

Acute Heart Failure

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Acute heart failure

- **Rapid onset of symptoms and signs secondary to abnormal cardiac function.**
- **Irrespective of the underlying cause (e.g., ischemic event) or precipitant (e.g., severe hypertension), pulmonary and systemic congestion due to elevated ventricular filling pressures with or without a decrease in cardiac output is a nearly universal finding in AHF**

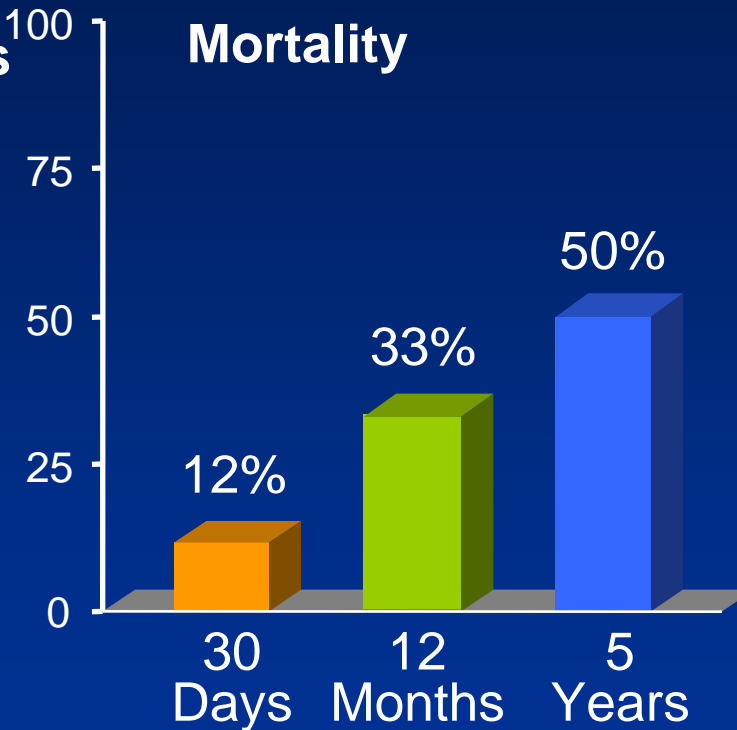
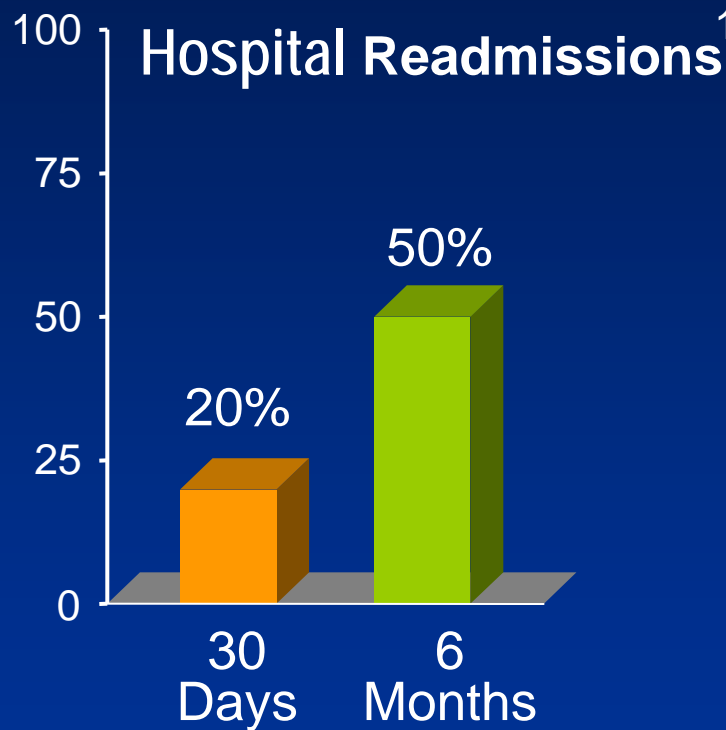
Acute heart failure

- 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

Admission for AHF is a “red -flag” for early morbidity and mortality



Who are the AHF patients?

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%

Adhere Registry - Demographics

All Enrolled Discharges (n=105,388)

Median Age (yrs)	75
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Gender

Male (%)	48
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Female (%)	52
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Past medical history

All Enrolled Discharges (n=105,388)

CAD (%)	57
MI (%)	31
AF (%)	31
CRF (%)	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

AHF; Hospital course

All Enrolled Discharges (n=105,388)

