Therapy for Acute Heart Failure: Time for Change ?!

ESC Guidelines for the management of acute heart failure

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Heart Failure ESC guidelines: two decades of history

European Heart Journal (2012) **33**, 1787–1847
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ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

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Committee for Practice Guidelines

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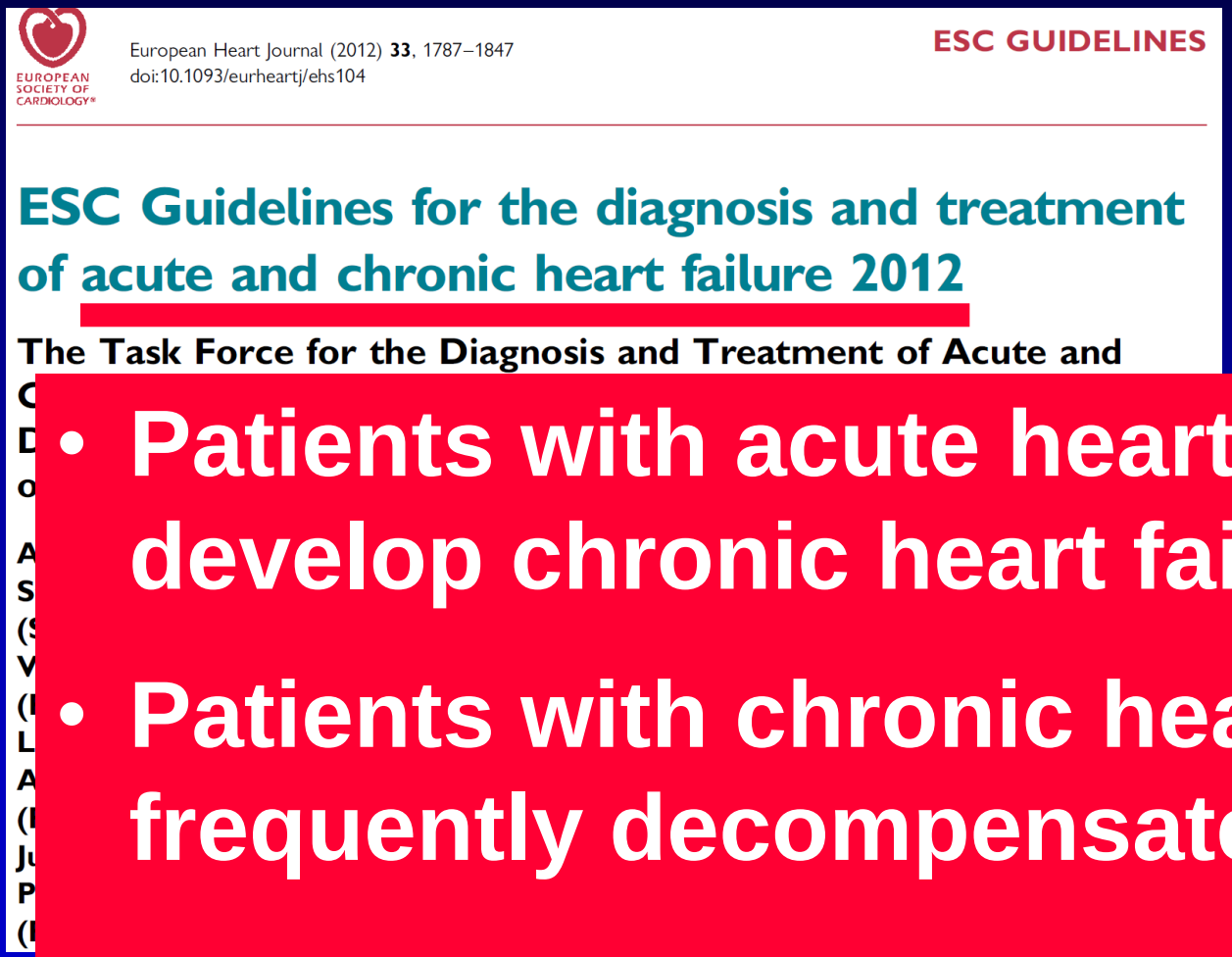

