

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

Dr. med. Raphael Koller | Dr. med. Franziska Rohner | Dipl. med. Dimitrios Koudonas

## Leitliniengerechte Herzinsuffizienztherapie

D. Koudonas  
herzteam wil

1

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

## 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?

2

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

## Herzinsuffizienz

- Komplexes klinisches Syndrom mit hoher Mortalität und Morbidität

Herzinsuffizienz in der Schweiz

ca. **200 000** jährlich sterben in der Schweiz ca. **18 000**  
HI-Patienten in der Schweiz Patienten an HI

Mortalität

**5 Jahre** nach Erstdiagnose\*\*  
jeder zweite HI-Patient verstorbt\*\*

- Überlebensrate schlechter als bei vielen Krebserkrankungen

1. Szucs, T.D., Gesundheitsökonomische Aspekte der chronischen Herzinsuffizienz, S. Ärztezeitung, Editor, 2003.  
2. Mohacsai, P., et al., Ein Curriculum für Herzinsuffizienz ist als Grundlage für die Entwicklung erforderlicher nationaler Strukturen unumgänglich: Positionspapier «Herzinsuffizienz-Curricula» der Arbeitsgruppe Herzinsuffizienz der SGG, Cardiovascular Medicine, 2018, 21(1): p. 26-32.  
3. Loefer, L.R., et al., Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study), Am J Cardiol, 2008, 101(7): p. 1019-22.  
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.

3

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

## Diagnostik

ESC

Mc Donagh et al. European Heart Journal (2021)

4

## Aktuelle Klassifikation

Type of HF	HFrEF	HFmrEF	HFpEF
1	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>
2	LVEF <40%	LVEF 41–49% <sup>b</sup>	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 <sup>c</sup>

© ESC 2021

Mc Donagh et al. European Heart Journal (2021)

5

## Therapie der Herzinsuffizienz (HFrEF)

Mc Donagh et al. European Heart Journal (2021)

6

## Therapie der Herzinsuffizienz (HFrEF)

### Management of HFrEF

To reduce mortality - for all patients

ACE-I/ARNI

BB

MRA

SGLT2i

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

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

© ESC 2021

Mc Donagh et al. European Heart Journal (2021)

7

## Therapie der Herzinsuffizienz (HFrEF) PARADIGM-HF

**A Primary End Point**

**B Death from Cardiovascular Causes**

**C Hospitalization for Heart Failure**

**D Death from Any Cause**

John J.V. McMurray, et al. NEJM 2014

8

### Therapie der Herzinsuffizienz (HF<sub>r</sub>EF) SGLT2 Inhibition

**Potential mechanisms**

- blood pressure ↓
- body weight ↓
- arterial stiffness ↓
- cardiac function ↑
- cardiac oxygen demand ↓
- lack of sympathetic nerve activation
- sodium depletion
- oxidative stress ↓
- glucagon secretion ↓
- additional unknown mechanisms

**Reduction of**

- CV death
- overall mortality
- HF hospitalization

**EMPA-REG OUTCOME**

Marx N et al. European Heart Journal (2016) 37, 3192–3200

### Therapie der Herzinsuffizienz (HF<sub>r</sub>EF) SGLT2 Inhibition

#### Dapagliflozin in Patients with Heart Failure and 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 HF<sub>r</sub>EF

#### „Moderne Therapie“ vs. Standard (ACEI und BB) bei HF<sub>r</sub>EF

Comparison	EMPEROR-ADD (N=202)	EMPEROR-PRESERVE (N=209)	EMPEROR-OUTCOME (N=204)
Primary outcome	2008 (50)	2096 (51)	2057 (51)
Relative risk reduction	12.0% (95% CI 7.0-16.9)	12.0% (95% CI 7.0-16.9)	12.0% (95% CI 7.0-16.9)

