

What's New on Treatment Guidelines for Heart Failure



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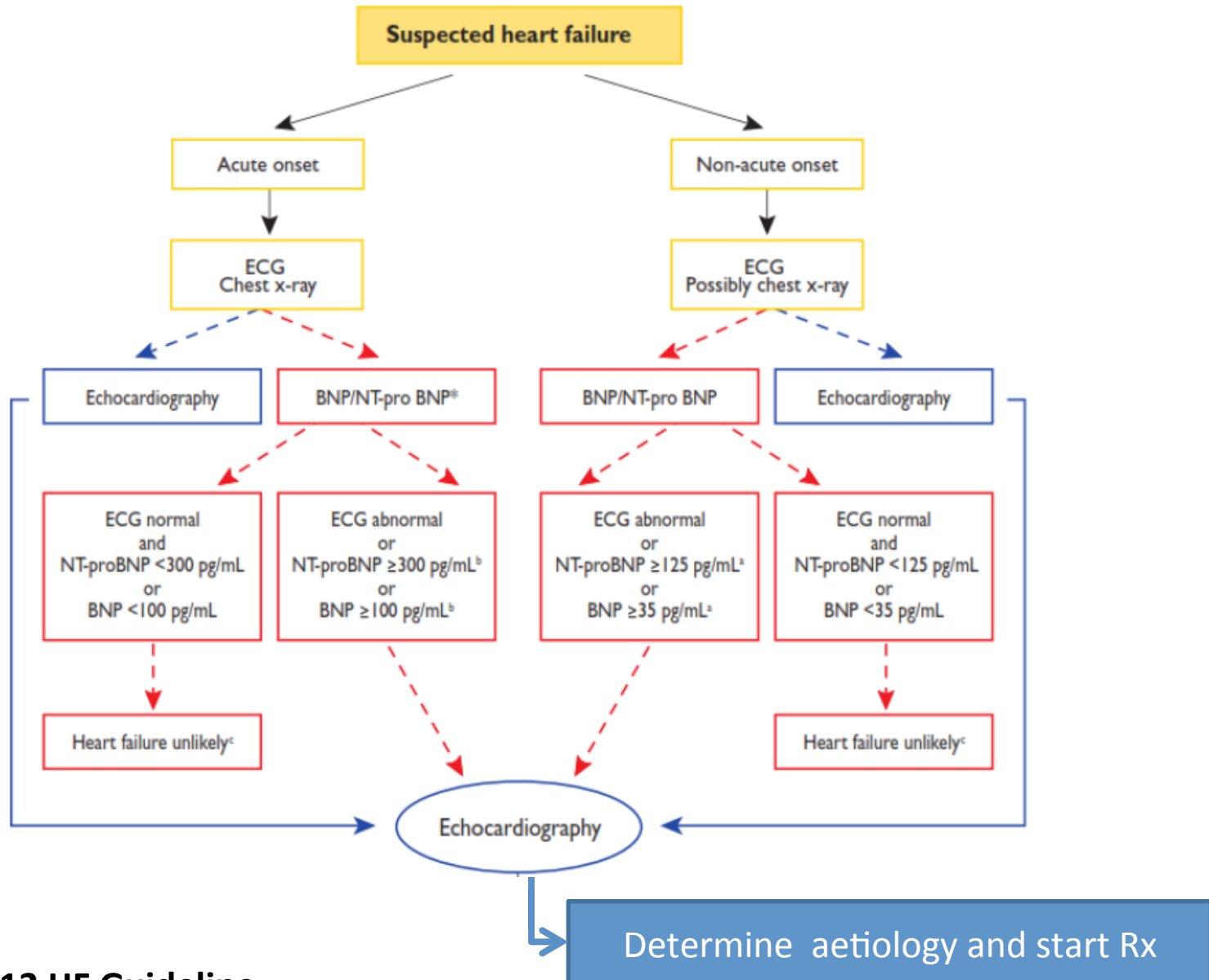
Outlines

- **Diagnosis of HF**
- **Pharmacological Treatment of HF**
- **Non-pharmacological Treatment of HF**
- **Management of AF in HF**

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Diagnosis of Heart Failure



Diagnosis of Heart Failure

What is new?

