УМБАЛ ЦАРИЦА ЙОАННА-ИСУЛ ЕАД

ОСТРА И ОБОСТРЕНА СЪРДЕЧНА НЕДОСТАТЪЧНОСТ

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ACUTE HEART FAILURE

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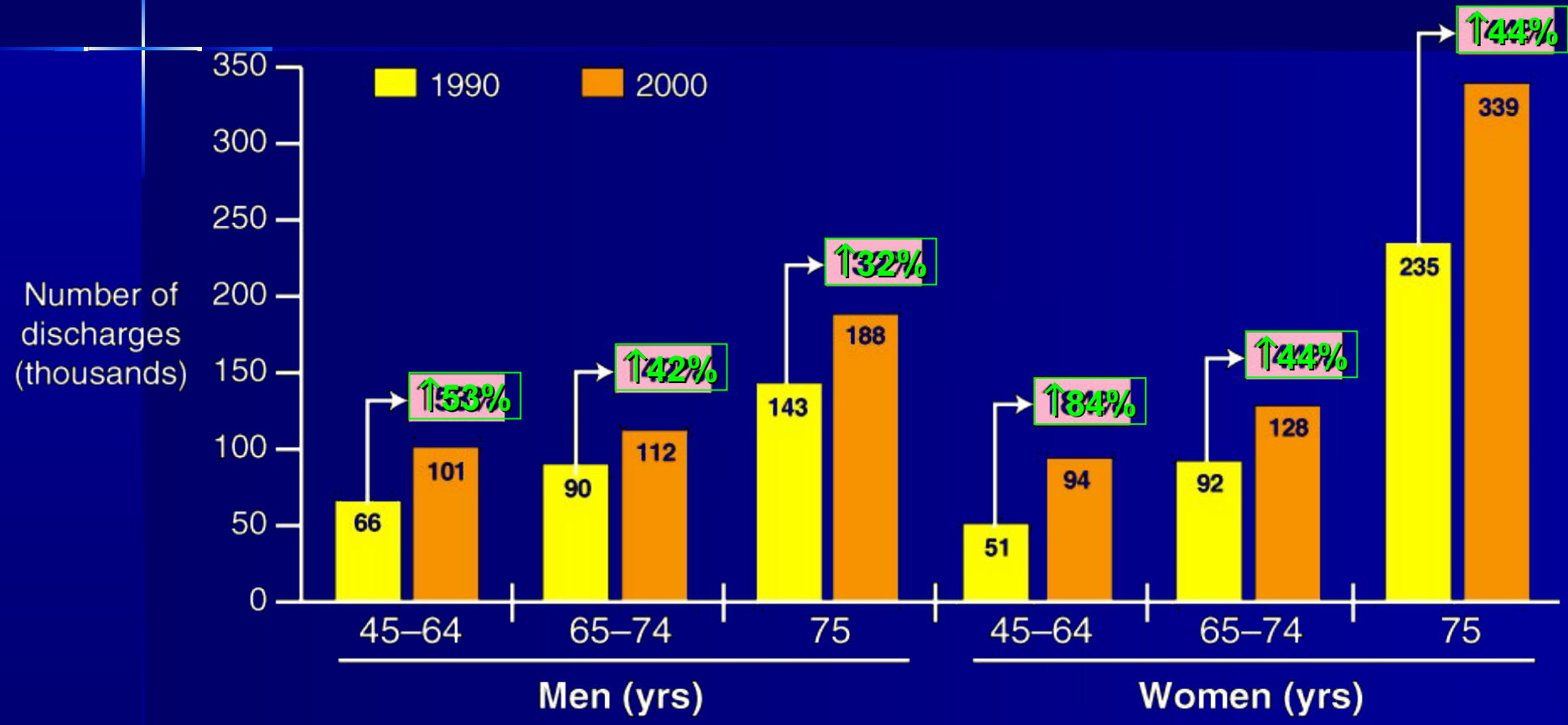
PROVIDENCE, RHODE ISLAND

