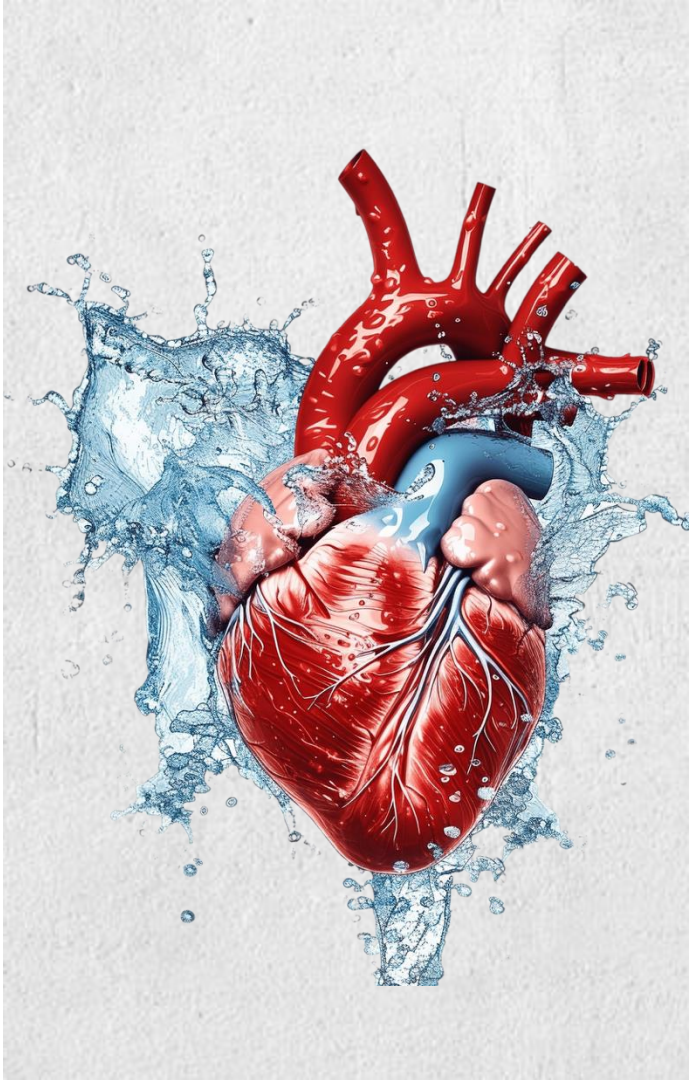
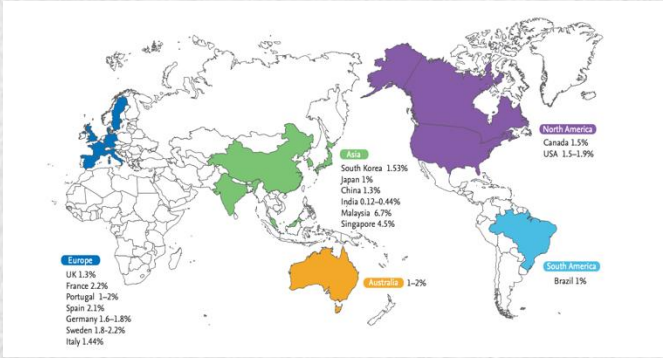
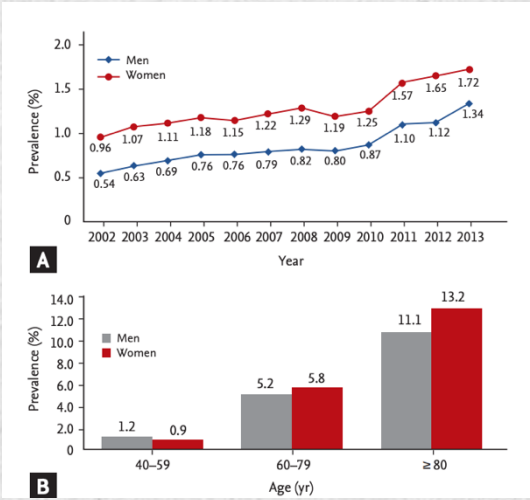
Bridging the Gap Between Guidelines & Practical Application in Heart Failure Management

Kannika Ratnachina M.D.







Heart failure

Prevalence 0.4-1%

1 hospitalization cause > 65 yrs

High morbidity and mortality

- In-hospital mortality 28%
- 1-year mortality 28.2%
- 5-year mortality 58.2%

High rehospitalization rate

- 30-day rehospitalization rate 34%
- 1-year1 rehospitalization rate 73%

Korean J Intern Med 2019;34:11-43

Terminology of HF staging and classification.

Universal** HF **Definition

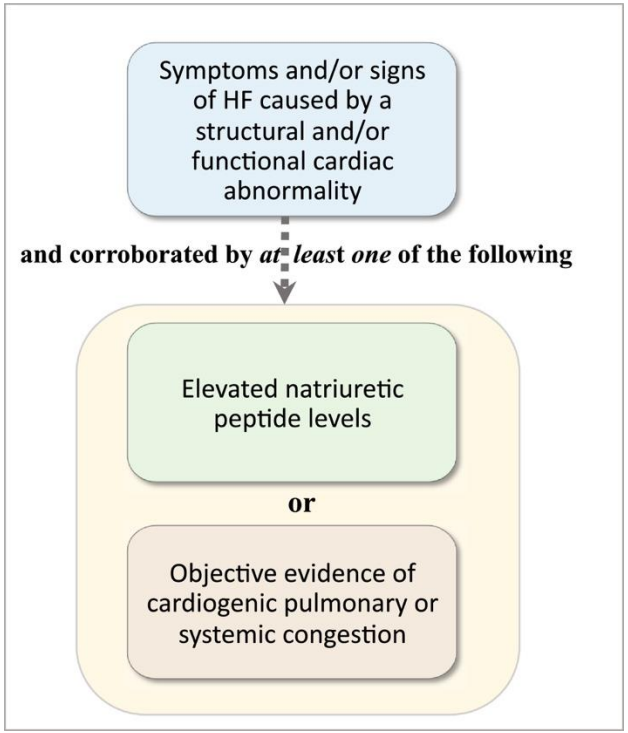
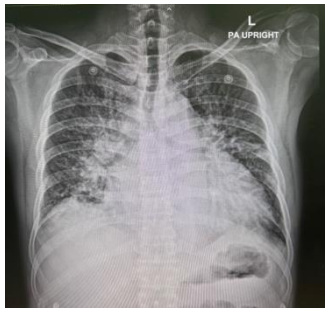


Table 1 Clinical features of heart failure and their accuracy for the detection of congestion

	Sensitivity	Specificity
Dyspnoea	50%	73%
Dyspnoea on exertion	66%	52%
Orthopnoea	66%	47%
Third heart sound	73%	42%
Bilateral leg oedema	94%	10%
Weight change	9%	97%
Jugular venous reflux	50%	75%
Resting jugular venous distention	70%	79%
Jugular venous distention >8 cm	48%	78%
Hepatomegaly	51%	62%
Chest X-ray findings		
Cardiomegaly	66%	96%
Redistribution	60%	68%
Interstitial oedema	60%	73%
Pleural effusion	43%	79%

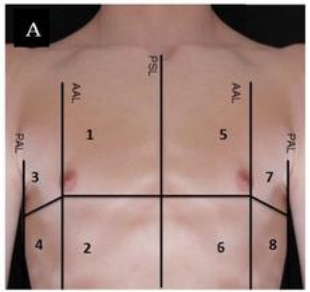
Data adapted from Mullens *et al.*[11]

Diagnostic Algorithm for Patients With Suspected HF



Assessment
- Clinical history
- Physical examination
- ECG, labs

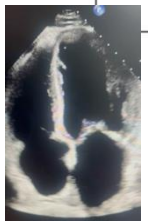
Natriuretic Peptide
- NT-proBNP >125 pg/mL
- BNP ≥35 pg/mL

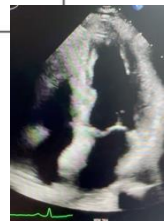


Transthoracic Echocardiography
- Additional testing, if necessary

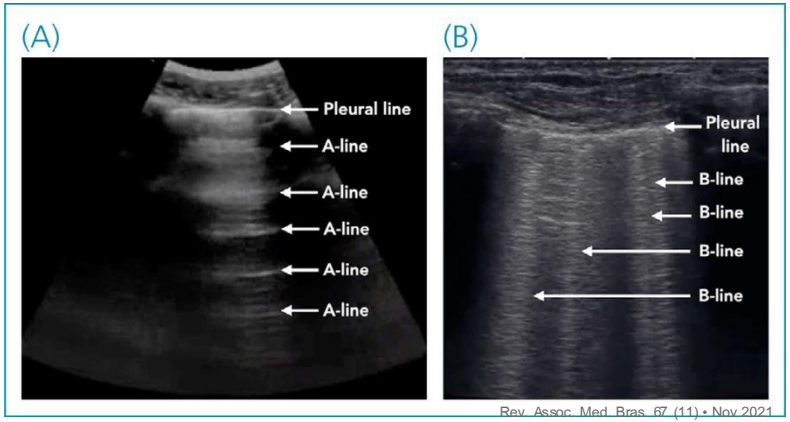
HF Diagnosis Confirmed
- Determine cause and classify

HFrEF	HFmrEF	HFpEF
LVEF ≤40%	LVEF 41%–49%	LVEF ≥50%





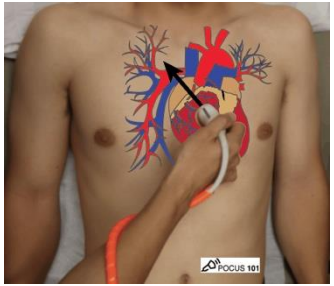
Management

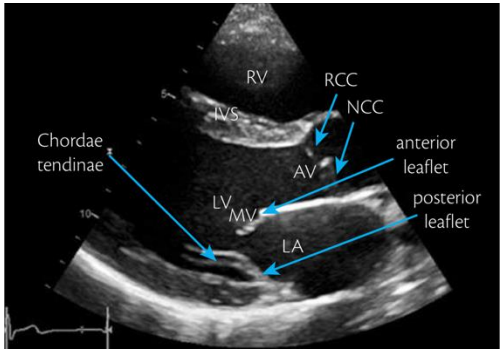


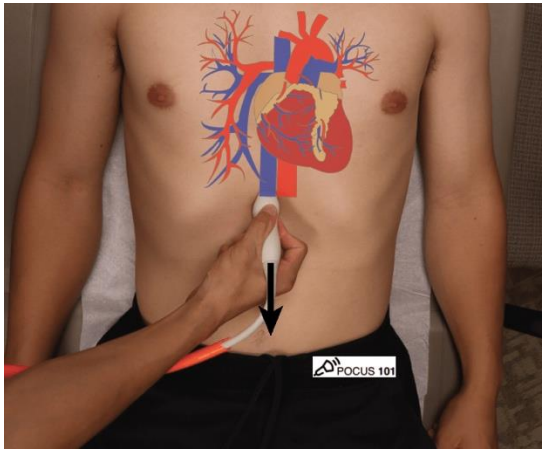
Rev. Assoc. Med. Bras. 67 (11) • Nov 2021

Causes of elevated NP other than HF
Cardiac causes
- Acute coronary syndrome
- Cardioversion
- Atrial fibrillation
- Cardiac surgery
Non-cardiac causes
- Advanced age
- Renal failure
- Sepsis
- Pulmonary causes: obstructive sleep apnea (OSA), severe pneumonia, pulmonary embolism, pulmonary hypertension
- Severe burn
- Anemia
- Patients receiving ARNI (elevated BNP, but not NT pro-BNP)

2022 HFCT Focused Update of the 2019 HFCT Heart Failure Guidelines


POCUS 101


RV
RCC
NCC
IVS
Chordae tendinae
anterior leaflet
AV
LV
MV
posterior leaflet
LA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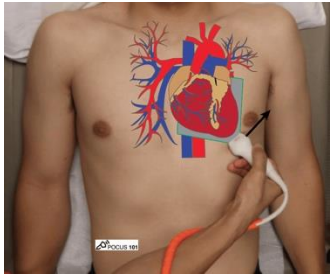
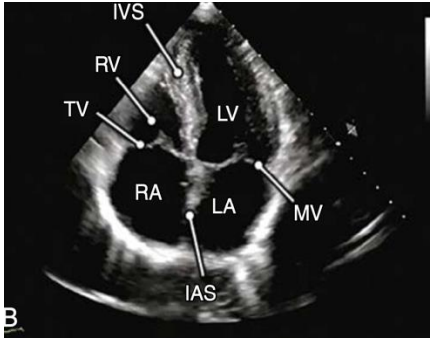
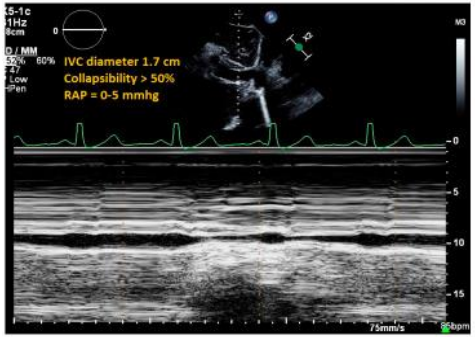
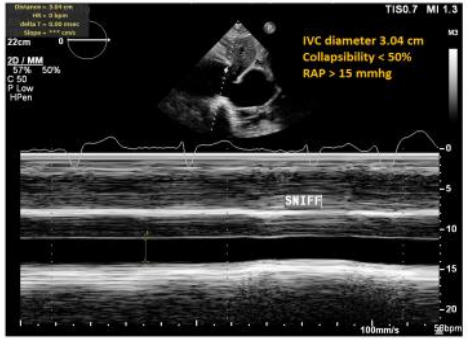
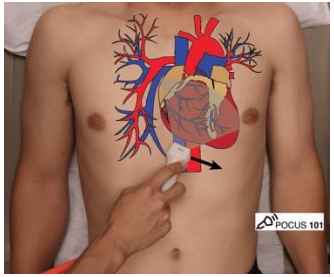
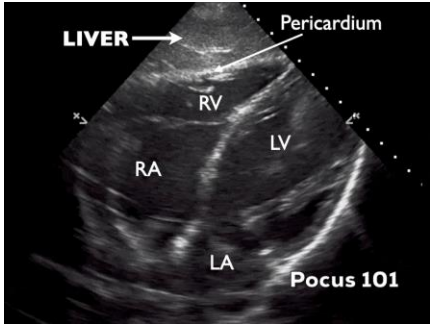



