHA class II–IV
- LVEF < 45%
- Guideline based HF therapies

after

“Worsening event”

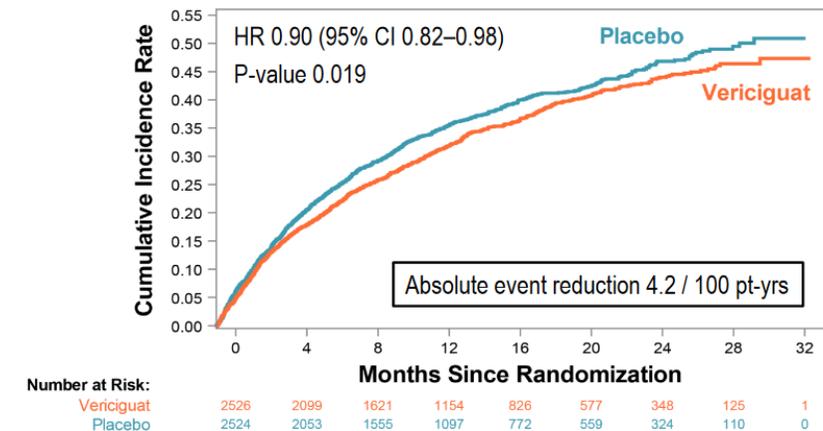
- Recent HFH or IV diuretic use
- With very elevated natriuretic peptides (BNP or NT-proBNP)

BNP ≥ 300 & pro-BNP ≥ 1000 pg/ml NSR
BNP ≥ 500 & pro-BNP ≥ 1600pg/ml AF

Patients may have been randomized as an inpatient or outpatient but must have met criteria for clinical stability (e.g., SBP ≥ 100 mmHg, off IV treatments ≥ 24 hours)

30-day screening period without run-in

Primary Composite Endpoint: CV Death or First HF Hospitalization



Einteilung

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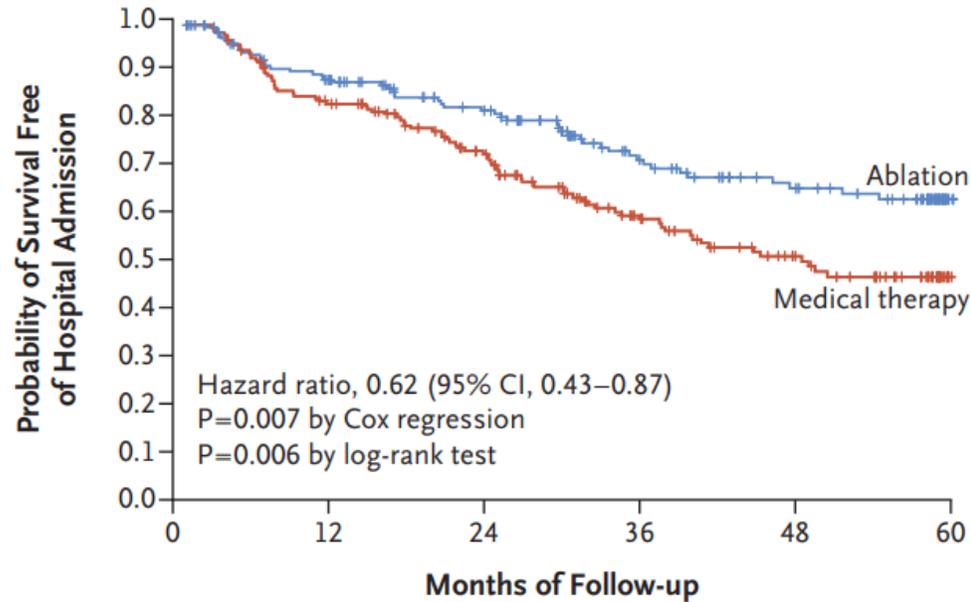
Individualisierte Therapie der Herzinsuffizienz

Device-Therapie

To reduce HF hospitalization/mortality - for selected patients				
<i>Volume overload</i>				
Diuretics				
<i>SR with LBBB ≥ 150 ms</i>		<i>SR with LBBB 130–149 ms or non LBBB ≥ 150 ms</i>		
CRT-P/D		CRT-P/D		
<i>Ischaemic aetiology</i>		<i>Non-ischaemic aetiology</i>		
ICD		ICD		
<i>Atrial fibrillation</i>	<i>Atrial fibrillation</i>		<i>Coronary artery disease</i>	<i>Iron deficiency</i>
Anticoagulation	Digoxin	PVI	CABG	Ferric carboxymaltose
<i>Aortic stenosis</i>	<i>Mitral regurgitation</i>	<i>Heart rate SR > 70 bpm</i>	<i>Black Race</i>	<i>ACE-I/ARNI intolerance</i>
SAVR/TAVI	TEE MV Repair	Ivabradine	Hydralazine/ISDN	ARB

Catheter Ablation for Atrial Fibrillation with Heart Failure

A Death or Hospitalization for Worsening Heart Failure



No. at Risk

Ablation	179	141	114	76	58	22
Medical therapy	184	145	111	70	48	12

AF catheter ablation

In cases of a clear association between paroxysmal or persistent AF and worsening of HF symptoms, which persist despite MT, catheter ablation should be considered for the prevention or treatment of AF.^{552–554,557}

IIa

B

Nach Entlassung

Recommendations	Class ^a	Level ^b
It is recommended that patients hospitalized for HF be carefully evaluated to exclude persistent signs of congestion before discharge and to optimize oral treatment. ^{427,472}	I	C
It is recommended that evidence-based oral medical treatment be administered before discharge. ^{103,513}	I	C
An early follow-up visit is recommended at 1–2 weeks after discharge to assess signs of congestion, drug tolerance and start and/or uptitrate evidence-based therapy. ^{517,518}	I	C
Ferric carboxymaltose should be considered for iron deficiency, defined as serum ferritin <100 ng/mL or serum ferritin 100–299 ng/mL with TSAT <20%, to improve symptoms and reduce rehospitalizations. ⁵¹²	IIa	B

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Zusammenfassung

- Komplexes klinisches Syndrom mit hoher Mortalität und Morbidität
- Basistherapie «4er-Kombi»
 - ARNI/ACEI-b-Blocker-Aldosteronantagonist (MRA)-SGLT2-Hemmer
- Strategiewechsel für alle Patienten mit **HFrEF** durch den raschen Beginn prognoseverbessernder Substanzen noch im Spital
- Vollständige Rekompensation und Verlaufskontrolle innerhalb 1-2 Wochen
- **HFmrEF** Patienten profitieren wahrscheinlich auch von diesem Therapieprinzip
- Eine deutliche Prognoseverbesserung der chronischen Herzinsuffizienz ist zu erwarten
- Trotz der Emperor-Preserved Studie wurden Empfehlungen für **HFpEF** noch nicht ausgesprochen, da Zulassungen für SGLT2-Hemmer bisher ausstehen

Vielen Dank für Ihre Aufmerksamkeit