#### „Moderne“ 4-fach Therapie bei HF<sub>r</sub>EF vs. Standardtherapie (ACEI, BB)

Vaduganathan et al., Lancet 2020

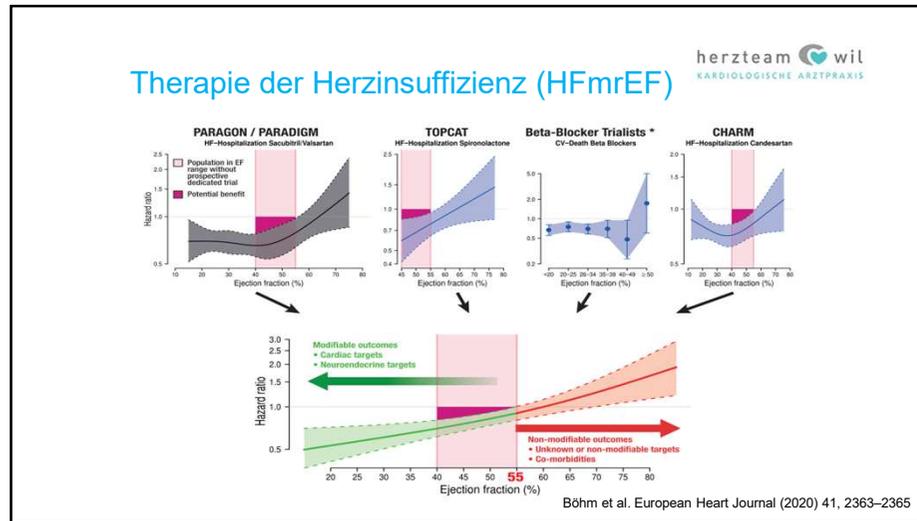
### Therapie der Herzinsuffizienz (HF<sub>m</sub>rEF)

Type of HF	HF <sub>r</sub> EF	HF <sub>m</sub> rEF	HFpEF
1	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>
2	LVEF <40%	LVEF 41–49% <sup>b</sup>	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

herzteam wil  
KARDIOLOGISCHE ANZTRAXIS

© ESC 2021

Mc Donagh et al. European Heart Journal (2021)



13

### Therapie der Herzinsuffizienz (HFmrEF)

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

© ESC 2021

Mc Donagh et al. European Heart Journal (2021)

14

### Therapie der Herzinsuffizienz (HFpEF)

Type of HF	HFREF	HFmrEF	HFpEF
1	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>	Symptoms ± Signs <sup>a</sup>
2	LVEF <40%	LVEF 41–49% <sup>b</sup>	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 peptide

Mc Donagh et al. European Heart Journal (2021)

15

### Therapie der Herzinsuffizienz (HFpEF)

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

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
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. <sup>137</sup>	I	C

© ESC 2021

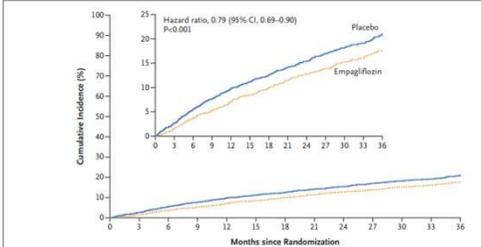
Mc Donagh et al. European Heart Journal (2021)

16

## EMPEROR-PRESERVED SGLT2-Hemmer bei HFpEF



KARDIOLOGISCHE ARZTPRAXIS



**Figure 1. Primary Outcome, a Composite of Cardiovascular Death or Hospitalization for Heart Failure.**

No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1006	709	402

FDA Approves Empagliflozin for Treatment of HFpEF, 24.02.2022

S.D. Anker et al. NEJM Oktober 21

17

## Einteilung



KARDIOLOGISCHE ARZTPRAXIS

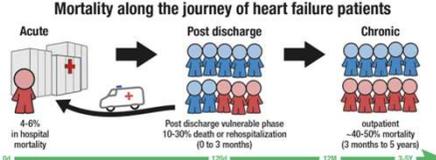
- Epidemiologie-Typen der Herzinsuffizienz
- Aktuelle Pharmakotherapie/ESC Leitlinien 2021
- Neue Konzepte in der Therapie-wann und wie behandeln
- Was kommt nach der medikamentösen Therapie?

18

## ‘Time is prognosis’ in heart failure



KARDIOLOGISCHE ARZTPRAXIS



**Mortality along the journey of heart failure patients**

Acute: 4-6% in hospital mortality

Post discharge: Post discharge vulnerable phase 10-30% death or rehospitalization (0 to 3 months)

Chronic: outpatient ~40-50% mortality (3 months to 5 years)

ASCEND-HF<sup>1</sup>, ATOMIC-AHF<sup>2</sup>, TACTICS-HF<sup>3</sup>, TRUE-AHF<sup>4</sup>, SECRET of CHF<sup>5</sup>, RELAX-AHF-2<sup>6</sup>