IVS
RV
TV
LV
RA
LA
MV
IAS

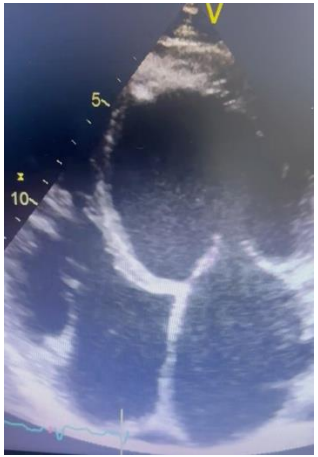

IVC diameter 1.7 cm
Collapsibility > 50%
RAP = 0-5 mmhg


IVC diameter 3.04 cm
Collapsibility < 50%
RAP > 15 mmhg
SNIFF

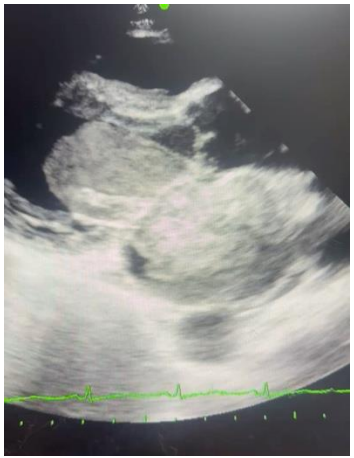

POCUS 101


LIVER
Pericardium
RV
LV
RA
LA
Pocus 101

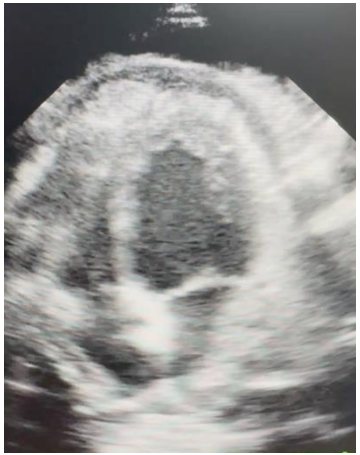
DCM



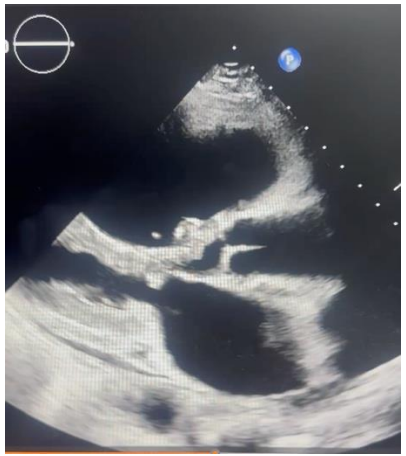
Myxoma



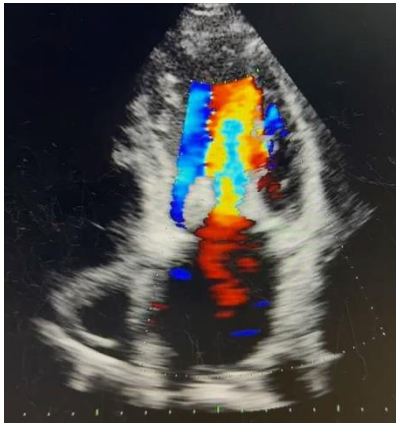
Constrictive pericarditis



PHT



IE with severe MR



Many face of heart failure

Similar symptoms –Different pathology

Etiology of HF with reduced LVEF

Ischemic cause-multivessel disease ,old MI

Non-ischemic cause : FIT STEP (+ end stage of any cardiomyopathy

Familial

Infection/inflammation (myocarditis)

Tachycardia-induced

Stress-induced (acute HF)

Toxin (Chemo ; doxorubicin ,Transtuzumab ,alcohol,amphetamine ,etc)

Endocrine (DM,thyroid,nutrition def,etc)

Peripartum cardiomyopathy

HF guideline

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

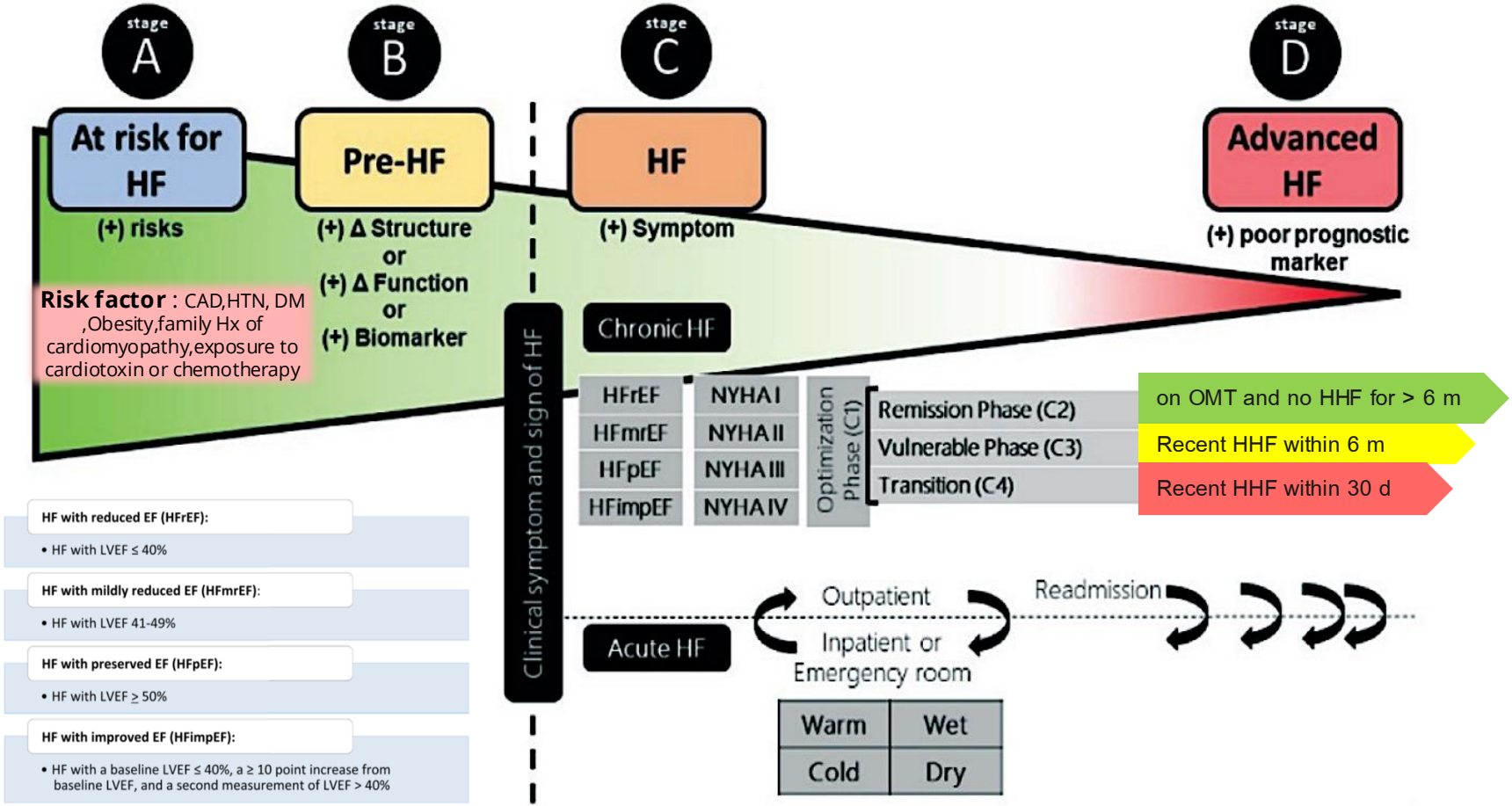
2022 HFCT Focused Update of the 2019 HFCT Heart Failure Guidelines: Part 1 - Heart Failure Classification and Pharmacological Treatment for Heart Failure with Reduced Ejection Fraction (HFrEF)

Aekarach Ariyachaipanich MD[1], Adisai Buakhamsri MD[2], Arintaya Phrommintikul MD[3], Srisakul Chirakarnjanakorn MD[4], Rungroj Krittayaphong MD[4], Vichai Senthong MD[5], Bundit Naratreekoon MD[6], Teerapat Yingchoncharoen MD[6]

2023 Focused Update of the 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

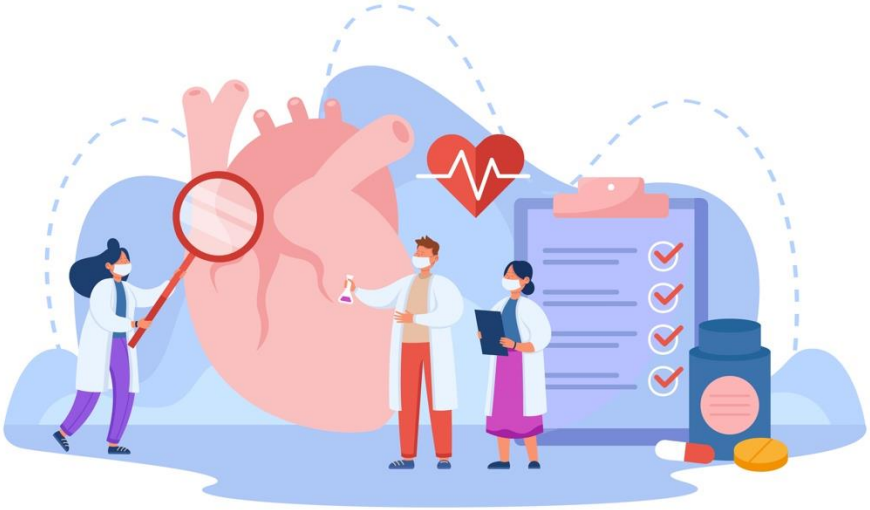
Developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