Median Total Hospital LOS = 4.3 days

Adverse Outcomes

In-hospital Mortality (%) = 4.0

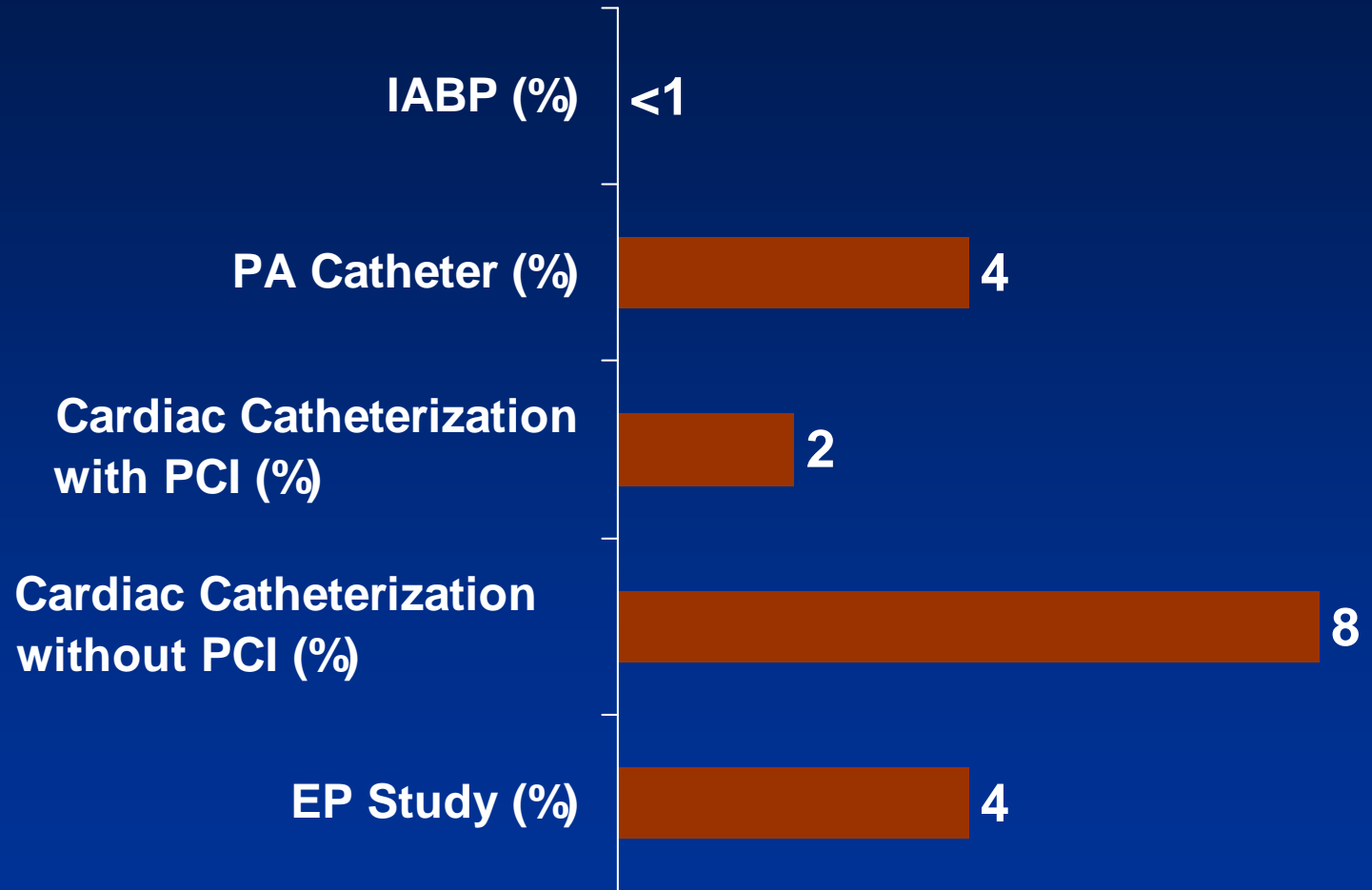
Mechanical Vent (%) = 4.8

Renal Dialysis (%) = 5.3

Defibrillation or CPR (%) = 1.5

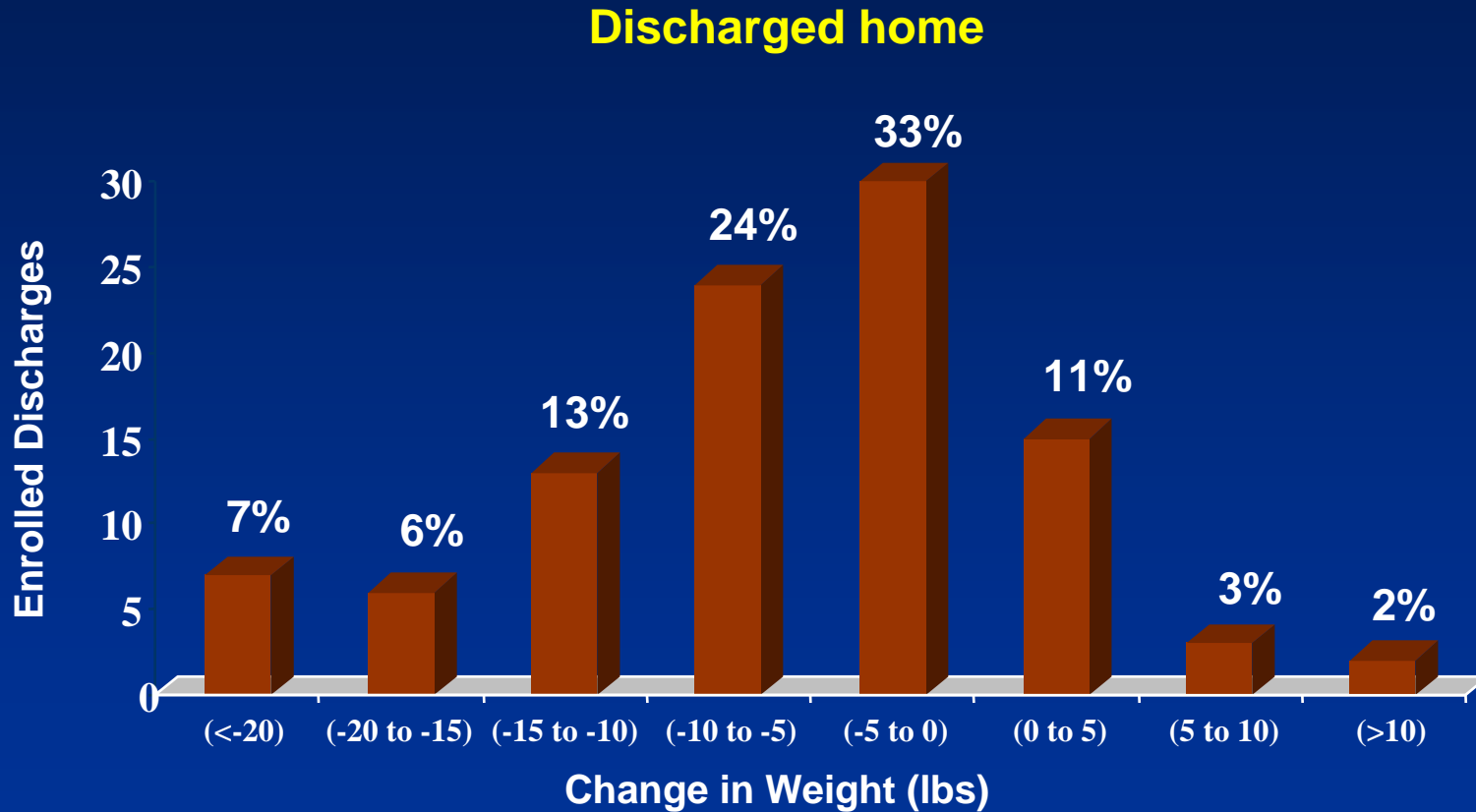
Hospital procedures

All Enrolled Discharges (n=105,388)



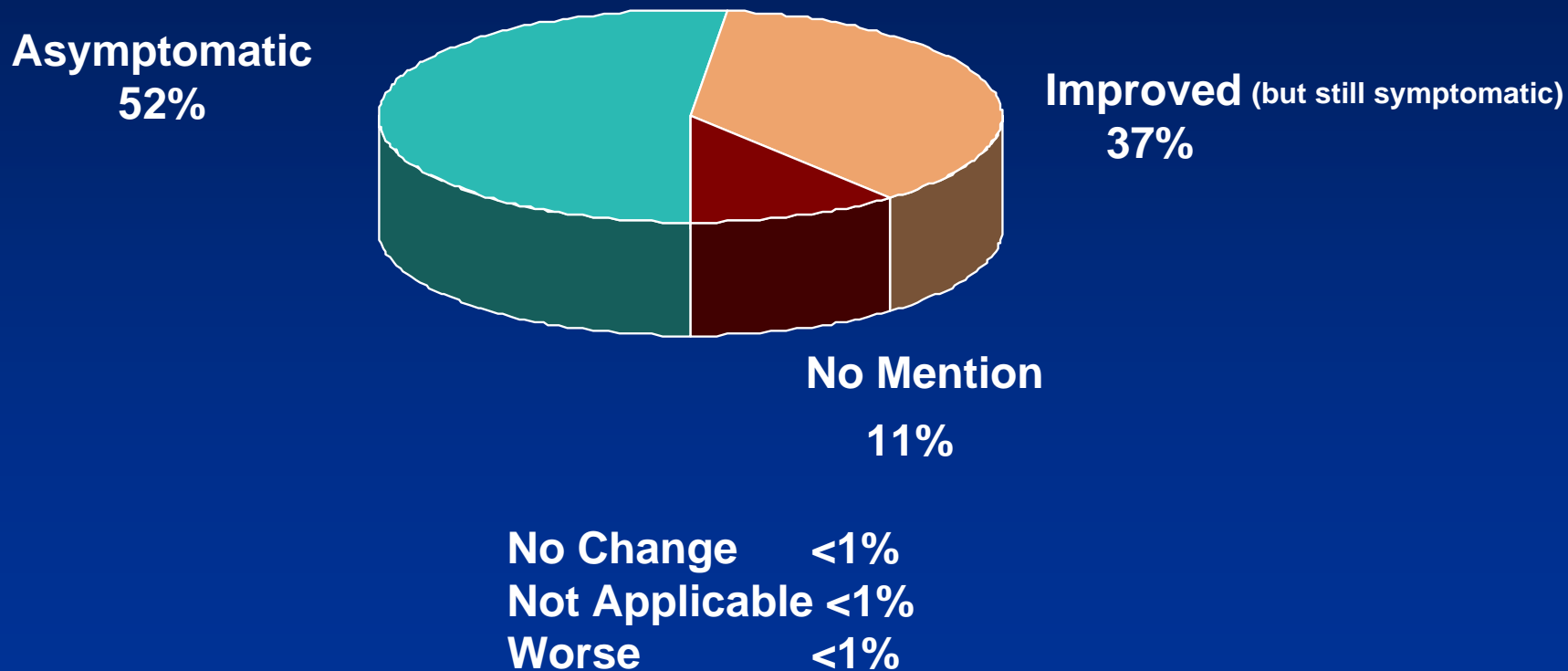
Lack of weight loss in HF

Change in weight was assessed in 51,013 patient episodes



Clinical status at time of discharge

All Enrolled Discharges (n=105,388)



What can be done better?

Different patients=Different measures

Classification of AHF%	All	Acute <i>de novo</i>	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 hypertension	10.1	11.4	9.2
RV HF	2.8	2.9	2.7

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

* $P < .001$

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
- Troponin may be elevated in AHF without ACS

Assessment of AHF patients

Cause of the AHF?

Risk stratification:

1. Clinical: Low BP, cold / wet

2. Cardio-renal Syndrome

3. Biomarkers: BNP, Troponin, sodium etc



The clinical hemodynamic profile

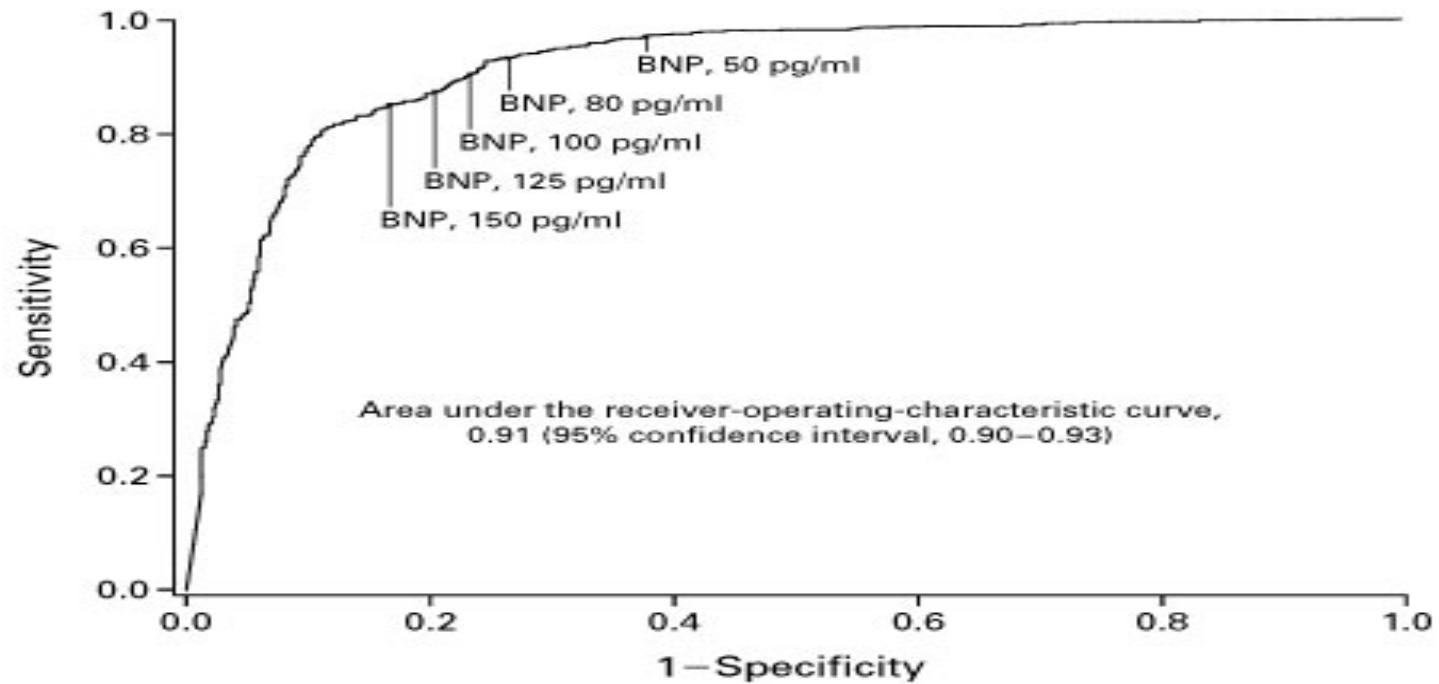
Dry & Warm	Wet & Warm
Dry & Cold	Wet & Cold

To Bnp or Not to Bnp ?

