WHAT'S NEW IN HEART FAILURE MANAGEMENT

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Outline:

1. Definitions and Stages of Heart failure
2. New 2023 ESC heart failure guideline recommendations
3. New 2022 ACC/AHA heart failure guideline recommendations
4. Role of Heart rate control in heart failure management

Background Literature & Guidelines:

- 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure
- 2023 Focused update of the 2021 ESC Guidelines for diagnosis and treatment of acute and chronic heart failure
- 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

Definition of Heart failure

- Is not a single pathological diagnosis, but a clinical syndrome
- Consisting of cardinal symptoms (e.g. breathlessness, ankle swelling, and fatigue)
- Accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles, and peripheral oedema)
- Due to a structural and/or functional abnormality of the heart
- Resulting in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)

Definition of heart failure with reduced ejection fraction, mildly reduced ejection fraction and preserved ejection fraction

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]

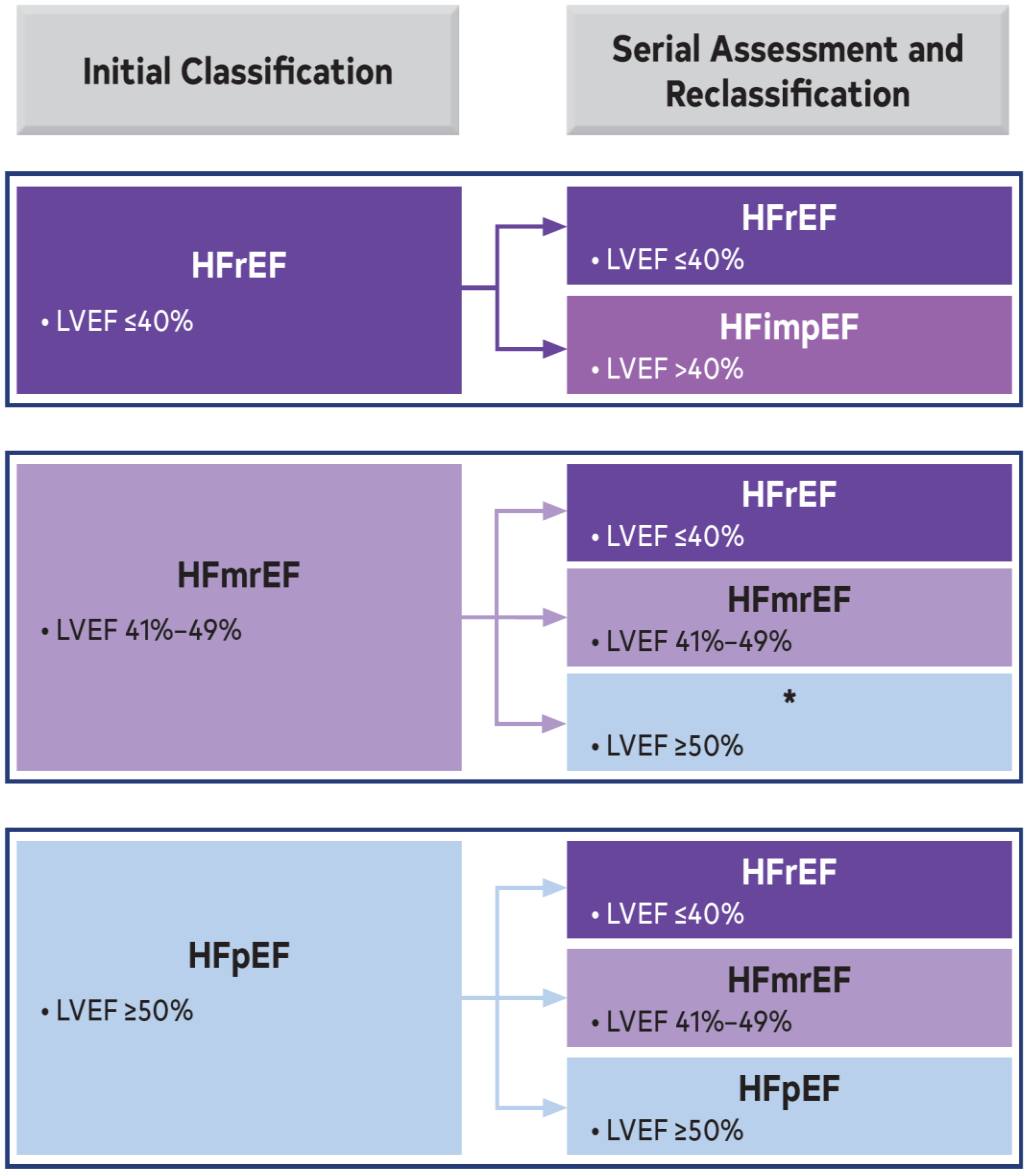
HF = heart failure; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LV = left ventricle; LVEF = left ventricular ejection fraction.

[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in optimally treated patients.

[b]For the diagnosis of HFmrEF, the presence of other evidence of structural heart disease (e.g. increased left atrial size, LV hypertrophy or echocardiographic measures of impaired LV filling) makes the diagnosis more likely.

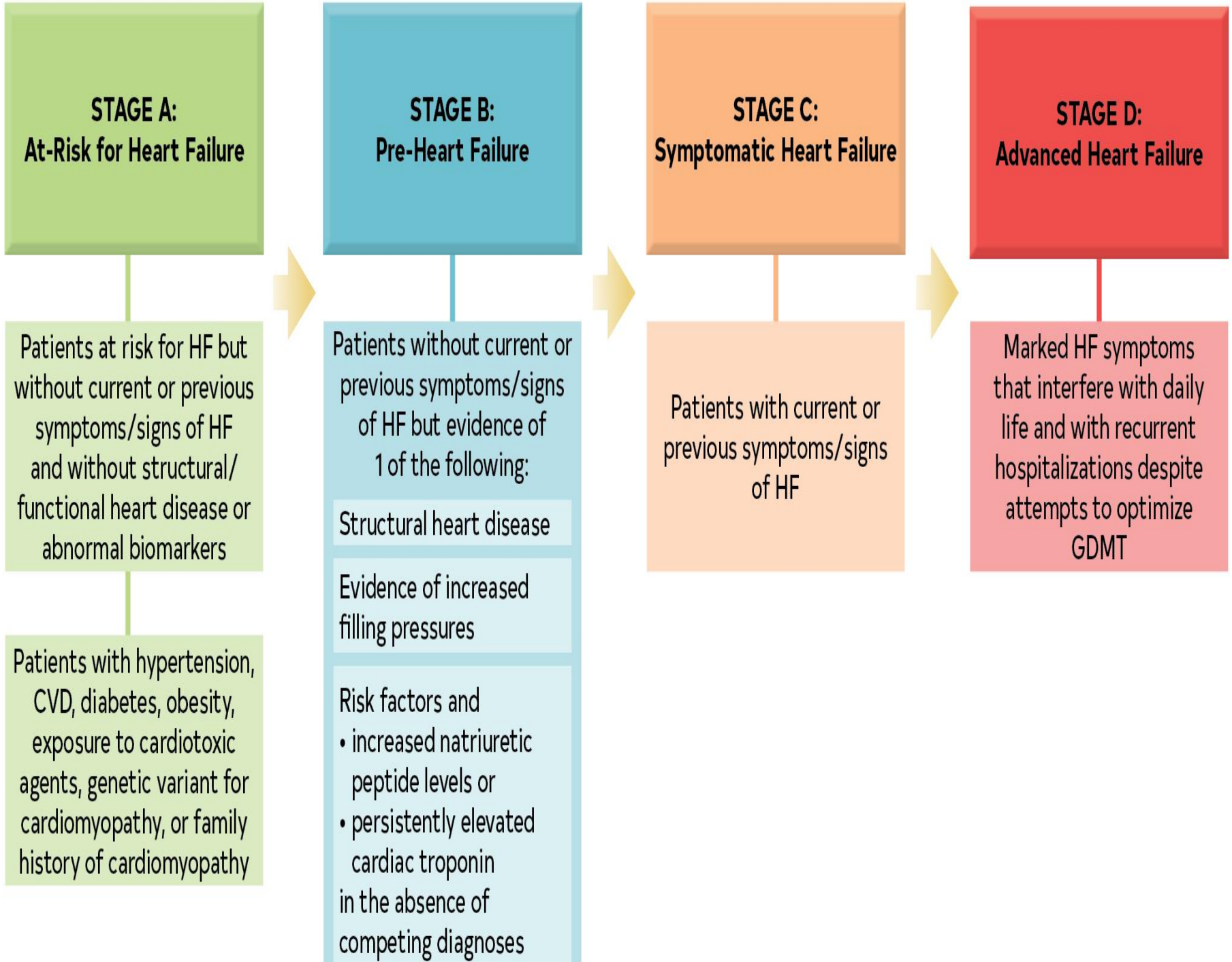
[c]For the diagnosis of HFpEF, the greater the number of abnormalities present, the higher the likelihood of HFpEF.

Classification and Trajectories of HF Based on LVEF



- **Patients with a history of overtly reduced LVEF (≤40%), who later present with LVEF ≥50%**
- **Should be considered to have "recovered HFrEF" or "HF with improved LVEF" (rather than HFpEF)**
- **Continued treatment for HFrEF is recommended**

ACC/AHA Stages of HF



The ACC/AHA stages of HF are shown.

ACC indicates American College of Cardiology; AHA, American Heart Association; CVD, cardiovascular disease; GDMT, guideline-directed medical therapy; and HF, heart failure.

STAGE B:
Pre-Heart Failure

Patients without current or previous symptoms/signs of HF but evidence of 1 of the following:

Structural heart disease

Evidence of increased filling pressures

Risk factors and
- increased natriuretic peptide levels or
- persistently elevated cardiac troponin

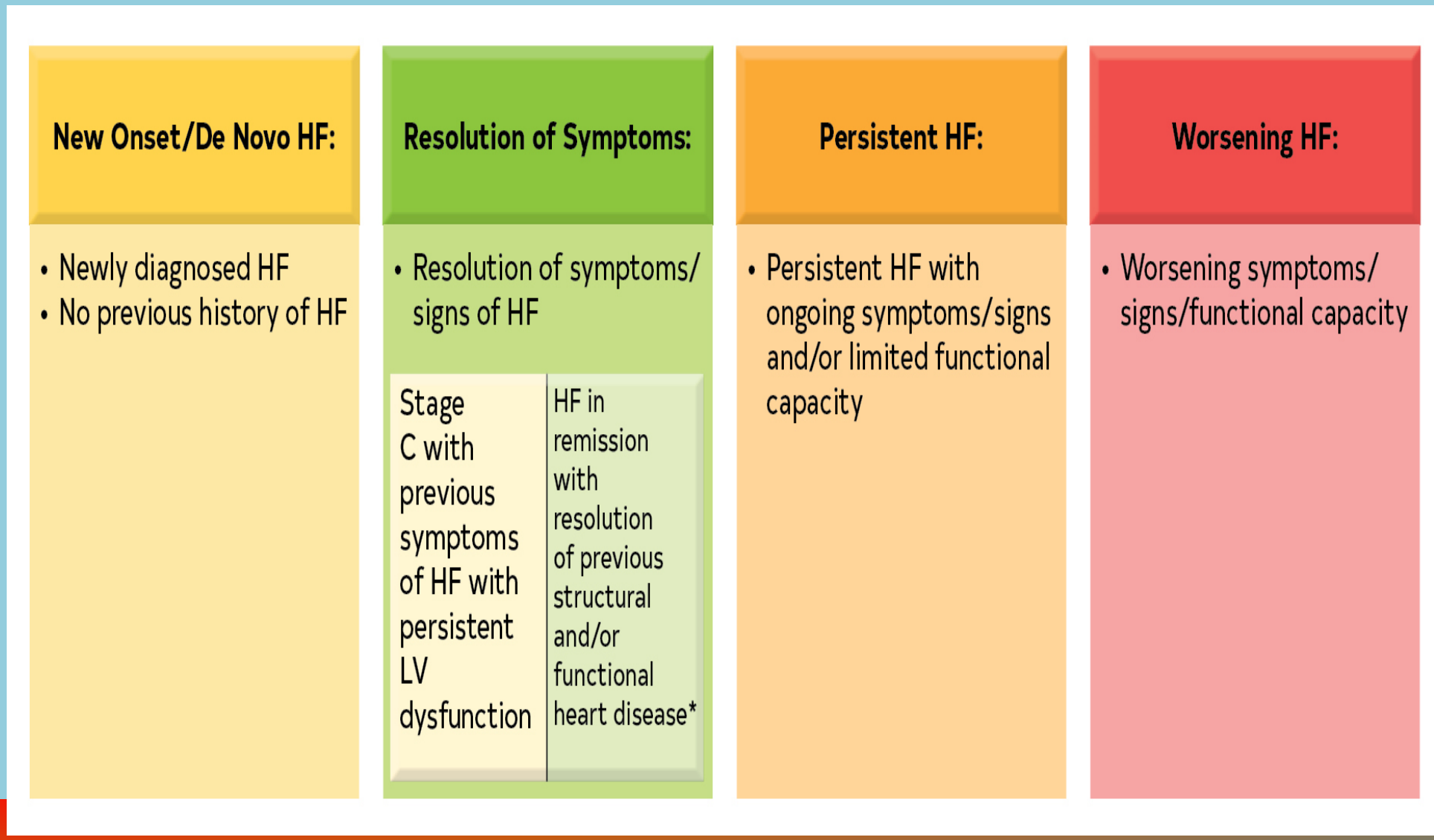
in the absence of competing diagnoses

- Reduced left or right ventricular systolic function
- Reduced ejection fraction, reduced strain
- Ventricular hypertrophy
- Chamber enlargement
- Wall motion abnormalities
- Valvular heart disease
- increase in left atrial size and volume (left atrial volume index) and/or an increase in LV mass (LV mass index)