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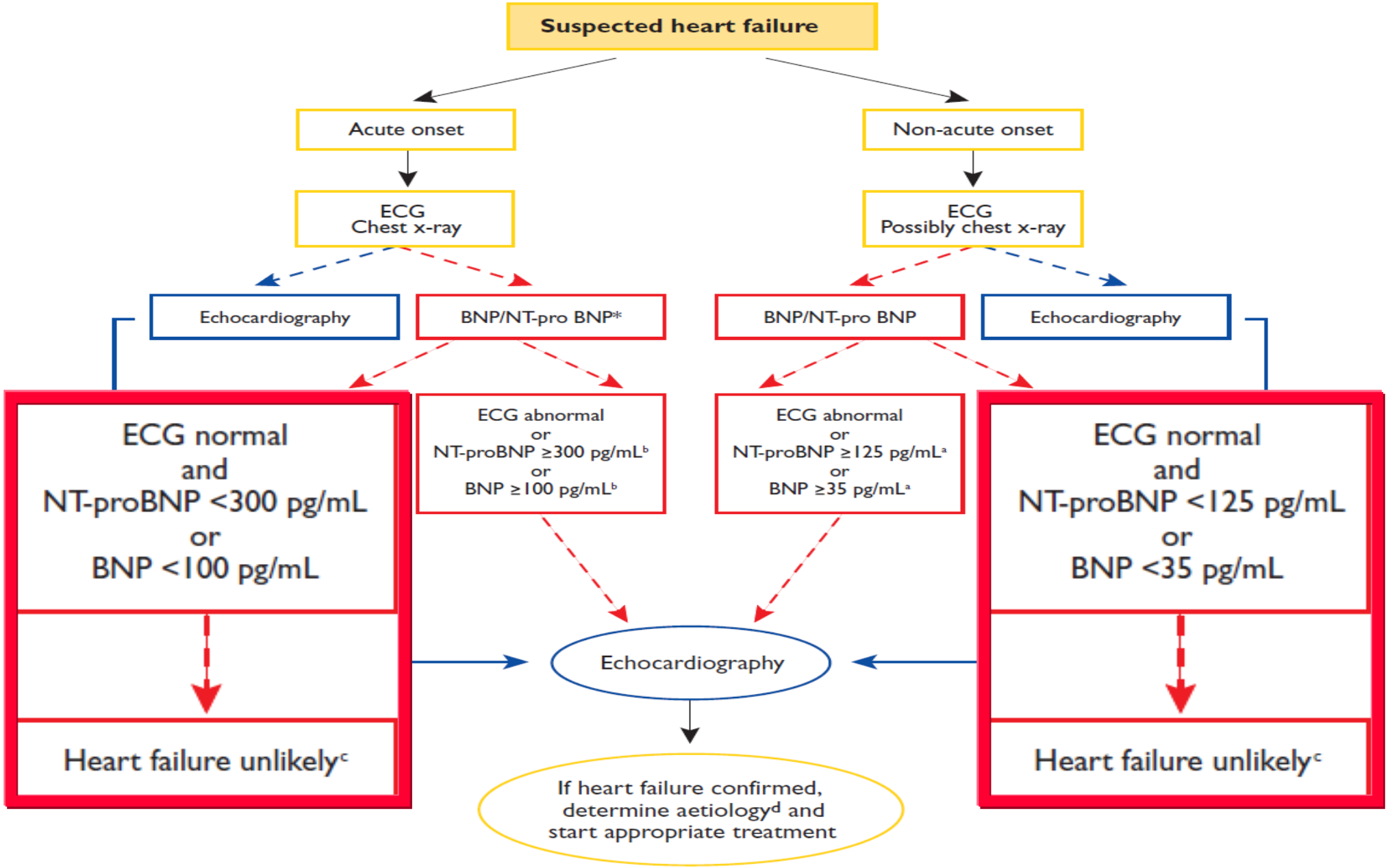
- **Patients with acute heart failure frequently develop chronic heart failure**
- **Patients with chronic heart failure frequently decompensate acutely**

K. Dickstein & P.A. Poole-Wilson, ESC HF Guidelines 2008

Diagnostic flowchart for patients with suspected heart failure



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Goals of Treatment in Acute Heart Failure

- Treat symptoms
- Restore oxygenation
- Improve organ perfusion & haemodynamics
- Limit cardiac/renal damage
- Prevent thrombo-embolism
- Minimize ICU length of stay

Immediate (ED/ICU/CCU)

Phases in the AHF management

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Need for paradigm shifting in acute heart failure:
short-term intervention and long-term goals (?)

What is needed ?

- **Targeted-approach**
  specific types of AHF, different pathophysiologies & therapies(?)
- **End-organ protection**
- **Early administration of therapy**
  „the earlier the better" (?)

Need for paradigm shifting in acute heart failure:
short-term intervention and long-term goals (?)

What is needed ?

→ prevention of tissue / organ damage caused by hypoxia, acidosis, under-perfusion;

→ phase with severe symptoms (high chance to be effective);

→ early clinical stabilization & chance to introduce other disease-modifying therapies;

→ no confounding effects of multiple concomitant therapies;

- **Early administration of therapy**

„the earlier the better" (?)

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- Prevent early readmission
- Improve symptoms, quality of life and survival

Long-term and pre-discharge management

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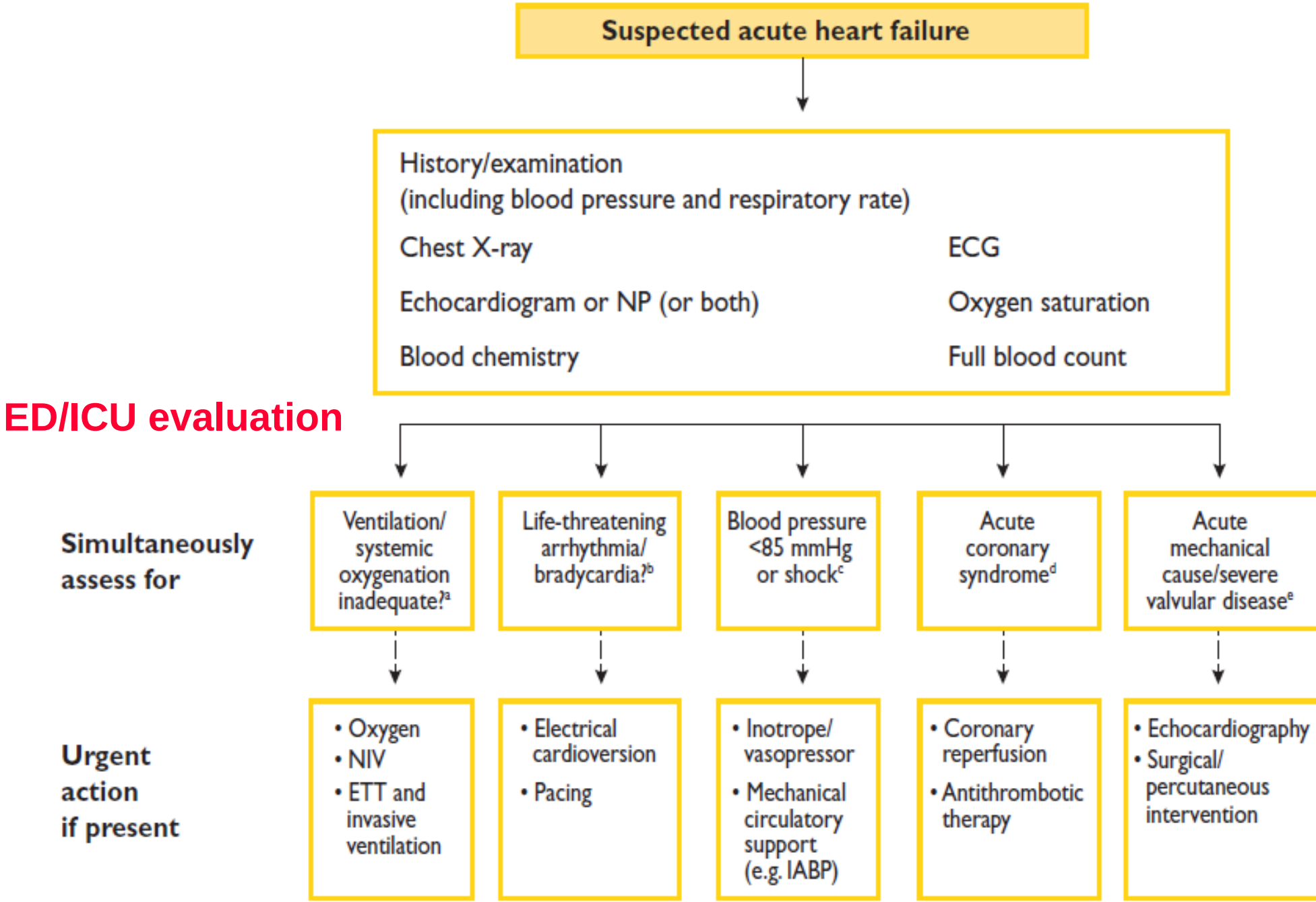