- **Biomarkers: MR-pro ANP (BACH)**
- **Echo- 3D, strain imaging**
- **CT coronary angiogram**
- **Cardiac MRI**
- **Genetic testing**

Definitions of Heart Failure

| Classification | EF (%) | Description |
|--|--------|--|
| I. Heart failure with reduced ejection fraction (HFrEF) | ≤40 | Also referred to as systolic HF. Randomized clinical trials have mainly enrolled patients with HFrEF, and it is only in these patients that efficacious therapies have been demonstrated to date. |
| II. Heart failure with preserved ejection fraction (HFpEF) | ≥50 | Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified. |
| a. HFpEF, borderline | 41-49 | These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF |
| b. HFpEF, improved | >40 | It has been recognized that a subset of patients with HFpEF previously had HFrEF. These patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF. Further research is needed to better characterize these patients. |

Diagnosis of Heart Failure

Definition:

Heart failure (HF) can be defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressure (or only at the expense of increased filling pressure)

Diagnosis of HFrEF:

1. Symptoms typical of HF
2. Signs typical of HF
3. Reduced LVEF

| Symptoms | Signs |
|--|------------------------------------|
| <i>Typical</i> | <i>More specific</i> |
| Breathlessness | Elevated jugular venous pressure |
| Orthopnoea | Hepatojugular reflux |
| Paroxysmal nocturnal dyspnoea | Third heart sound (gallop rhythm) |
| Reduced exercise tolerance | Laterally displaced apical impulse |
| Fatigue, tiredness, increased time to recover after exercise | Cardiac murmur |
| Ankle swelling | |

Diagnosis of Heart Failure

Diagnosis of HFpEF:

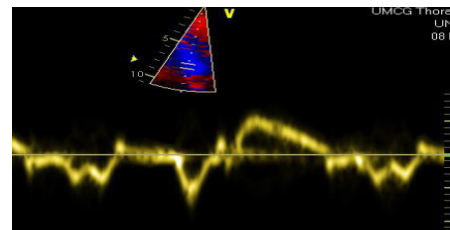
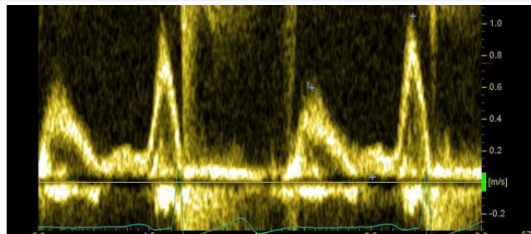
1. Symptoms typical of HF

2. Signs typical of HF

3. Normal or mildly reduced LVEF and LV not dilated

4. Relevant structural heart disease:

- LV hypertrophy: LV mass index $>95\text{g}/\text{m}^2$ (F) or $>115\text{g}/\text{m}^2$ (M)
- LA enlargement: $>34\text{ mL}/\text{m}^2$
- Diastolic dysfunction: Mitral inflow E/A ratio, tissue Doppler velocities (e'), or E/ e' ratio



Diagnosis of Heart Failure

Clinical
evidence of HF

+

EF \geq 45-50%+
LVEDI $<$ 97 ml/m² or LVEDDI $<$ 29 mm²

+

**Invasive
Hemodynamic :**
LVEDP $>$ 16 mmHg
or
Tau $>$ 48 msec
or
B $>$ 0.27
or
mPCWP $>$ 12 mmHg

or

**Structural
abnormalities :**
LAVI $>$ 34 mL/m²
or
LV mass index $>$ 95 g/m²
(F) or $>$ 115 g/m² (M)

or

**Functional
abnormalities:**
E/e' avg $>$ 8
or
e' average (lateral-
septal) $<$ 9 cm/s

| ACCF/AHA Stages of HF | | NYHA Functional Classification | |
|-----------------------|--|--------------------------------|---|
| A | At high risk for HF but without structural heart disease or symptoms of HF | None | |
| B | Structural heart disease but without signs or symptoms of HF | I | No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF. |
| C | Structural heart disease with prior or current symptoms of HF | I | No limitation of physical activity. Ordinary physical activity does not cause symptoms of HF. |
| | | II | Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of HF |
| | | III | Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of HF. |
| | | IV | Unable to carry on any physical activity without symptoms of HF, or symptoms of HF at rest. |
| D | Refractory HF requiring specialized interventions | | |