- **Screening**
- **Diagnosis**
- **Prognosis**
- **Treatment and guided treatment?**

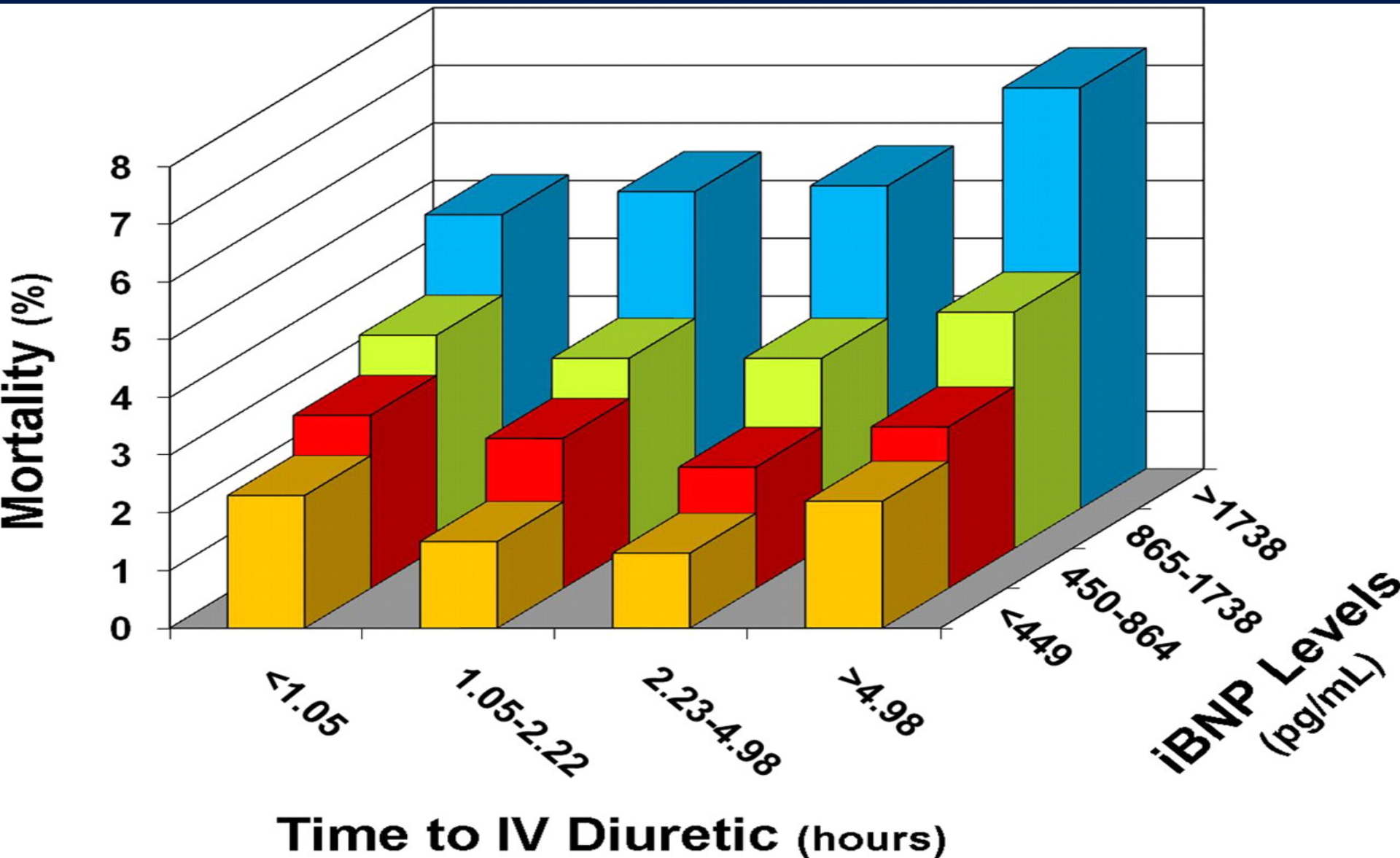
BNP study;

Differentiating between dyspnea due to congestive HF vs. other causes

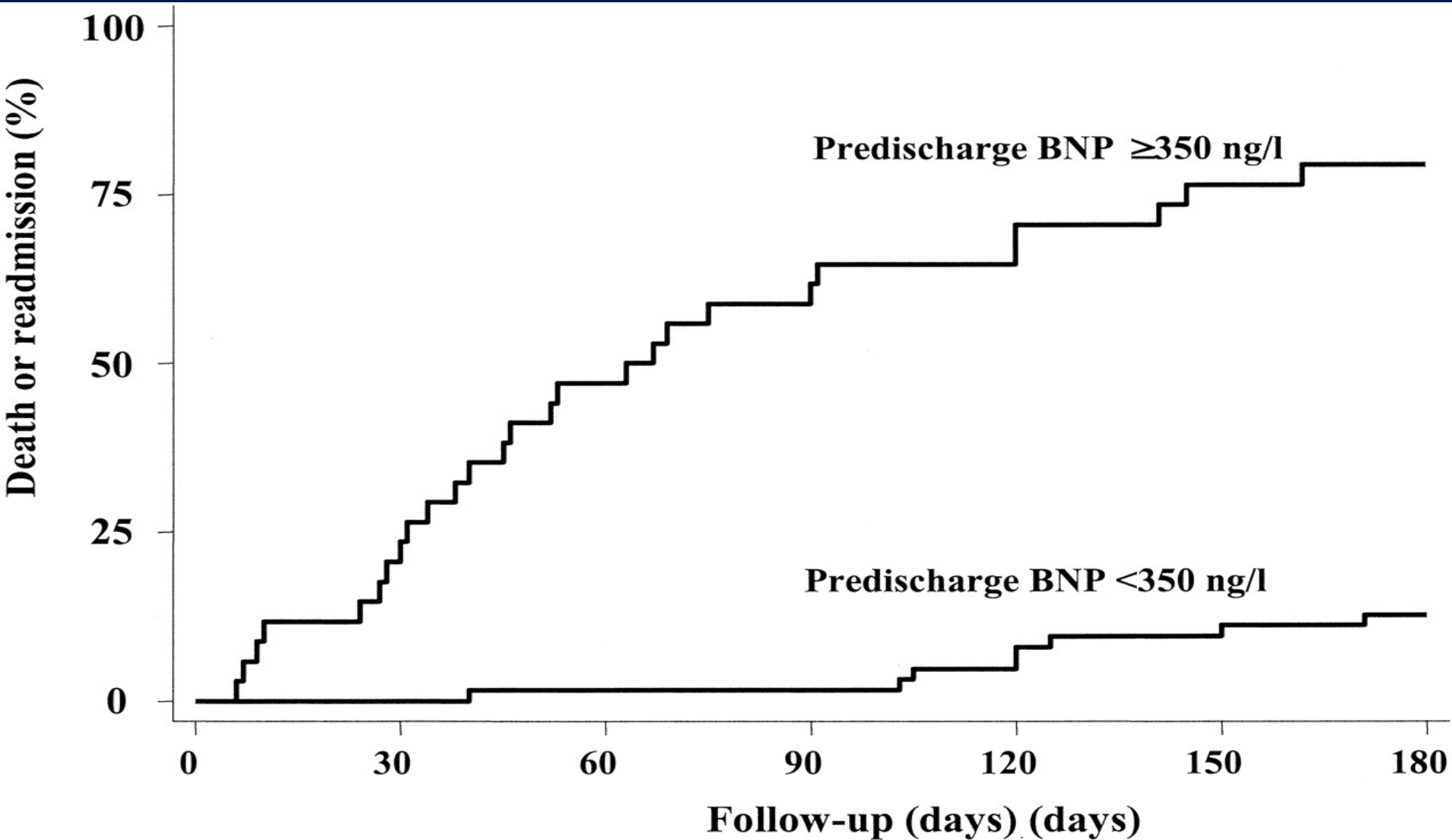


BNP pg/ml	SENSITIVITY	SPECIFICITY	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE	ACCURACY
	(95 percent confidence interval)				
50	97 (96–98)	62 (59–66)	71 (68–74)	96 (94–97)	79
80	93 (91–95)	74 (70–77)	77 (75–80)	92 (89–94)	83
100	90 (88–92)	76 (73–79)	79 (76–81)	89 (87–91)	83
125	87 (85–90)	79 (76–82)	80 (78–83)	87 (84–89)	83
150	85 (82–88)	83 (80–85)	83 (80–85)	85 (83–88)	84

Hospital Mortality, Time to Treatment, and BNP Level



Predischarge BNP



The Cardio-Renal Syndrome

Intrinsic Renal Disease

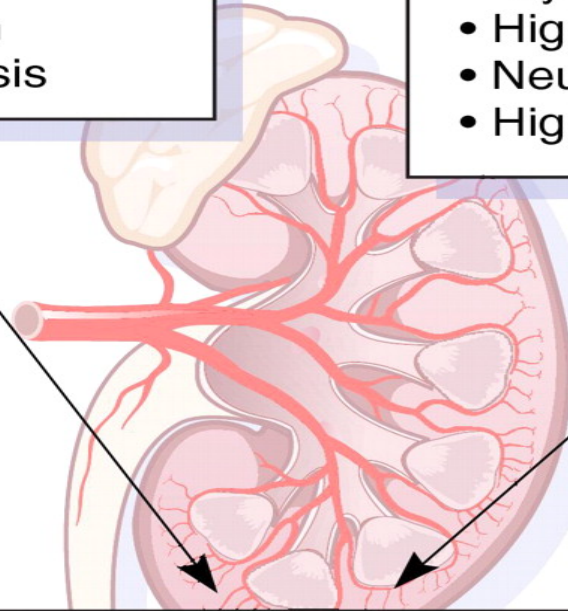
- Diabetes
- Hypertension
- Arteriosclerosis