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Acute Heart Failure – in hospital management

Pharmacological therapy

1. Acute management

- Oxygen
- Diuretics
- Opiates
- Vasodilators
- Nesiritide
- Inotropes
- Vasopressors

2. After stabilization

- ACE inhibitor / ARB
- Beta-blocker
- Mineralocorticoid receptor antagonist
- Digoxin

Non-pharmacological therapy

1. Sodium and fluid intake restriction

2. Ventilation

- non-invasive
- invasive

3. **Mechanical circulatory support**

- IABP
- VAD

4. **Ultrafiltration**

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EURO*observational Research Programme*
Euro Heart Surveys and Registries

AHFS: acute treatment

5118 pts
enrolled by 136 centres
period: Oct 2009-May 2010

3226 (63%)
outpatients with CHF

1892 (37%)
in-hospital patients with AHFS

	Total
Furosemide, %	78.9
Furosemide *median [IQR], daily dosage*	60 [40-100]
IV diuretics, %	84.6
IV nitrates, %	18.5
Inotropes, %	10.5
Dobutamine, %	4.6
Levosimendan, %	2.4
Other, %	3.5

Courtesy of A. Maggioni

Initial, short-term therapies (hours-days)

Target	„Traditional" therapeutic approach	**Effects on long-term outcome**
Alleviate congestion	i.v. diuretics	**?** **May be detrimental**
Reduce ↑ LV filling pressure	i.v. nitrates	**?** **Potentially favourable**
Hypoperfusion Poor cardiac performance	i.v. inotropes	**Detrimental**

Dissociation between symptomatic improvement, clinical stabilisation & favourable long-term outcome

Modified from Pang PS et al. Eur Heart J 2010;31:784-93

Interventions to Relieve Congestion

- Sodium & fluid restriction
- **Diuretics***
- Vasodilators
- Ultrafiltration / dialysis
  - BNP (nesiritide)
  - Vasopressin antagonists

Patients with pulmonary congestion/oedema without shock		
An i.v. loop diuretic is recommended to improve breathlessness and relieve congestion. Symptoms, urine output, renal function, and electrolytes should be monitored regularly during use of i.v. diuretic.	I	B

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Practical considerations in treatment of heart failure with loop diuretics

Insufficient response or diuretic resistance

- Check compliance& fluid intake
- Increase dose of diuretic
- Consider switching from furosemide to bumetanide or torasemide
- Add aldosterone antagonist
- Combine loop diuretic and thiazide/metolazone
- Consider short-term i.v. infusion of loop diuretic

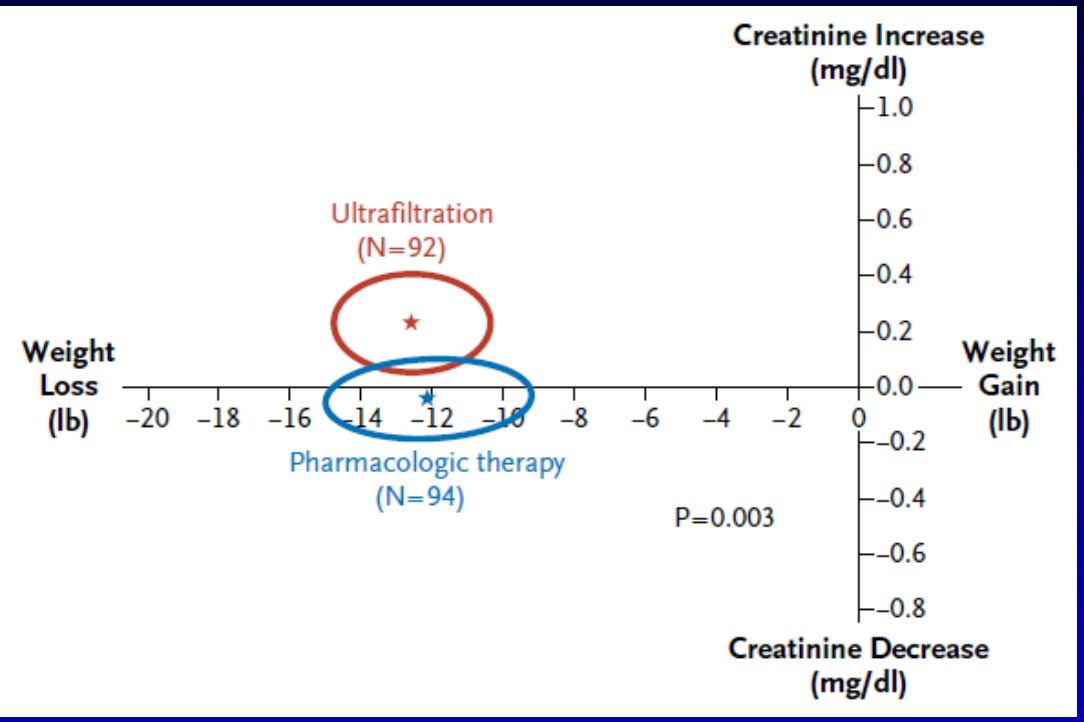
Renal failure (excessive rise in urea/BUN and/or creatinine)

