Acute Heart failure

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Acute heart failure
ESC Guidelines 2008

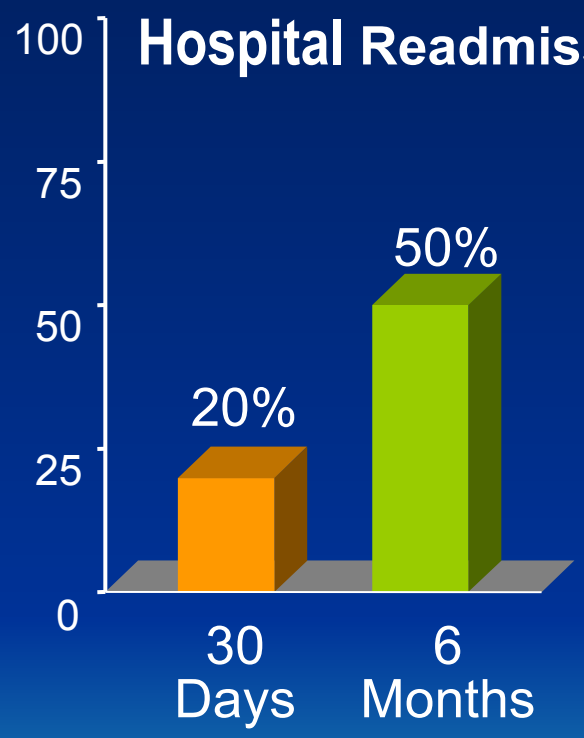
rapid onset of symptoms and signs secondary to abnormal cardiac function.

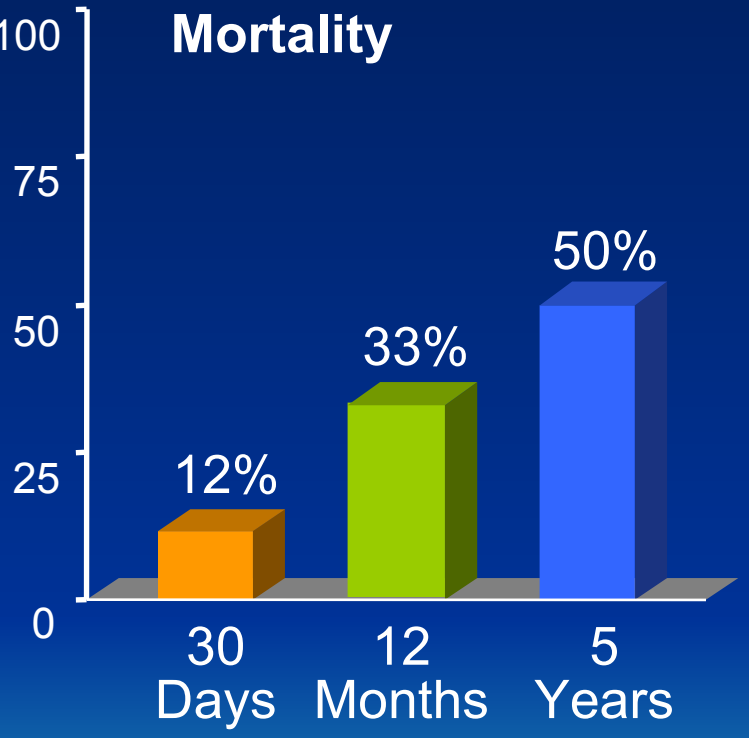
- often life threatening
- requires urgent treatment
- It may occur with or without previous cardiac disease

The cardiac dysfunction can be related to:

- systolic or diastolic dysfunction
- abnormalities of cardiac rhythm
- preload and afterload mismatch

Patient Outcomes in Hospitalized with Heart Failure (n = 38,702)





Median LOS: 6 days{ Mean length of staying in EuroHeart Survey II was 9 days}

Jong P et al. *Arch Intern Med. 2002*

Admission for ADHF is a "red -flag" for early morbidity and mortality

Gaps in Knowledge Before Adhere

What we learned from Clinical Trials in Heart Failure:

Age: 50-60 years old

Sex: 70-80% men

Comorbidities:

*Diabetes: 20-25%

*Renal Insufficiency: infrequent (mean Cr 1.1-1.3)

Ventricular Function:

*75-80% Systolic Dysfunction (LVEF < 0.40)

PAC use: 30-40%

In-hospital Mortality: 1.5-2.5%

The Adhere® Registry

- **Adhere –**
  - **Acute Decompensated HEart failure national REgistry Core Module (CM)**
    - **Multi-Center**
    - **Observational**
    - **Open-Label**
    - **Electronic web-based**
- Registry of the management of patients treated in hospitals for acutely decompensated heart failure in the US

Adhere Registry - Demographics

All Enrolled Discharges (n=105,388)

Median Age (yrs)	**75**
Gender	
Male (%)	**48**
Female (%)	**52**

Past Medical History

All Enrolled Discharges (n=105,388)

Coronary Artery Disease (%)	57
Myocardial Infarction (%)	31
Atrial Fibrillation (%)	31
Chronic Renal Insufficiency (%)	30
COPD or Asthma (%)	31