- By invasive hemodynamic measurements at rest or exercise
  - Pulmonary capillary wedge pressure or LV end diastolic pressures, pulmonary artery [PA] pressures, stroke volumes, and cardiac output

- By noninvasive imaging suggesting elevated filling pressures (eg, Doppler echocardiography E/e' >9)

Trajectory of Class C HF

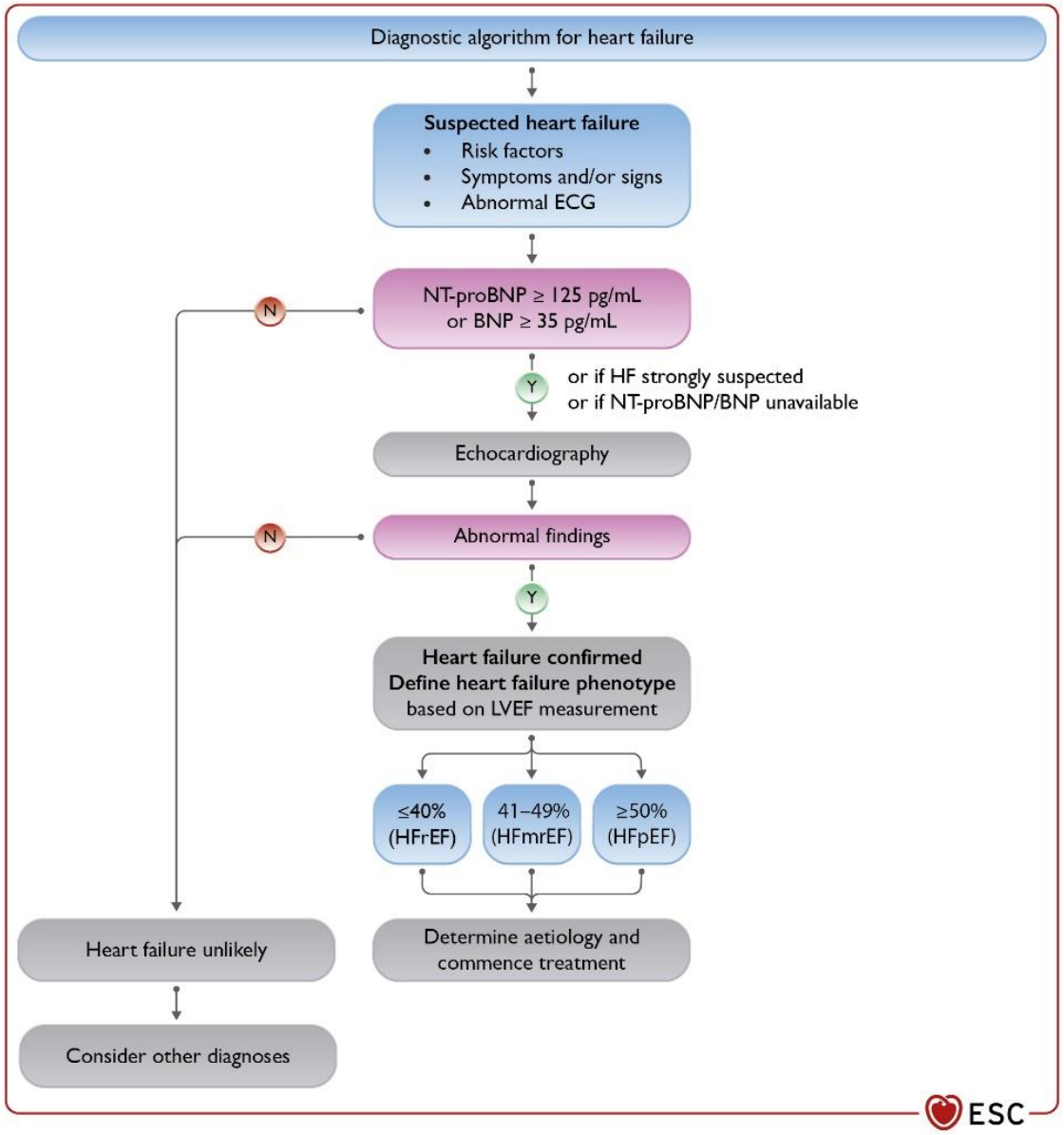


The trajectory of stage C HF is displayed. Patients whose symptoms and signs of HF are resolved are still stage C and should be treated accordingly. If all HF symptoms, signs, and structural abnormalities resolve, the patient is considered to have HF in remission.

***Full resolution of structural and functional cardiac abnormalities is uncommon.**

HF indicates heart failure; and LV, left ventricular.

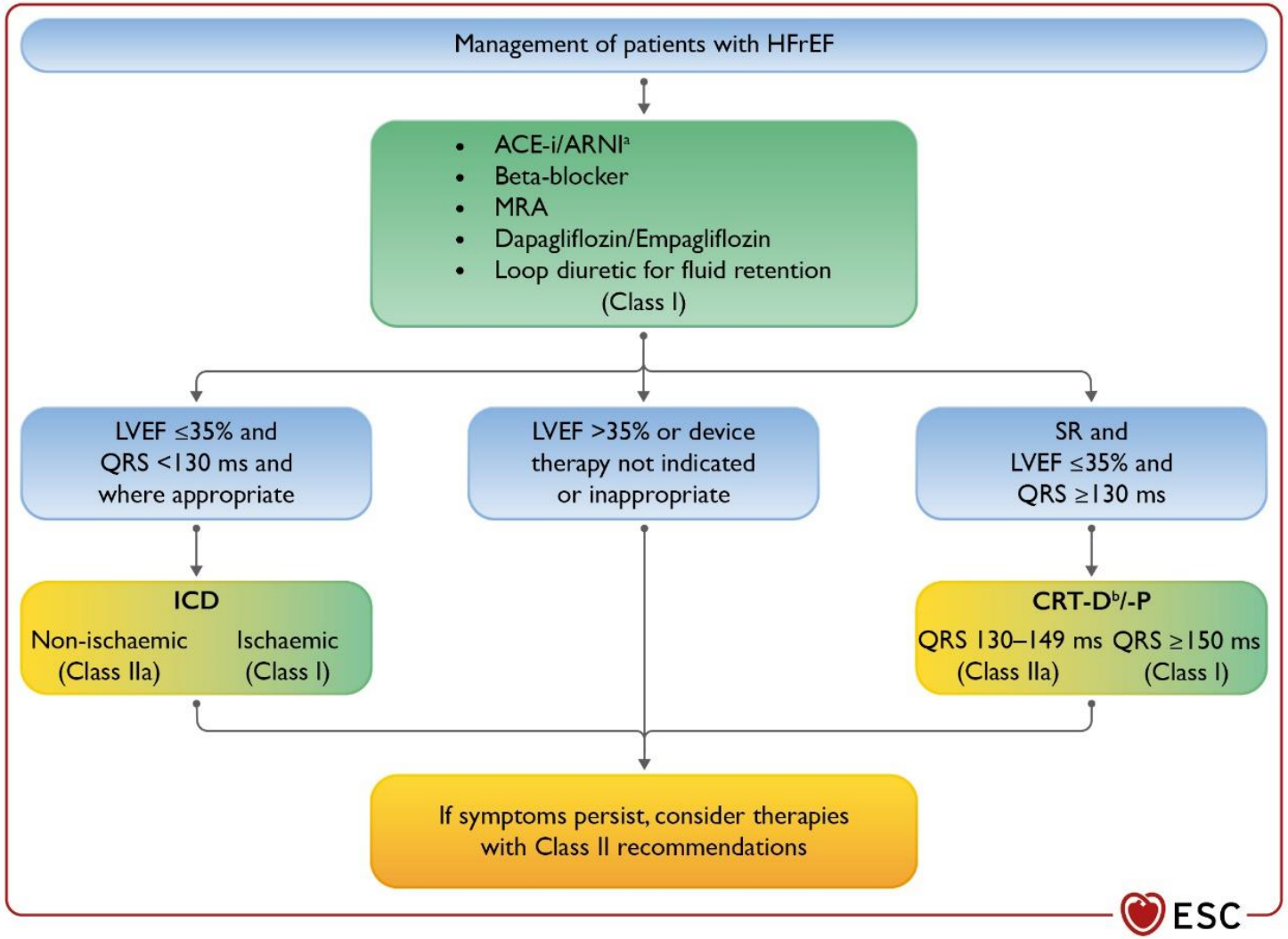
The diagnostic algorithm for heart failure



ECG = electrocardiogram; HFmrEF = heart failure with mildly reduced ejection fraction;
HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B type natriuretic peptide.
The abnormal echocardiographic findings are described in more detail in the respective sections onHFrEF (section 5), HFmrEF (section 7), and HFpEF (section 8).

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)10

Therapeutic algorithm of Class I Therapy Indications for a patient with heart failure with reduced ejection fraction