Outlines

- Diagnosis of HF
- **Pharmacological Treatment of HF**
- Non-pharmacological Treatment of HF
- Management of AF in HF

Pharmacological Rx of HF

Diuretics to relieve symptoms/signs of congestion^a

+

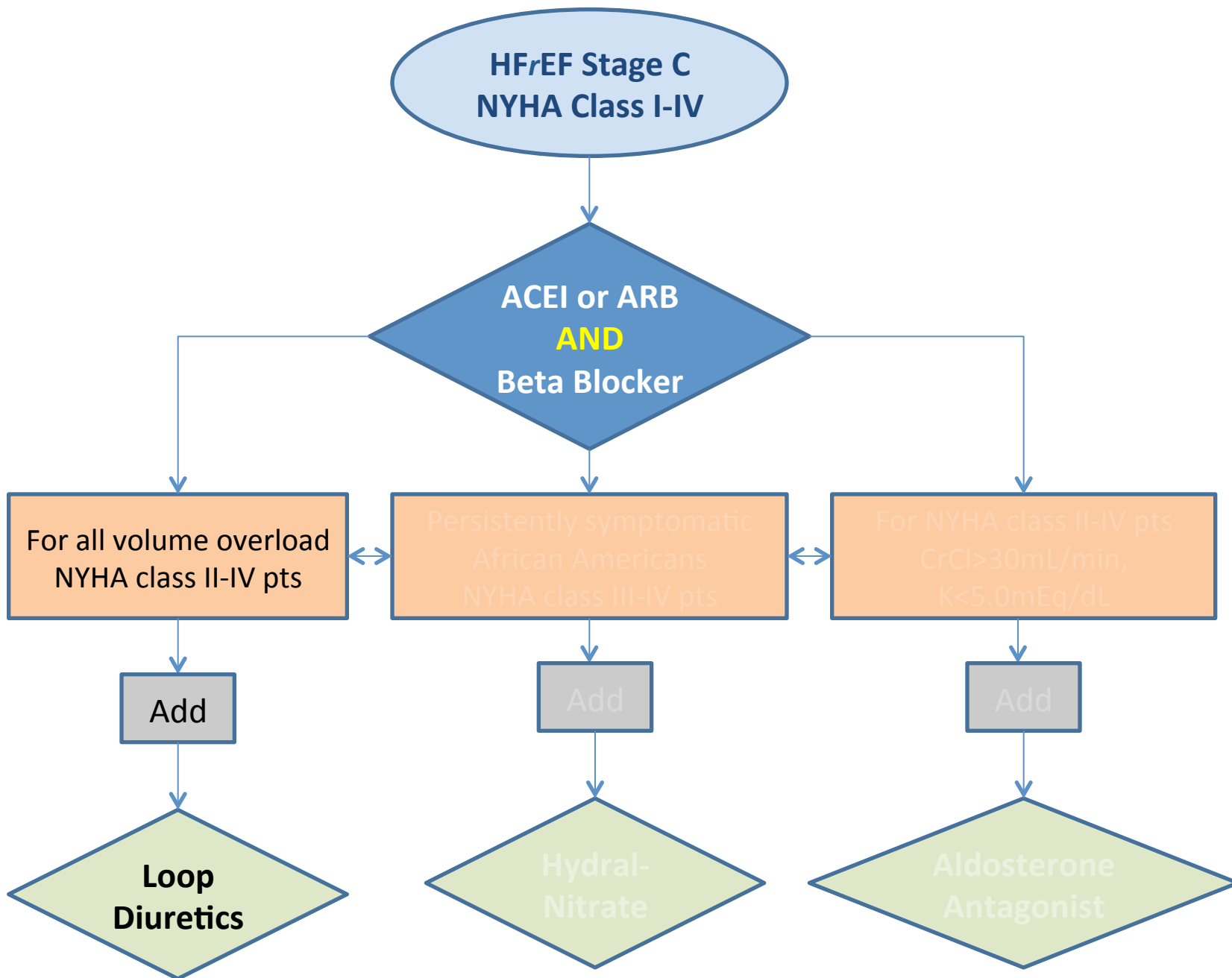
ACE inhibitor (or ARB if not tolerated)^b

ADD a beta-blocker^b

Still NYHA class II–IV?