With the special contribution of the Heart Failure Association (HFA) of the ESC

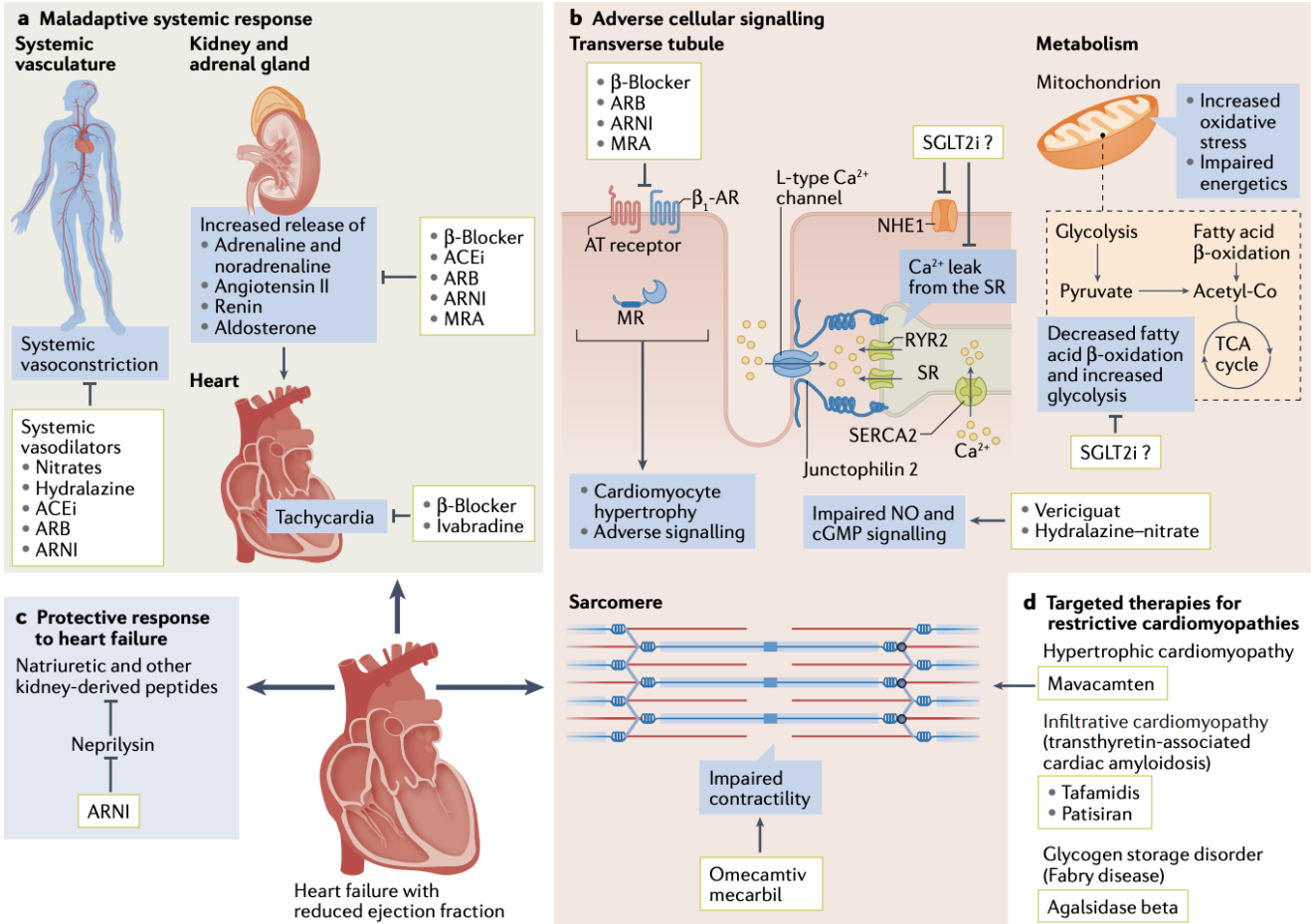


2022 HFCT Focused Update of the 2019 HFCT Heart Failure Guidelines

Heart failure management

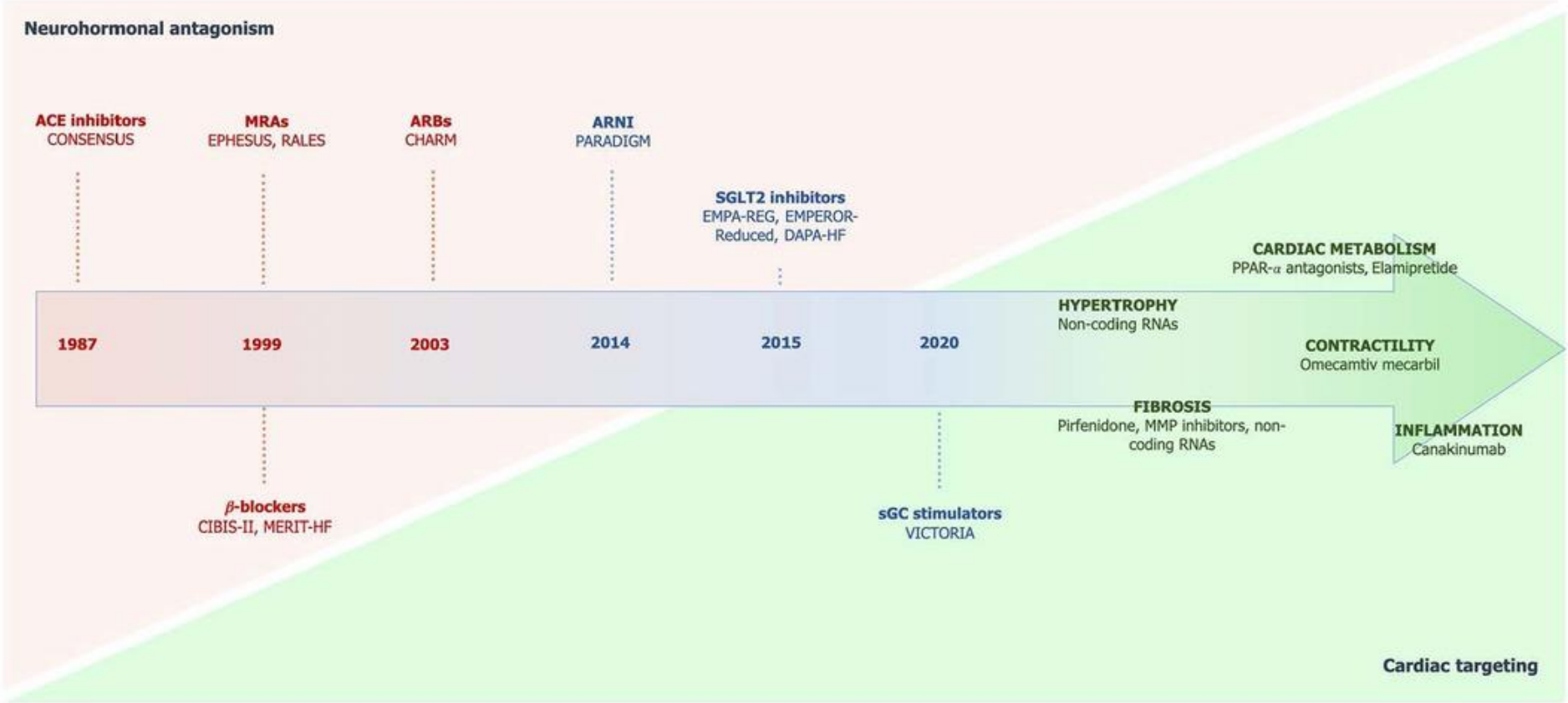


- ✓ Nonpharmacological interventions
- ✓ Pharmacological treatment for HFrEF
  - Foundational
  - Additional therapy
- ✓ Device and interventional therapy
- ✓ Co-morbidity in patients with HF

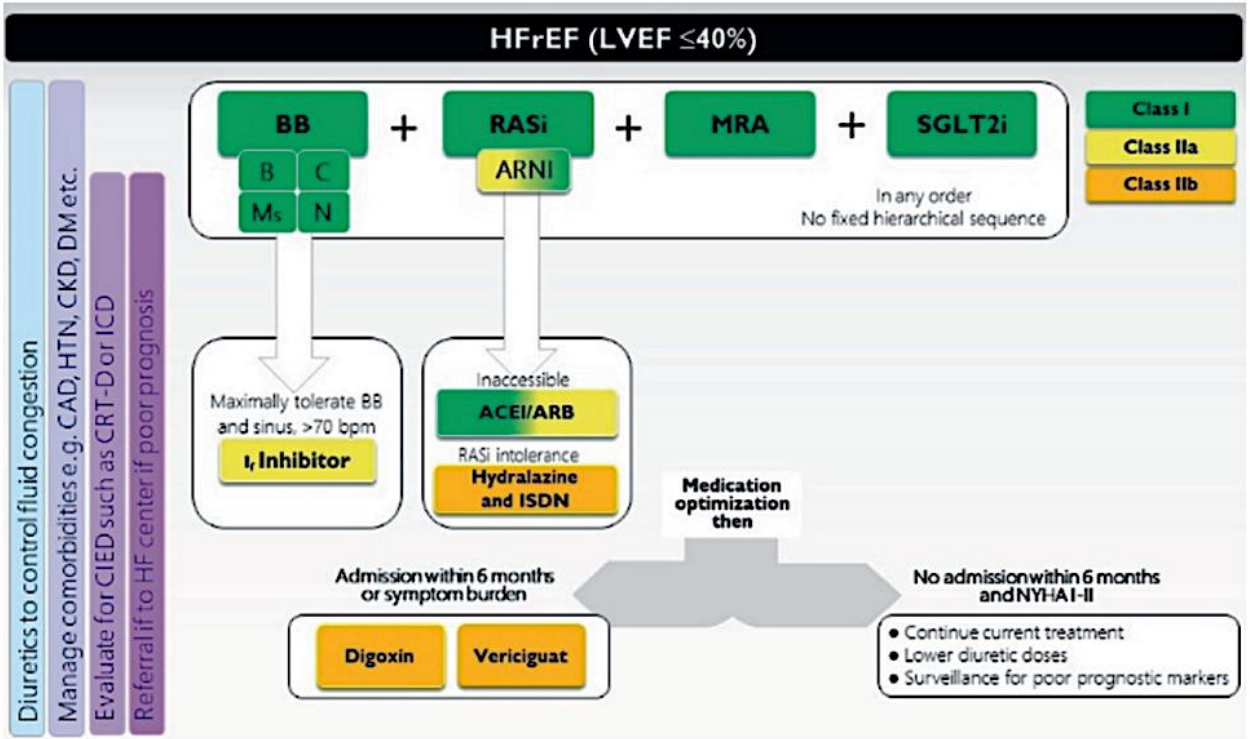


Heart failure therapeutics and their mechanisms of effect.

Nature Reviews Cardiology **volume 18**, pages745–762 (2021)

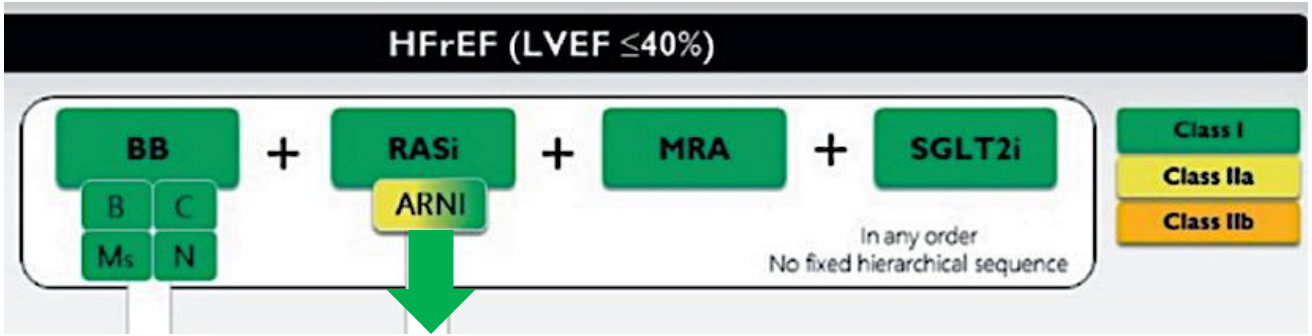

Neurohormonal antagonism
ACE inhibitors
CONSENSUS
MRAs
EPHESUS, RALES
ARBs
CHARM
ARNI
PARADIGM
SGLT2 inhibitors
EMPA-REG, EMPEROR-Reduced, DAPA-HF
CARDIAC METABOLISM
PPAR-α antagonists, Elamipretide
HYPERTROPHY
Non-coding RNAs
CONTRACTILITY
Omecamtiv mecarbil
FIBROSIS
Pirfenidone, MMP inhibitors, non-coding RNAs
INFLAMMATION
Canakinumab
1987
1999
2003
2014
2015
2020
β-blockers
CIBIS-II, MERIT-HF
sGC stimulators
VICTORIA
Cardiac targeting

Pharmacological therapy for chronic HFrEF



2022 HFCT Focused Update of the 2019 HFCT Heart Failure Guidelines

Pharmacological therapy for chronic HFrEF : RASi



Recommendations regarding the use of ACEIs in patients with HF	COR	LOE
ACEIs are recommended in all patients with asymptomatic LV systolic dysfunction regardless of etiology in order to prevent or delay the onset of symptomatic HF unless contraindicated	I	A
ACEIs are recommended in all patients with HFrEF and current or prior HF symptoms to reduce HF hospitalization and mortality.	I	A
In patients intolerant to ACEIs, angiotensin-receptor blockers (ARBs) are recommended unless contraindicated.	IIa	A

Pharmacological therapy for chronic HFrEF : RASi

Drug class	Drug	Initial dose (mg)	Target dose (mg)	Mean dose achieved in clinical trials
ACEIs	Captopril Enalapril Lisinopril Peridonpril Quinapril Ramipril	6.25 mg b.i.d. 2.5 mg b.i.d. 2.5-5 mg o.d. 2 mg o.d. 5 mg b.i.d. 1.25 to 2.5 mg o.d.	50 mg b.i.d. 10-20 mg b.i.d. 20 to 40 mg o.d. 8 to 16 mg o.d. 20 mg b.i.d. 10 mg o.d.	122.7 mg/d 16.6 mg/d 32.5-35mg/d n/a n/a n/a
ARBs	Candesartan Valsartan Losartan	4-8 mg o.d. 20-40 mg b.i.d 25-50 mg o.d.	32 mg o.d. 160 mg b.i.d 50-150 mg o.d.	24 mg/d 254 mg/d 129 mg/d

- ✓ **Assess baseline renal function before initiation**
- ✓ **Start low dose ,titrate q 2-4 week**
  - Check BUN/Cr, K+ and BP
  - Expected some rise in cr
  - Stop NSAIDs and other nephrotoxic drug
  - Avoid excessive diuresis
- ✓ **Try lower the dose before discontinue permanently**

Absolute contraindication of ACE-I /ARBs

1.Bilateral renal artery stenosis. 2.Angioedema 3.Pregnancy

Cough while taking ACEI

- Exclude pulmonary edema or bronchial disease
- Intolerable, disturbs sleep and proven to be due to ACE-I (withdrawal/rechallenge)
- Substitute with ARB