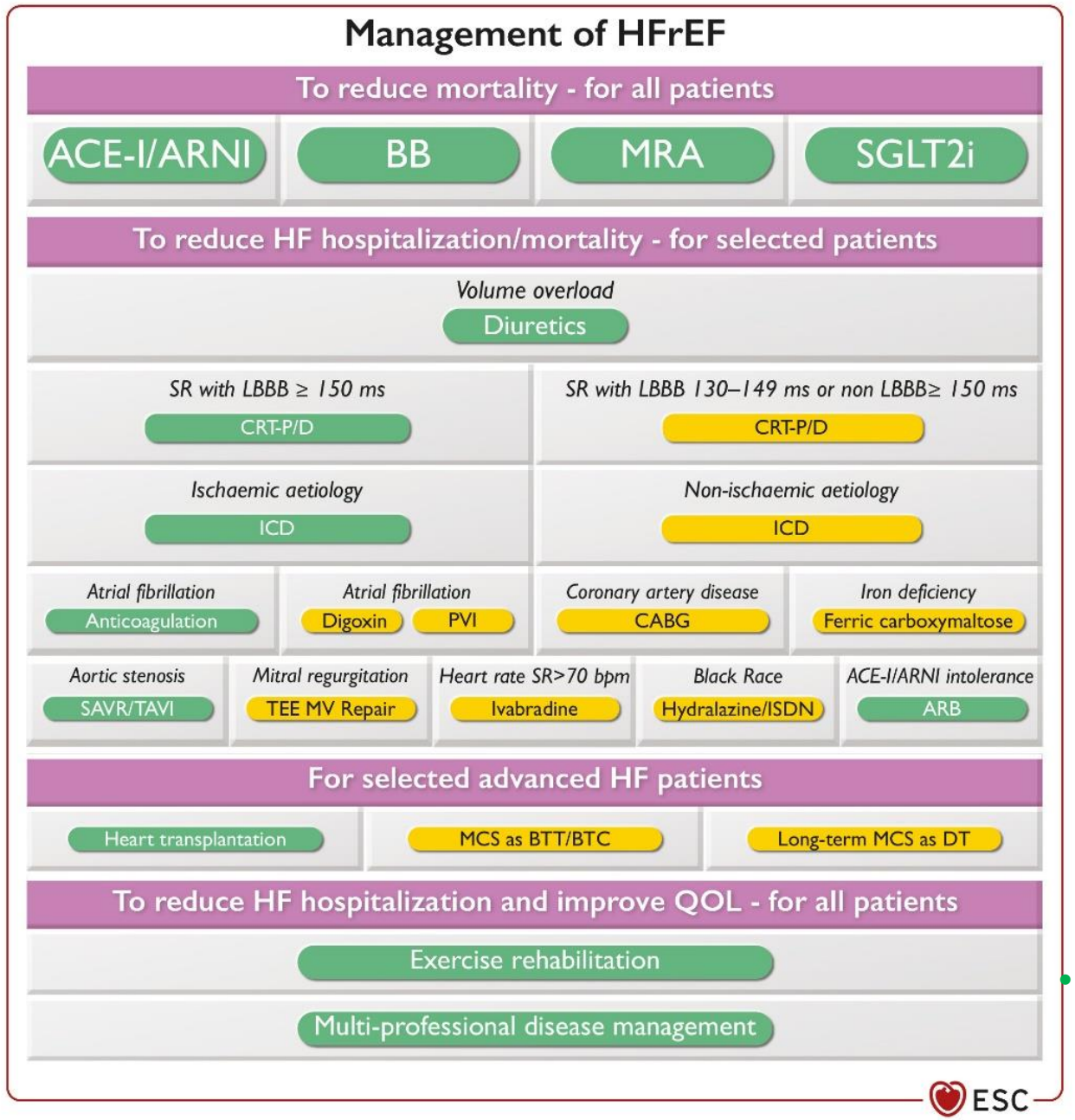


ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; CRT-D = cardiac resynchronization therapy with defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; ICD = implantable cardioverter-defibrillator; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; QRS = Q, R, and S waves of an ECG; SR = sinus rhythm.

[a]As a replacement for ACE-I.

[b]Where appropriate. Class I=green. Class IIa=Yellow.

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368) 11



Strategic phenotypic overview of the management of heart failure with reduced ejection fraction

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; BB = beta-blocker; b.p.m. = beats per minute; BTC = bridge to candidacy; BTT = bridge to transplantation; CABG = coronary artery bypass graft; CRT-D = cardiac resynchronization therapy with defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; DT = destination therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter-defibrillator; ISDN = isosorbide dinitrate; LBBB = left bundle branch block; MCS = mechanical circulatory support; MRA = mineralocorticoid receptor antagonist; MV = mitral valve; PVI = pulmonary vein isolation; QOL = quality of life; SAVR = surgical aortic valve replacement; SGLT2i = sodium-glucose co-transporter 2 inhibitor; SR = sinus rhythm; TAVI = transcatheter aortic valve replacement; TEE = transcatheter edge to edge. Colour code for classes of recommendation: Green for Class of recommendation I; Yellow for Class of recommendation IIa (see Table 1 for further details on classes of recommendation).
The Figure showsmanagement options with Class I and IIa recommendations. See the specific Tables for those with Class IIb recommendations.

- **4 agents placed side-by-side because positive effects on patient outcomes occur early after treatment initiation and these benefits are additive**

www.escardio.org/guidelines

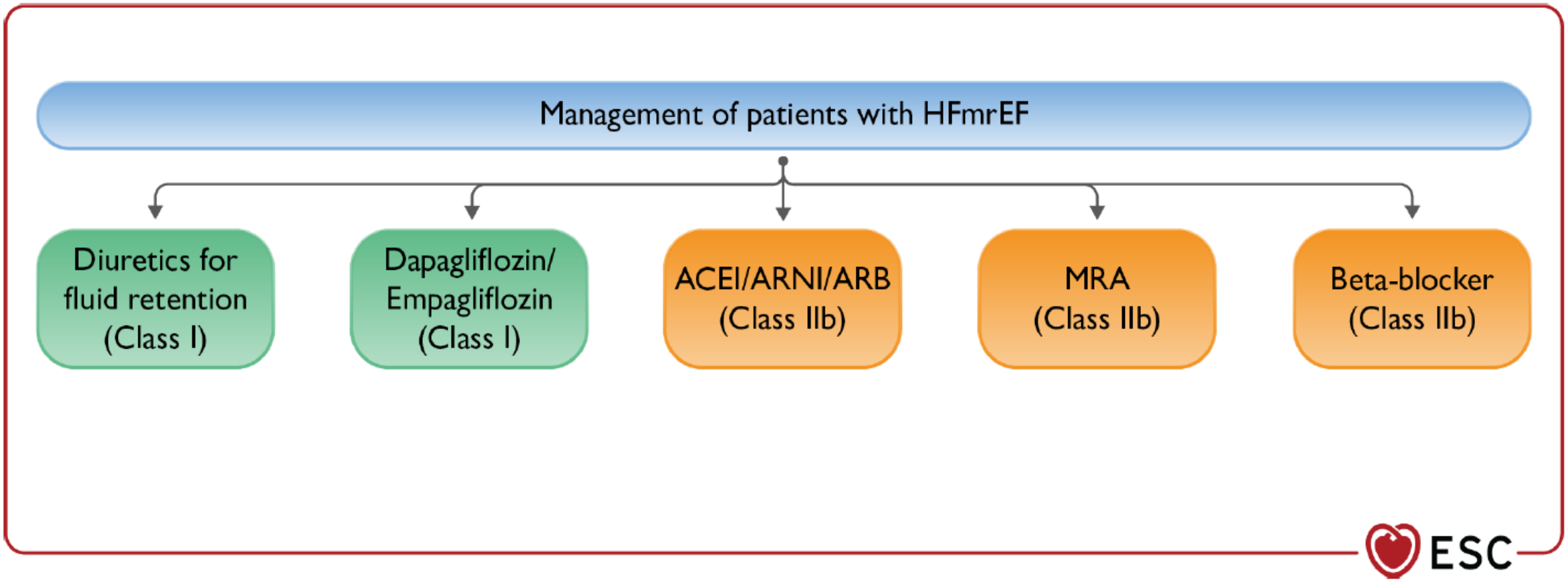
2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368)[12]

Other pharmacological treatments indicated in selected patients with NYHA class II-IV heart failure with reduced ejection fraction (LVEF ≤40%) (2)

Recommendations	Class	Level
I_f-channel inhibitor		
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.	IIa	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.	IIa	C

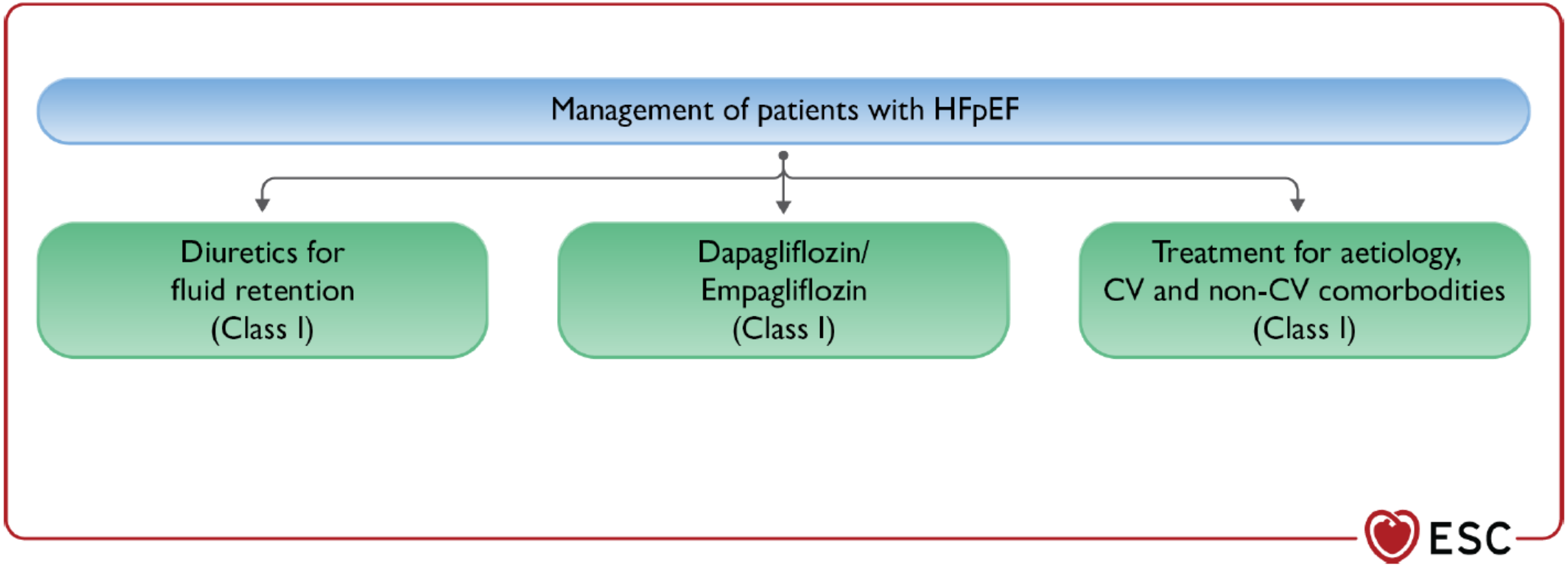
ACE-I = angiotensin-converting enzyme inhibitor; ARNI = angiotensin receptor-neprilysin inhibitor; b.p.m. = beats per minute; CV = cardiovascular; HF = heart failure; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NYHA= New York Heart Association; SR = sinus rhythm.

Figure 1. Management of patients with heart failure with mildly reduced ejection fraction



ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor–neprilysin inhibitor; HFmrEF, heart failure with mildly reduced ejection fraction; MRA, mineralocorticoid receptor antagonist.

Figure 2. Management of patients with heart failure with preserved ejection fraction



CV, cardiovascular; HFpEF, heart failure with preserved ejection fraction.

Recommendation for the treatment of patients with symptomatic heart failure with mildly reduced ejection fraction

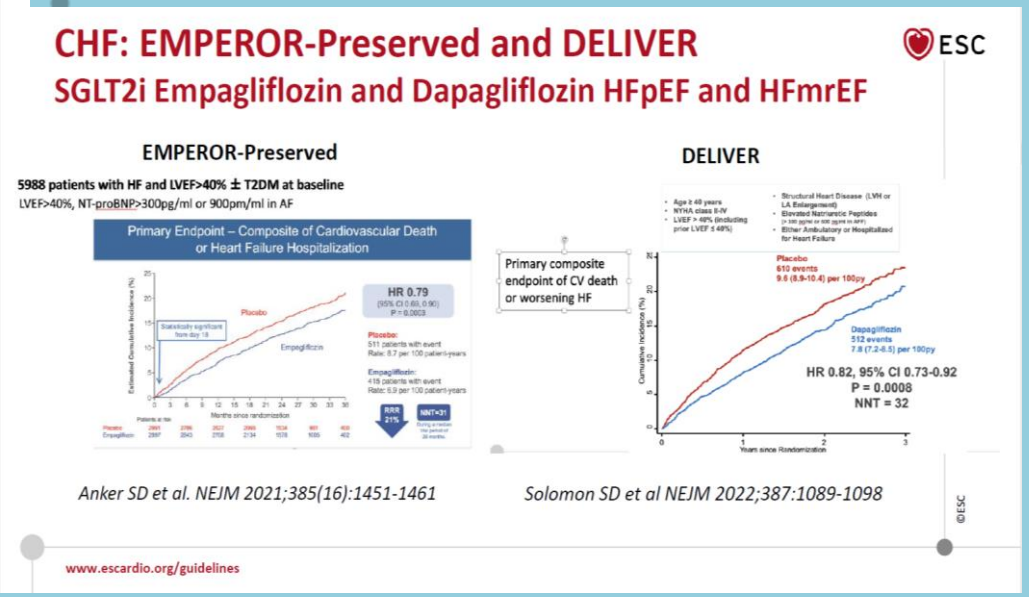
I A

- An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFmrEF to reduce the risk of HF hospitalization or CV death.