ASTRONAUT<sup>7</sup>

PIONEER-HF<sup>8</sup>

VICTORA<sup>9</sup>, GALACTIC-HF<sup>10</sup>, SOLOIST-WHF<sup>11</sup>

PARADIGM-HF<sup>12</sup>, DAPA-HF<sup>13</sup>, EMPEROR-Reduced<sup>14</sup>, RAASII<sup>15</sup>, Beta-blocker trials<sup>16</sup>

PARAGON-HF<sup>17</sup>, CHARM-Preserved<sup>18</sup>, TOPCAT<sup>19</sup> other HFpEF trials

<sup>1</sup> HFpEF, <sup>2-11</sup> HF with EF, <sup>12-19</sup> HFpEF

■ Met the primary endpoint  
■ Did not meet the primary endpoint

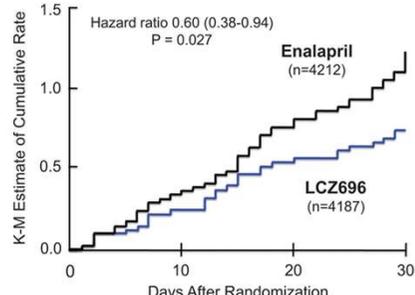
Abdin et al. ESC Heart Failure 2021; 8: 4444-4453

19

## Früher Nutzen von Sacubitril/Valsartan



KARDIOLOGISCHE ARZTPRAXIS



Hazard ratio 0.60 (0.38-0.94)  
P = 0.027

Enalapril (n=4212)

LCZ696 (n=4187)

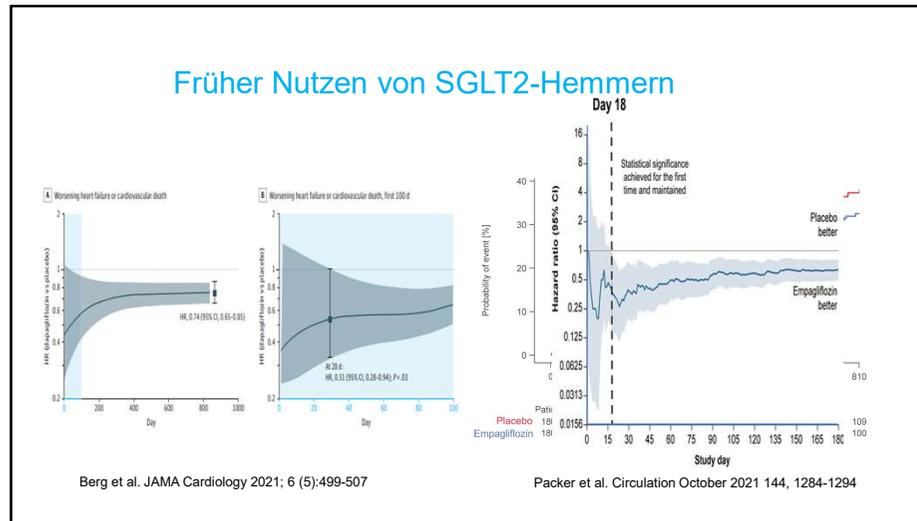
K-M Estimate of Cumulative Rate

Days After Randomization

Patients at Risk	0	10	20	30
LCZ696	4187	4174	4153	4140
Enalapril	4212	4192	4166	4143