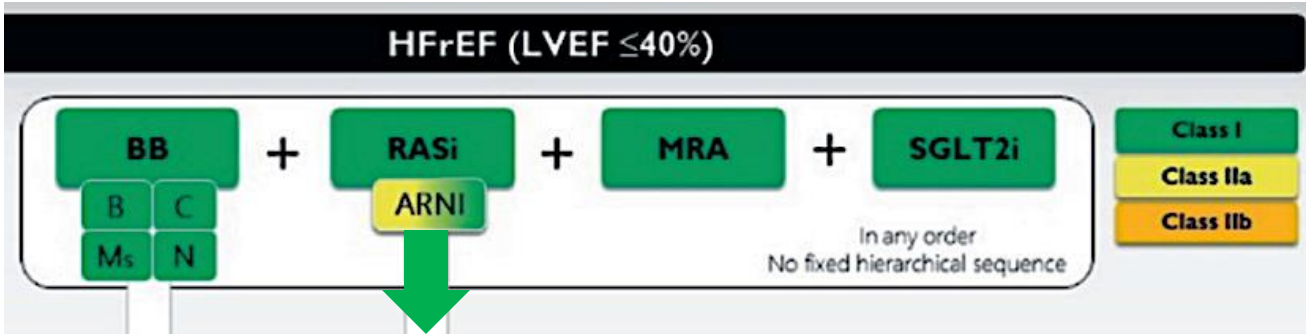
Serum cr /GFR drop during uptitration

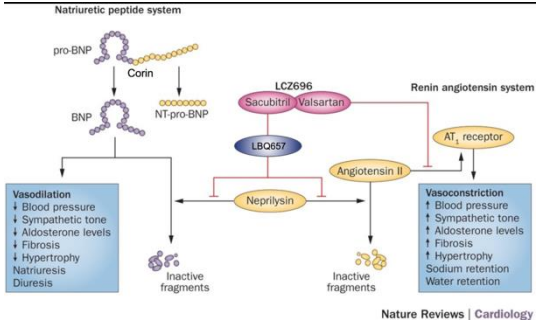
Effect on Renal Function		
ACE inhibitors cause efferent glomerular vasodilation, decreasing Filtration Fraction, preserving RBF and leading to a (reversible) decline in GFR [34]		
Early decline in eGFR after initiation (up to 5-10 mL/min/1.73m^2)[26,27]	Long term slope ~ - 0.5-1.0 mL/min/1.73m^2/year (not different from placebo in SOLVD)[26]	WRF during uptitration of ACEi-inhibition not associated with worse outcomes[39]

Management of substantial increase in serum creatinine/drop in eGFR during initiation/uptitration				
In the context of uptitration of ACE inhibitors some increase in serum creatinine / drop in eGFR is expected and acceptable. The survival benefit seen with this class of drugs far outweigh the risks associated with this perceived worsening of renal function (WRF)				
Δ serum creatinine (%)	**Max serum creatinine** (mg/dL)	**Min eGFR** mL/min/1.73m^2	**Max serum potassium** (mmol/L)	**Action advised**
< 50	**3 mg/dL**	**25**	**5.0**	None, uptitrate and evaluate renal function and electrolytes
50-100	**3.5 mg/dL**	**20**	**5.5**	Evaluate clinical status and other causes of WRF. Consider halving ACEi and re-evaluate
> 100	**> 3.5 mg/dL**	**< 20**	**> 5.5**	Evaluate clinical status and other causes of WRF. Consider stopping ACEi and re-evaluate
Rechallenge after 2-4 weeks (if possible at lower dose) when dosing reduced or stopped all together if renal function has improved				

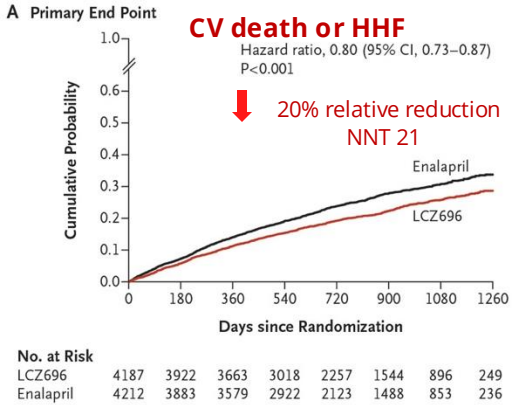
Evidence-Based Medical Therapy in Patients With Heart Failure With Reduced Ejection Fraction and Chronic Kidney Disease.Circulation 2022

Pharmacological therapy for chronic HFrEF : ARNI





Recommendations regarding the use of ARNI in patients with HF	COR	LOE
An ARNI (sacubitril/valsartan) is recommended as a **replacement** for an ACEI or ARB to reduce the risk of HF hospitalization and death.	I	B
An ARNI (sacubitril/valsartan) should be considered in patients with ACEI or ARB naïve	IIa	C

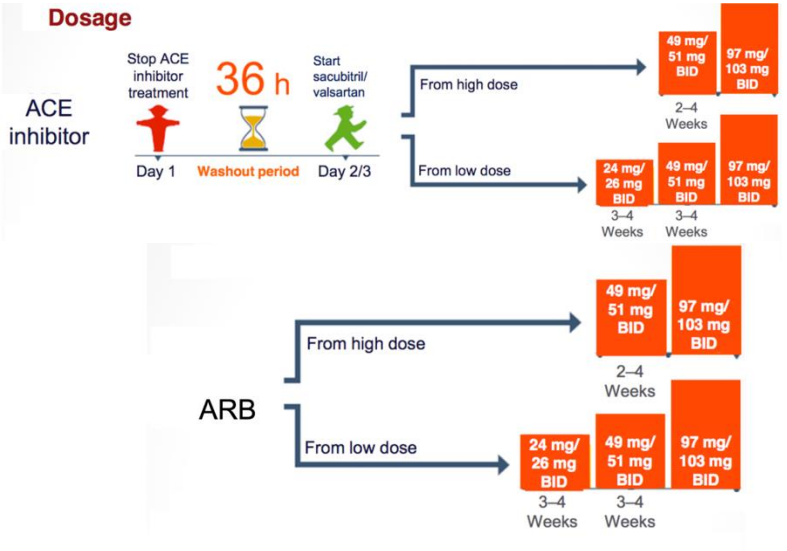


Pharmacological therapy for chronic HFrEF : ARNI

Initial dose (mg)	Target dose (mg)	Mean dose achieved in clinical trials
24/26 mg b.i.d. 49/51 mg b.i.d.	97/103 b.i.d.	375 mg/d

Table 3. Recommended initial dose of ARNI

Current dose RAAS blockade		Initial dose of ARNI
ACEIs	ARBs	Sacubitril/valsatan
Enalapril ≥10 mg/day	Losartan ≥50 mg/day	49/51 mg b.i.d.
Lisinopril ≥10 mg/day	Valsartan ≥160 mg/day	
Perindopril ≥4 mg/day	Candesartan ≥16 mg/day	
Ramipril ≥5 mg/day	Irbesartan ≥150 mg/day	
	Olmesartan ≥10 mg/day	
	Telmisartan ≥40 mg/day	
Low-dose RAAS blockade		24/26 mg b.i.d.
RAAS blockade naïve		24/26 mg b.i.d.
High risk of hypotension		



Cautions

1.**Renal impairement (eGFR < 30 mL/min/1.73 m²)**
2.CTP B
3.SBP < 100 mmHg
4. K > 5.2 mEq/L
5.Volume depletion

Contraindication

1. **ACEI use < 36 hrs**
2. Angioedema
3. Preg ,lactation (no data)
4. Bilat RAS
5. CTP C
6. Hypersenitivity to ARB,ARNI
7. Concomitant aliskiren use in DM patients

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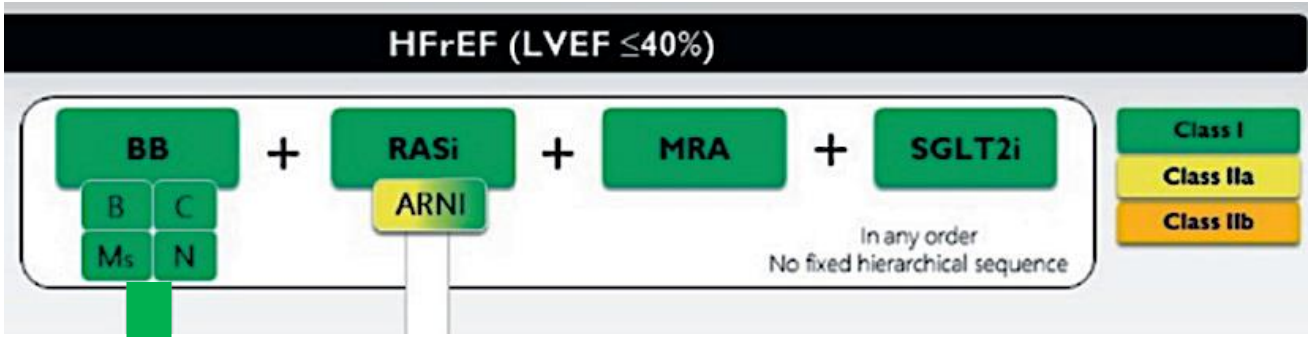
Pharmacological therapy for chronic HFrEF : Beta blocker



Recommendations regarding the use of beta-blockers in patients with HF	COR	LOE
BB are recommended in all patients with asymptomatic LV systolic dysfunction and history of myocardial infarction in order to prevent or delay the onset of symptomatic HF and to reduce mortality	I	B
BB are recommended in all patients with asymptomatic LV systolic dysfunction, including those with no history of myocardial infarction, in order to prevent or delay the onset of symptomatic HF	I	C
A beta-blocker **(bisoprolol, carvedilol, sustained-release metoprolol succinate, or nebivolol)** is recommended	I	A

2022 HFCT Focused Update of the 2019 HFCT Heart Failure Guidelines

Pharmacological therapy for chronic HFrEF : Beta blocker

Drug	Initial dose (mg)	Target dose (mg)	Mean dose achieved in clinical trials
Bisoprolol	1.25 mg o.d.	10 mg o.d.	8.6 mg/d
Carvedilol	3.125 mg b.i.d.	25 mg bi.d.	37 mg/d
Metroprolol succinate	12.5-25 mg o.d.	200 mg o.d.	159 mg/d
Nebivolol	1.5 mg o.d.	10 mg 0.d.	7.7 mg/day

Generation	β-Blocker	β1 Antagonism	β2 Antagonism	α1 Antagonism	Nitric Oxide Production	Lipophilic
First	Propranolol	Yes	Yes	No	No	Yes
	Timolol	Yes	Yes	No	No	Mild
Second	Metoprolol Succinate	Yes	No	No	No	Yes
			Less neuropsychiatric side effect			
	Bisoprolol	Yes	No	No	No	Mild
Third	Carvedilol	Yes	Yes	Yes	Yes	Yes
	Bucindolol	Yes	Yes	No	Mild	Yes
	Nebivolol	Yes	No	No	Yes	Yes

Clinical scenario	Beta blocker
HTN	Carvedilol ,bisoprolol
Asthma and COPD	Bisoprolol,nebivolol
DM	Carvedilol,bisoprolol
AF	Metoprolol,bisoprolol
PAD	Carvedilol ,nebivolol

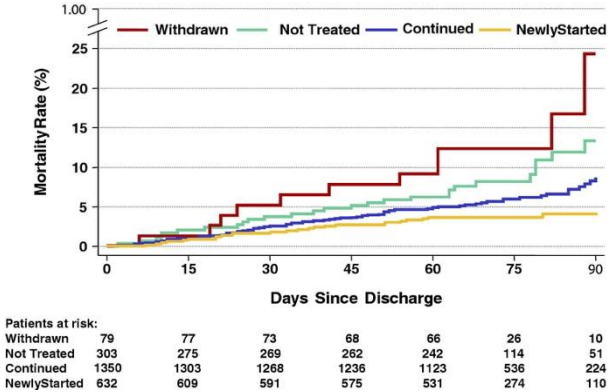
J Am Coll Cardiol 2017;69:20 2542

Practical use: Beta blocker

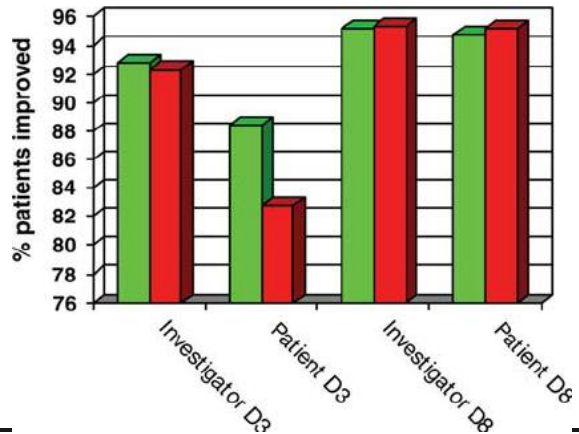
- **When** : euvolemia ,no IV medication for HF (inotropes ,diuretic)
- **How** : start low ,go slow (every 2 week)
- **Congestion at 3-5 day** : Increase diuretic ,Halve dose BB if not improve
- **Fatigue** ; resolve in weeks to months
  Trick ; Switch to **“hs”**
- **Depression ; lipophilic** BB
- **Asthma** (relative contraindication)

Practical use: Beta blocker

- **Hospitalized for ADHF** : *Don ‘t stop ,if no cardiogenic shock*
- **Low BP or Low HR with symptoms**
  - Off or lower dose of other drugs,half dose BB if not improve
    - Nitrate ,CCB , alpha blocker ,Diuretics if no congestion
    - Digitalis ,Amiodarone ,Ivabradine ,Non-DHP CCBs