Clinical Presentation at Registry Hospital

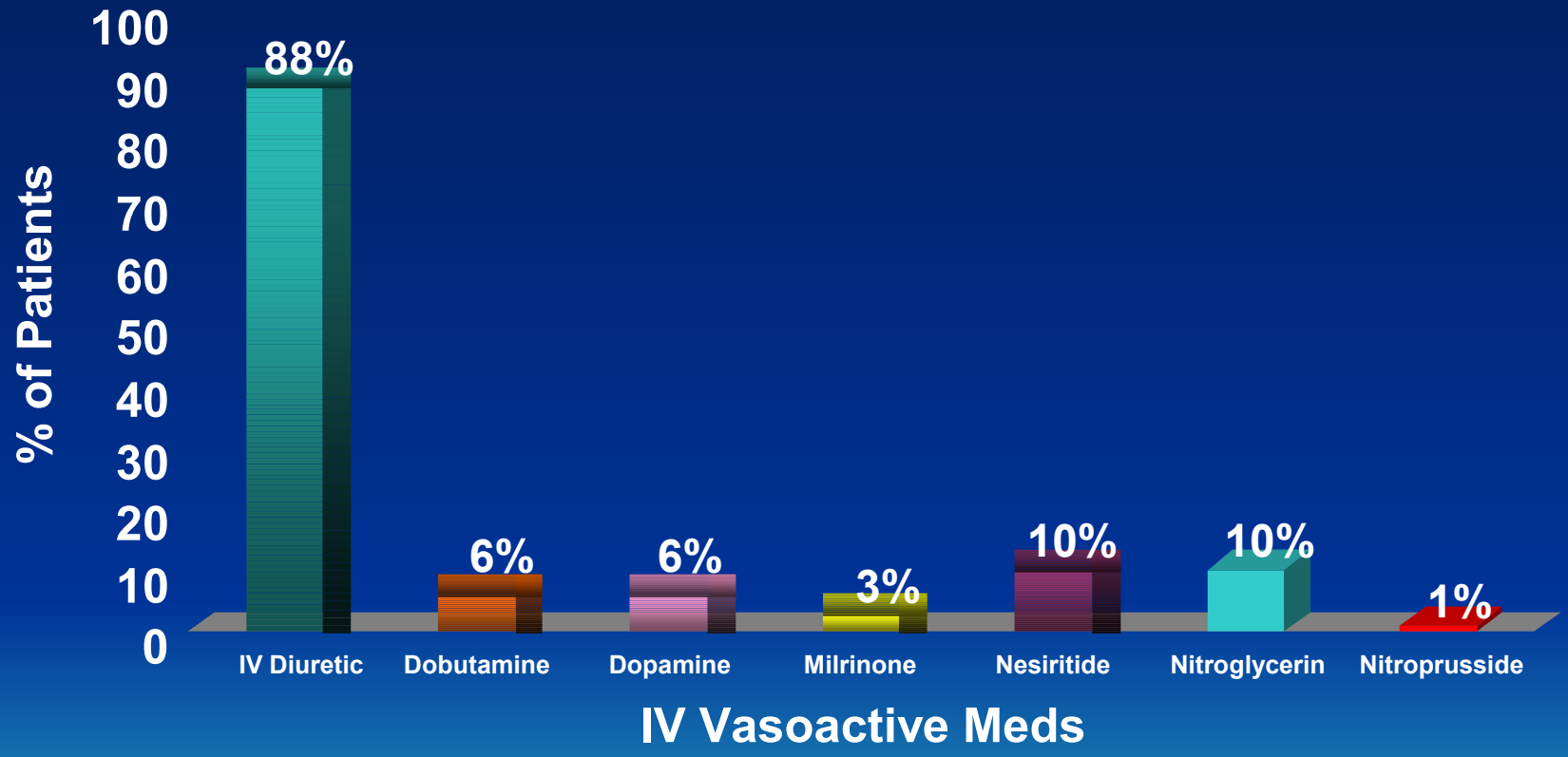
All Enrolled Discharges (n=105,388)

Any Dyspnea (%)	89
Dyspnea at Rest (%)	34
Fatigue (%)	32
Rales (%)	68
Peripheral Edema (%)	66
NYHA Class Assessed (%)	11 (n=11,555)
NYHA Class I (%)	2
NYHA Class II (%)	11
NYHA Class III (%)	40
NYHA Class IV (%)	47
Systolic Blood Pressure Assessed (%)	99 (n=104,573)
SBP <90 mmHg (%)	2*
SBP 90-140 mmHg (%)	48
SBP >140 mmHg (%)	50