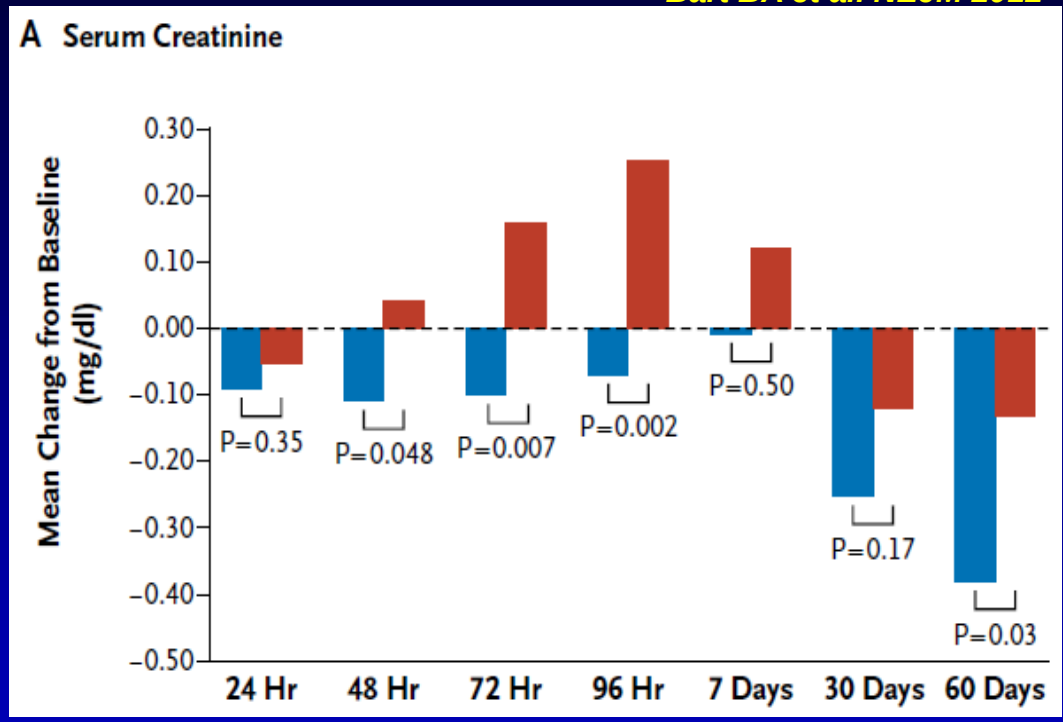
- check for hypovolaemia/dehydration
- Exclude use of other nephrotoxic agents, e.g. NSAIDs, trimethoprim
- Withhold aldosterone antagonist
- If using concomitant loop and thiazide diuretic stop thiazides
- Consider reducing dose of ACEi/ARB
- Consider ultrafiltration

ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008

Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome – CARRESS-HF Results

Bart BA et al. NEJM 2012





Conclusion:… the use of a stepped pharmacologic-therapy algorithm was superior to a strategy of ultrafiltration for the preservation of renal function at 96 hours, with a similar amount of weight loss with the two approaches. Ultrafiltration was associated with a higher rate of adverse events.

Reconsidering Ultrafiltration in the Acute Cardiorenal Syndrome

W.H. Wilson Tang, M.D.

NEJM 2012

Fluid redistribution	Fluid accumulation
"Vascular" Failure	"Cardiac" Failure
• High blood pressure	• Normal blood pressure
• Rapid worsening	• Gradual worsening (days)
• Pulmonary congestion	• Systemic rather than pulmonary congestion
• PCWP acutely increased	• PCWP chronically high
• Rales: present	• Rales: may be absent
• Severe radiographic congestion	• Radiographic congestion may be absent
• Weight gain minimal	• Weight gain significant (edema)
• LVEF relatively preserved	• LVEF usually low
• Response to therapy: relatively rapid	• Response to therapy: continue to have systemic congestion in spite of the initial symptomatic response

Gheorghiade M et al.; Am J Cardiol 2005;96[suppl]:11G–17

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Gheorghiade M et al.; Am J Cardiol 2005;96[suppl]:11G–17

Patients with pulmonary congestion/oedema without shock		
An i.v. infusion of a nitrate should be considered in patients with pulmonary congestion/oedema and a systolic blood pressure >110 mmHg, who do not have severe mitral or aortic stenosis, to reduce pulmonary capillary wedge pressure and systemic vascular resistance. Nitrates may also relieve dyspnoea and congestion. Symptoms and blood pressure should be monitored frequently during administration of i.v. nitrates.	IIa	B

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Limitations of Inotropic Agents

- **Tachyarrhythmias**
  - ↑ ventricular arrhythmias
  - ↑ ventricular rate in atrial fibrillation
- **Myocardial ischemia → progression of LV dysfunction?**
  - Hypotension / coronary hypoperfusion
  - ↑ myocardial VO_2 (contractility & HR)
- **Mechanisms**
  - ↑ cytoplasmic Ca^{2+}
  - Myocardial efficiency (work/VO_2)?
  - Vasodilation /hypotension