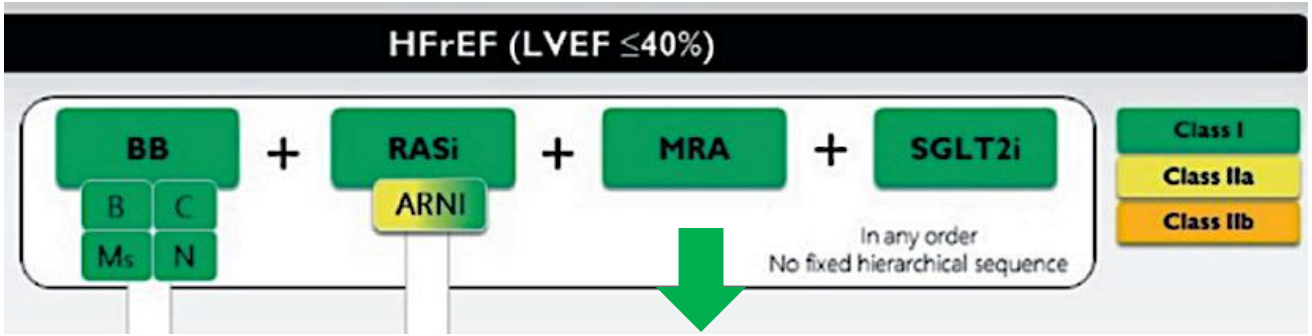


OPTIMIZE-HF trial



B-CONVINCED

Pharmacological therapy for chronic HFrEF : Mineralocorticoid receptor agonist



Recommendations regarding the use of MRA in patients with HF	COR	LOE
Unless contraindicated, **low-dose MRA (spironolactone)** is recommended in symptomatic chronic HFrEF , preferably after treatment with ACEI/ARBs and BB, to further reduce HF hospitalization and mortality.	I	A

Pharmacological therapy for chronic HFrEF : Mineralocorticoid receptor agonist

Drug	Initial dose (mg)	Target dose (mg)	Mean dose achieved in clinical trials
Spironolactone	12.5-25 mg o.d.	25-50 mg o.d.	26 mg/d
Eplerenone	25 mg o.d.	50 mg o.d.	42.6 mg/d

Cautions
- K > 5.0 mmol/L
- Cr > 2.5 mg/dl
- Concomitant use with NSAID,RASi,High K diet

Side effect
- Gynecomastia (spironolactone)
- Sexual dysfunction
- Abnormal menstruation
- Hyperkalemia (dose response)

Dosing in renal insufficiency

Spironolactone	Initial dose (mg)	Target dose (mg)
GFR > 50 **GFR 31-49**	12.5-25 mg o.d. 12.5 mg once or every other day	25(50) mg o.d.

- Minimal effect on BP
- Up-titration after 4-8 weeks,check Cr K at 1 and 4 week after starting/increasing

Effect on Renal Function

The precise pathophysiology of the effect of MRA on renal function is unclear

Early decline in eGFR after initiation (2.3 to 6.7 mL/min/1.73m^2)[48]	Long term slope in eGFR slightly steeper with eplerenone vs placebo (-0.3 vs -0.1 mL/min/1.73m^2/year)[48,51]	WRF during uptitration of MRA-inhibition not associated with worse outcome [39,43]

Management of substantial increase in serum creatinine/drop in eGFR during initiation/uptitration

In the context of uptitration of MRAs some increase in serum creatinine / drop in eGFR is expected and acceptable. The survival benefit seen with this class of drugs far outweigh the risks associated with this perceived worsening of renal function (WRF)

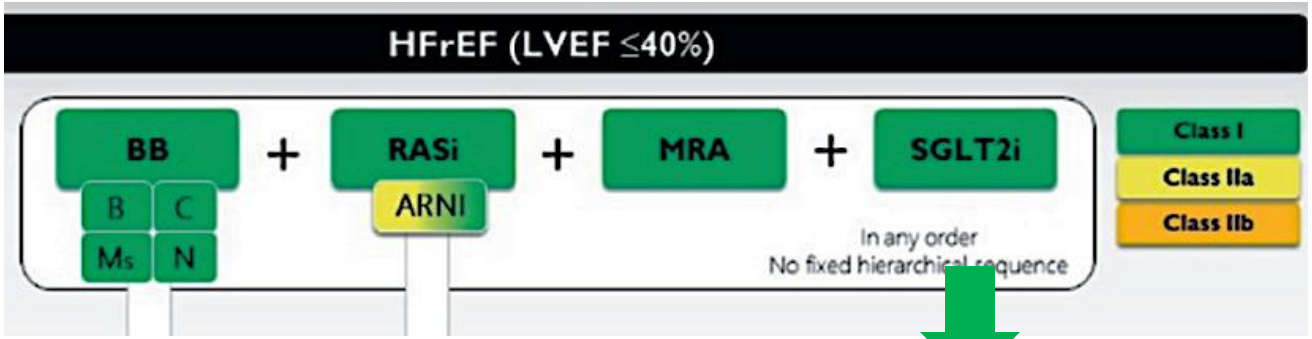
Δ serum creatinine (%)	Max serum creatinine (mg/dL)	Min eGFR mL/min/1.73m^2	Max serum potassium (mmol/L)	Action advised
< 50	2.5 mg/dL	30	5.0	None, uptitrate and evaluate renal function and electrolytes
50-100	3.5 mg/dL	20	5.5	Evaluate clinical status and other causes of WRF. Consider halving MRA and re-evaluate
> 100	> 3.5 mg/dL	< 20	> 6.0	Evaluate clinical status and other causes of WRF. Consider stopping MRA and re-evaluate

Rechallenge after 2-4 weeks (if possible at lower dose) when dosing reduced or stopped all together if renal function and/or potassium has improved

Current Cardiology Reviews, **2015**, *11*, **23-3**

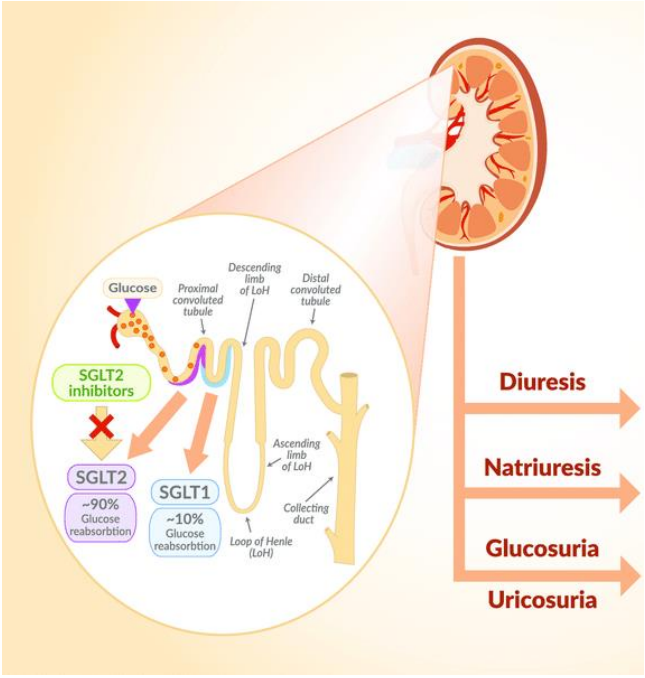
Evidence-Based Medical Therapy in Patients With Heart Failure With Reduced Ejection Fraction and Chronic Kidney Disease.Circulation 2022

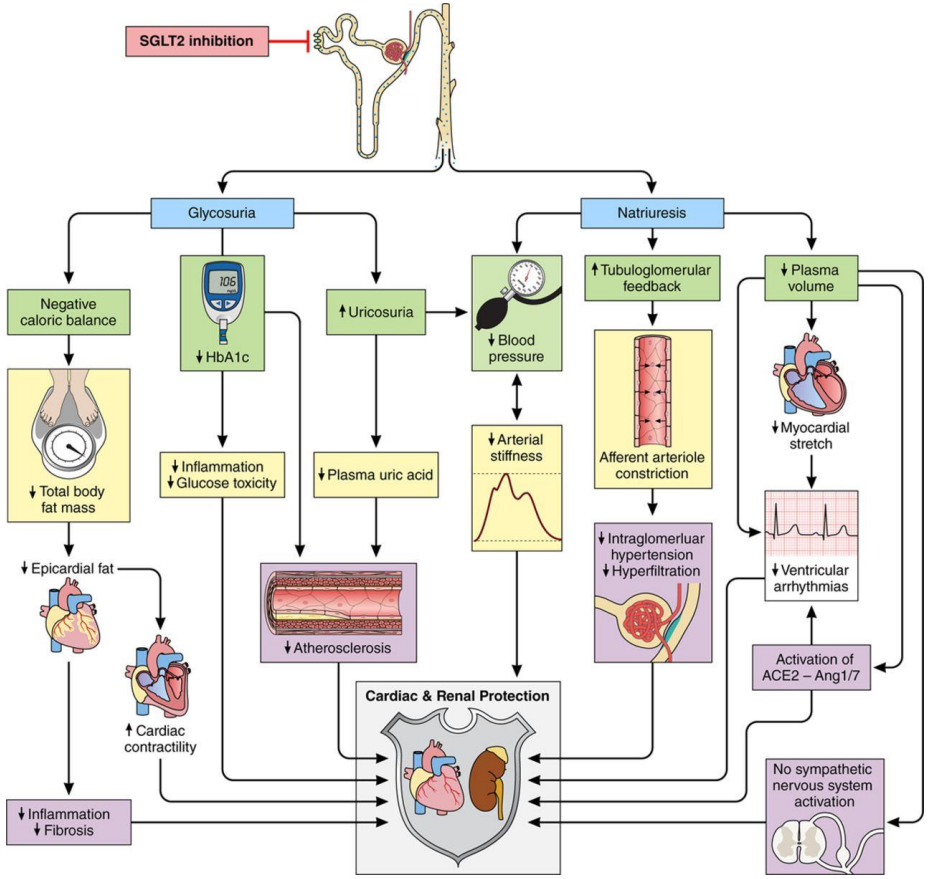
Pharmacological therapy for chronic HFrEF :SGLT2 inhibitor



Recommendations regarding the use of SGLT2i in patients with HF	COR	LOE
Dapagliflozin or empagliflozin are recommended for symptomatic patients with HFrEF to reduce the risk of heart failure hospitalization and death	I	A
SGLT2i are recommended for diabetic patients who are at risk for heart failure and asymptomatic left ventricular systolic	I	A

Sodium-Glucose Cotransporter 2 inhibitor Cardiorenal pretection





1. Heart Failure Reviews. 26. 1-20 2. Circulation.2016;134:752-722

SGLT2 inhibitor : practical use

Drug	Initial dose (mg)	Target dose (mg)
Dapagliflozin	10 mg o.d.	10 mg o.d.
Empagliflozin	10 mg.o.d.	10 mg o.d.

Contraindication

1.Type I DM
2. Hypersensitivity
3. Lactation (no data)
4. Dialysis
5. Pregnancy

Cautions

1. Hx of DKA
2. Hypovolemia
3. Concomitant use with diuretics
4. **eGFR < 30 (Dapagliflozin)**
5. **eGFR <20 (Empagliflocin)**

Side effect

1. Ketoacidosis
2. Urinary tract infection
3. Genital mycotic infection
4. AKI
5. Volume depleteion

Patient education

- ✓ Avoid dehydration
- ✓ Genital hygiene
- ✓ Sick day rules
- ✓ Stop before surgery

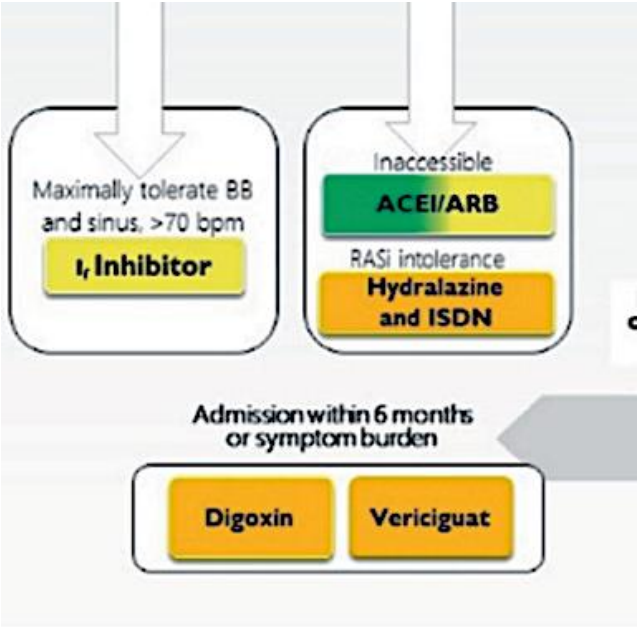
Pharmacological therapy in HFrEF

	ARNI	ACEI/ARB	BB	MRA	SGLT2i
SBP <90	⚠	⚠	✓	✓	✓
HR <55	✓	✓	⚠	✓	✓
GFR <30	⚠	⚠	✓	⚠	⚠
K >5.0	⚠	⚠	✓	⚠	✓
Congestion	✓	✓	⚠	✓	✓
Cost	฿฿฿	฿	฿	฿	฿฿฿

⚠ Caution and closely monitor ✓ Consider initiate or up titrate

- ✓ **RASi+BB+MRA+SGLT2i**
- ✓ In any order ,No fiexed hierarchical sequence
- ✓ Patient profie