Recommendation for the treatment of patients with symptomatic heart failure with preserved ejection fraction

- An SGLT2 inhibitor (dapagliflozin or empagliflozin) is recommended in patients with HFpEF to reduce the risk of HF hospitalization or CV death

I A



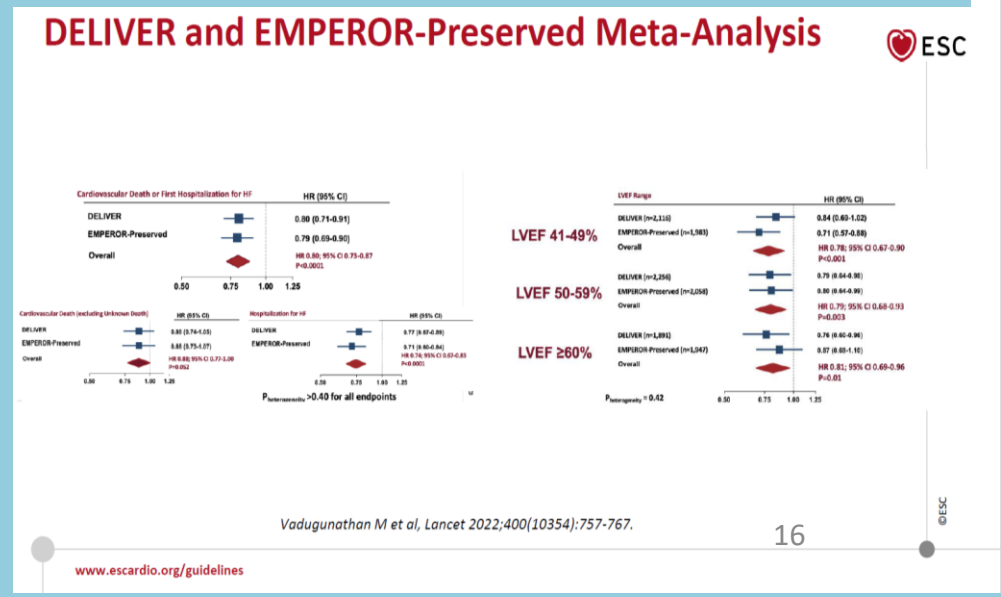
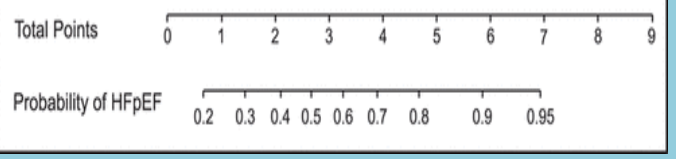


Figure 5. Recommendations (Class 1 and 2a) for Patients at Risk of HF (Stage A) and Those With Pre-HF (Stage B)

	Clinical Variable	Values	Points
H_2	Heavy	Body mass index > 30 kg/m^2	2
	Hypertensive	2 or more antihypertensive medicines	1
F	Atrial Fibrillation	Paroxysmal or Persistent	3
P	Pulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E	Elder	Age > 60 years	1
F	Filling Pressure	Doppler Echocardiographic E/e' > 9	1
H_2FPEF score			Sum (0-9)



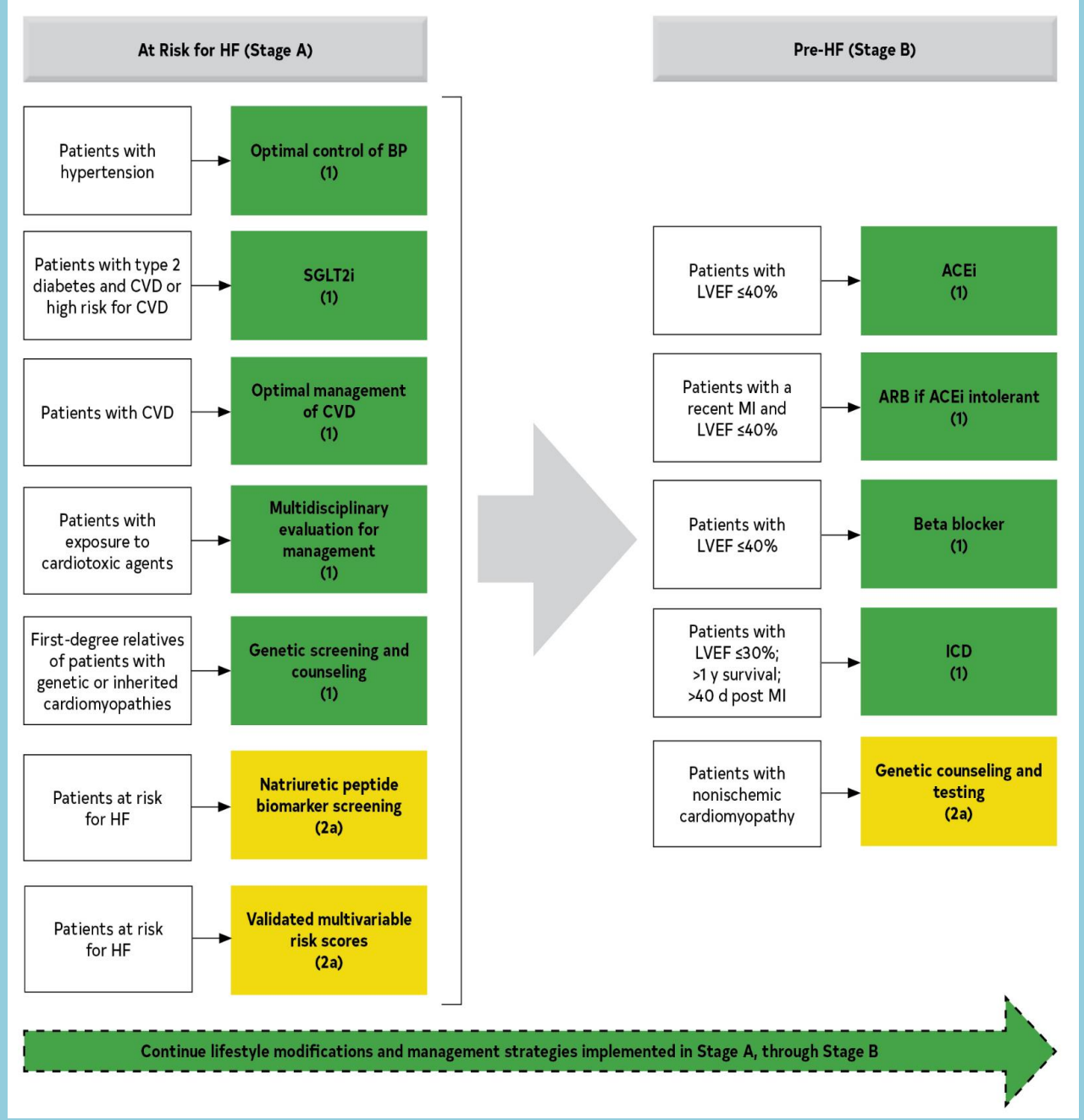


Figure 6. Treatment of HFrEF Stages C and D

Colors correspond to COR in Table 2.

Treatment recommendations for patients with HFrEF are displayed. Step 1 medications may be started simultaneously at initial (low) doses recommended for HFrEF. Alternatively, these medications may be started sequentially, with sequence guided by clinical or other factors, without need to achieve target dosing before initiating next medication. Medication doses should be increased to target as tolerated.

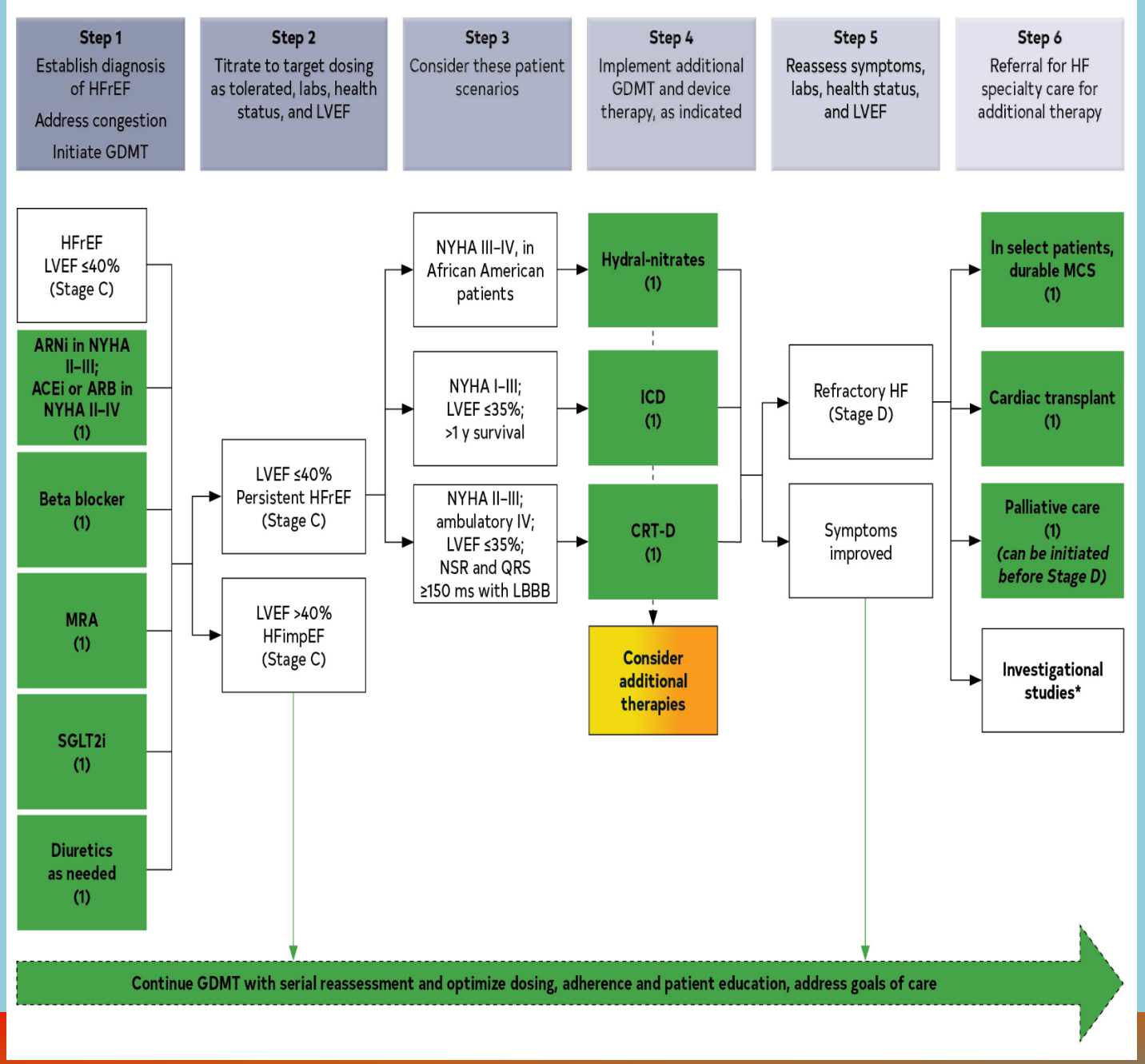
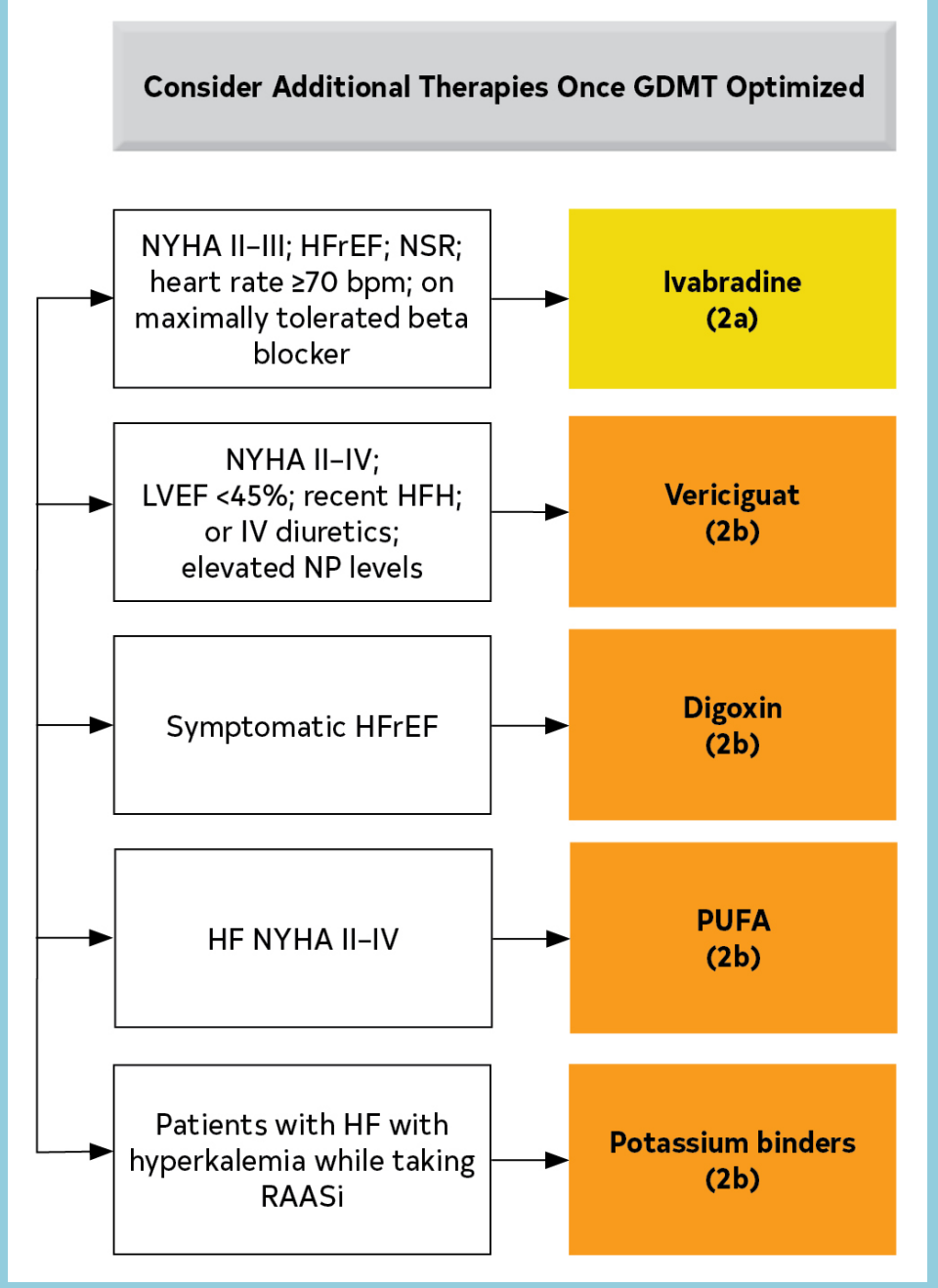