“Vasomotor” Nephropathy

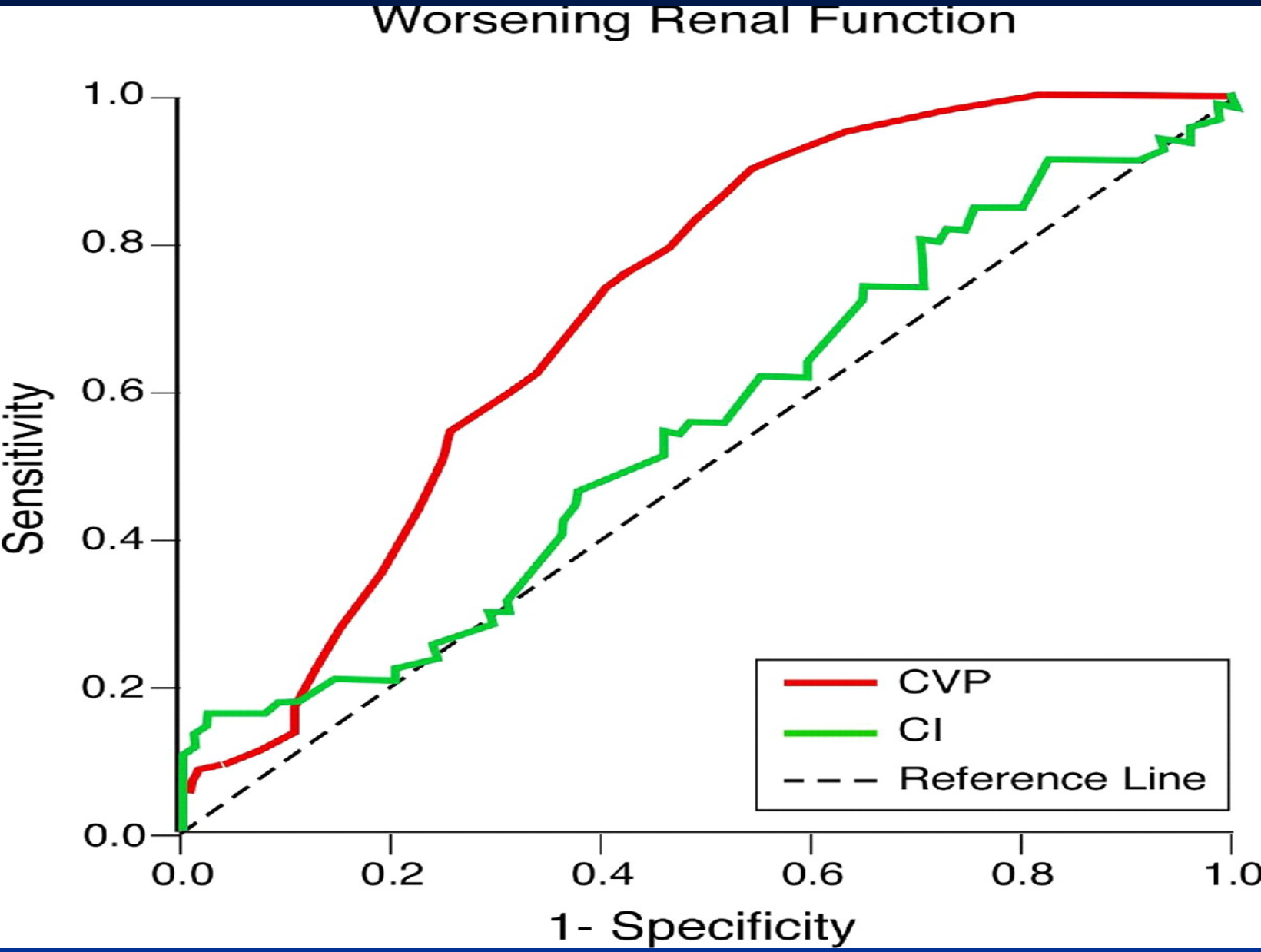
- Decreased cardiac output and/or systemic vasodilation
- High renal venous pressures
- Neurohormonal activation
- High dose loop diuretic therapy

Cardio-renal Syndrome

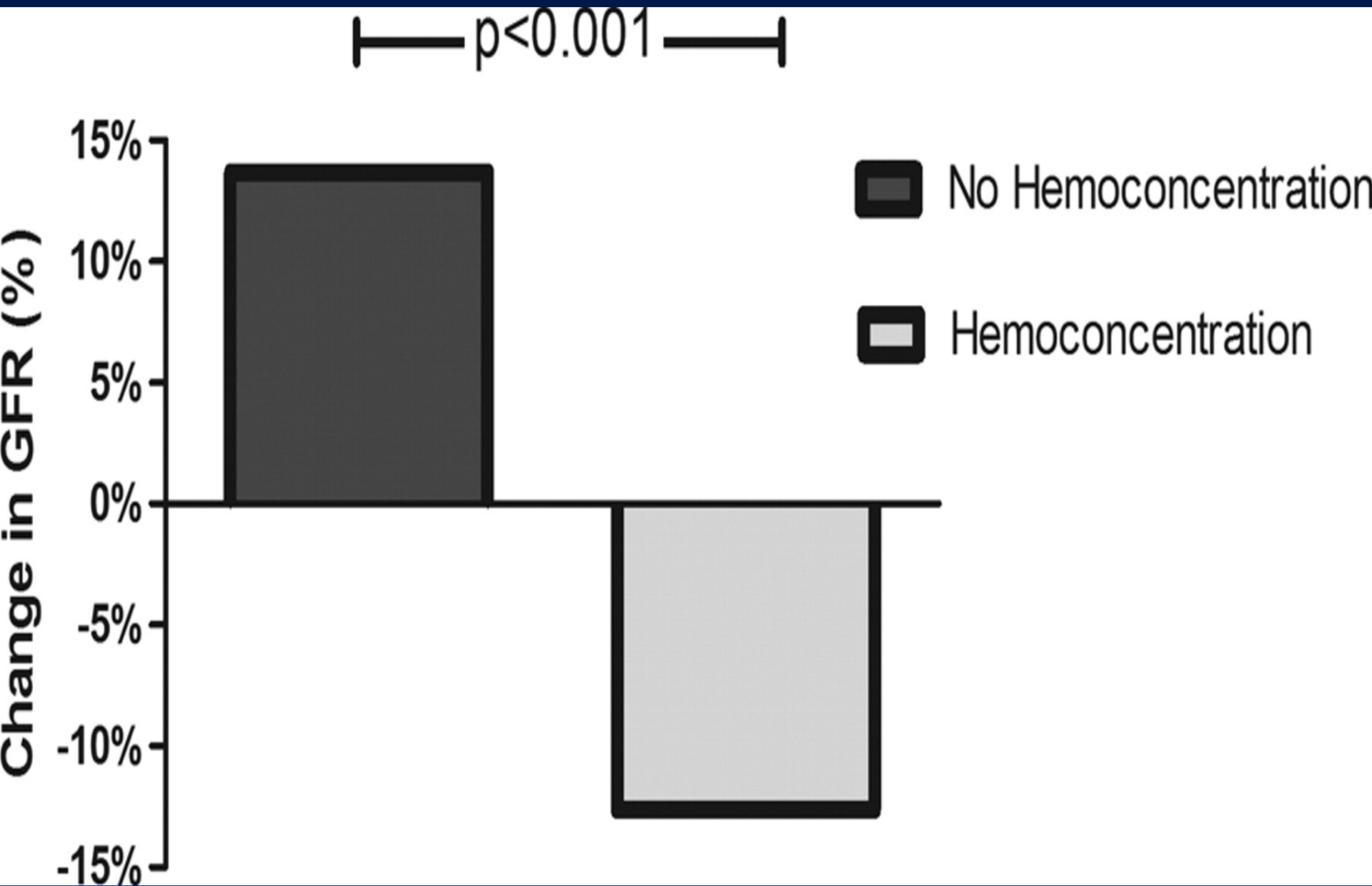
Worsening renal function during hospitalization, in spite of clinical improvement in response to therapy for HF and adequate intravascular volume



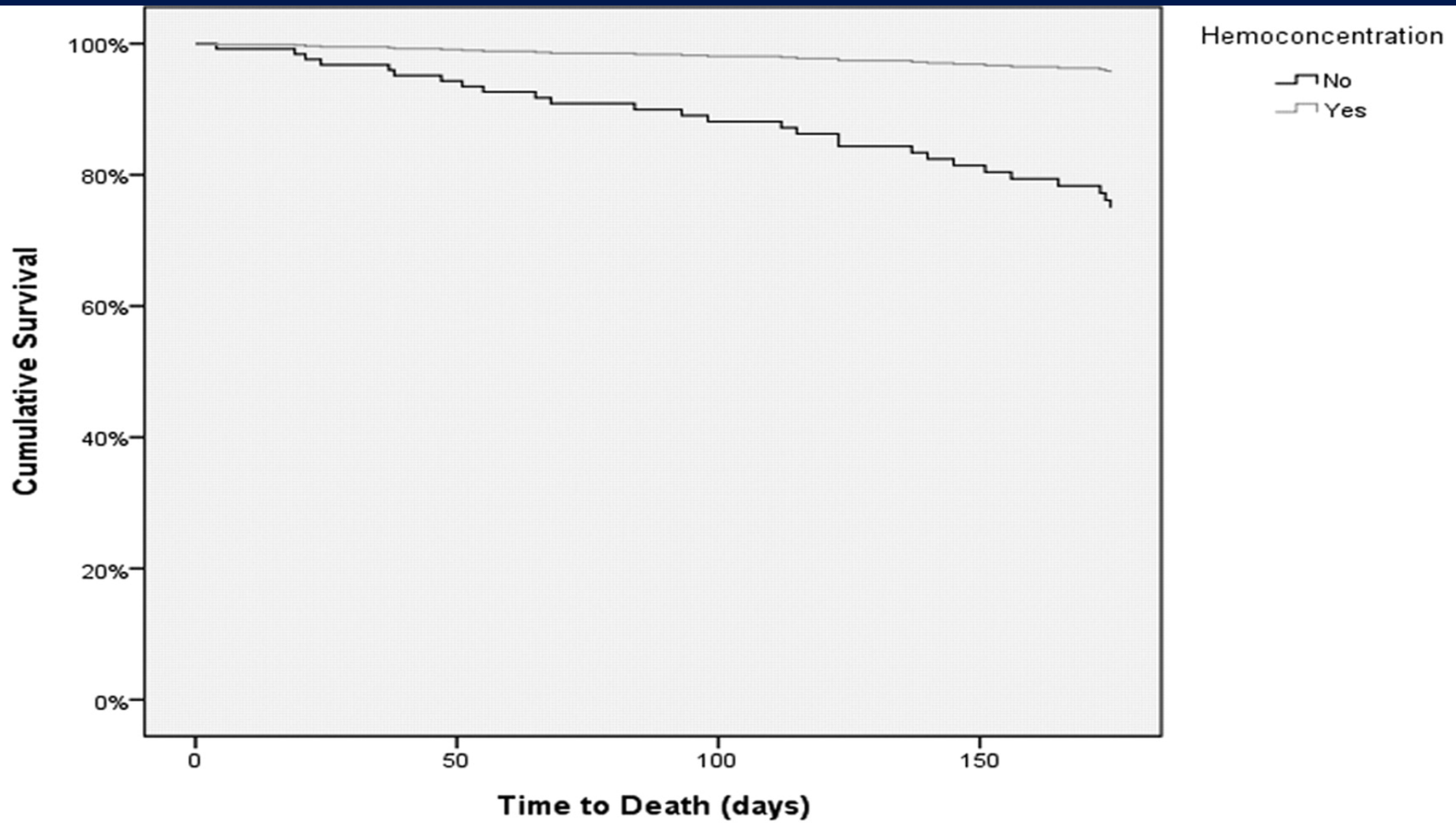
CVP and CI ; development of Cardio-renal syndrome