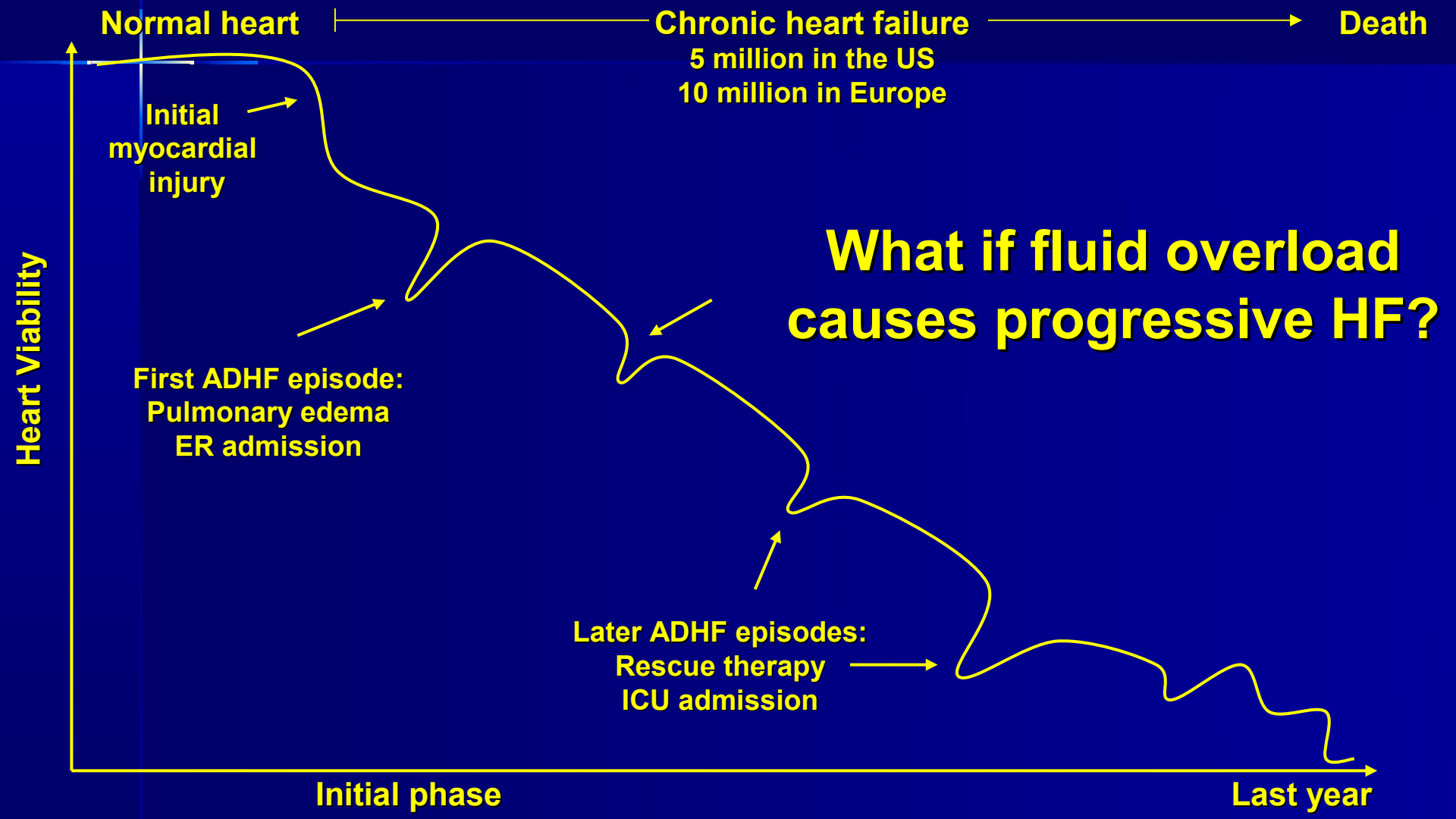
ACUTE heart failure is almost invariably a result of some chronic abnormality of function or structure. Cardiac disease runs progressively through a number of stages which merge into each other. This progress is more or less gradual, but the change may be greatly hastened and acute heart failure induced by some aggravating cause such as infection of the respiratory tract, cough, pregnancy, obesity, marked anemia, tachycardia, disturbances of rhythm or emotional and mental strain. Excessive exertion frequently brings about the signs of acute heart failure in persons previously free of symptoms.

Hospital discharges for HF by age: 1990 vs 2000



CDC. National Center for Health Statistics. National Hospital Discharge Survey. 2002.

Natural History of Chronic and Acute Heart Failure



Gheorghiade M. Am J Cardiol. 2005;96(suppl 6A):1-4G.