Additional medication for selected patient



Drug	Initial dose (mg)	Target dose (mg)
Ivabradine	5 mg bid	7.5 mg bid
Hydralazine and nitrate		
Hydralazine	25-50 mg tid	300 mg/d
Isosorbide dinitrate	10-20 mg tid	120 mg/d
Digoxin	0.125-0.25 mg od	Variable dose Drug level 0.5-0.9 ng/ml
Vericiquat	2.5 mg od	10 mg od

Vaccination

Table 5. Summary of recommendations regarding vaccines and multidisciplinary care in patients with HF

Recommendations	COR	LOE
Annual influenza vaccine is recommended in all patients with HF.	I	B
Combined pneumococcal vaccine and influenza vaccine are recommended in all patients with HF.	IIa	B
Multidisciplinary care management program is recommended for patients with high-risk HF to reduce the risk of HF hospitalization and mortality.	I	A
Routine use of coenzyme Q10 is not recommended in patients with HFrEF due to insufficient data	III	B

COR=class of recommendation; HF=heart failure; LOE=level of evidence

Predicharge planning

Clinical optimization

- ❑ Decongest
- ❑ Address precipitating factors
- ❑ Address comorbidities
- ❑ Deprescribe unnecessary therapy
- ❑ Initiate GDMT pillars

Discharge preparation

- ❑ Switch from IV to oral therapies
- ❑ Ensure adequate decongestion with stable oral dose for 2 days prior to discharge
- ❑ Address barriers to GDMT access or uptake
- ❑ Provide education

Transitional care

- ❑ Schedule postdischarge follow-up visit, ideally in an HF clinic to optimize GDMT
- ❑ Refer to cardiac rehabilitation
- ❑ If appropriate, refer to palliative care

Follow up

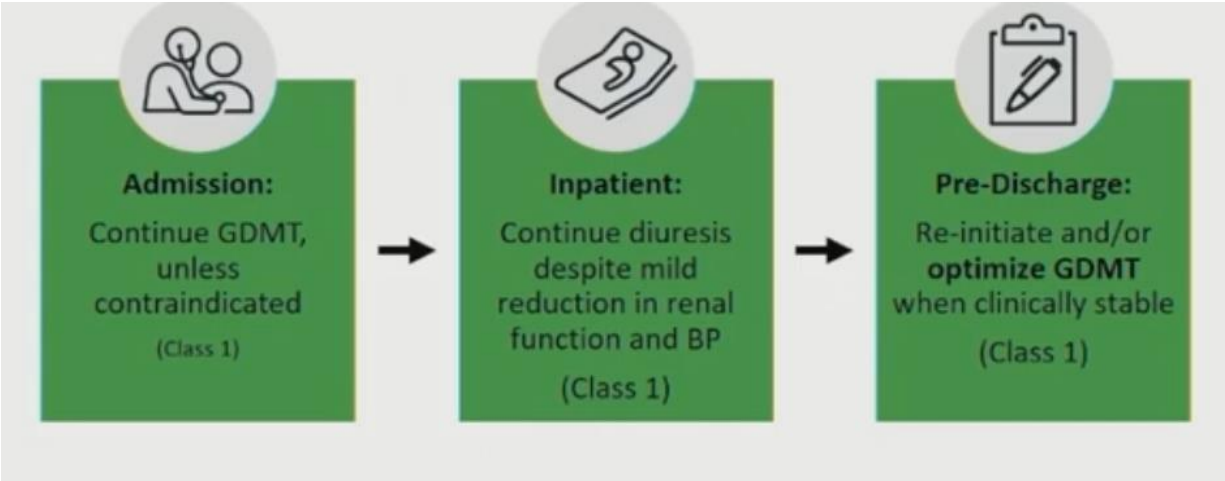
Phase	Name	Definition	Suggested goal	Suggested follow up
C1	Optimization	Not optimally on GDMT, usually recently diagnosed HF	Intensive HF education, up titrate pharmacologic treatment to maximally tolerated doses or as tolerate within 3-6 months.	2-4 weeks
C2	Remission	Already on OMT and no HF hospitalization for >6 months	Surveillance for alteration in symptoms. Consider reducing diuretic if possible. Evaluation for CIED if needed. Routine functional capacity assessment.	2-6 months
C3	Vulnerable	Recent hospitalization within 6 months, but not within 30 days	Similar to optimization phase with more urgency. Consider medications that can reduce HF hospitalization.	2-8 weeks
C4	Transition	Recent hospitalization within 30 days	Transition of care from inpatient to outpatient.	1-2 weeks

CIED=cardiac implantable electronic devices; GDMT=guideline-directed medical therapy; OMT=optimal medical therapy

GDMT in specific situation

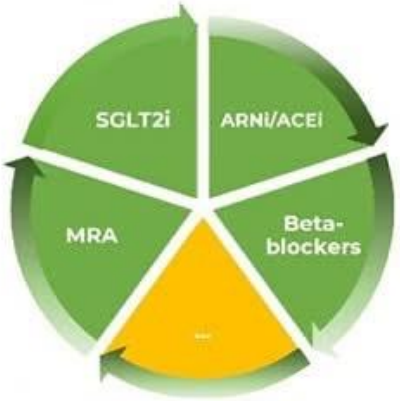
GDMT During hospitalization

Oral GDMT should be continued and optimized on admission ,as doing so is associated with lower post diischarge death and readmission



Heidenreich,P.A.et al. (2022) AHA/ACC/HFSA Guideline for HF.Circulation

HOW TO TREAT WORSENING HF IN HFrEF EARLY



Chronic HFrEF

WHF event/progression
Improvement needed

Patient Settings:

- Patient on full dose GDMT
- Patient on suboptimal GDMT (due to impaired kidney function, hyperkalemia, hypotension, heart rate, or other)

Vericiguat

- NYHA II-III
- **Stabilization after a WHF event**
- SBP > 100 mmHg
- eGFR > 15 mL/min/1.73m²
- IV diuretics > 24h

Ivabradine

- NYHA II-III
- NSR
- Heart rate ≥ 70 bpm
- On maximally tolerated beta blocker

Ferric carboxymaltose

- In patients with iron deficiency

Digoxin

- May be considered in patients with symptomatic HFrEF in NSR

Hydralazine and isosorbide dinitrate

- For Black patients with LVEF ≤ 35% or with an LVEF < 45% combined with a dilated LV in NYHA class III-IV

ESC 2021 - Classes of Recommendation:

- Class I (recommended/indicated)
- Class IIa (should be considered)
- Class IIb (may be considered)

Diuretics as needed
Early treatment of **comorbidities**

GDMT with CKD patient

ESC European Society of Cardiology

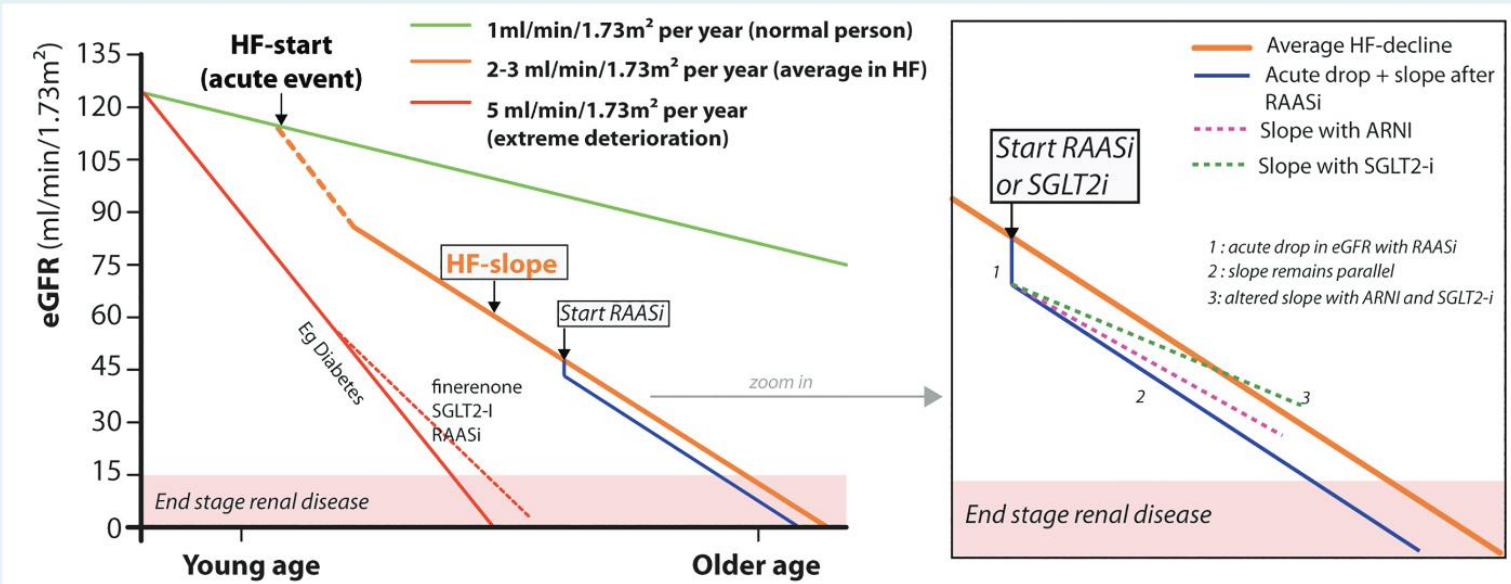
European Journal of Heart Failure (2022) **24**, 603–619
doi:10.1002/ejhf.2471

POSITION PAPER

Renal effects of guideline-directed medical therapies in heart failure: a consensus document from the Heart Failure Association of the European Society of Cardiology

Table 4 Initiation of heart failure drugs in relation to baseline chronic kidney disease status

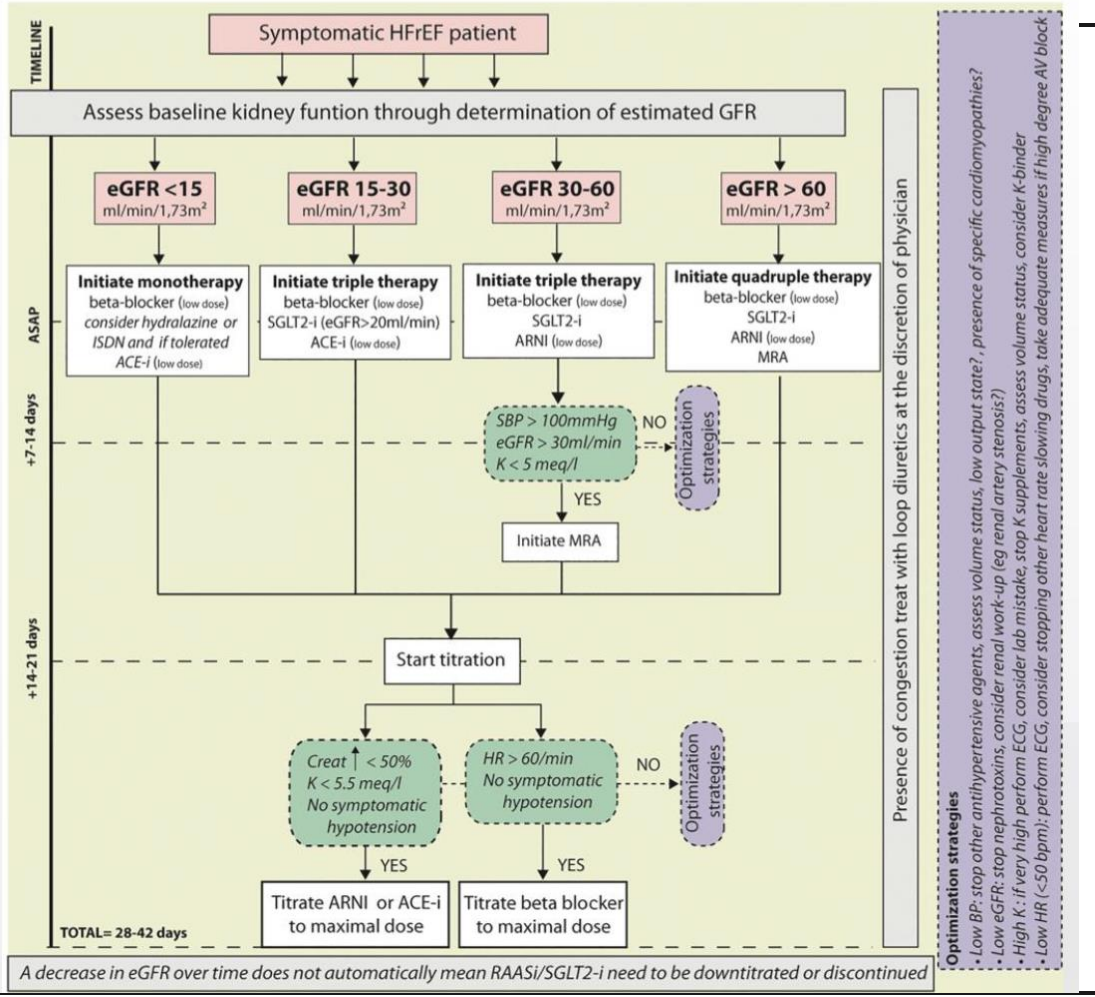
Drug	Evidence across GFR strata according to baseline eGFR enrolment criteria	Acute drop GFR	Impact on GFR slope in HF trial	CKD treatment interaction	Treatment effect with CKD
	ESKD 15–30 30–60 >60				
ACE-I/ARB	Moderate evidence if dialysis, weak evidence if not on dialysis	Yes	No (beneficial effect of around 1–2 ml/min/1.73 m^2 per year in CKD trials)	No	Relative benefit: ~ Absolute benefit: ↑
Beta-blockers		No	No	Yes (potentially but some conflicting results)	Relative benefit: ~ Absolute benefit: ↑
MRA		Yes	No	No	Relative benefit: ~ Absolute benefit: ↑
ARNI		Yes	Yes (around 0.5 ml/min/1.73 m^2 per year)	No	Relative benefit: ~ Absolute benefit: ↑
SGLT2-i	>20	Yes	Yes (around 1–2 ml/min/1.73 m^2 per year)	No	Relative benefit: ~ Absolute benefit: ↑
Ivabradine		No	No	No	Relative benefit: ~ Absolute benefit: ↑
Vericiguat		No	No	No	Relative benefit: ~ Absolute benefit: ↑
Omecamtiv mecarbil		No	No	No	Relative benefit: ~ Absolute benefit: ↑



Key messages

1. Acute drop in GFR with RAASi, ARNI and SGLT2-i does not diminishes treatment effect
2. A reduction in slope deterioration in HFrEF with ARNI and SGLT2-i is associated with reduced hard renal endpoints

Figure 2 Effect of drugs on renal slope. ARNI, angiotensin receptor–neprilysin inhibitor; eGFR, estimated glomerular filtration rate; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; RAASi, renin–angiotensin–aldosterone system inhibitor; SGLT2-i, sodium–glucose cotransporter 2 inhibitor. Adapted from Mullens *et al.*[3]



European Journal of Heart Failure(2022) 24, 603–619.