**ESCAPE TRIAL: Hemoconcentration {HT/Protein levels} ;
Admission-to-discharge percentage change in GFR**



Survival curves grouped by presence or absence of hemoconcentration after adjustment for baseline characteristics

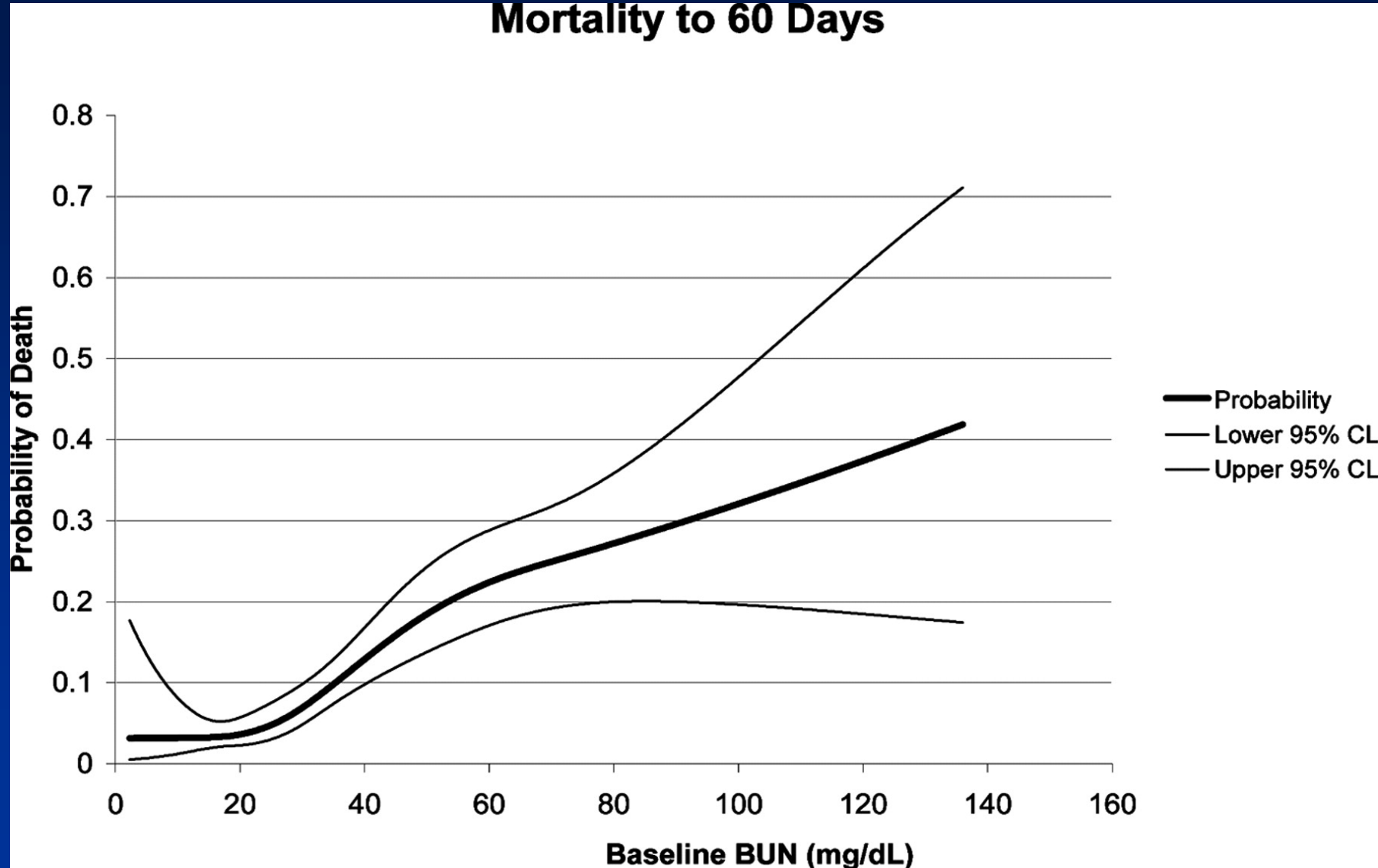


Number at Risk	102	93	80	71	No Hemoconcentration
	49	45	43	39	Yes Hemoconcentration

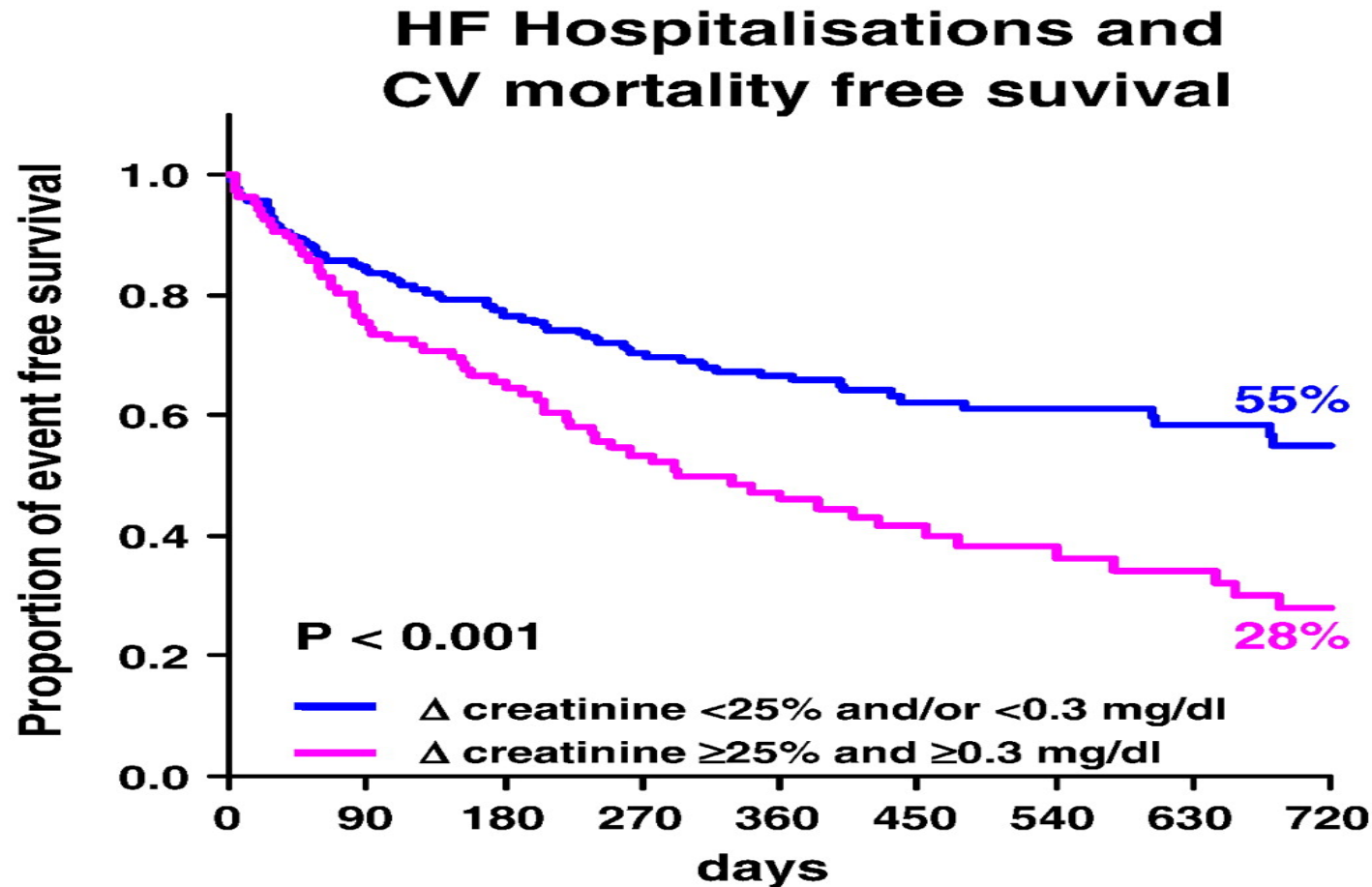
Baseline BUN and 60-day probability of death

OPTIME Trial

Mortality to 60 Days



Survival in AHF and s-CR



Pts. at risk

Absolute and percent s-Cr change:

<0.3 or 25%	211	143	92	55	36
\geq 0.3 & 25%	107	64	36	19	14

Predicting mortality :