Courtesy M.Metra

Patients with hypotension, hypoperfusion or shock		
An i.v. infusion of an inotrope (e.g. dobutamine) should be considered in patients with hypotension (systolic blood pressure <85 mmHg) and/or hypoperfusion to increase cardiac output, increase blood pressure, and improve peripheral perfusion. The ECG should be monitored continuously because inotropic agents can cause arrhythmias and myocardial ischaemia.	IIa	C
An i.v. infusion of levosimendan (or a phosphodiesterase inhibitor) may be considered to reverse the effect of beta-blockade if beta-blockade is thought to be contributing to hypoperfusion. The ECG should be monitored continuously because inotropic agents can cause arrhythmias and myocardial ischaemia, and, as these agents are also vasodilators, blood pressure should be monitored carefully.	IIb	C
A vasopressor (e.g. dopamine or norepinephrine) may be considered in patients who have cardiogenic shock, despite treatment with an inotrope, to increase blood pressure and vital organ perfusion. The ECG should be monitored as these agents can cause arrhythmias and/or myocardial ischaemia. Intra-arterial blood pressure measurement should be considered.	IIb	C

Patients with pulmonary congestion/oedema without shock		
Inotropic agents are NOT recommended unless the patient is hypotensive (systolic blood pressure <85 mmHg), hypoperfused, or shocked because of safety concerns (atrial and ventricular arrhythmias, myocardial ischaemia, and death).	III	C

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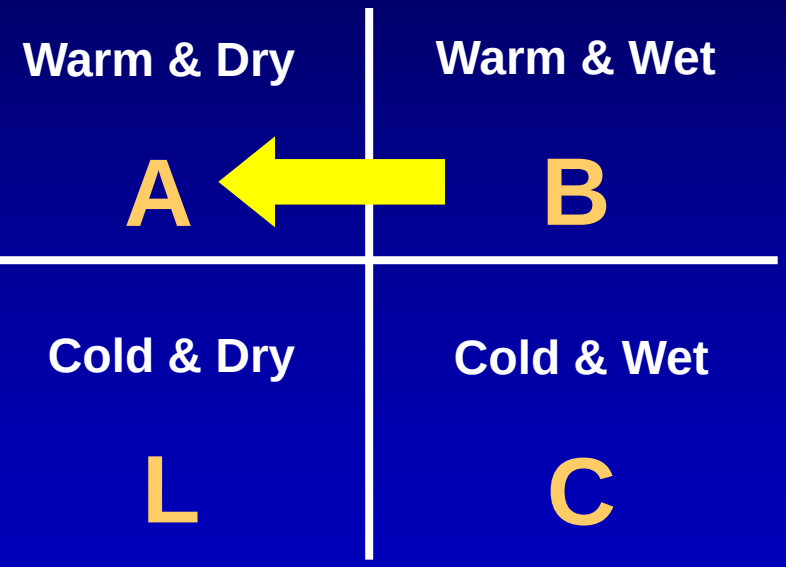
Assessment of hemodynamic profile: therapeutic implications

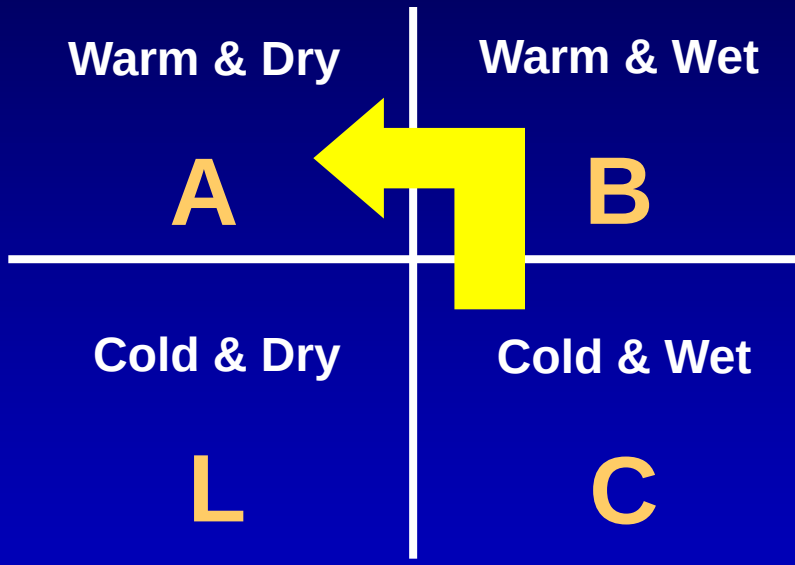
„dry-out”

- diuretics
- ultrafiltration



Vasodilators
- **nitroglycerin**
- **nesiritide**
- nitroprusside

„warm-up” & „dry-out”



Inotropes
- **dobutamine**
- **dopamine**
- levosimendan
- nitroprusside

Fluid retention or redistribution ?

Adapted from Stevenson LW, Eur J Heart Failure 2005;7:323

Invasive monitoring – for whom ?

Intra-arterial line

Insertion of an intra-arterial line should only be considered in patients with persistent HF and a **low systolic blood pressure** despite treatment.

Pulmonary artery catheterization

Right heart catheterization does not have a general role in the management of AHF, but may help in the treatment of a minority of selected patients.