Yes

No^c



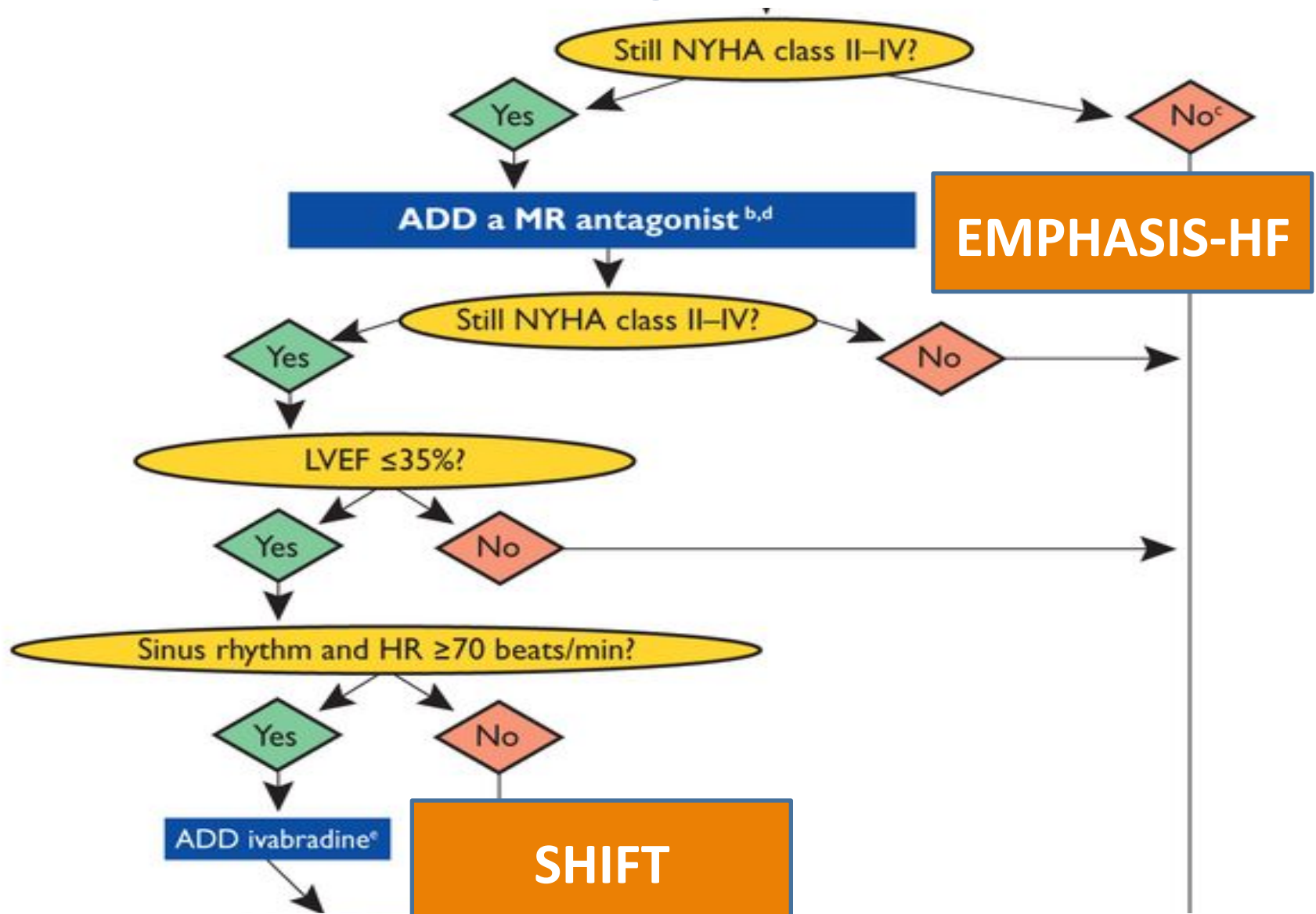
Pharmacological Rx of HF

| Recommendations | Class ^a | Level ^b |
|--|--------------------|--------------------|
| An ACE inhibitor is recommended, in addition to a beta-blocker, for all patients with an EF \leq 40% to reduce the risk of HF hospitalization and the risk of premature death. | I | A |
| A beta-blocker is recommended, in addition to an ACE inhibitor (or ARB if ACE inhibitor not tolerated), for all patients with an EF \leq 40% to reduce the risk of HF hospitalization and the risk of premature death. | I | A |

| | Starting dose (mg) | Target dose (mg) |
|------------------------------|--------------------|------------------|
| ACE inhibitor | | |
| Captopril [†] | 6.25 t.i.d. | 50 t.i.d. |
| Enalapril | 2.5 b.i.d. | 10–20 b.i.d. |
| Lisinopril [†] | 2.5–5.0 o.d. | 20–35 o.d. |
| Ramipril | 2.5 o.d. | 5 b.i.d. |
| Trandolapril [†] | 0.5 o.d. | 4 o.d. |
| Beta-blocker | | |
| Bisoprolol | 1.25 o.d. | 10 o.d. |
| Carvedilol | 3.125 b.i.d. | 25–50 b.i.d. |
| Metoprolol succinate (CR/XL) | 12.5/25 o.d. | 200 o.d. |
| Nebivolol [†] | 1.25 o.d. | 10 o.d. |
| ARB | | |
| Candesartan | 4 or 8 o.d. | 32 o.d. |
| Valsartan | 40 b.i.d. | 160 b.i.d. |
| Losartan ^{b,c} | 50 o.d. | 150 o.d. |

All patients with HFrEF should start on ACEI (or ARB)
AND Beta-blocker unless contraindicated