Hospital course

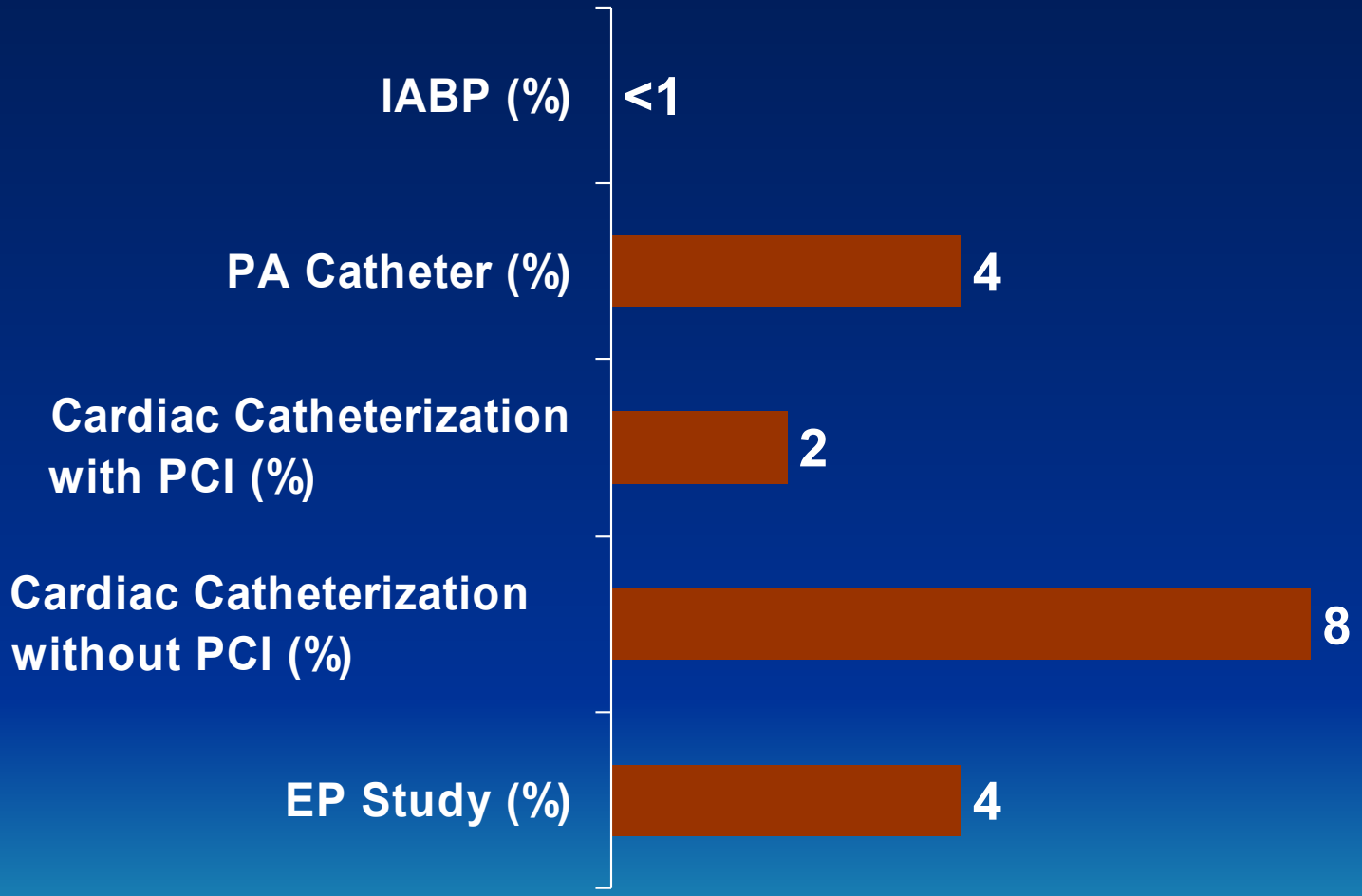
Most Common IV Medications

All Enrolled Discharges (n=105,388)



Procedures at Registry Hospital

All Enrolled Discharges (n=105,388)



AHF; Admission results

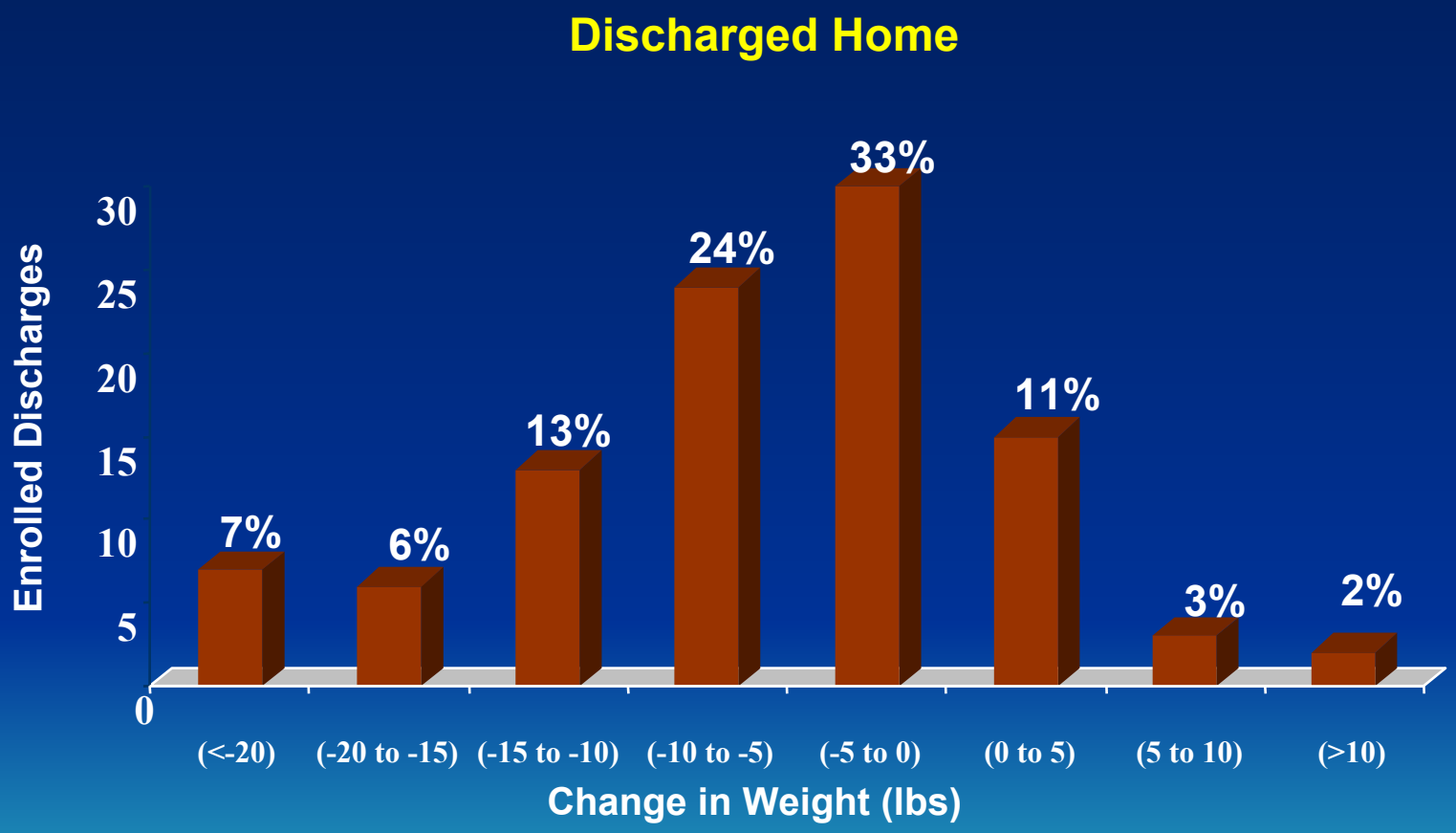
Adhere Clinical Outcomes

All Enrolled Discharges (n=105,388)