Figure 7. Additional Medical Therapies for Patients With HFrEF



Colors correspond to COR in Table 2

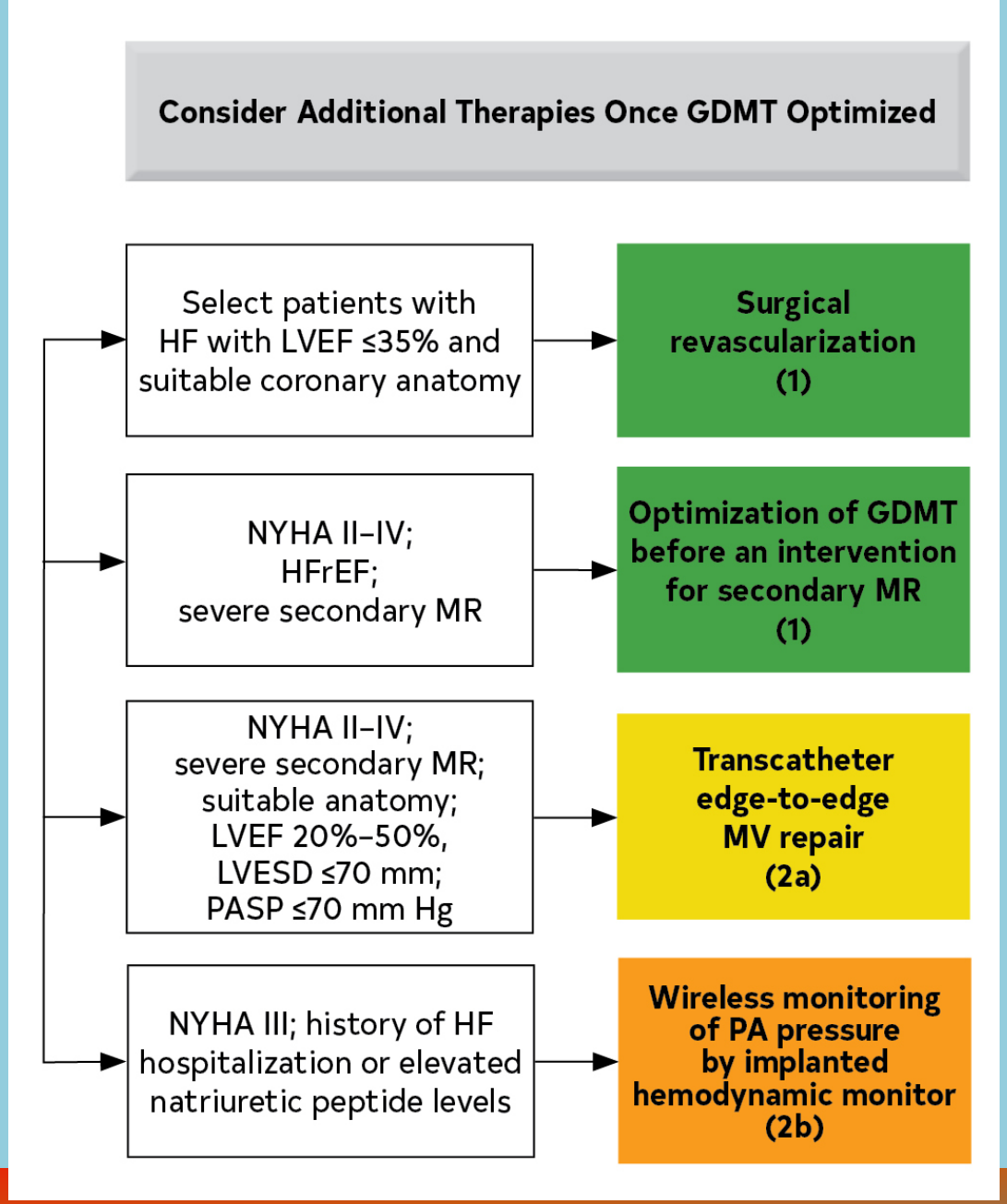
Recommendations for additional medical therapies that may be considered for patients with HF are shown.

GDMT indicates guideline-directed medical therapy; HF, heart failure; HFH, heart failure hospitalization; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; LVEF, left ventricular ejection fraction; LVESD, left ventricular end systolic dimension; MV, mitral valve; MR, mitral regurgitation; NP, natriuretic peptide; NSR, normal sinus rhythm; and NYHA, New York Heart Association; RAASi, renin-angiotensin-aldosterone system inhibitors.

Management of Stage C HF: Ivabradine

Recommendation for the Management of Stage C HF: Ivabradine Referenced studies that support the recommendation are summarized in the Online Data Supplements.		
COR	**LOE**	**Recommendation**
2a	**B-R**	**1. For patients with symptomatic (NYHA class II to III) stable chronic HFrEF (LVEF ≤35%) who are receiving GDMT, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of ≥70 bpm at rest, ivabradine can be beneficial to reduce HF hospitalizations and cardiovascular death.**

Figure 9. Additional Device Therapies

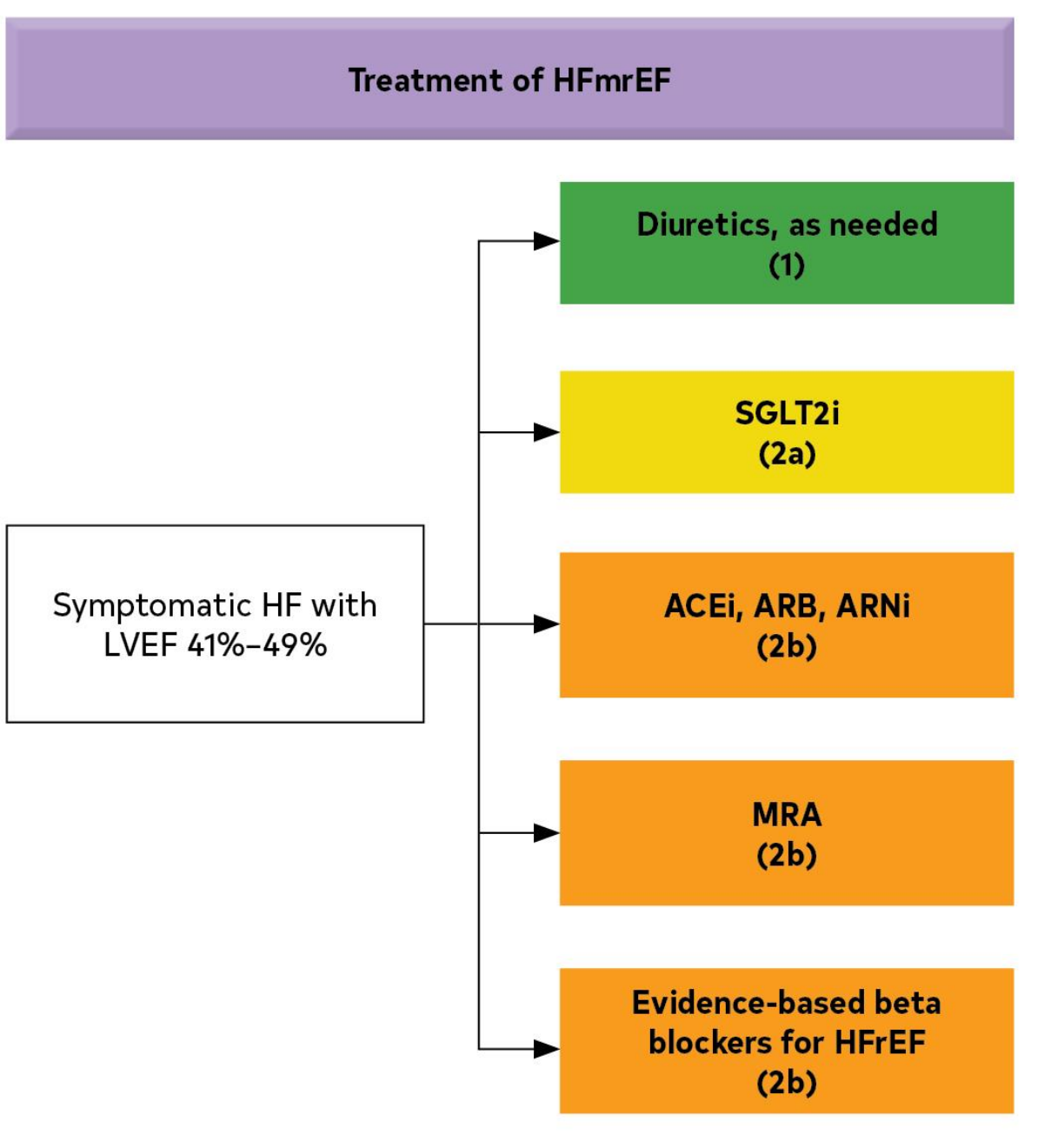


Colors correspond to COR in Table 2.

Recommendations for additional nonpharmaceutical interventions that may be considered for patients with HF are shown.

GDMT indicates guideline-directed medical therapy; HF, heart failure; HFH, heart failure hospitalization; HFrEF, heart failure with reduced ejection fraction; IV, intravenous; LVEF, left ventricular ejection fraction; LVESD, left ventricular end systolic dimension; MV, mitral valve; MR, mitral regurgitation; NP, natriuretic peptide; NSR, normal sinus rhythm; NYHA, New York Heart Association; and PASP, pulmonary artery systolic pressure.