Pulmonary artery catheterization **should only be considered** in patients:

(i) who are refractory to pharmacological treatment

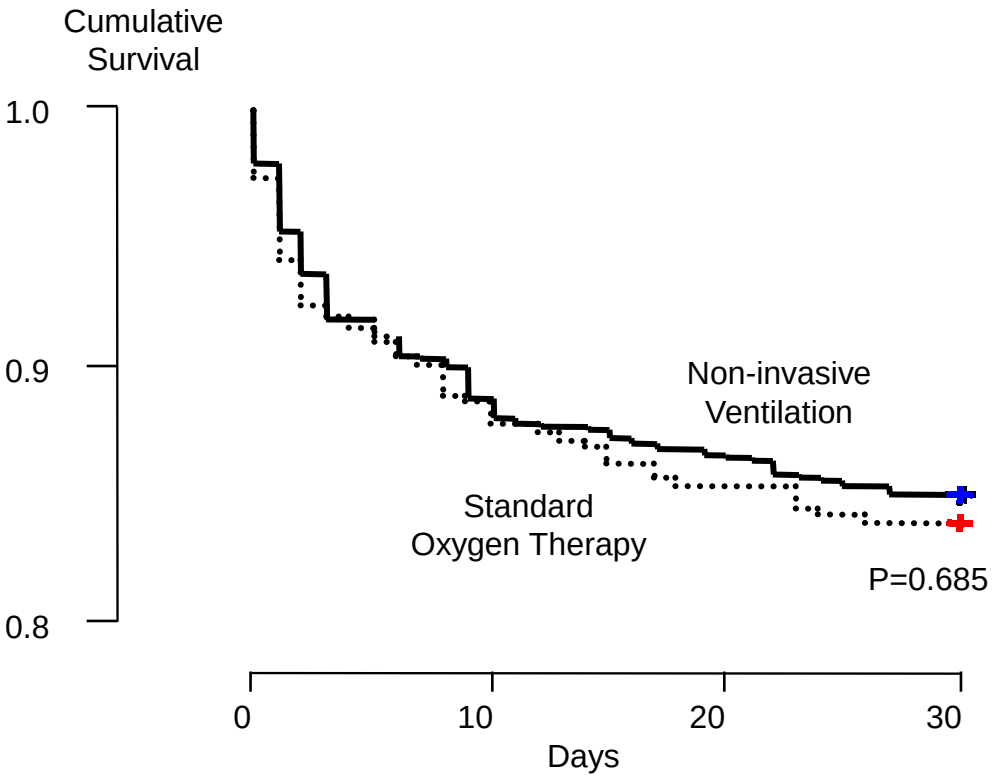
(ii) who are persistently hypotensive

(iii) in whom LV filling pressure is uncertain

(iv) who are being considered for cardiac surgery

3CPO study

Primary Outcome: *Mortality*
Standard Oxygen Therapy
versus
Non-invasive Ventilation



Non-invasive ventilation (e.g. CPAP) should be considered in **dyspnoeic patients with pulmonary oedema and a respiratory rate >20 breaths/min** to **improve breathlessness and reduce hypercapnia and acidosis**. Non-invasive ventilation can reduce blood pressure and should not generally be used in patients with a SBP<85 mmHg (and blood pressure should be monitored regularly when this treatment is used). (Class IIa , level B)

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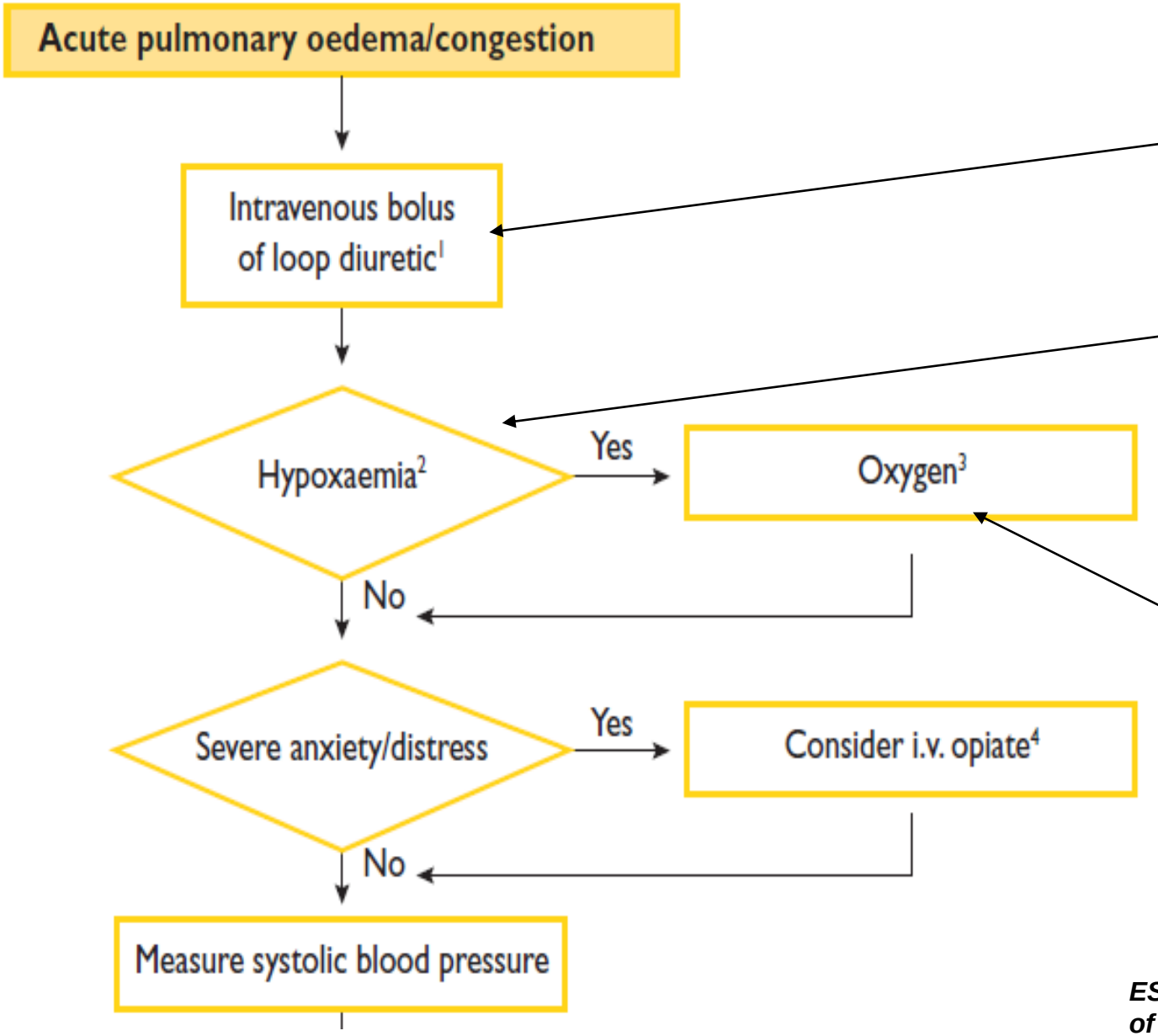
Algorithm for management of acute pulmonary oedema/congestion