GDMT with low blood pressure patient

ESC European Society of Cardiology

European Journal of Heart Failure (2025)
doi:10.1002/ejhf.3618

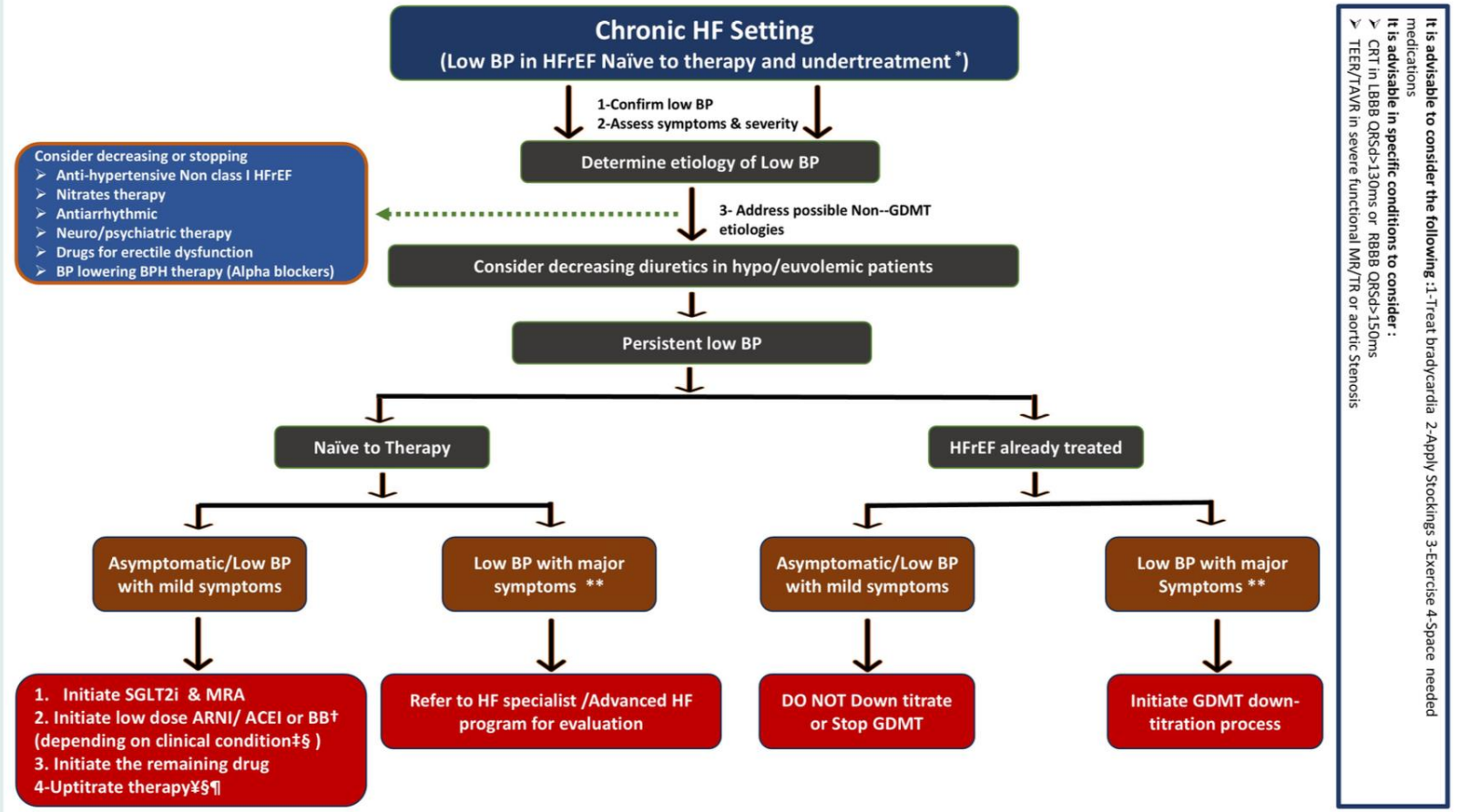
POSITION PAPER

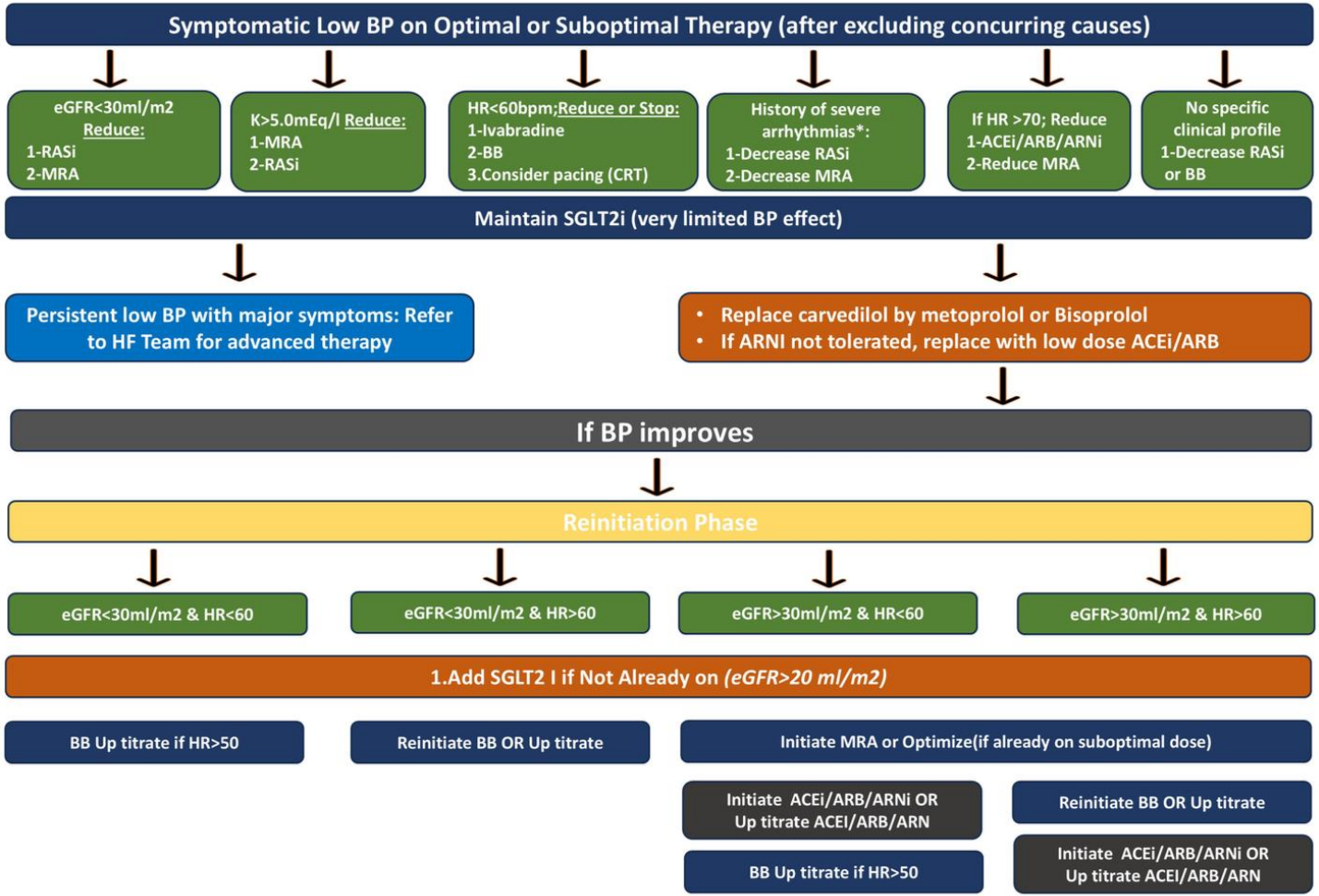
Clinical management and therapeutic optimization of patients with heart failure with reduced ejection fraction and low blood pressure. A clinical consensus statement of the Heart Failure Association (HFA) of the ESC

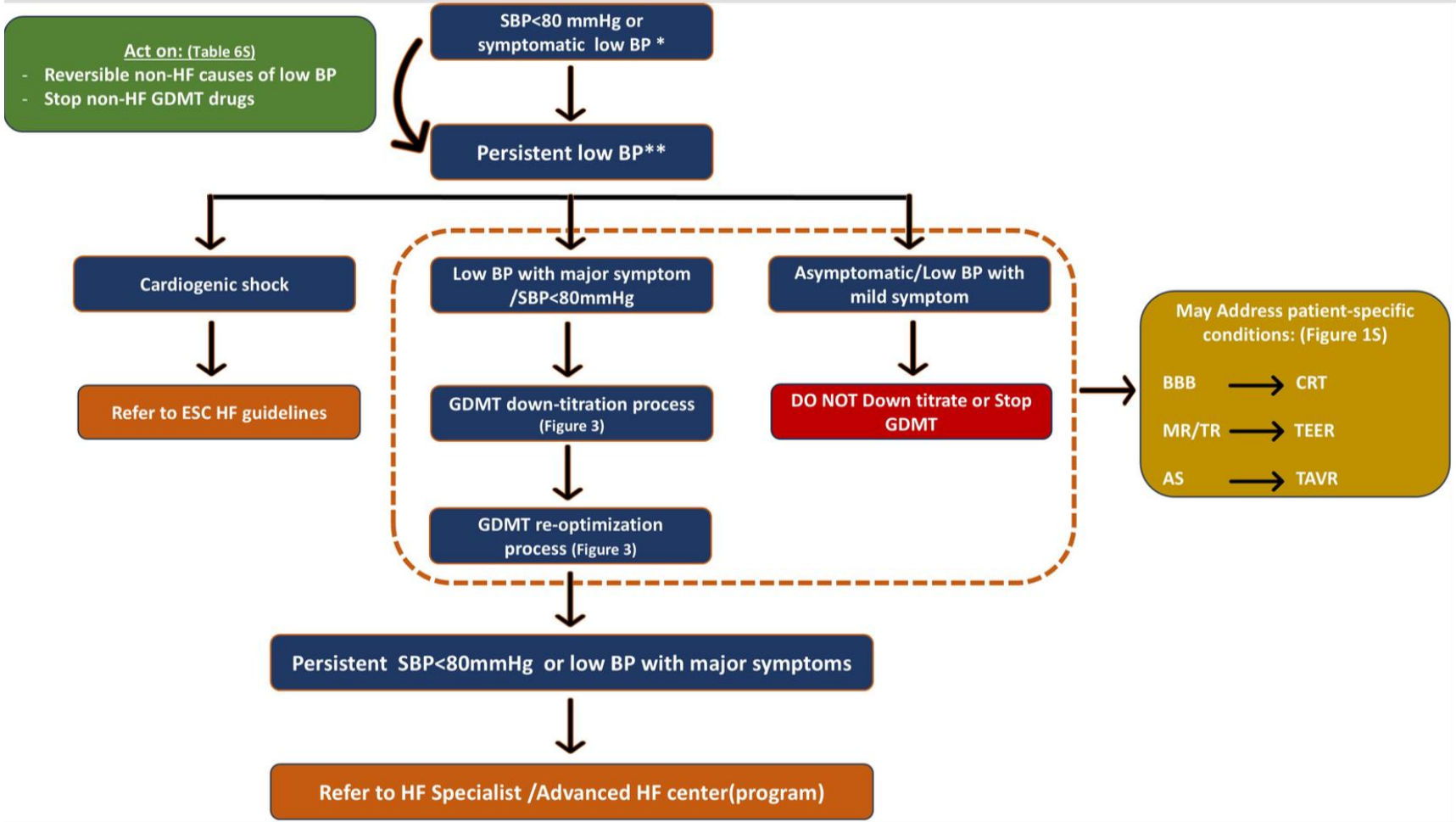
Table 1 **Cardiovascular and non-cardiovascular potential causes of low blood pressure**