Figure 11. Recommendations for Patients With Mildly Reduced LVEF (41%–49%)

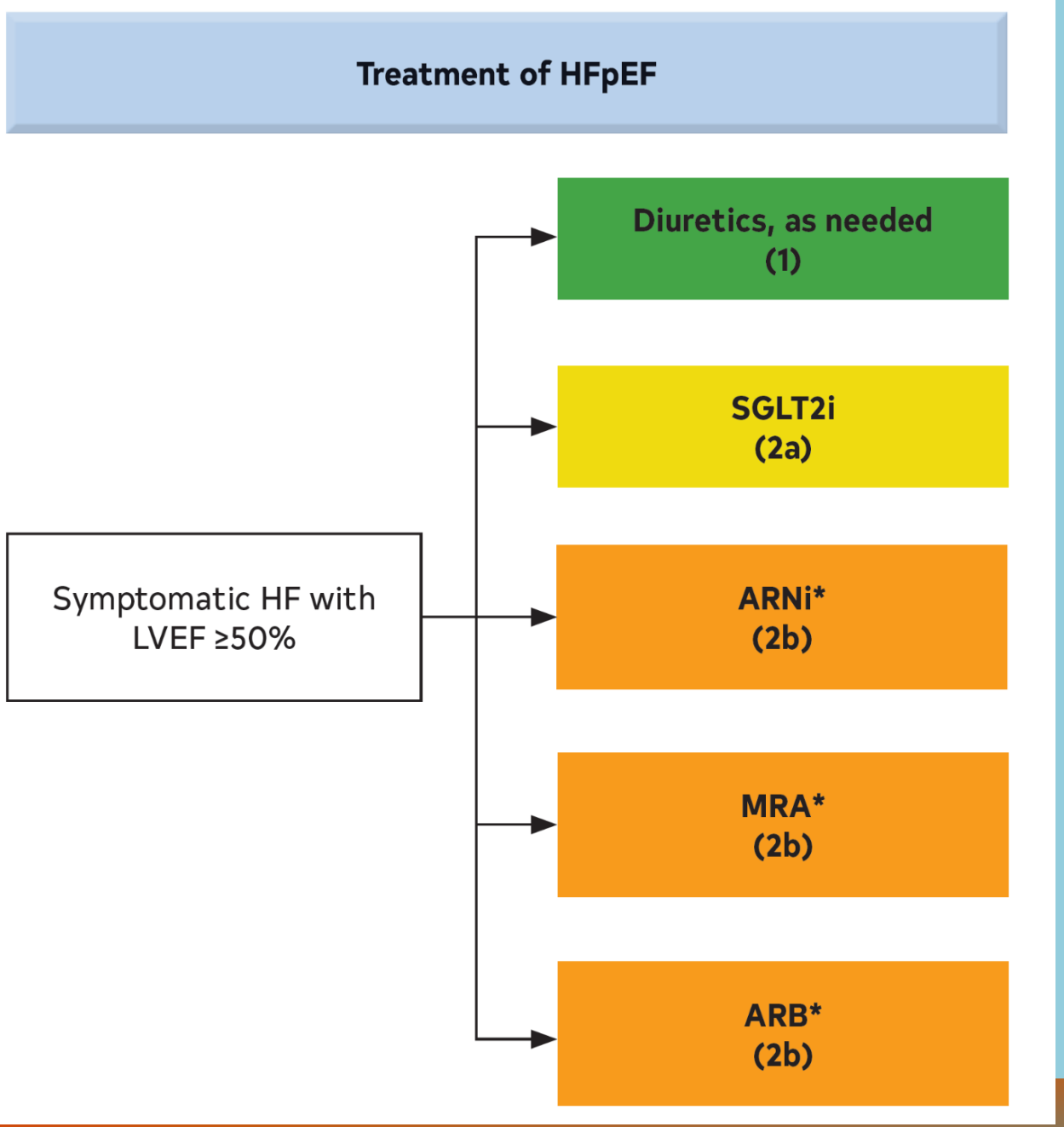


Colors correspond to COR in Table 2.

Medication recommendations for HFmrEF are displayed.

ACEi indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HRmrEF, heart failure with mildly reduced ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium- glucose cotransporter 2 inhibitor.

Figure 12. Recommendations for Patients With Preserved LVEF (≥50%)



Colors correspond to COR in Table 2.

Medication recommendations for HFpEF are displayed.

*Greater benefit in patients with LVEF closer to 50%.

ARB indicates angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitor; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and SGLT2i, sodium-glucose cotransporter 2 inhibitor.

Recommendations for pre-discharge and early post-discharge follow-up of patients hospitalized for acute heart failure

- Evidence-based oral medical treatment be administered before discharge

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.

- An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death.

I | B

Pre-discharge management: STRONG-HF

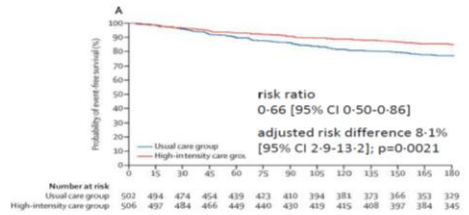
Patients
- 1078 patients hospitalized for acute HF
- Not already on full doses of GRMT
- Haemodynamically stable
- NT-proBNP >2500 pg/mL at screening, >10% decrease screening to randomization

Randomization
- High-intensity care (HIC) vs usual care (UC)

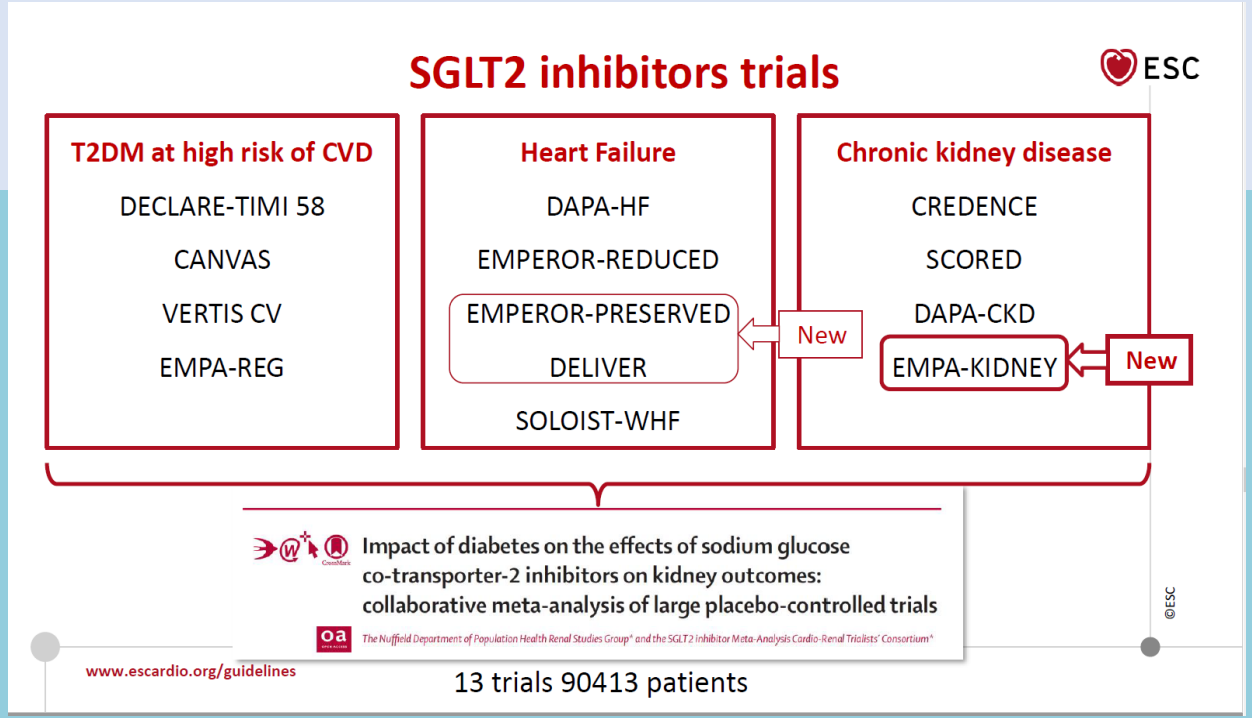
High intensity care
- Early (2 days before discharge) and rapid intensification of oral HF treatment with ACE-I/ARB/ARNI, beta-blockers and MRA

Results

Full doses of oral therapies. HIC vs UC
- ACEi/ARB/ARNI 55% vs. 2%,
- beta-blockers 49% vs. 4%
- MRA 84% vs. 46%



Mebazaa A et al Lancet. 2022 Dec 3;400(10367):1938-1952.



Recommendations for the prevention of heart failure in patients with type 2 diabetes and chronic kidney disease

ESC

Recommendations	Class	Level
In patients with type 2 diabetes and CKD, SGLT2 inhibitors (dapagliflozin or empagliflozin) are recommended to reduce the risk of HF hospitalization or CV death.	I	A

In patients with type 2 diabetes and CKD, finerenone is recommended to reduce the risk of HF hospitalization.

I A

Finerenone trials

Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes

George L. Bakris, M.D., Rajiv Agarwal, M.D., Stefan D. Anker, M.D., Ph.D., Bertram Pitt, M.D., Luis M. Ruilope, M.D., Peter Rossing, M.D., Peter Kolkhof, Ph.D., Christina Nowack, M.D., Patrick Schloemer, Ph.D., Amer Joseph, M.B., B.S., and Gerasimos Filippatos, M.D., for the FIDELIO-DKD Investigators*

No. 5734 patients
Primary endpoint: composite of kidney failure, sustained ↓ eGFR ≥40% or death from renal causes.

Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes

B. Pitt, G. Filippatos, R. Agarwal, S.D. Anker, G.L. Bakris, P. Rossing, A. Joseph, P. Kolkhof, C. Nowack, P. Schloemer, and L.M. Ruilope, for the FIGARO-DKD Investigators*

No. 7437 patients
Primary endpoint: composite of CV death, non-fatal MI, non-fatal stroke, or HF hospitalization

ESC European Society of Cardiology European Heart Journal (2022) 43, 474–484 https://doi.org/10.1093/eurheartj/ehab777

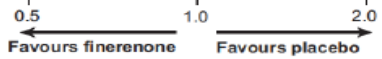
FASTTRACK CLINICAL RESEARCH
Diabetes and metabolic disorders

Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis

No. = 13026 patients; Median FU= 3 ys

ESC

Outcome	Finerenone (n = 6519)		Placebo (n = 6507)		Hazard ratio (95% CI)	*P*-value[a]
	Number of patients with event (%)	Number of patients with event per 100 patient-years	Number of patients with event (%)	Number of patients with event per 100 patient-years		
Composite cardiovascular outcome[b]	825 (12.7)	4.34	939 (14.4)	5.01	0.86 (0.78–0.95)	0.0018
Death from cardiovascular causes	322 (4.9)	1.61	364 (5.6)	1.84	0.88 (0.76–1.02)	0.092
Non-fatal myocardial infarction	173 (2.7)	0.88	189 (2.9)	0.97	0.91 (0.74–1.12)	0.36
Non-fatal stroke	198 (3.0)	1.01	198 (3.0)	1.02	0.99 (0.82–1.21)	0.95
Hospitalization for heart failure	256 (3.9)	1.31	325 (5.0)	1.68	0.78 (0.66–0.92)	0.0030
eGFR ≥57% composite kidney outcome[c]	360 (5.5)	1.96	465 (7.1)	2.55	0.77 (0.67–0.88)	0.0002
Kidney failure	254 (3.9)	1.38	297 (4.6)	1.62	0.84 (0.71–0.99)	0.039
End-stage kidney disease[d]	151 (2.3)	0.76	188 (2.9)	0.96	0.80 (0.64–0.99)	0.040[e]
Sustained decrease in eGFR to <15 mL/min/1.73 m²	195 (3.0)	1.06	237 (3.6)	1.29	0.81 (0.67–0.98)	0.026[e]
Sustained ≥57% decrease in eGFR from baseline	257 (3.9)	1.40	361 (5.5)	4.03	0.70 (0.60–0.83)	< 0.0001
Renal death	2 (<0.1)	0.01	4 (<0.1)	0.02	0.53 (0.10–2.91)	0.46[e]
eGFR ≥40% composite kidney outcome[f]	854 (13.1)	4.81	995 (15.3)	5.64	0.85 (0.77–0.93)	0.0004
Sustained ≥40% decrease in eGFR from baseline	817 (12.5)	4.60	962 (14.8)	5.45	0.84 (0.76–0.92)	0.0002
Death from any cause	552 (8.5)	2.76	614 (9.4)	3.10	0.89 (0.79–>1.00[g])	0.051[e]
Hospitalization for any cause	2836 (43.5)	19.04	2926 (45.0)	19.91	0.96 (0.91–1.01)	0.087[e]