[1] - In patients' already taking diuretic, 2.5 times existing oral dose recommended. Repeat as needed.

[2] - Pulse oximeter oxygen saturation <90% or PaO_2 <60 mmHg (<8.0 kPa).

[3] - Usually start with 40–60% oxygen, titrating to SpO_2 >90%; caution required in patients at risk of CO_2 retention.

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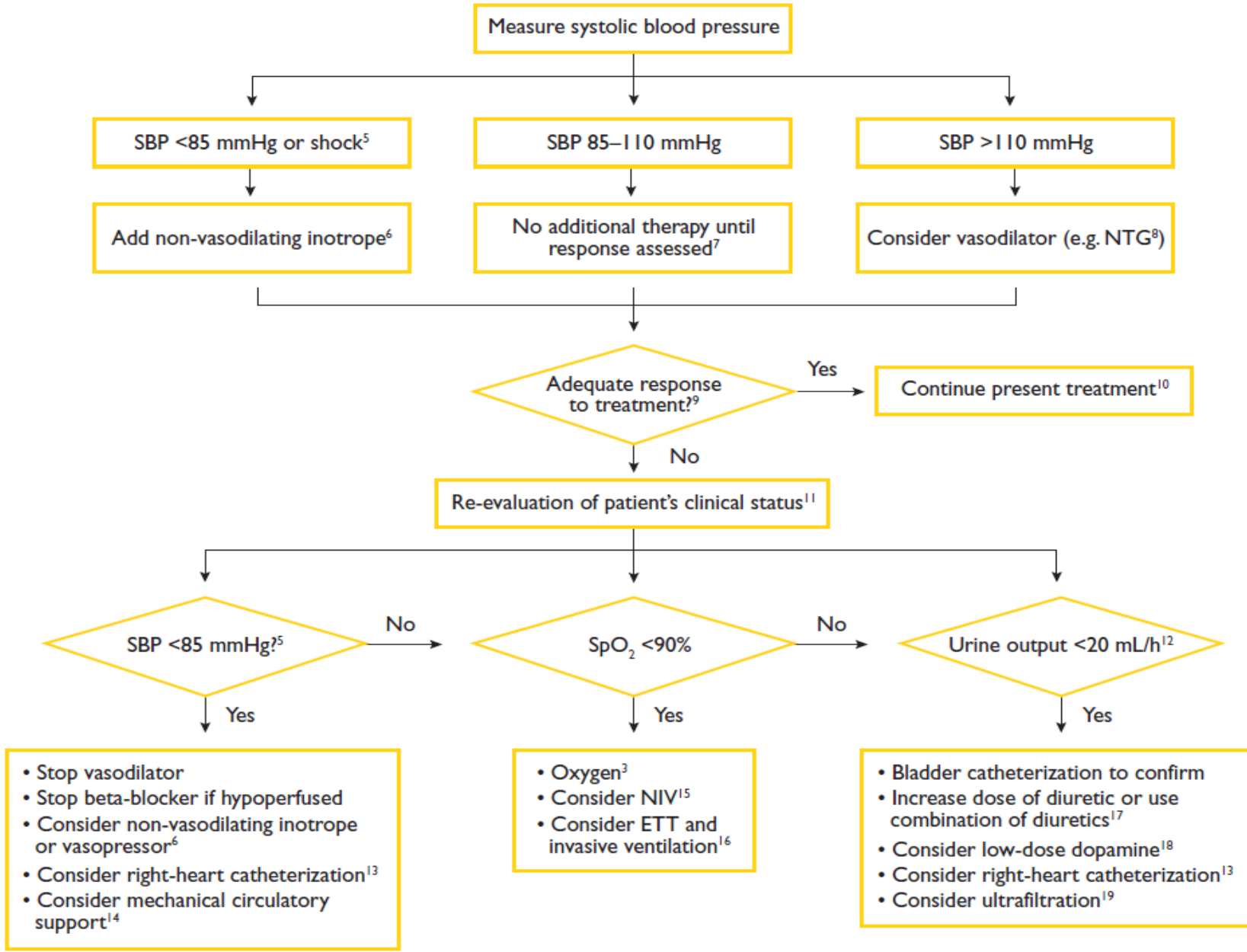

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AHF: management after stabilization

ACE inhibitor/angiotensin receptor blocker

In patients with reduced EF not already receiving an ACE inhibitor(or ARB), this treatment should be started as soon as possible, blood pressure and renal function permitting*.

Beta-blocker

In patients with reduced EF not already receiving a beta-blocker, this treatment should be started as soon as possible after stabilization, blood pressure and heart rate permitting*. Beta-blocker treatment may be continued in many patients during an episode of decompensation

Mineralocorticoid receptor antagonist

In patients with reduced EF not already receiving an MRA, this treatment should be started as soon as possible, renal function and potassium permitting*. As the dose of MRA used to treat HF has a minimal effect on blood pressure, even relatively hypotensive patients may be started on this therapy during admission.