Median Total Hospital LOS	= 4.3 days
Adverse Outcomes	
In-hospital Mortality (%)	= 4.0
Mechanical Vent (%)	= 4.8
Renal Dialysis (%)	= 5.3
Defibrillation or CPR (%)	= 1.5

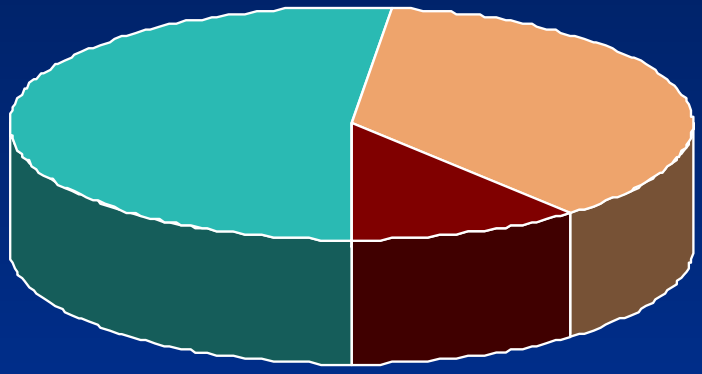
Lack of Weight Loss in Large Fraction of Patients Admitted for Acute Heart Failure

Change in weight was assessed in 51,013 patient episodes



Clinical Status at Time of Discharge

All Enrolled Discharges (n=105,388)



No Change <1%

Not Applicable <1%

Worse <1%

What can be done better?

Different patients- different measures:
Classification of AHF

- Acute decompensated heart failure, *de novo*, or decompensation of chronic heart failure
- Hypertensive AHF
- Pulmonary edema
- Low cardiac output syndrome to cardiogenic shock
- Right heart failure
- High output failure

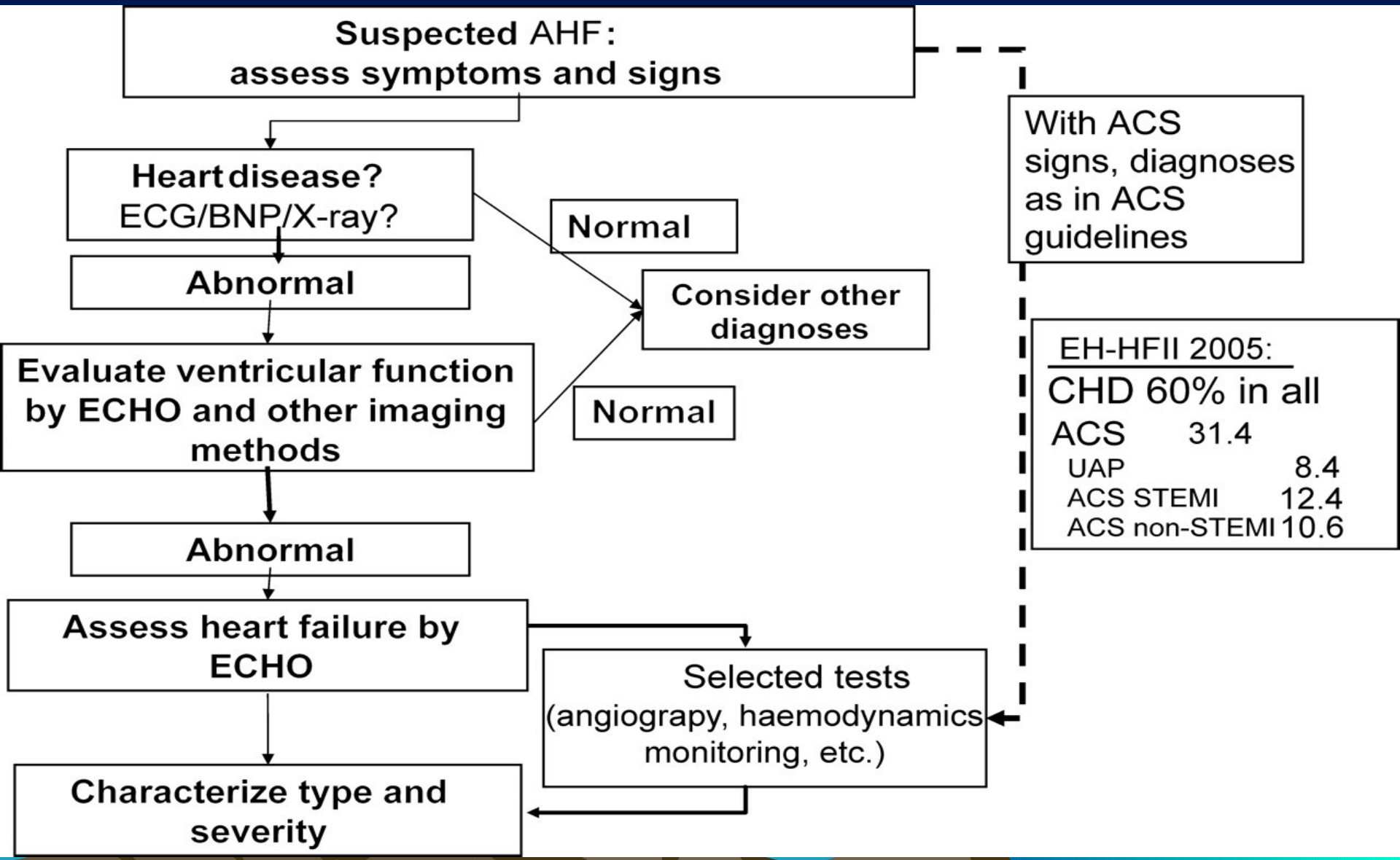
Severity and type of AHF in acute *de novo*, or in chronic decompensated AHF

Classification of AHF%	All	Acute *de novo*	Chronic decompensated
Decompensated HF	66	53.7	74.5*
Pulmonary edema	16.6	24.8	11.4*
Cardiogenic shock	4.2	7.2	2.3*
HF and hypertensive	10.1	11.4	9.2
RV HF	2.8	2.9	2.7

EuroHeart survey on AHF presented at ESC congress, Stockholm, 2005

*P<0.001

Diagnostic algorithm of AHF



Nieminen, M. S. Eur Heart J Suppl 2006

Pitfalls in the diagnosis of AHF

- May not be trivial (COPD, Pneumonia)
- 60% of HF pts have CAD
- 30% of AHF pts have ACS; most commonly-acute MI/AHF
- 15% of ACS have HF signs &symptoms
- Troponin may be elevated in AHF without ACS

To BNP or not to BNP?