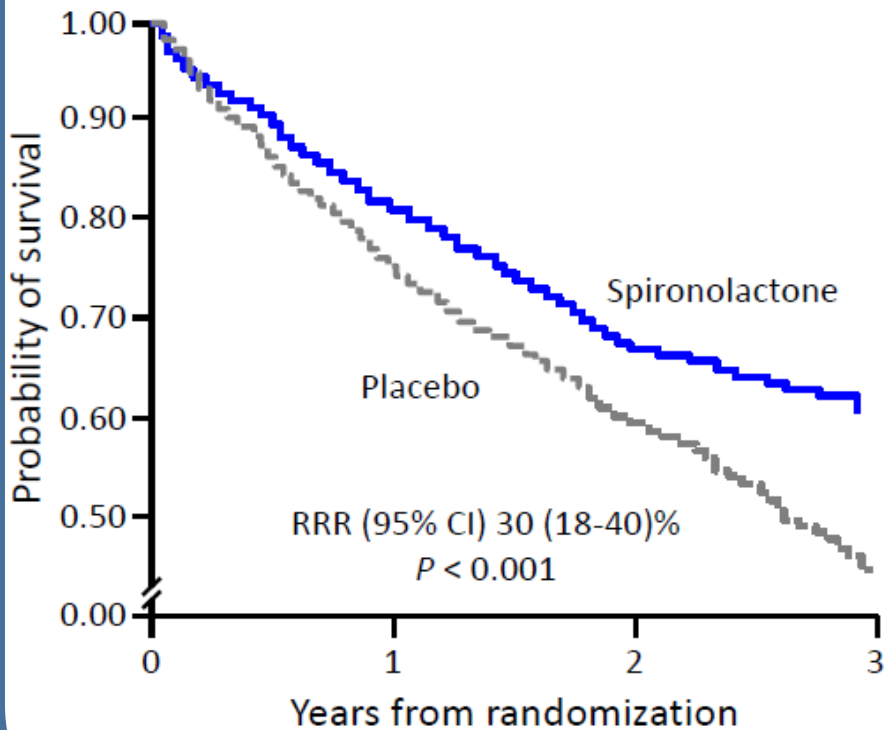
Pharmacological Rx of HF



Pharmacological Rx of HF

RALES

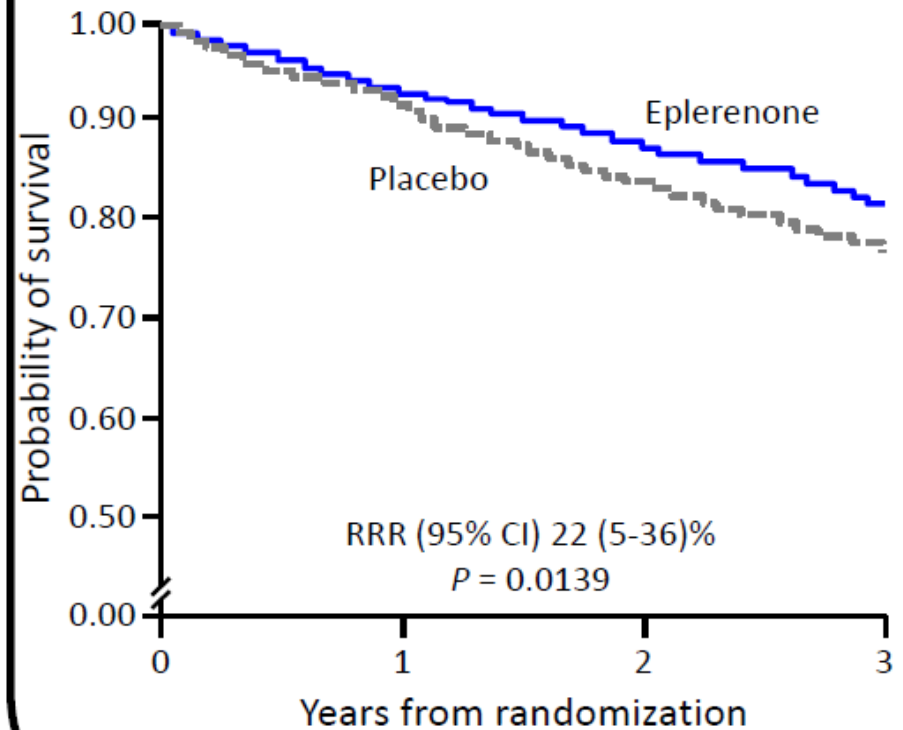
1663 NYHA class III/IV patients
95% ACE-I/10% β -blocker



Pitt B, et al. *N Engl J Med.* 1999;341:709-717.

EMPHASIS-HF

2737 NYHA class II patients
93% ACE-I or ARB/87% β -blocker



Zannad F, et al. *N Engl J Med.* 2010;364:11-21.

Pharmacological Rx of HF

An MRA is recommended for all patients with persisting symptoms (NYHA class II–IV) and an EF \leq 35%, despite treatment with an ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated) and a beta-blocker, to reduce the risk of HF hospitalization and the risk of premature death.

I **A**

| MRA | | |
|--------------|---------|------------|
| Eplerenone | 25 o.d. | 50 o.d. |
| Spirolactone | 25 o.d. | 25–50 o.d. |

Practical guidance

Cautions:

- Significant hyperK (K $>$ 5.0 mmol/L)
- Significant renal dysfunction (Cr $>$ 221 μ mol/L or eGFR $<$ 30ml/min)