** - The dose of ACEi/ARB, beta-blockers, MRA should be up-titrated as far as possible before discharge, and a plan made to complete dose up-titration after discharge.*

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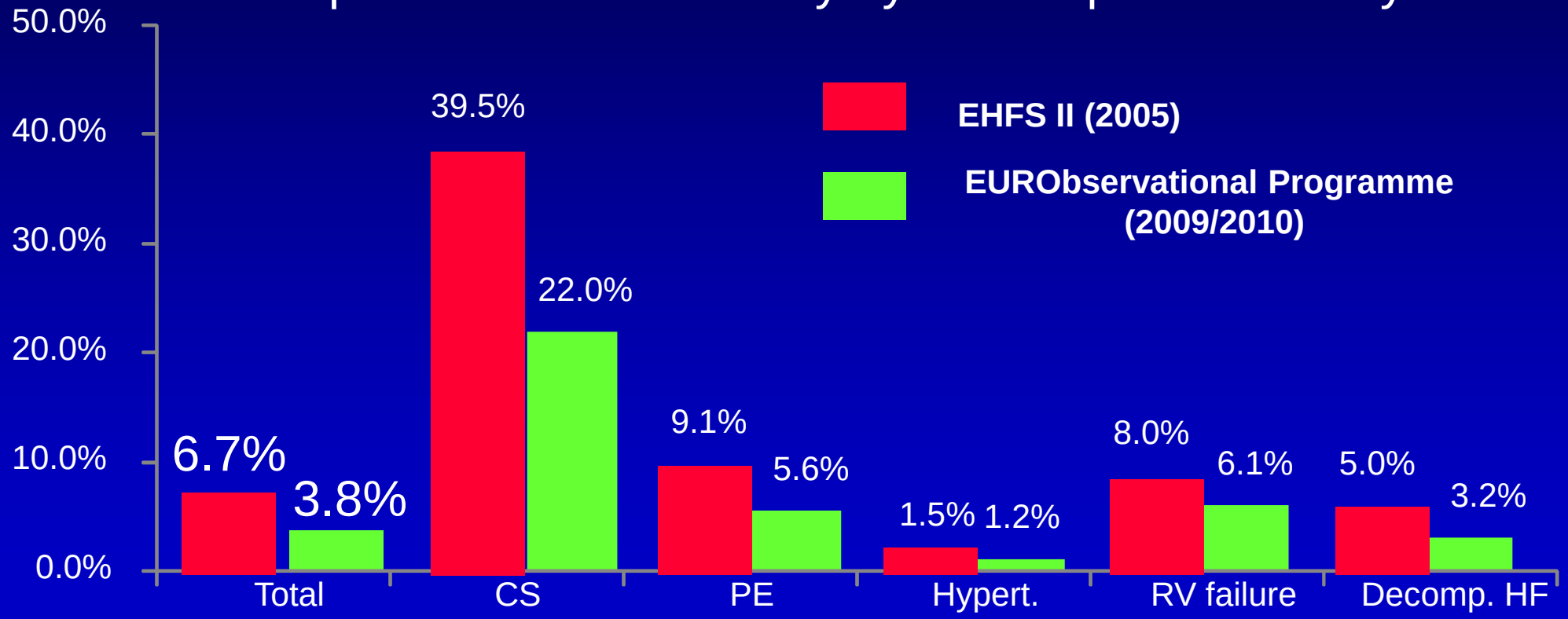
Acute Heart Failure Management 2012:
Optimization leading to in-hospital mortality improvement

AHS – outcome data

In-hospital all-cause mortality by clinical profile at entry



CS=Cardiogenic shock; PE=Pulmonary edema

Nieminen M et al., Eur Heart J 2006
& Courtesy of A. Maggioni

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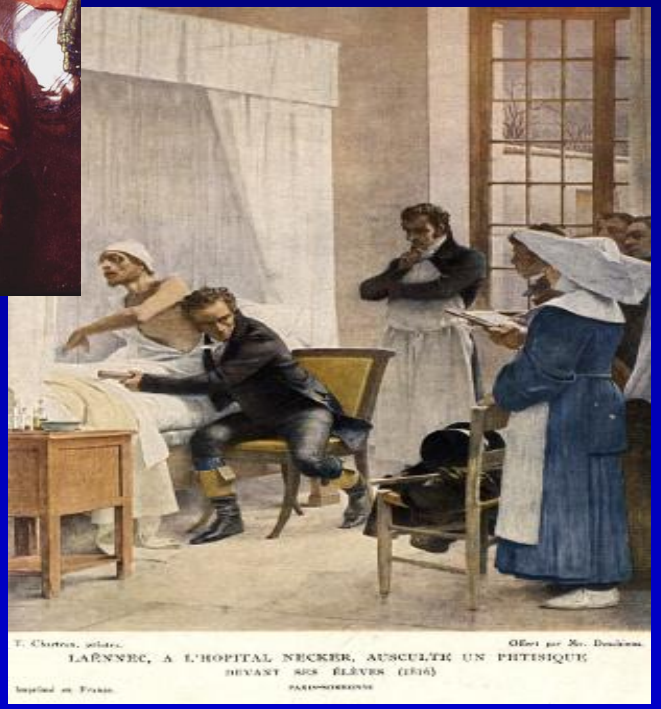
HF management: principal changes from the 2008 guidelines

- an expansion of the indication for mineralocorticoid receptor antagonists;
- a new indication for the sinus node inhibitor ivabradine;
- an expanded indication for cardiac resynchronization therapy;
- new information on the role of coronary revascularization in HF;
- recognition of the growing use of ventricular assist devices;
- the emergence of transcatheter valve interventions;

Management of heart failure: summary



„The best physician for a patient with HF would be one with ***excellent training, extensive experience, and superb judgment*** with regard to all aspects of the disease.

He or she ***would not necessarily follow guidelines slavishly***."

J.N. Cohn, Circ Heart Fail 2008;1:87-88