ADHERE Registry

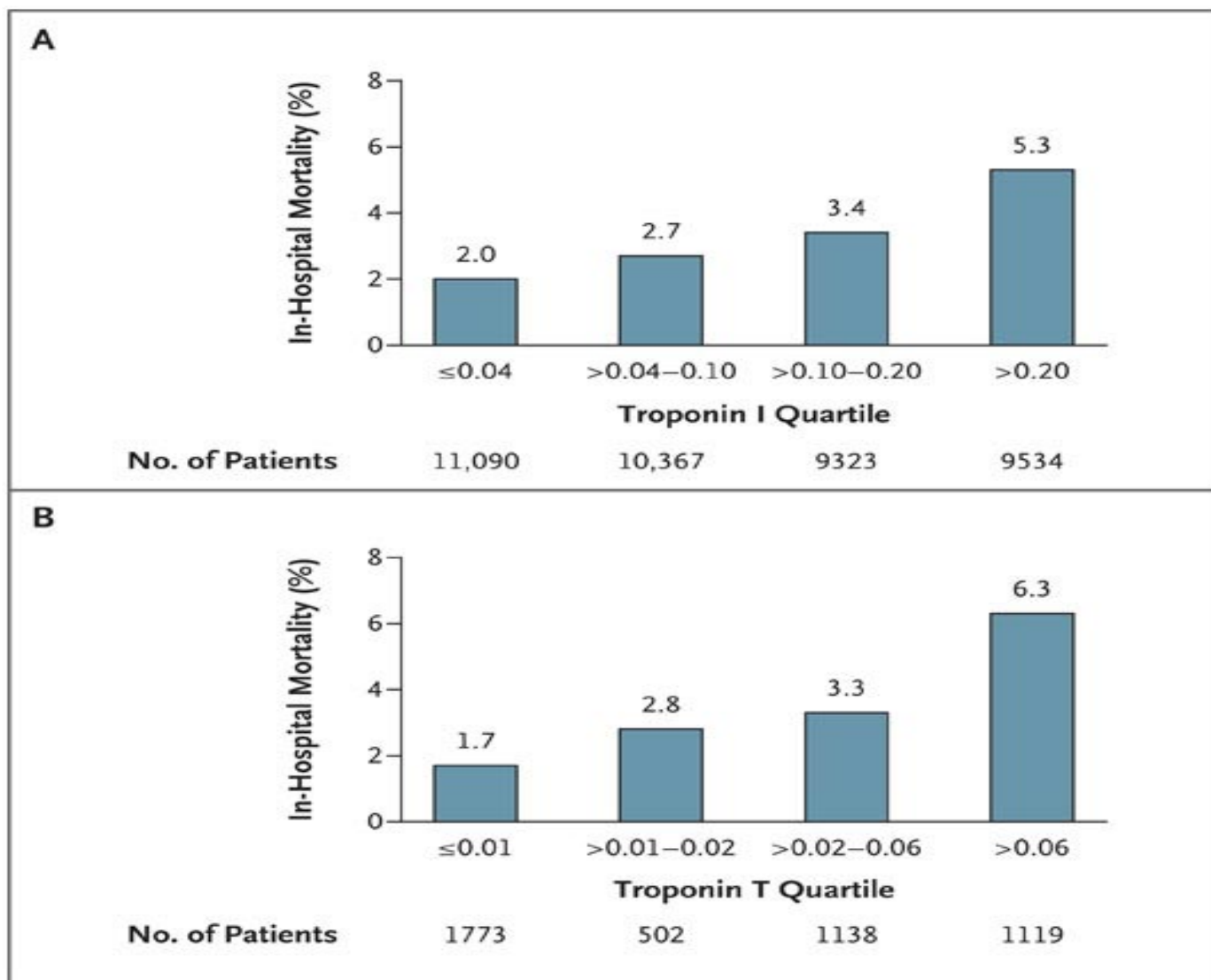
Recursive partitioning of the derivation cohort for 39 variables :

- Best single predictor for mortality was high admission levels of blood urea nitrogen (≥ 43 mg/dL)
- Low admission systolic blood pressure (<115 mm Hg) – second place
- High levels of serum creatinine (≥ 2.75 mg/dL) - third place

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

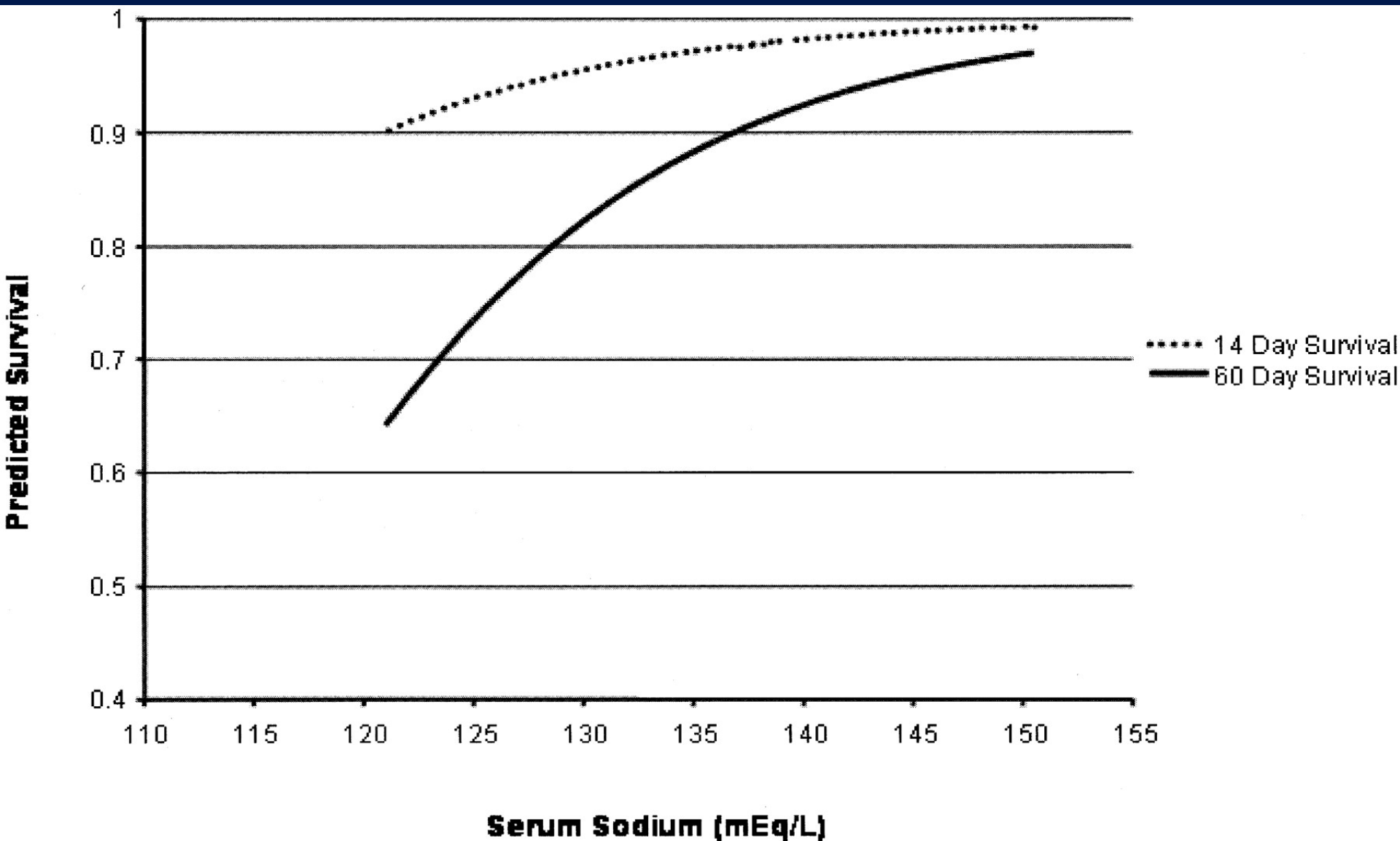
In-Hospital Mortality According to Troponin I or Troponin T Quartile (ADHERE)