European Heart Journal (2010) **31**, 784–793
doi:10.1093/eurheartj/ehq040

CLINICAL REVIEW

Frontiers in cardiovascular medicine

The current and future management of acute heart failure syndromes

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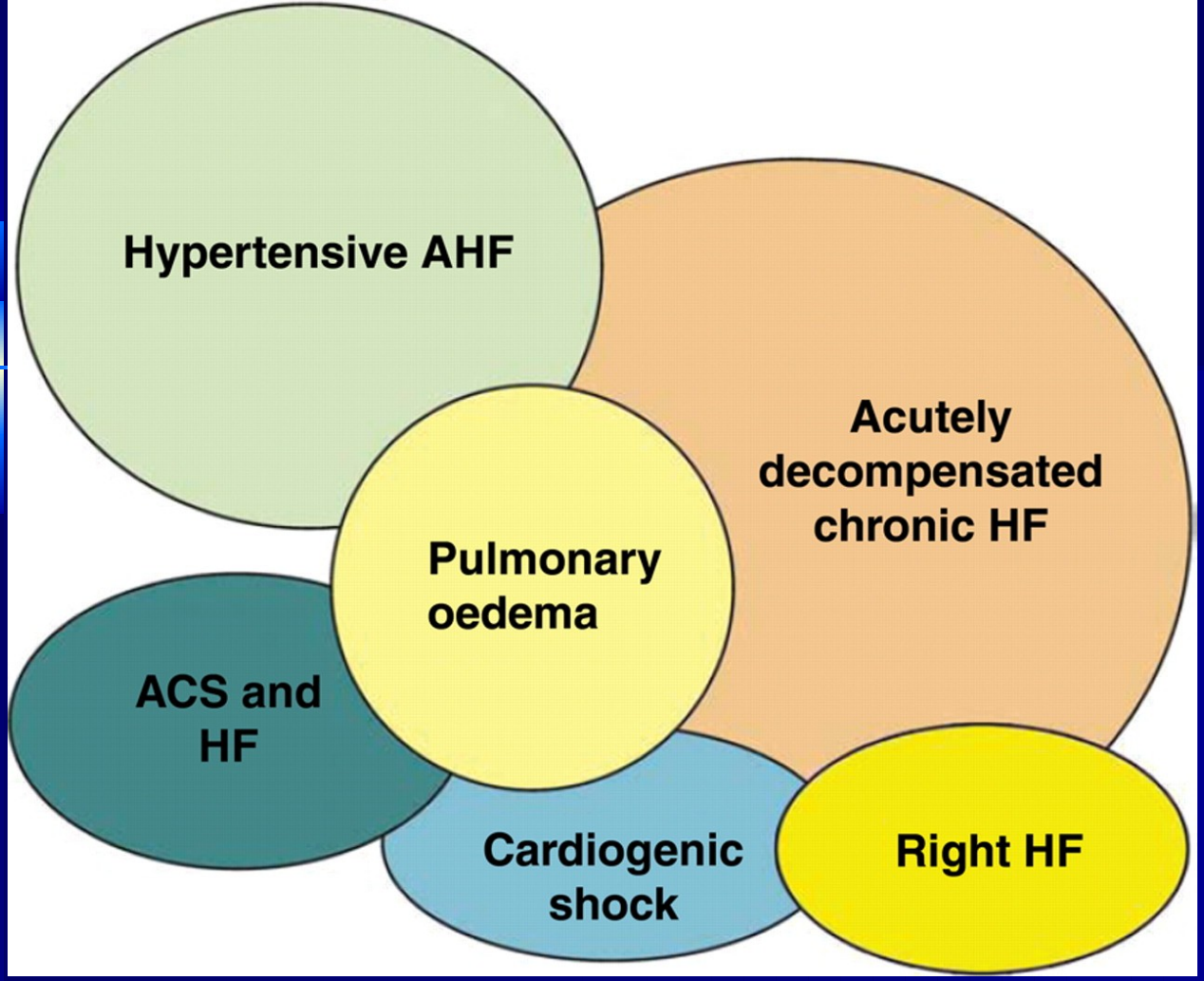
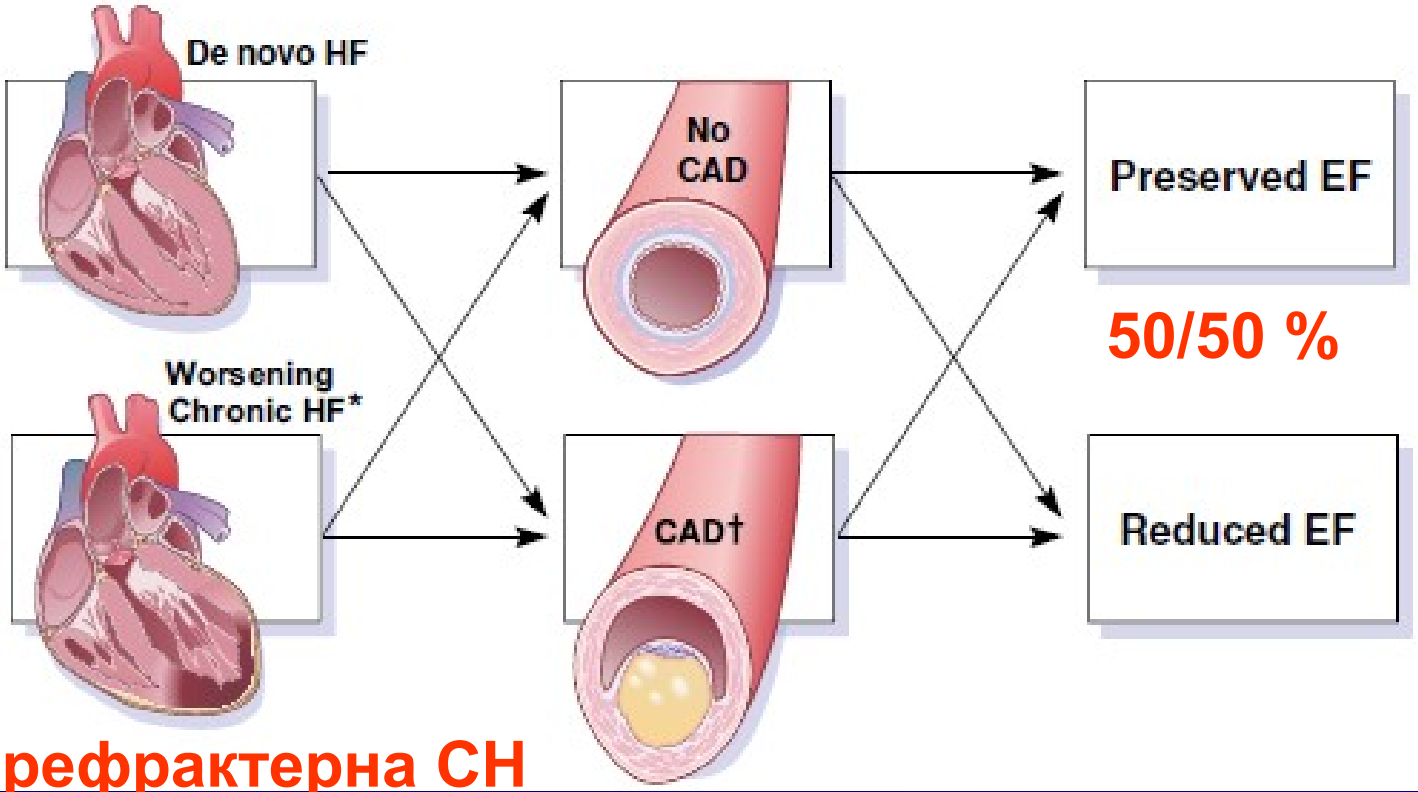