2023 Focused update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (European Heart Journal; 2023 – doi:10.1093/eurheartj/ehad195)

www.escardio.org/guidelines

Intravenous iron supplementation is recommended in symptomatic patients with HFrEF and HFmrEF and iron deficiency, to alleviate HF symptoms and improve quality of life.	I	A
Intravenous iron supplementation with ferric carboxymaltose or ferric derisomaltose should be considered in symptomatic patients with HFrEF and HFmrEF and iron deficiency to reduce the risk of HF hospitalization.	IIa	A

ESC European Society of Cardiology
European Journal of Heart Failure (2023)
doi:10.1002/ejhf.2810
RESEARCH ARTICLE

Intravenous iron in patients with heart failure and iron deficiency: an updated meta-analysis

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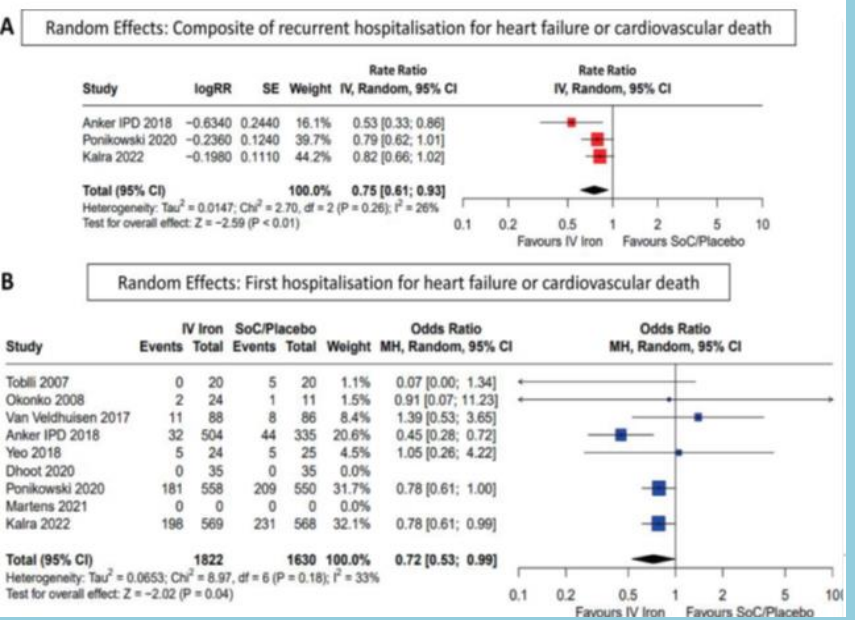

Effect of intravenous iron replacement on recurrent heart failure hospitalizations and cardiovascular mortality in patients with heart failure and iron deficiency: A Bayesian meta-analysis

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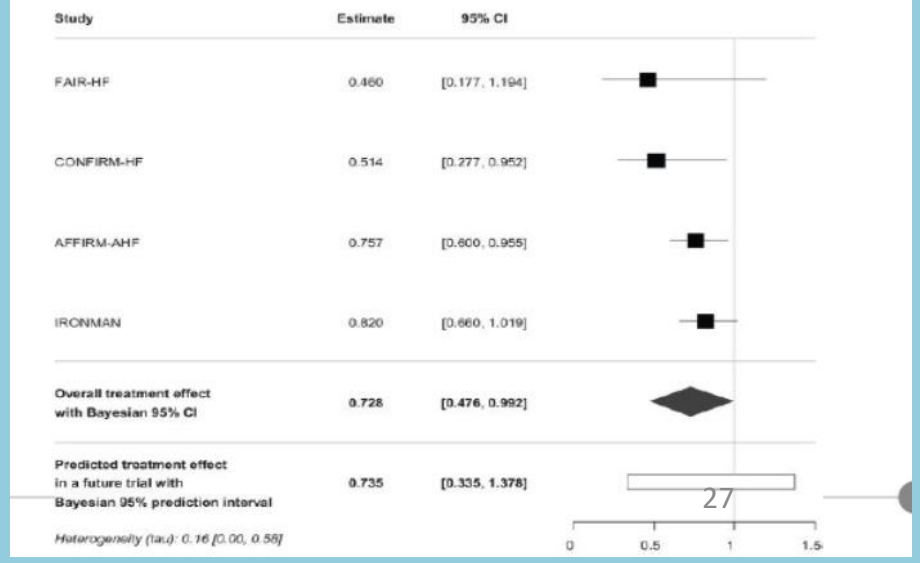
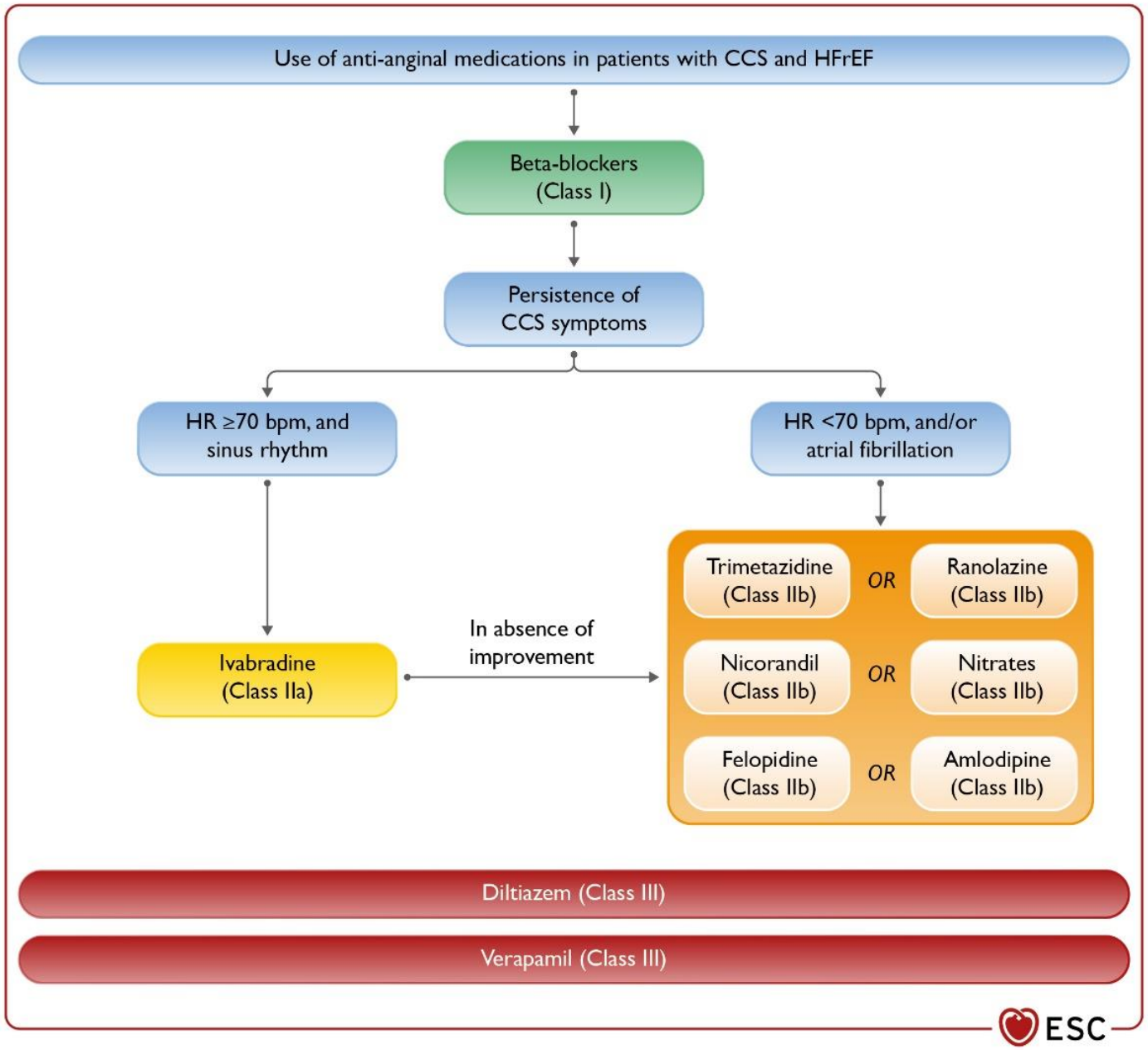
Total HF hospitalization or CV death



Algorithm for the medical treatment of chronic coronary syndrome in patients with heart failure with reduced ejection fraction



CCS = chronic coronary syndrome; HFrEF = heart failure with reduced ejection fraction; HR = heart rate.
Colour code for classes of recommendation: Green for Class of recommendation I; Yellow for Class of recommendation IIa; Orange for Class of recommendation IIb; Red for Class of recommendation III (see Table 1 for further details on classes of recommendation).

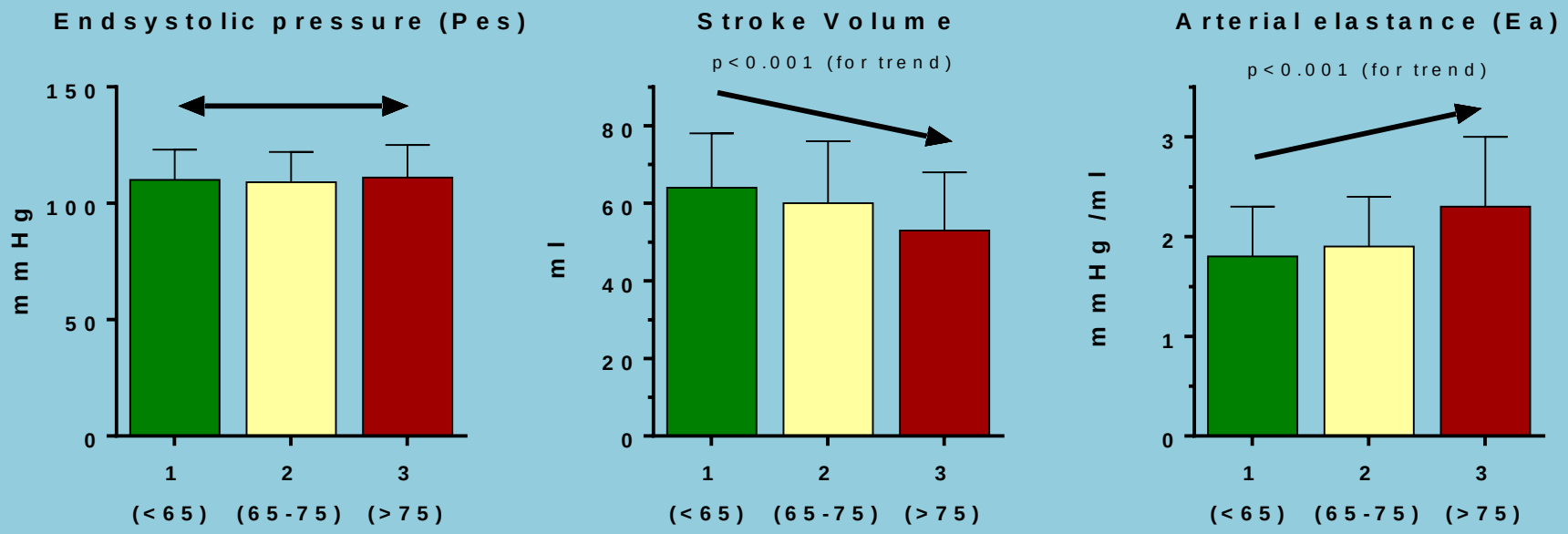
www.escardio.org/guidelines

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure (European Heart Journal 2021 – doi:10.1093/eurheartj/ehab368) 28

Increased heart rate is associated with reduced stroke volume and increased afterload

Echocardiography substudy (SHI_fT)

n=275 pat. with CHF from SHI_fT
(n=132 placebo; n=143 ivabradine)



Tertiles for Heart Rate (bpm)