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



Fourteen-day and 60-day mortality rates by serum sodium levels

OPTIME trial



Six-month end points and serum Sodium Concentration

ESCAPE Trial

Table 2. Six-Month End Points and Serum Sodium Concentration^a

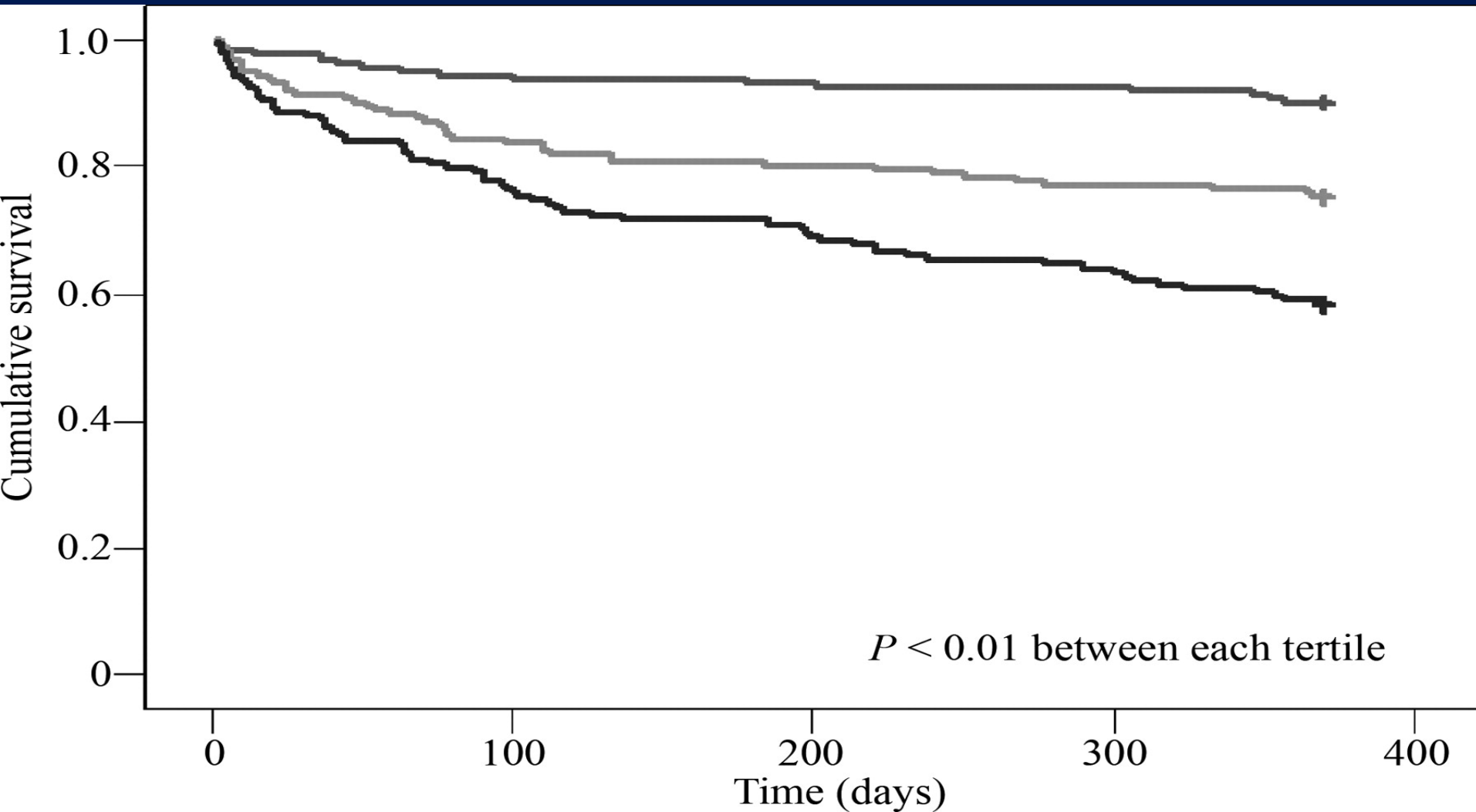
Hyponatremia Factor	Mortality	<i>P</i> Value	HF Hospitalization	<i>P</i> Value	Mortality or HF Hospitalization	<i>P</i> Value
Baseline Serum Sodium as a Continuous Variable						
Per 3-mEq/L decrease	1.23 (1.05-1.43)	.01	1.06 (0.96-1.17)	.29	1.09 (0.99-1.19)	.07
Serum Sodium Pattern During Hospitalization						
Persistent hyponatremia vs normonatremia	1.82 (1.03-3.22)	.04	1.52 (1.05-2.22)	.03	1.54 (1.09-2.17)	.01
Persistent hyponatremia vs corrected hyponatremia	1.71 (0.38-7.68)	.48	1.80 (0.73-4.43)	.20	1.47 (0.67-3.22)	.03

Abbreviations: CPR, cardiopulmonary resuscitation; HF, heart failure; SUN, serum urea nitrogen level.

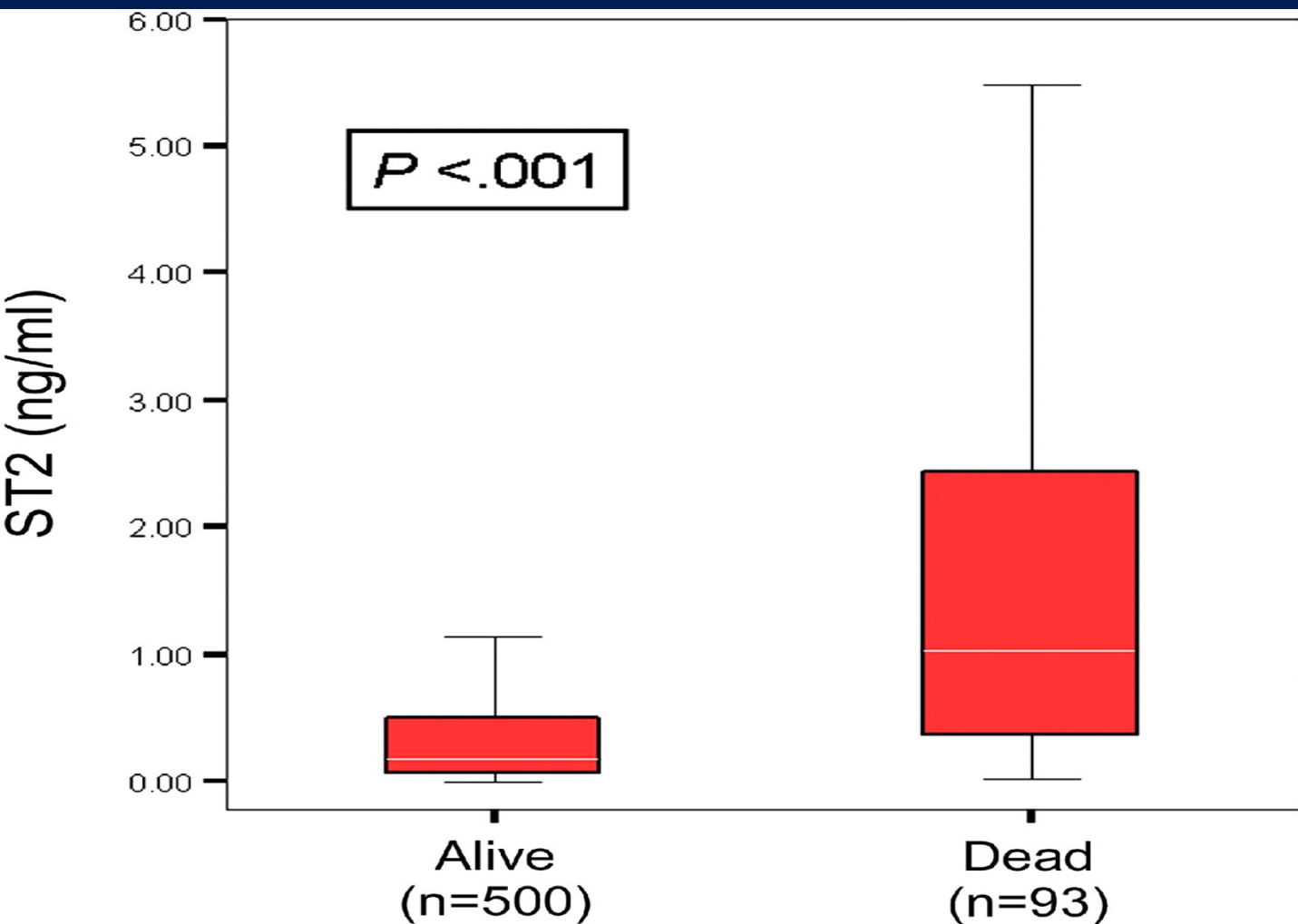
SI conversion factor: To convert serum sodium to millimoles per liter, multiply by 1.0.

^aUnless otherwise indicated, data are presented as hazard ratio (95% confidence interval). Models were adjusted for randomized treatment, discharge systolic blood pressure, discharge diuretic dose, weight change during hospitalization, and other identified predictors of each end point. For mortality, these other predictors were age, baseline 6-minute walk distance, discharge SUN, and whether patient received CPR or mechanical ventilation in the hospital. For heart failure rehospitalization and the composite end point, these other predictors were baseline heart rate and hemoglobin level, discharge SUN, 6-minute walk distance, β -blocker use, and whether patient received CPR or mechanical ventilation in the hospital.

One year survival by tertiles of cystatin C.



ST2 concentrations at presentation as a function of survival at 1 Year PRIDE study



Risk Stratification Data Points in ED Patients With Suspected Acute Heart Failure

Low Risk 20% of AHFS	Moderate 70% of AHFS	High 10% of AHFS
SBP > 160 ¹⁴ BUN < 30 ¹⁵ Normal Troponin ¹⁴	BUN 30-43 mg/dL SBP 115-160 mmHg	BUN > 43 mg/dL ¹⁶ Creat > 2.75 mg/dL ¹⁶ SBP < 115 mmHg ¹⁶ Elevated troponin ¹⁷ Significantly elevated BNP ¹⁸ Na < 136 ⁴
Discharge w/in 24 hrs & no 30 day readmits	Hospitalization 24 hrs to 7 days, no ↑ mortality	↑ Mortality and/or Hospitalized > 7 days

Treatments in AHF

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

Therapy/medication	Level of recommendation	Level of evidence
CPAP/NIPV	IIa	B
Morphine	IIb	B
Diuretics	I	B
Vasodilators (nitrates, nitroprusside)	I	B
ACE-I	Not recommended	
Angiotensin II blocking agents	Not recommended	
Beta-blocking agents	IIa	B
Inotropic agents		
Dopamine	IIb	C
Dobutamine	IIa	C
PDE- Inhibitors	IIb	C
Levosimendan	IIa	B

Treatment options in AHF*-Start with the cause!