1. Обемно обременяване
2. Преразпределение на течностите
3. Силно намален МСО
4. Комбинация от ↓МСО и застой
5. Проинфламаторни механизми

European Heart Journal

Pang P S et al. Eur Heart J 2010;31:784-793

15-20%

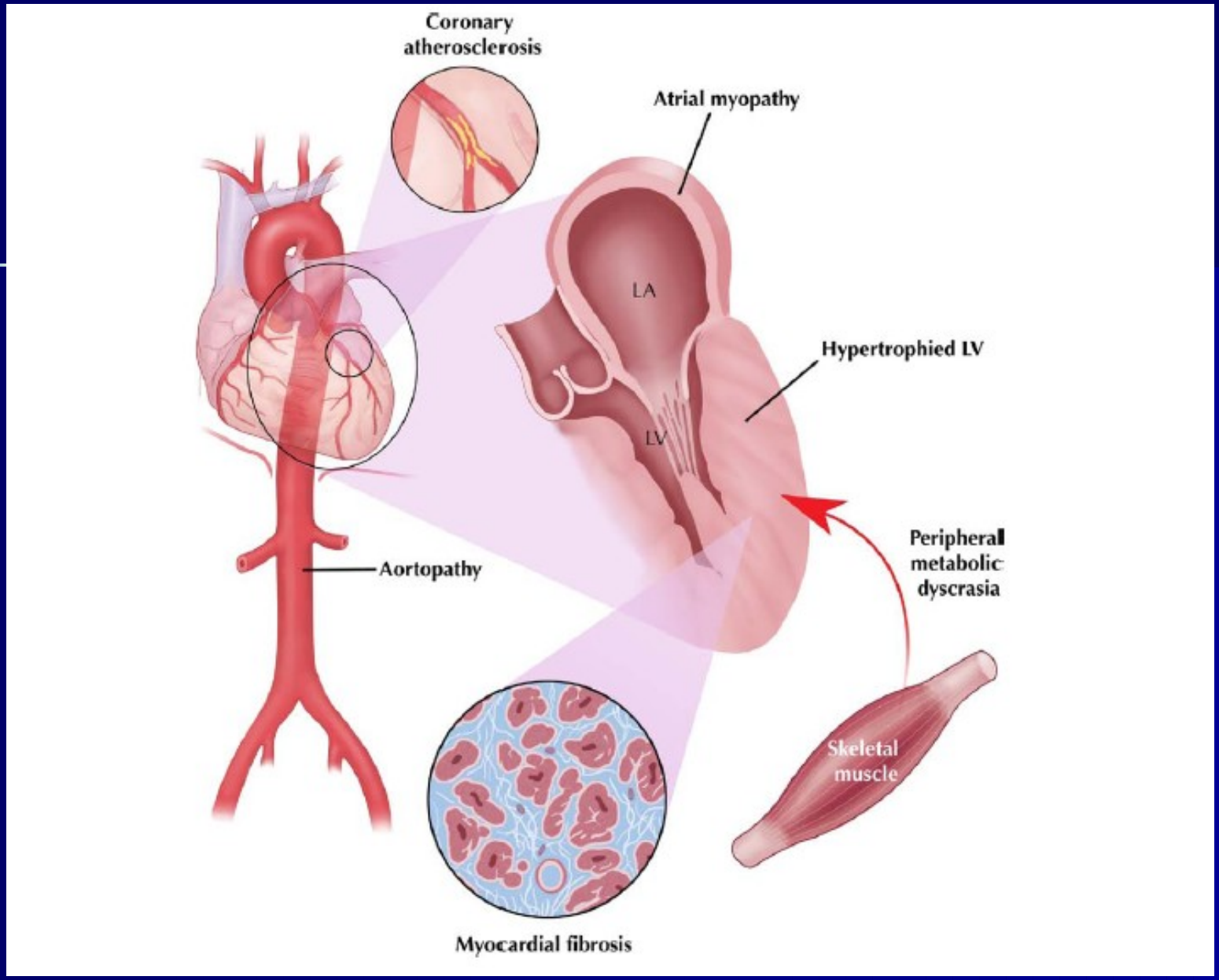


50/50 %

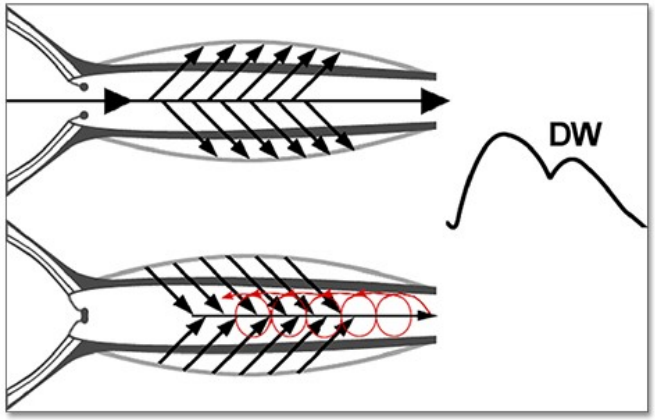
80 %

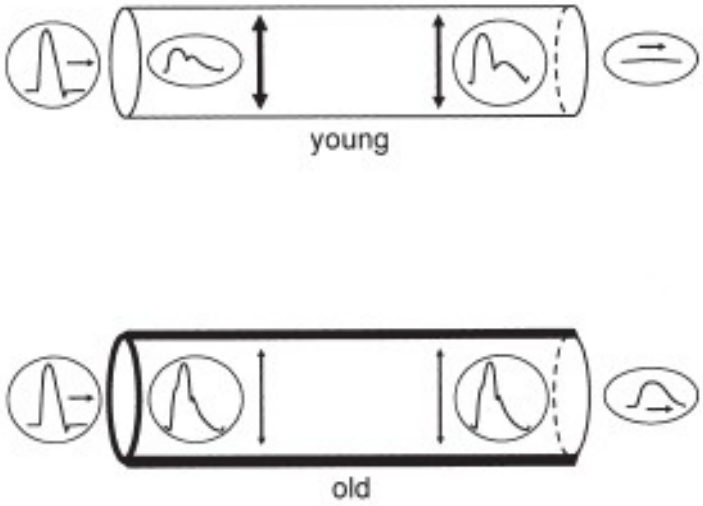
10% рефрактерна СН

JACC, 2009;53:557

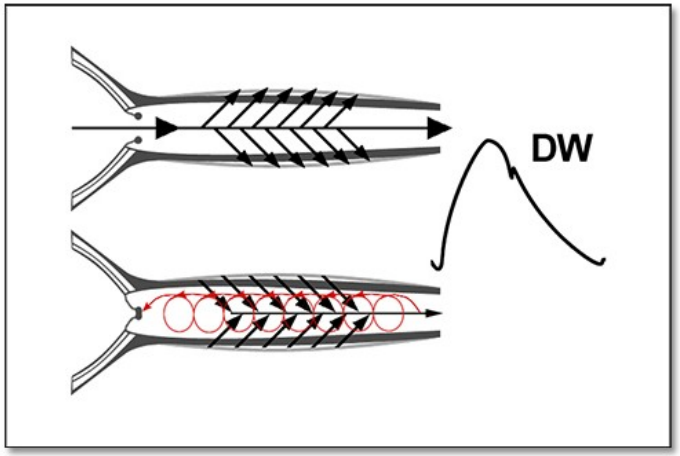