- BNP Study: in Patients with acute dyspnea in the ER, BNP is better than Framingham Criteria for the Diagnosis of Heart Failure.

  (NEJM;2002;347:161).

- REDHOT Study :BNP was a better prognostic marker than " Clinical Assessment".

  (JACC 2004;44:1328).

- BASEL Study: BNP is cost effective: Less time to discharge and less total costs.

  (NEJM 2004;350:647).

To BNP

- Very High BNP is practically equivalent to Acute Heart Failure
- Elevated BNP is not equivalent to AHF
- No BNP=No CHF (High Negative Predictive Value)

Assessment of Mortality

Hemodynamic Assessment:

- Low BP, Cold and wet

Cardio-renal Syndrome:

- Any rise in Cr is a marker of poor outcome
- The higher the Cr elevation , the worse is the prognosis
- High BUN

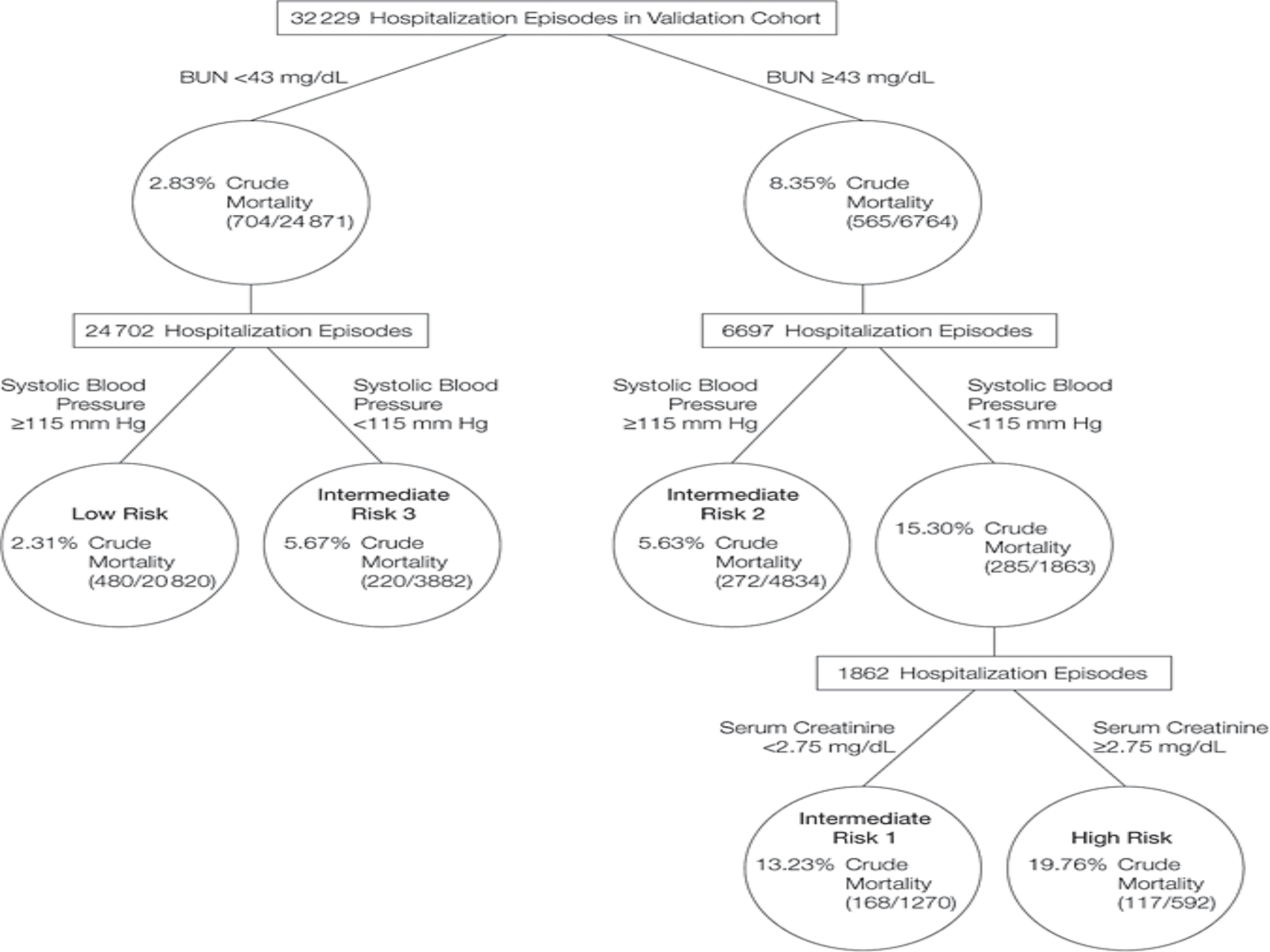
Others: High Troponin, low sodium, elevated TB

Assessment of mortality in the ADHERE*

In-hospital mortality :