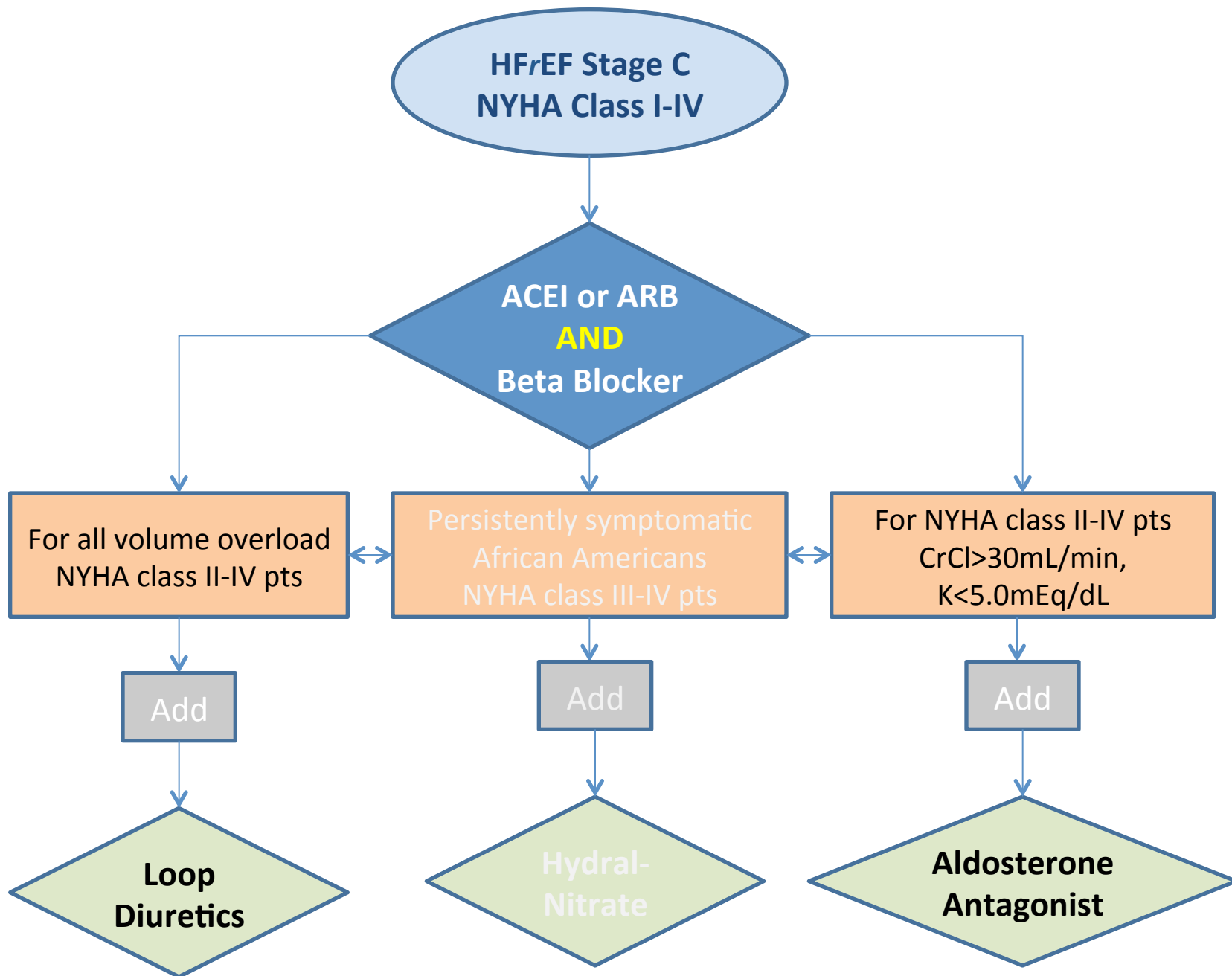
Drug Interactions:

- K supplement/sparing diuretic
- ACEI/ARB
- Trimethoprim/trimethoprim-sulfamethoxazole
- Low-salt substitutes with high K

Contraindications:

- Eplerenone: strong CYP3A4 inhibitors. Eg ketoconazole

- Start with low dose and dose up-titration after 4-8 weeks
- Check RFT before and 4 weeks after starting/increasing dose
- Half dose if Cr $>$ 221 μ mol/L or eGFR $<$ 30ml/min or K $>$ 5.5mmol/L
- Stop if if Cr $>$ 310 μ mol/L or eGFR $<$ 20ml/min or K $>$ 6.0mmol/L