M. Packer et al. Circulation 2015;131:54-61

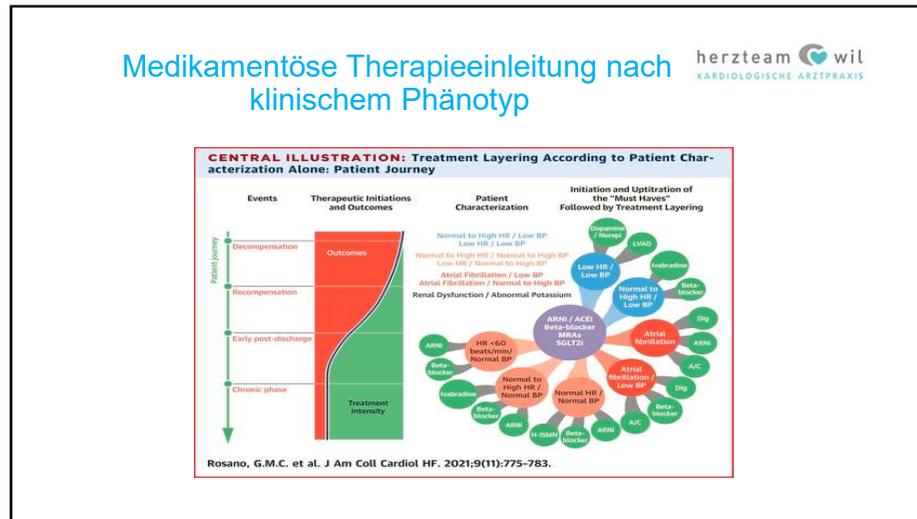
20



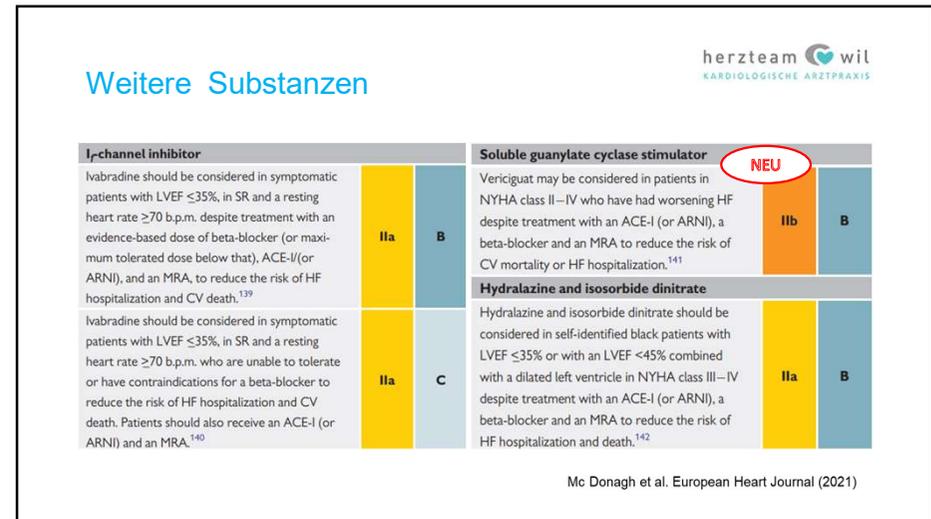
21



22



23



24

## VICTORIA - Vericiguat

**Inclusion Criteria**

**“Chronic HF”** after **“Worsening event”**

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

**“Worsening event”**

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

BNP ≥ 300 & pre-BNP ≥ 1000 ng/ml NRSR  
 NT-proBNP ≥ 5000 & pre-NT-proBNP ≥ 10000 ng/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**

Armstrong et al. NEJM Mai 2020, 382

25

## Einteilung

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

- Epidemiologie-Typen der Herzinsuffizienz
- Aktuelle Pharmakotherapie/ESC Leitlinien 2021
- Neue Konzepte in der Therapie-wann und wie behandeln

- Was kommt nach der medikamentösen Therapie?

26

## Individualisierte Therapie der Herzinsuffizienz Device-Therapie

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

To reduce HF hospitalization/mortality - for selected patients

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

Mc Donagh et al. European Heart Journal (2021)

27

## Catheter Ablation for Atrial Fibrillation with Heart Failure

A Death or Hospitalization for Worsening Heart Failure

**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.<sup>352–354,557</sup>

IIa B

Marrouche et al. NEJM 2018; 378:417-27

28

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

## Nach Entlassung

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
It is recommended that patients hospitalized for HF be carefully evaluated to exclude persistent signs of congestion before discharge and to optimize oral treatment. <sup>427,472</sup>	I	C
It is recommended that evidence-based oral medical treatment be administered before discharge. <sup>103,513</sup>	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 up-titrate evidence-based therapy. <sup>517,518</sup>	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. <sup>512</sup>	IIa	B

© ESC, 2021  
Mc Donagh et al. European Heart Journal (2021)

29

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

## 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 **HF<sub>r</sub>EF** durch den raschen Beginn prognoseverbessernder Substanzen noch im Spital
- Vollständige Rekompensation und Verlaufskontrolle innerhalb 1-2 Wochen
- **HF<sub>mr</sub>EF** Patienten profitieren wahrscheinlich auch von diesem Therapieprinzip
- Eine deutliche Prognoseverbesserung der chronischen Herzinsuffizienz ist zu erwarten
- Trotz der Emperor-Preserved Studie wurden Empfehlungen für **HF<sub>p</sub>EF** noch nicht ausgesprochen, da Zulassungen für SGLT2-Hemmer bisher ausstehen

30

herzteam wil  
KARDIOLOGISCHE ARZTPRAXIS

## Vielen Dank für Ihre Aufmerksamkeit

31