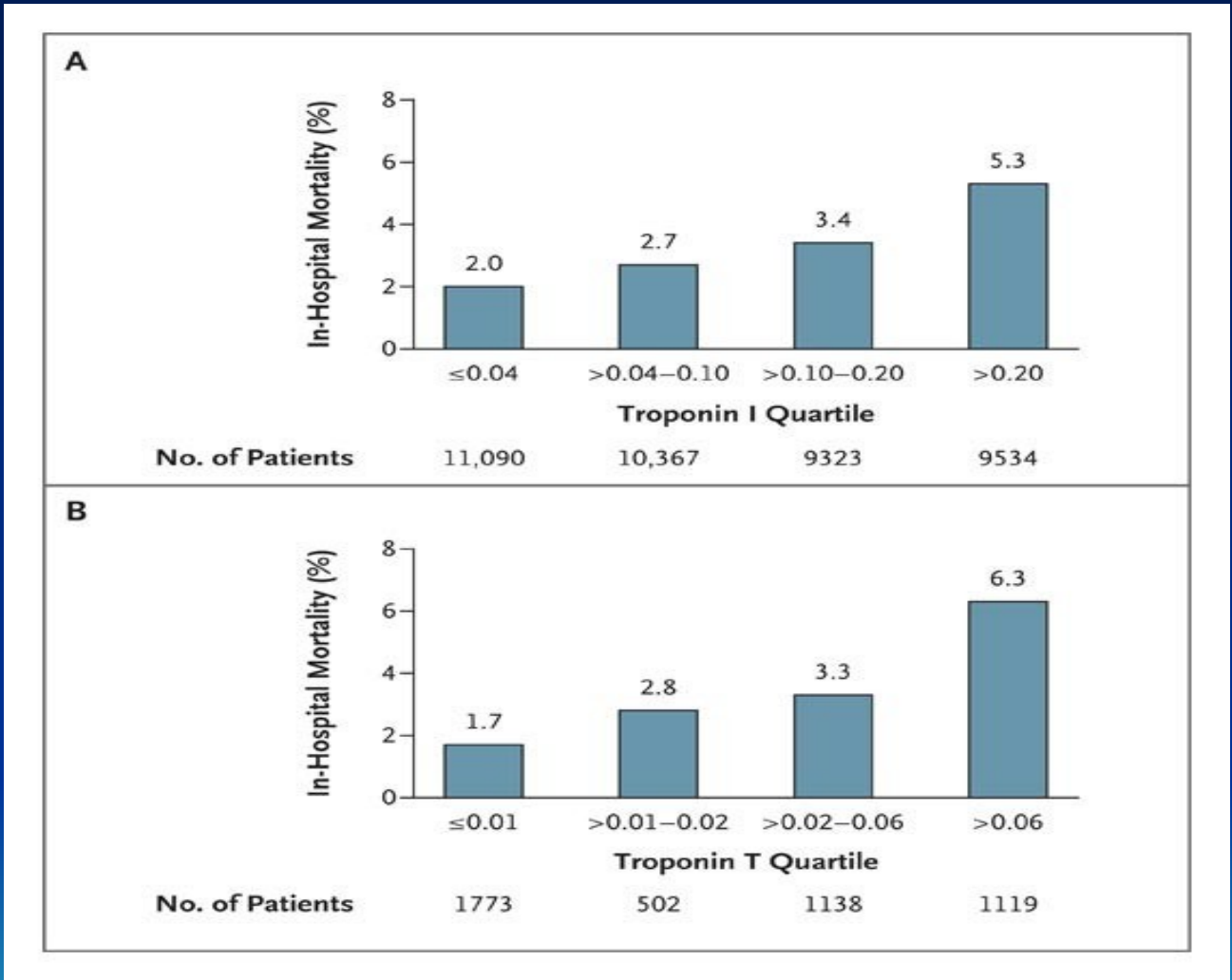
- similar between men and women (p = 0.727). Recursive partitioning of the derivation cohort for 39 variables :
- best single predictor for mortality was high admission levels of blood urea nitrogen (≥ 43 mg/dL)
- low admission systolic blood pressure (<115 mm Hg) high levels of serum creatinine (≥ 2.75 mg/dL)

A simple risk tree identified patient groups with mortality ranging from 2% to 22%.


32 229 Hospitalization Episodes in Validation Cohort
BUN <43 mg/dL
BUN ≥43 mg/dL
2.83% Crude Mortality (704/24 871)
8.35% Crude Mortality (565/6764)
24 702 Hospitalization Episodes
6697 Hospitalization Episodes
Systolic Blood Pressure ≥115 mm Hg
Systolic Blood Pressure <115 mm Hg
Systolic Blood Pressure ≥115 mm Hg
Systolic Blood Pressure <115 mm Hg
Low Risk
2.31% Crude Mortality (480/20 820)
Intermediate Risk 3
5.67% Crude Mortality (220/3882)
Intermediate Risk 2
5.63% Crude Mortality (272/4834)
15.30% Crude Mortality (285/1863)
1862 Hospitalization Episodes
Serum Creatinine <2.75 mg/dL
Serum Creatinine ≥2.75 mg/dL
Intermediate Risk 1
13.23% Crude Mortality (168/1270)
High Risk
19.76% Crude Mortality (117/592)

In-Hospital Mortality According to Troponin I or Troponin T Quartile (ADHERE)

* (troponin I level >1.0 microg per liter ; troponin T level > 0.1 microg per liter)



Peacock WF 4th et al. N Engl J Med 2008

Treatments in AHF

- Lack of studies
- Lack of evidence: IIa, IIb, B, C

Therapy/medication	Level of recommendation	Level of evidence	Comments
CPAP/NIPV	IIa	B	For hypoxaemia and congestion or oedema
Morphine	IIb	B	Restlessness and dyspnoeaVenodilation and mild arterial vasodilation, and decrease in heart rate
Anticoagulation LMWH/UFH			Well established in ACS or AF, with or without AHFLess evidence in AHFCareful monitoring of coagulation system, if creatinine clearance <30 mL/min
Diuretics	I	B	Dosing individualPrefer IV loop diuretics (i.e. furosemide) Thiazides and spironolactone can be used in combination with loop diuretics
Vasodilators (nitrates, nitroprusside)	I	B	Effective therapy when clinically indicated Tolerance on continuous use, isocyanate toxicity
ACE-I	Not recommended		Not as initial therapy, indicated after stabilization
Angiotensin II blocking agents	Not recommended		Not as initial therapy, indicated if ACE-I intolerant
Beta-blocking agents	IIa	B	Indicated when tolerated, first line therapy in tachycardia or after AMI Intravenous BBs should be considered in patients with ischaemic chest pain resistant to opiates, recurrent ischaemia, hypertension, tachycardia, tachyarrhythmias
Inotropic agents			Peripheral hypoperfusion/hypotension, with decreased renal function
Dopamine	IIb	C	With or without congestion or pulmonary oedema
Dobutamine	IIa	C	Refractory to diuretics and vasodilators at optimal doses
PDE- Inhibitors	IIb	C	In cardiogenic shock
Levosimendan	IIa	B	In decompensated congestive heart failure