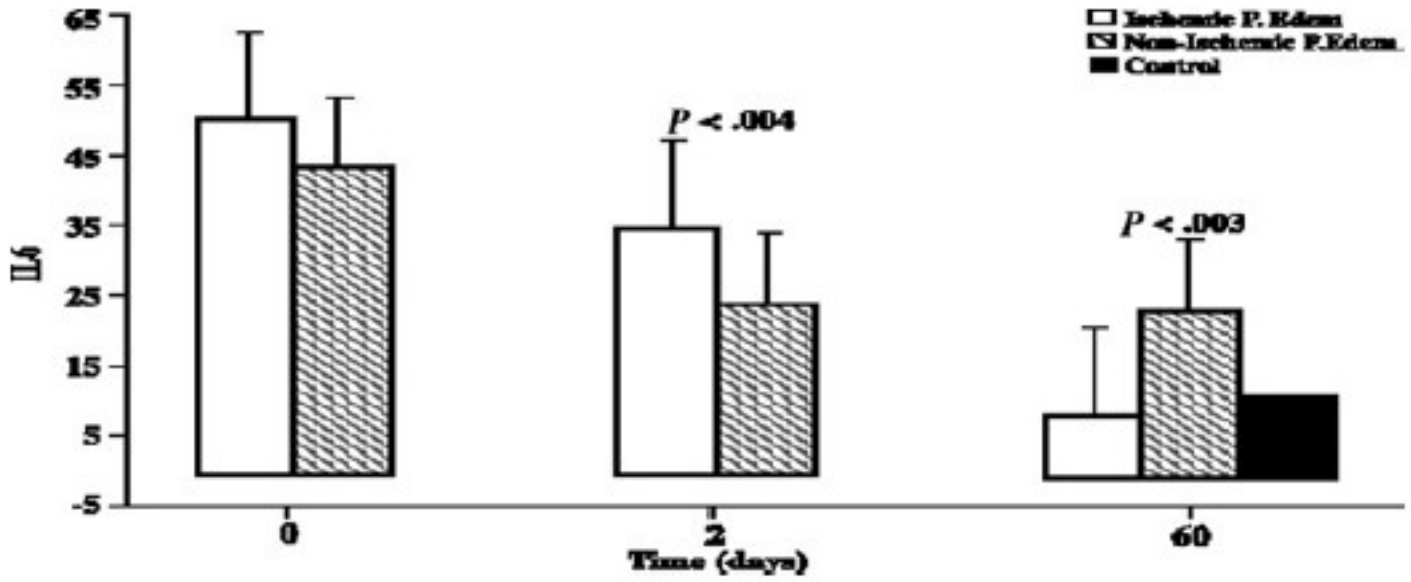
S. Raman, JACC 2010;55:91



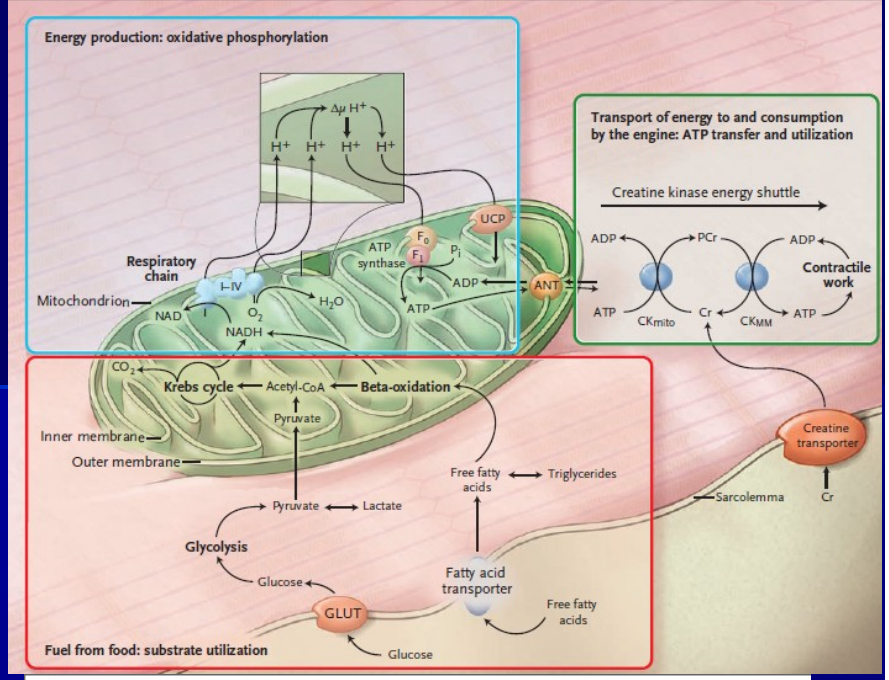


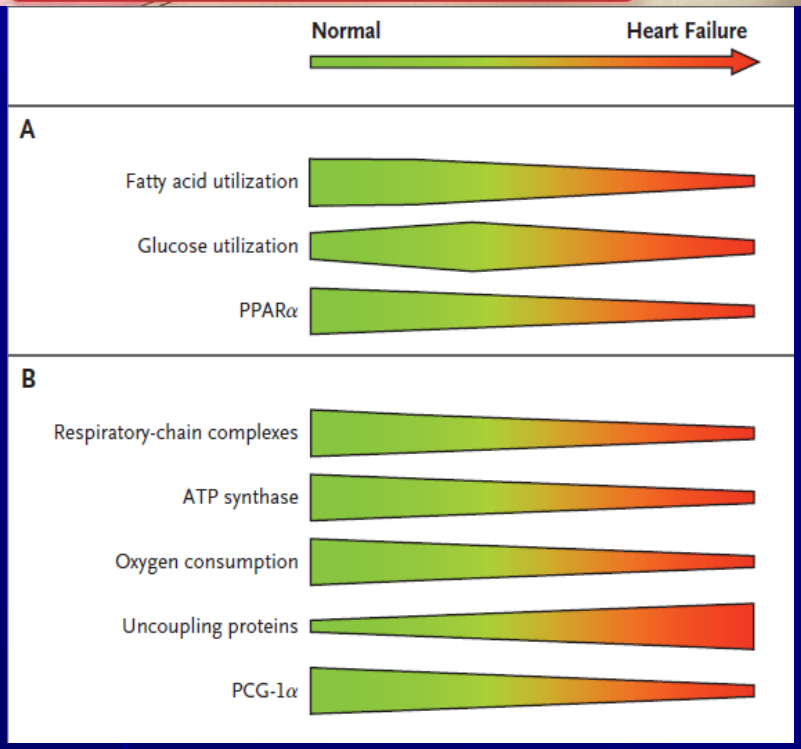
Pulse Wave Velocity and
Reflected Wave Velocity in Stiff Aorta