Cardiovascular-related	Non-cardiovascular-related
• Advanced HF (low output state-NYHA IIIb–IV; hyponatraemia) • Decrease blood volume (recent bleed, trauma …) • Valve disease (significant MR, TR, and AS) • Bradycardia (AV blocks …) • Dehydration (over diuresis; high temperature, diarrhoea) • An increase in diuretic dose in the previous week • Prolonged bed rest (OH) • Pregnancy 1st 24 weeks • BP-lowering medications: CCB; alpha-blockers, centrally acting; diuretics (thiazides …); ACEis; ARBs; BB • Angina medications: BB; CCB; nitrates • HF non class I: hydralazine/nitrates • Neurally mediated syncope • Altered vasoreactivity related to comorbidities (diabetes) Acute–rapidly progressive • Peripartum cardiomyopathy • Myocarditis • Intraabdominal hypertension (ascites) • Persistent signs of congestion requiring high doses of diuretics or vasodilators	• Elderly (higher age group) • CKD • Endocrine problems: hypothyroidism; adrenal insufficiency (Addison's disease); hypoglycaemia; diabetes • Infection (when severe): UTI, septic shock • Allergic reaction (anaphylaxis) • Nutrient deficiency: vitamin B12 and folate causing anaemia • Iron deficiency • Liver disease: hepatic cirrhosis • COPD • Dementia • Parkinson's • Depression • Medications (see online supplementary *Table S6*) - Antidepressants - Antipsychotics (2nd generation) - Dopamine antagonist - PDE5 inhibitors (erectile dysfunction) - Alfa-blockers (BPH) - Complementary and alternative medicine - Narcotics and alcohol - Intraocular beta-blockers (glaucoma)

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor antagonist; AS, aortic stenosis; AV, atrio-ventricular; BB, beta-blocker; BPH, benign prostatic hypertrophy; CCB, calcium channel blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MR, mitral regurgitation; NYHA, New York Heart Association; OH, orthostatic hypotension; PDE5, phosphodiesterase 5; TR, tricuspid regurgitation; UTI, urinary tract infection.


Chronic HF Setting
(Low BP in HFrEF Naïve to therapy and undertreatment *)
1-Confirm low BP
2-Assess symptoms & severity
Determine etiology of Low BP
Consider decreasing or stopping
Anti-hypertensive Non class I HFrEF
Nitrates therapy
Antiarrhythmic
Neuro/psychiatric therapy
Drugs for erectile dysfunction
BP lowering BPH therapy (Alpha blockers)
3- Address possible Non--GDMT etiologies
Consider decreasing diuretics in hypo/euvolemic patients
Persistent low BP
Naïve to Therapy
HFrEF already treated
Asymptomatic/Low BP with mild symptoms
Low BP with major symptoms **
Asymptomatic/Low BP with mild symptoms
Low BP with major Symptoms **
1. Initiate SGLT2i & MRA
2. Initiate low dose ARNI/ ACEI or BB† (depending on clinical condition‡§)
3. Initiate the remaining drug
4-Uptitrate therapy¥§¶
Refer to HF specialist /Advanced HF program for evaluation
DO NOT Down titrate or Stop GDMT
Initiate GDMT down-titration process
It is advisable to consider the following :1-Treat bradycardia 2-Apply Stockings 3-Exercise 4-Space needed medications
It is advisable in specific conditions to consider :
CRT in LBBB QRSd>130ms or RBBB QRSd>150ms
TEER/TAVR in severe functional MR/TR or aortic Stenosis

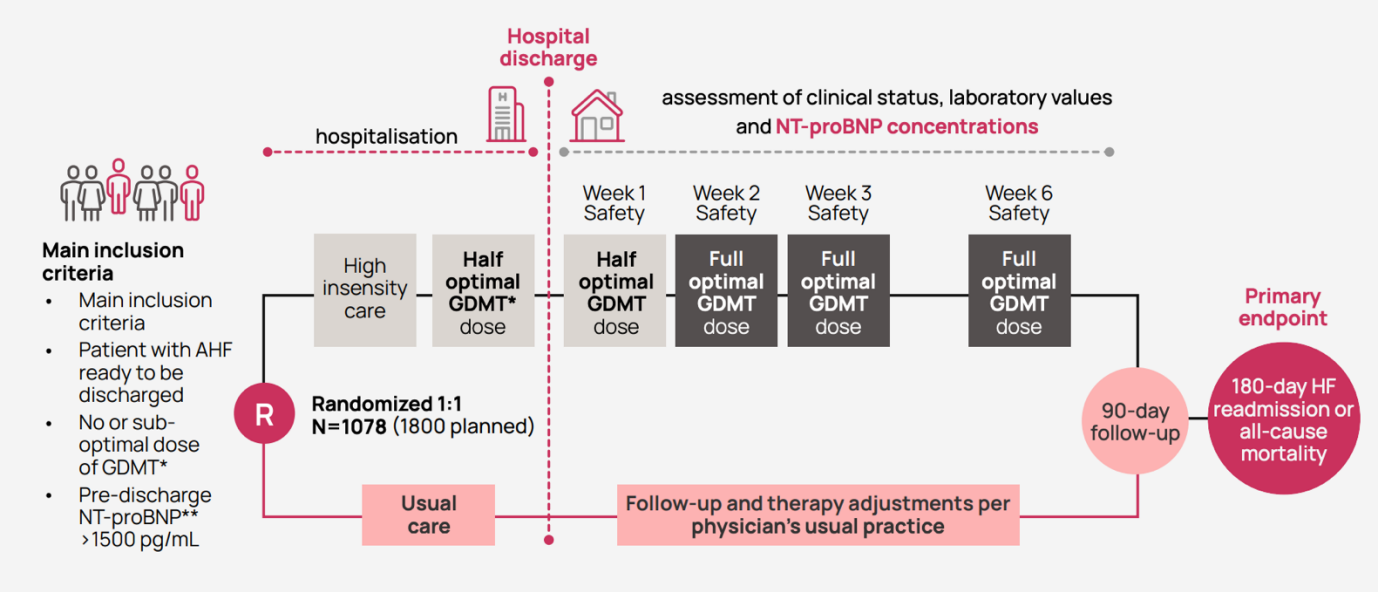

Symptomatic Low BP on Optimal or Suboptimal Therapy (after excluding concurring causes)
eGFR<30ml/m2 Reduce: 1-RASi 2-MRA
K>5.0mEq/l Reduce: 1-MRA 2-RASi
HR<60bpm;Reduce or Stop: 1-Ivabradine 2-BB 3.Consider pacing (CRT)
History of severe arrhythmias*: 1-Decrease RASi 2-Decrease MRA
If HR >70; Reduce 1-ACEi/ARB/ARNi 2-Reduce MRA
No specific clinical profile 1-Decrease RASi or BB
Maintain SGLT2i (very limited BP effect)
Persistent low BP with major symptoms: Refer to HF Team for advanced therapy
• Replace carvedilol by metoprolol or Bisoprolol
• If ARNI not tolerated, replace with low dose ACEi/ARB
If BP improves
Reinitiation Phase
eGFR<30ml/m2 & HR<60
eGFR<30ml/m2 & HR>60
eGFR>30ml/m2 & HR<60
eGFR>30ml/m2 & HR>60
1.Add SGLT2 I if Not Already on (eGFR>20 ml/m2)
BB Up titrate if HR>50
Reinitiate BB OR Up titrate
Initiate MRA or Optimize(if already on suboptimal dose)
Initiate ACEi/ARB/ARNi OR Up titrate ACEI/ARB/ARN
BB Up titrate if HR>50
Reinitiate BB OR Up titrate
Initiate ACEi/ARB/ARNi OR Up titrate ACEI/ARB/ARN
It is advisable to consider the following :1-Treat bradycardia 2-Apply Stockings 3-Exercise 4-Space needed medications
It is advisable in specific conditions to consider :
CRT in LBBB QRS>130ms or RBBB QRS>150ms
TEER/TAVR in severe functional MR ,TR or aortic stenosis


Act on: (Table 6S)
- Reversible non-HF causes of low BP
- Stop non-HF GDMT drugs
SBP<80 mmHg or symptomatic low BP *
Persistent low BP**
Cardiogenic shock
Refer to ESC HF guidelines
Low BP with major symptom /SBP<80mmHg
GDMT down-titration process (Figure 3)
GDMT re-optimization process (Figure 3)
Asymptomatic/Low BP with mild symptom
DO NOT Down titrate or Stop GDMT
May Address patient-specific conditions: (Figure 1S)
BBB → CRT
MR/TR → TEER
AS → TAVR
Persistent SBP<80mmHg or low BP with major symptoms
Refer to HF Specialist /Advanced HF center(program)

GDMT with low blood pressure patient

- Asymptomatic or mildly symptomatic low BP **should not be** a reason for GDMT reduction or cessation
- Reduction or cessation of one or more GDMT is advisable in case of systolic BP <80mmHg or low BP with relevant symptoms
- In chronic HF always evaluate symptoms of hypotension/orthostatic hypotension
- In acute HF always assess organ perfusion (shock or pre-shock)
- **SGLT2is and MRAs** have the **least effect** on BP and in low BP groups they may increase BP

Safety, tolerability, and efficacy of up-titration of guideline-directed medical therapies for acute heart failure (STR NG-HF): a multinational, open-label, randomized, trial



High-intensity care ; Up-titration of GDMT (B blockers, ACEIs/ARBs/ARNI, MRA) to ≥ 50% of recommended dose at discharge and up-titration to 100% of recommended doses within 2 weeks of discharge and 4 scheduled outpatient visits over the 2 months after discharge that closely monitored clinical status, laboratory values, and NT-proBNP concentrations.
Usual care ; followed usual local practice.

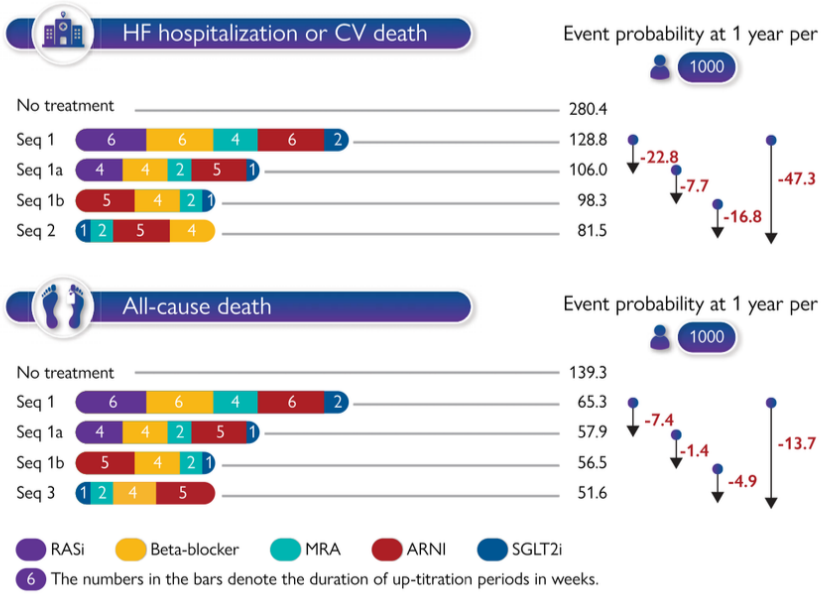
STRONG-HF

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

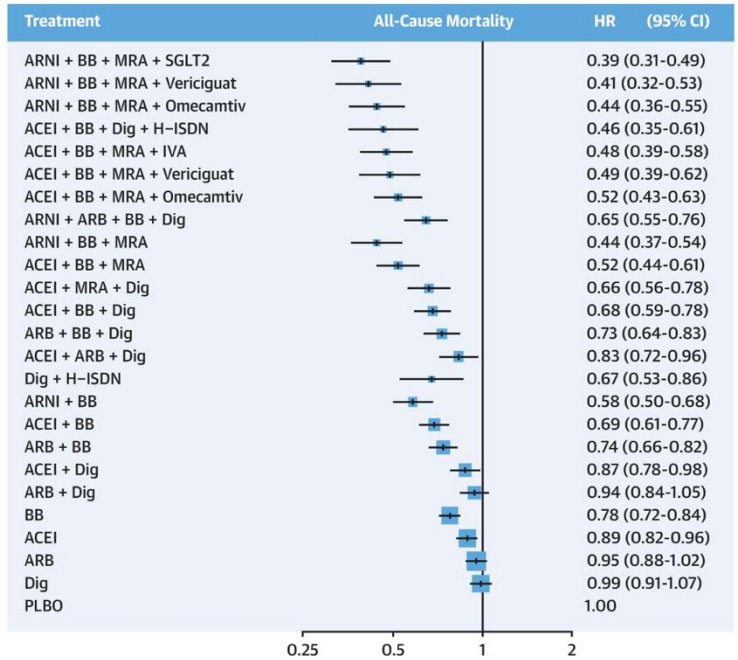
CV (cardiovascular) death	HF readmission	All-cause death
26% lower	**44% lower**	**16% lower**

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

Strategies to rapid achievement of 4-pillars GDMT safely



CENTRAL ILLUSTRATION: Relative Risk Reduction of Different Pharmacological Treatment Combinations for Heart Failure



European Heart Journal (2022) 43, 2573–2587

Tromp J *et al. JACC Heart Fail.* 2022;10:73.

THANK YOU