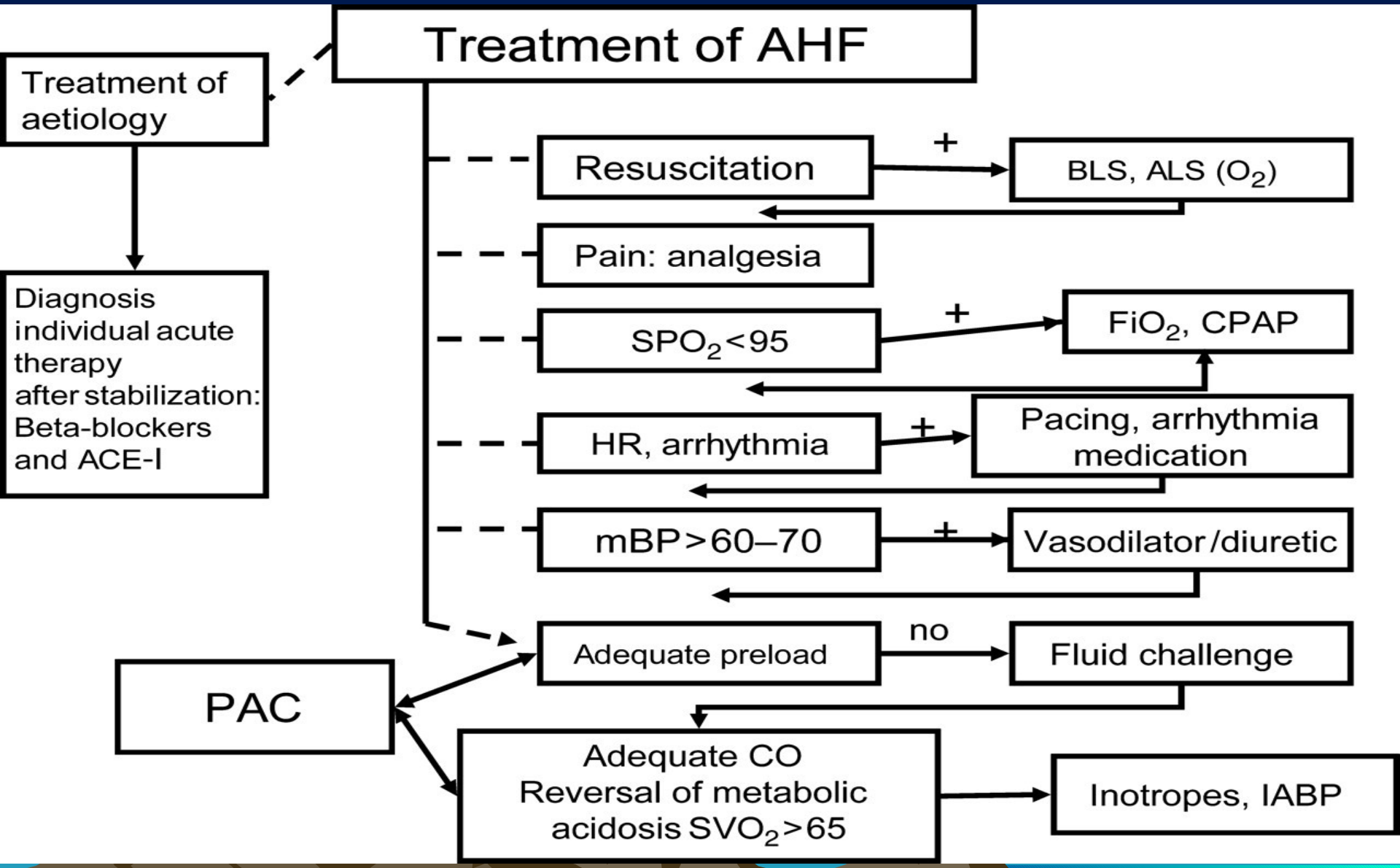
Treatment options in AHF ESC Guidelines 2008

General care/management:

- O2 (I), Morphine
- PEEP (IIa) decrease the need for intubations, possibly decrease mortality
- Lines; PAC (IIb) if etiology not clear or no response to therapy
- Labs: BNP+ CBC+ electrolytes+ ABG+ RFT+ LFT +troponin if ACS suspected
- Coronary angiogram (I)
- Anticoagulation
- Vasodilators (I)
- ACE-I(I) Diuretics (I)
- Beta-blocking agents (IIa)- decrease or delete in low CO
- Inotropes (dobutamine IIa/ dopamine IIb/ Milrinone IIb/ Levosimendan IIa)
- Digoxin (IIb)
- Vasopressors-Norepinephrine IIb
- Surgical management and , CRTP

Tailoring Heart Failure Therapy

Treatment algorithm of AHF



The Clinical Hemodynamic Profile
The modified Forrester* hemodynamics post MI classification{*AJC 1977};or
The “HF KILLIP classification”

Dry & Warm	Wet & Warm
Dry & Cold	Wet & Cold

" ADHF: The shrinking role of inotropic therapy"*

OPTIME-CHF: Short-term intravenous milrinone for acute exacerbation of chronic heart failure {JAMA- 2002}

- **951 patients admitted with an exacerbation of systolic heart failure not requiring intravenous inotropic support (mean age, 65 years; 92% with baseline New York Heart Association class III or IV; mean left ventricular ejection fraction, 23%)**
- **CONCLUSION: These results do not support the routine use of intravenous milrinone as an adjunct to standard therapy in the treatment of patients hospitalized for an exacerbation of chronic heart failure.***
- **Heart failure etiology and response to milrinone in decompensated heart failure: results from the OPTIME-CHF study ; Milrinone may have a bidirectional effect based on etiology in decompensated HF. Milrinone may be deleterious in ischemic HF, but neutral to beneficial in nonischemic cardiomyopathy**{Am Coll Cardiol. 2003}**

Levosimendan- the new kid in the block?