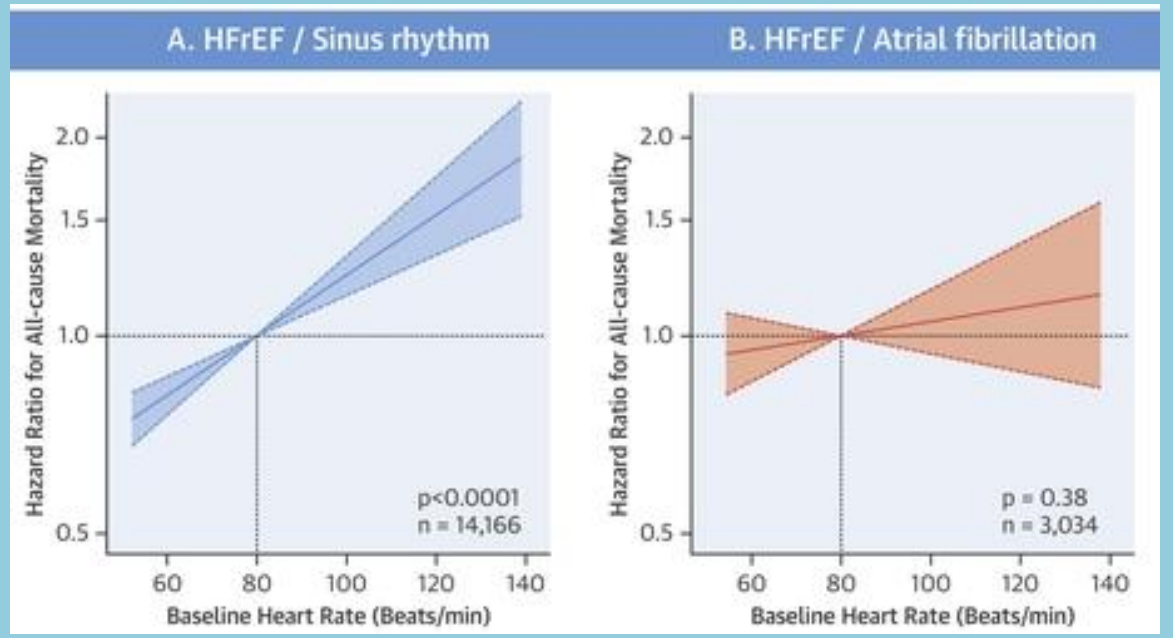
(means ±SD)

Reil et al. *J Am Coll Cardiol*. 2013;62:1977-85

Association of heart rate with outcomes in HFrEF

Simple marker to help improve patients' lives

- These results[1] conclusively demonstrate the predictive value of pulse rate measured at time of diagnosis of HFrEF and during patient follow up
- A **lower pulse rate** at the time diagnosis and across follow-up encounters was strongly associated with **lower risk of mortality and hospitalization outcomes**, **independent of BB treatment and dose**
- Patients who had a **pulse rate ≥70 bpm in the past 6 months had 36% ↑mortality, 25% ↑all-cause hospitalizations, and 51% ↑HF hospitalization**, compared to patients with pulse rates <70 bpm
- Meta-analysis of 11 RCTs of BB in HF patients in SR showed significant positive linear association between HR at time of enrollment and all-cause mortality[2]

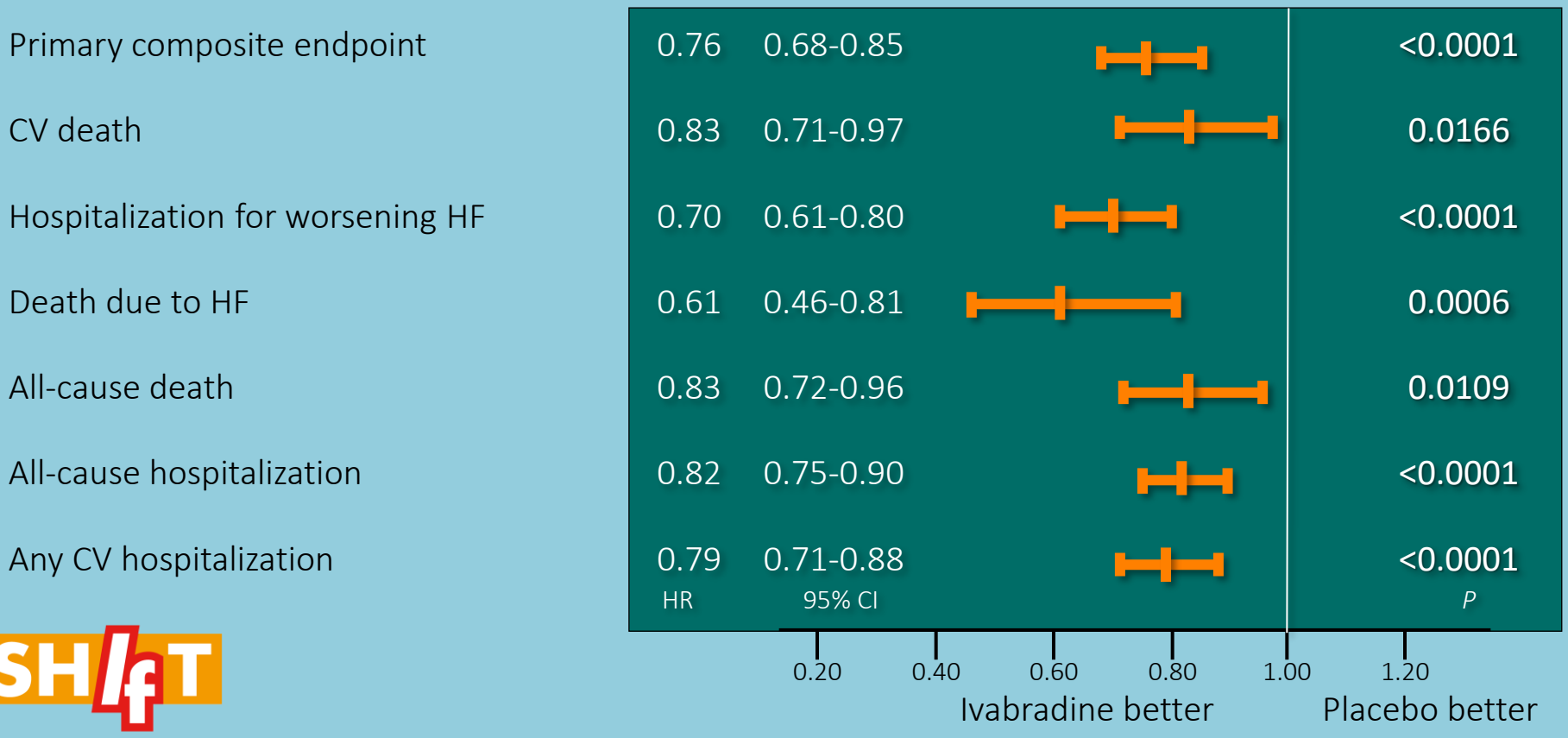


Veterans Affairs (VA) national cohort: 51,194 incident HFrEF cases (67 ± 12 years, 98% male) between 2006 and 2012. Average of 6.3 ± 3.6 pulse measurements per patient updated at 6 month intervals over a median follow-up of 3.2 years. Objective: examine the associations of both baseline (time of HF diagnosis) and serially measured pulse rates, with mortality and days hospitalized per year for HF and for any cause.

1. Kurgansky KE et al. BMC Cardiovasc Dis 2020; 20: 92. 2. Kotecha D et al. J Am Coll Cardiol 2017;69:2885-96.

Ivabradine improves outcomes in HFrEF

Effects in subgroup of patients with baseline HR ≥75 bpm



SHIFT: 6505 patients with HF and LVEF≤35%, NYHA II-IV, SR ≥70 bpm, and at least one HF hospitalization in the past 12 months. Patients were randomly assigned to ivabradine titrated to a maximum of 7.5 mg bid or matching placebo.

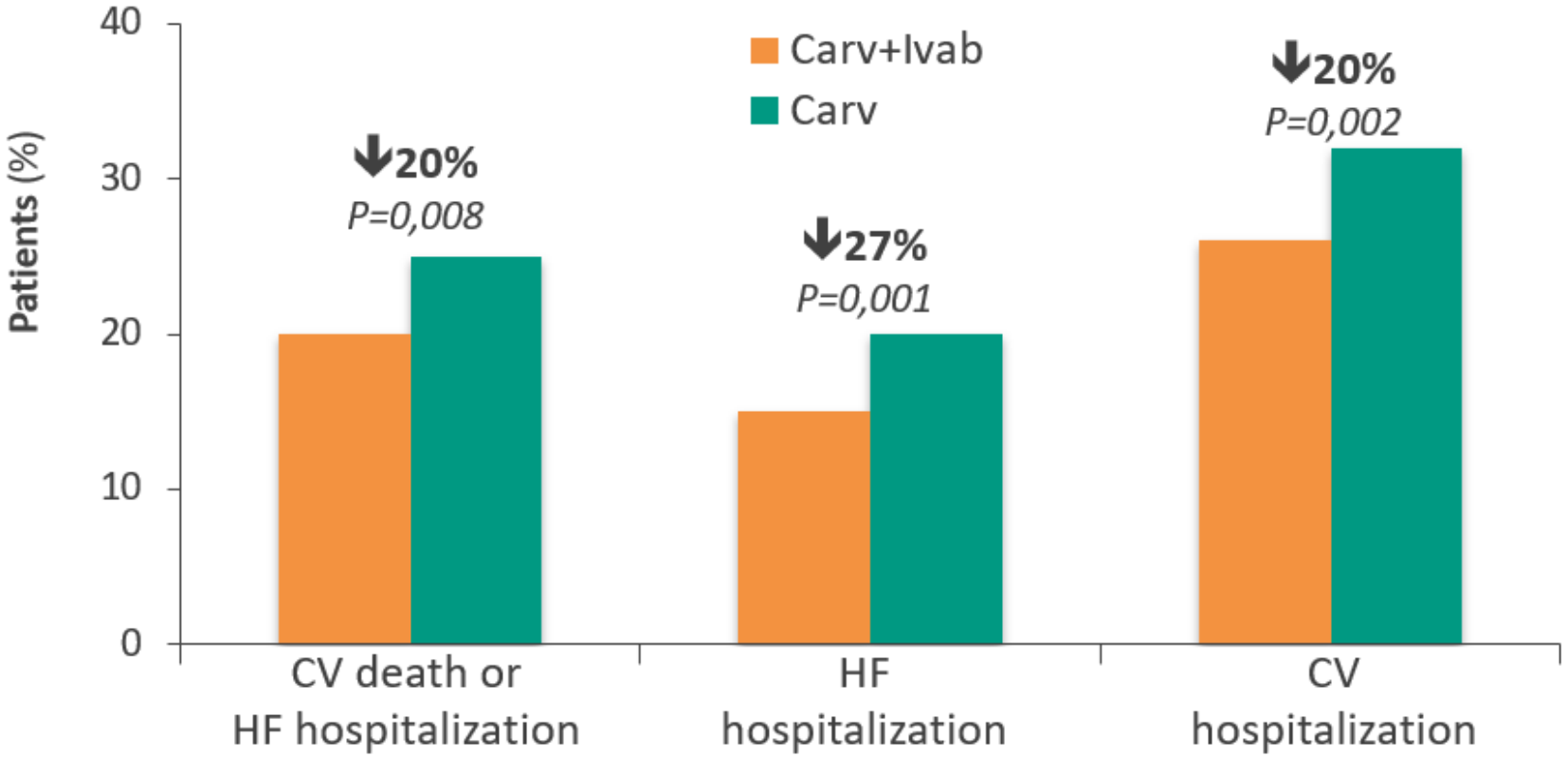
Medical therapy at baseline included 91% ACEi/ARB and 90% BB. Median follow up 23 months. Primary endpoint: CV death or HF hospitalization.

Bohm M et al. Clin Res Cardiol 2013; 102: 11-22

Ivabradine and carvedilol combination therapy

Long term benefits

Increased life expectancy and survival free from HF hospitalizations



SHIFT-Carvedilol: 6505 patients with HF and LVEF≤35%, NYHA II-IV, SR ≥70 bpm, and at least one HF hospitalization in the past 12 months. Patients were randomly assigned to ivabradine titrated to a maximum of 7.5 mg bid or matching placebo.

Medical therapy at baseline included 91% ACEi/ARB and 90% BB. Median follow up 23 months. Primary endpoint: CV death or HF hospitalization. 2596 Dts tratados com Carvedilol (45% dos tratados com BB).

Bocchi EA et al. Cardiology 2015;131:218

Key Message

High heart rate, both at the time of diagnosis and during follow-up, is strongly associated with increased risk of adverse outcomes in HFrEF patients, independent of the use of beta-blockers

Key Message

In HFrEF patients, ivabradine and carvedilol combination therapy improves life expectancy, free from HF hospitalizations, and this benefit is mediated by favorable effects on cardiac remodeling.

Improvements in systolic function and functional capacity, and reductions in HF hospitalizations are noticed early after treatment initiation.

THANK YOU