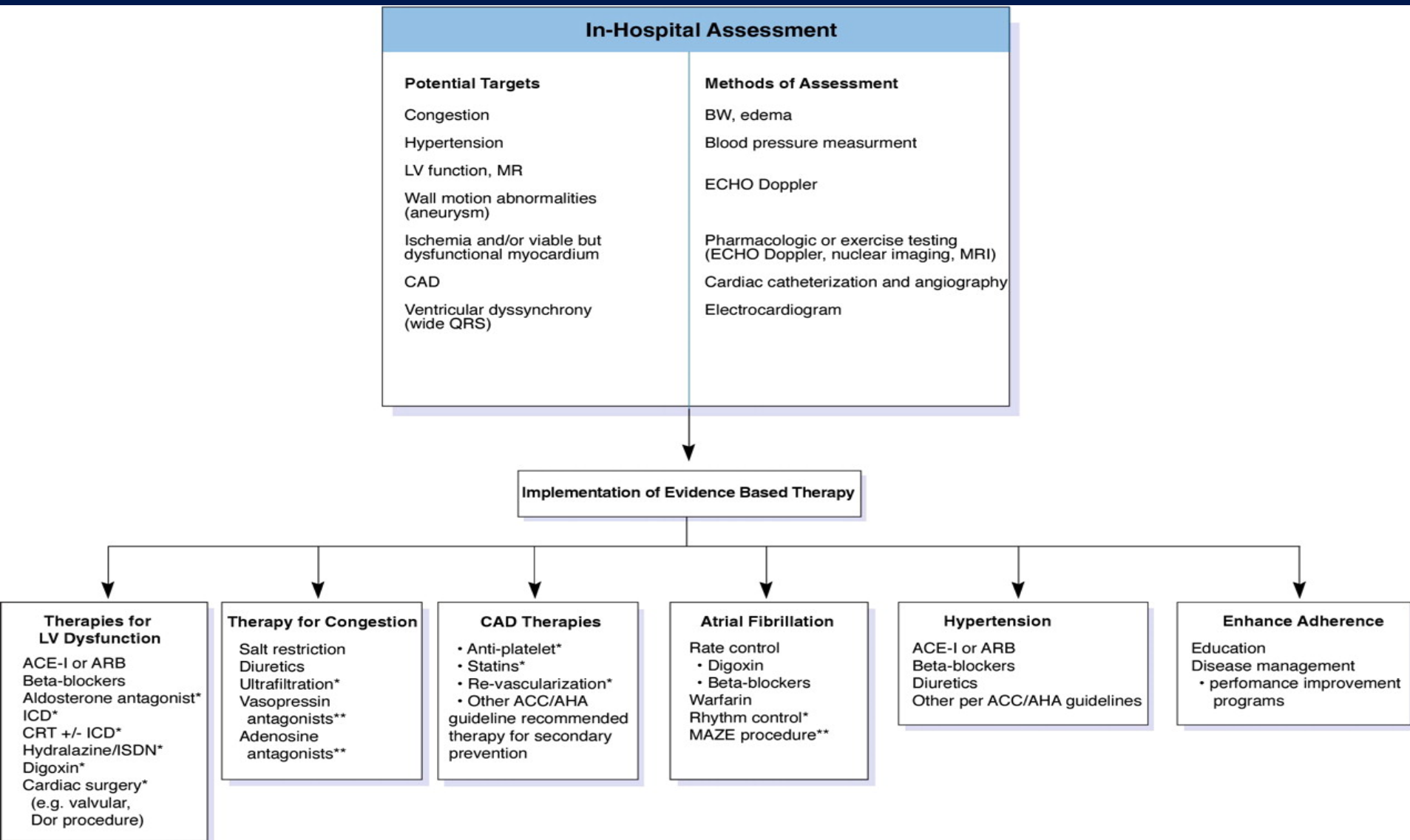
- General care/management
- IV, O2 (mask/CPAP), IV lines
- monitoring (rhythm, saturation, PAC, A.L, urine output)
- Labs: cbc+ electrolytes+ RFT+ LFT etc
- **Morphine-Increases mortality ?**
- Anticoagulation
- **Vasodilators: Ularitide, Adrenomedullin*****
- ACE-I
- Diuretics {Tolvaptan – V2 antagonist, Conivaptan- V1+V2 antagonists}
- Digoxin
- Aldactone for RHF?- No studies of Aldactone in AHF}
- Beta-blocking agents
- Direct anti- renin ; Aliskerin trial: ASTRONAUT
- Inotropes{ investigational regimens: **Istaroxime**, Cardiac myosin activators – improved contractility without Ca elevation}
- Surgical management and , CRT
- Devices and heart transplantation

*Gheorghide, M. et al. J Am Coll Cardiol 2009;53:557-573 & Acute Cardiac Care 2009,83-87.

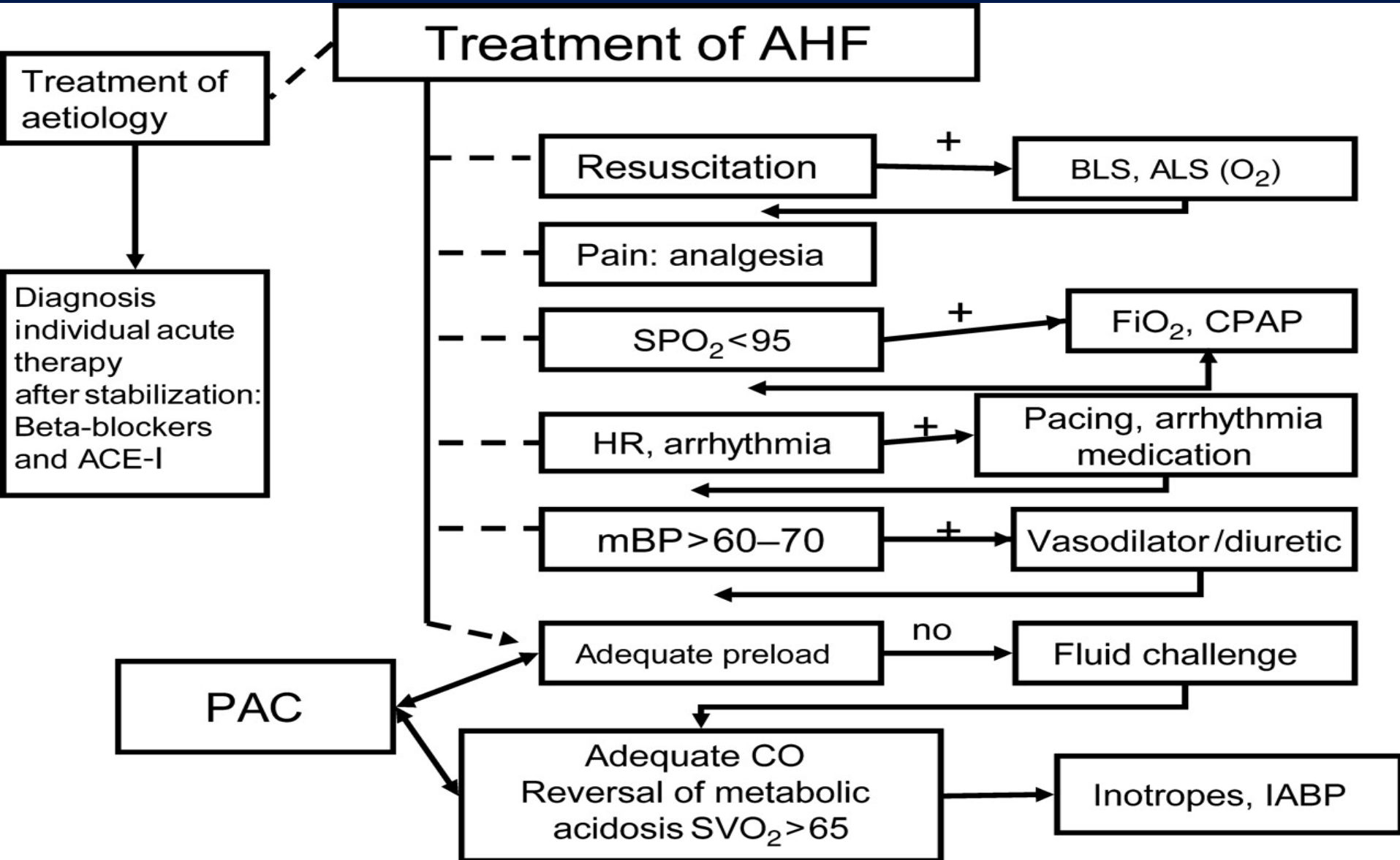
**Pwacock WF, et al; Emerg Med J 2008;25:205

***Nishikimi t et al; Cir J 2009:892

Assessment and Targeted Implementation of Evidence-Based Therapy in AHF



Treatment algorithm of AHF



Tailoring Heart Failure Therapy



Inotropes and hemodynamic profile

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}**

*Editorial- JAMA 2005

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 (ie, dobutamine or milrinone)

Three favourable trials:

- LIDO (AHF:levo vs dobutamine)
- RUSSLAN (AHF- post mi pts : levo vs placebo)
- CASINO (AHF: three arms: levo vs. placebo vs. dobutamine)

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 (FDA requirement)**

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.

Beta Blockers what to do?

In patients admitted to hospital with AHF, continuing BB does not worsen immediate outcomes AND-it is associated with an increased likelihood of subsequent beta-blocker.

- 169 pts, analysis of 147 pts-been on beta blockers for systolic heart failure
- patients with AHF who do not require dobutamine
- The study was open label and underpowered to detect differences in hard clinical endpoints

Not “convinced”

- In AHF, beta-blockers should not be withdrawn routinely.

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

- **Body weight and serum sodium effects persisted long after discharge.**

But:

- **No effect on long-term mortality or HF related morbidity.**

Treatments for Cardio-renal syndrome:

- **UNLOAD trial**
- **Selective A1 Adenosine Receptor Antagonist KW-3902 -PROTECT study**



{Does not } PROTECT study

- "Although there was a pharmacological basis on which to expect improvement, the benefits seen in a small pilot trial, as frequently happens, could not be replicated in a larger trial."

Tailoring Heart Failure Therapy:

The crushing & burning patient

INTERMACS Patient Profiles and Timing of Mechanical Circulatory Support* (Wilson SR; Circ 2009;119,2225)

Intermacs profile	Patient Characteristics	Time frame for intervention
1	Critical cardiogenic shock despite escalating support	Within a few hours
2	Progressive decline with inotrope dependence	Within a few days
3	Clinically stable with mild to moderate inotrope dependence	Elective implantation over the next few weeks
4	Recurrent, not refractory, advanced heart failure that can be stabilized with intervention	Elective implantation over weeks to months
5	Exertion intolerant but is comfortable at rest and able to perform activities of daily living with slight difficulty	Variable; depends on nutrition, organ function, and activity
6	Exertion limited; is able to perform mild activity, but fatigue results within a few minutes of any meaningful physical exertion	Variable; depends on nutrition, organ function, and activity
7	Advanced NYHA functional class III	At this time, mechanical circulatory support is not indicated

Act Quick!





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.



FUCK IT

I'm going home.

The End