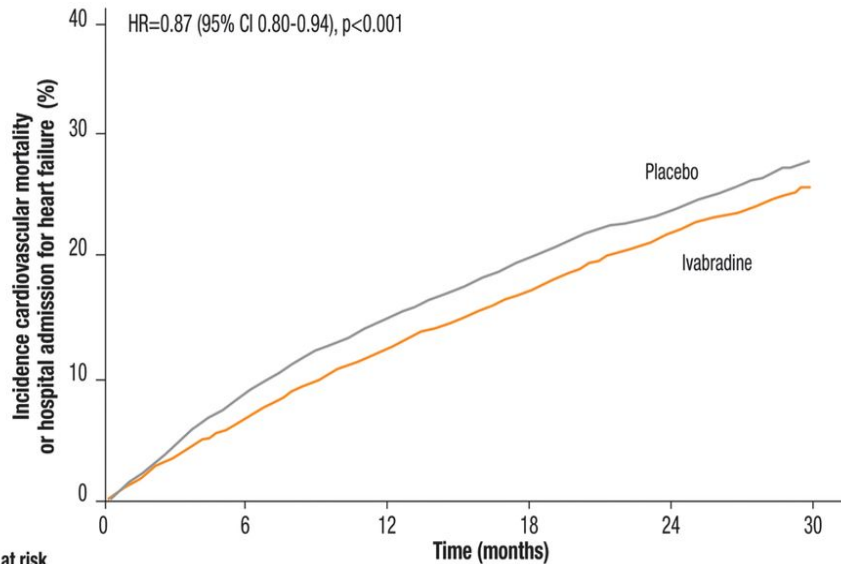


BEAUTIFUL and SHIFT

Composite endpoint of CV mortality or HF hospital

Composite endpoint of CV mortality, HF hospital admission or hospital admission for MI

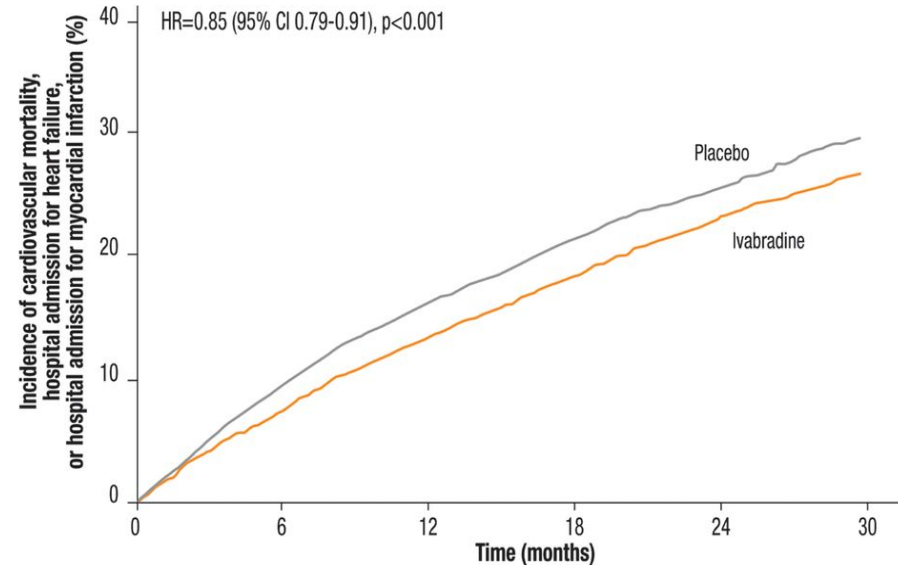
A



Number at risk

| | | | | | | |
|------------|------|------|------|------|------|-----|
| Ivabradine | 5940 | 5451 | 4881 | 3610 | 1789 | 469 |
| Placebo | 5957 | 5348 | 4754 | 3497 | 1682 | 457 |

B



Number at risk

| | | | | | | |
|------------|------|------|------|------|------|-----|
| Ivabradine | 5940 | 5420 | 4838 | 3564 | 1765 | 460 |
| Placebo | 5957 | 5317 | 4690 | 3438 | 1651 | 447 |

Pharmacological Rx of HF

Agents with less certain benefit

| Ivabradine | | |
|--|-----|---|
| Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF \leq 35%, a heart rate remaining \geq 70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB). ^c | IIa | B |
| May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF $<$ 35% and a heart rate \geq 70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB). ^c | IIb | C |

Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with a heart rate remaining \geq 70 beats per minute and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB) and an MRA (or ARB).

Caveat about EMA labelling: \geq 75 b.p.m.