Levosimendan:

- calcium-sensitizing agent
- different from the classic inotropic agents activating the beta-receptor-cyclic adenosine monophosphate (cAMP) pathway

Three favourable trials:

- LIDO RUSSLAN
- CASINO

Levosimendan

Revive:

- **ADHF patients who received a single infusion of levosimendan together with standard therapy did significantly better than patients who received standard therapy alone: patients dyspnea assessment**

Adverse events in REVIVE-2

Selected adverse events	Levosimendan (%)	Placebo (%)
Hypotension	49.2	35.5
Headache	29.4	14.6
Ventricular tachycardia	24.1	16.9
Cardiac failure	22.4	26.6
Atrial fibrillation	8.4	0.2
Ventricular extrasystoles	7.4	0.2

Packer M et al. American Heart Association Scientific Sessions 2005; November

Levosimendan

SURVIVE :

- **Levosimendan vs dobutamine for patients with acute decompensated heart failure:**

  Despite an initial reduction in plasma B-type natriuretic peptide level in patients in the levosimendan group compared with patients in the dobutamine group, levosimendan did not significantly reduce all-cause mortality at 180 days or affect any secondary clinical outcomes.

hBNP

Yoshimara et al, 1991 show that administration of externally produced hBNP produces:

- vasodilation;
- antagonism of the hormone system that helps
- regulate long term blood
- increase in urine output containing large amounts of salt.
- VMAC, FUSION vs. Dr. Jonathan Sackner-Bernstein

Selective Oral Vasopressin V2-Receptor Antagonist

ACTIV in CHF*:

- Tolvaptan, a selective oral vasopressin V2-receptor antagonist, in addition to standard therapy in 319 patients with left ventricular ejection fraction of less than 40% and hospitalized for heart failure with persistent signs and symptoms of systemic congestion despite standard therapy

- increased fluid loss resulting in decreased body weight, and improved edema and serum sodium without affecting blood pressure, heart rate, or renal functions in patients with HF

* JAMA 2004

Selective Oral Vasopressin V2-Receptor Antagonist

EVERST*:

Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study With Tolvaptan:

- 4133 patients who were hospitalized with heart failure .
- significantly improved secondary end points of day 1 patient-assessed dyspnea
- day 1 body weight
- day 7 edema
- body weight and serum sodium effects persisted long after discharge.
- no effect on long-term mortality or heart failure-related morbidity at 1 year.

Cardio-renal syndrome; looking for treatment options:

- UNLOAD trial :Patients hospitalized for HF with > or =2 signs of hypervolemia were randomized to ultrafiltration or intravenous diuretics. Ultrafiltration safely produces greater weight and fluid loss than intravenous diuretics, reduces 90-day resource utilization for HF, and is an effective alternative therapy. {JACC 2007}

- Selective A1 Adenosine Receptor Antagonist KW-3902 for Patients Hospitalized With Acute HF and Volume Overload to Assess Treatment Effect on Congestion and Renal Function
  {PROTECT study}

Discharge with appropriate medications and doses:

ADHERE :Discharge medication (n=79,704)

Diuretic (%)	86 (70)
ACE Inhibitor (%)	55 (41)
Angiotensin II Receptor Blocker (%)	14 (12)
Nitrate (%)	30 (26)
Antiarrhythmic (%) (a)	14 (11)
Beta-Blocker (%)	59 (48)
Calcium Channel Blocker (%)	22 (23)
Hydralazine (%)	6 (4)
Digoxin (%)	34(28)
Warfarin	27 (24)
Aspirin (%)	48 (38)
Lipid-Lowering (%)	36 (31)
NSAID (%)	3 (6)

(a) Antiarrhythmics other than beta-blockers, calcium channel blockers, or digoxin

שאלות

שאלה 1

עיקר היעילות במדידת רמות בנסיוב של הורמונים נטריופפטידים במיון בחולה חשוד לאי ספיקת לב חריפה:

א. פרוגנוזה באשפוז

ב. אישור אבחנה של אי ספיקת לב חריפה

ג. שלילת אבחנה של אי ספיקת לב חריפה

ד. נוכחות אירוע כלילי חריף

ה. סיכון לפתח אי ספיקת כליות

שאלה 2

מה **<u>לא נכון</u>** לגבי עליית טרופונין בחולה חשוד לאי ספיקת לב חריפה?

א. מנבא פרוגנוזה באשפוז

ב. יכול להיות כחלק ממצאי מעבדה של תסחיף ריאתי

ג. שולל אבחנה של אי ספיקת לב חריפה ללא אירוע כלילי נלווה

ד. תומך בנוכחות אירוע כלילי חריף

ה. לא מתנהג בעקומה "רגילה" של אירוע כלילי חריף

שאלה 3

מה **<u>לא נכון</u>** לגבי החמרת תפקודי כיליה במאושפז עם אי ספיקת לב חריפה?

א. מנבא פרוגנוזה באשפוז

ב. נובע לרוב מייבוש יתר ע"י הדיורטיקה

ג. יתכן ויגרמו ממתן טיפולי עם הורמון נטריופפטידי רה-קומביננטי

ד. בולמי רצפטורים לאדנוזין יתכנו כטיפול אפשרי

ה. שכיח שמלווים עם היפונטרמיה