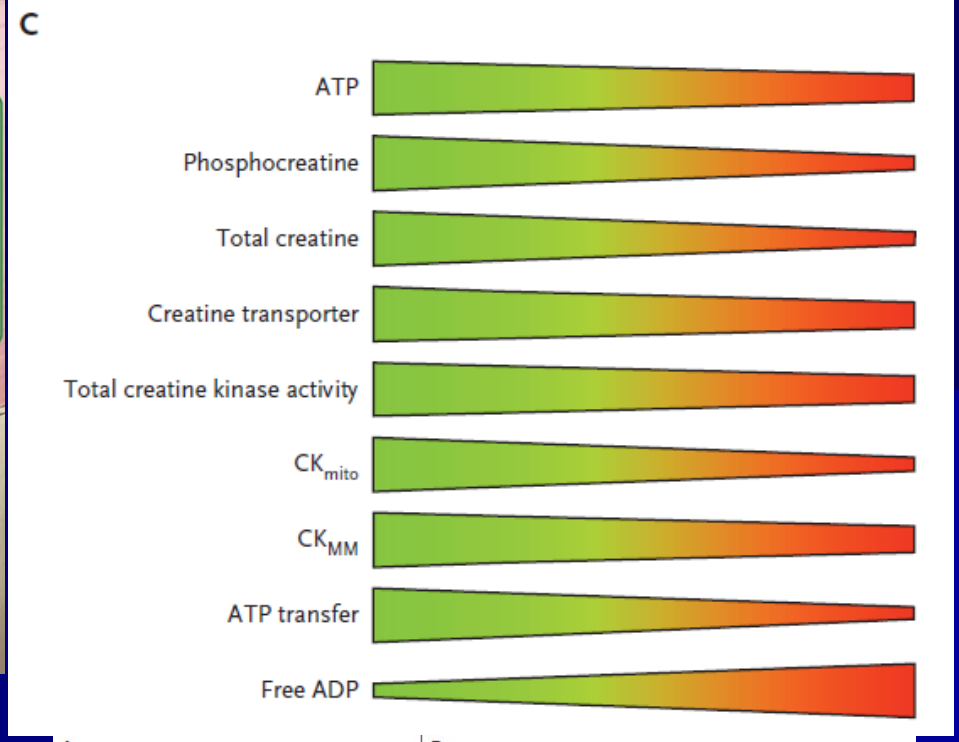


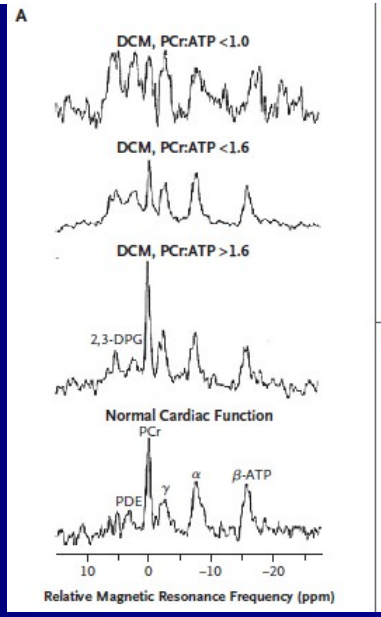


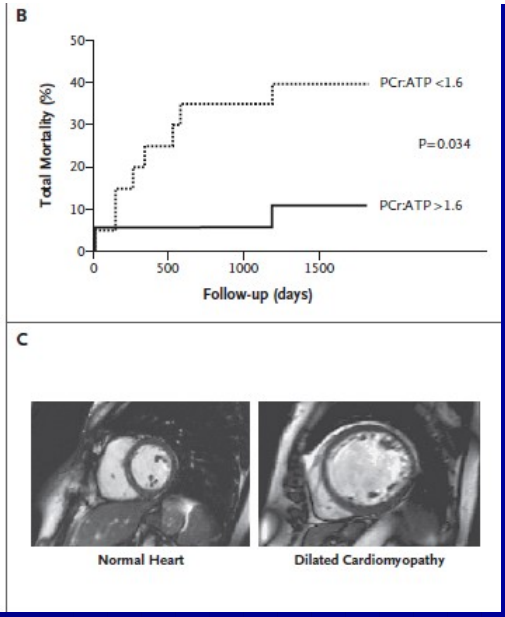
Changes in inflammatory markers in patients admitted with acute HF (interleukin 6 pg/mL).





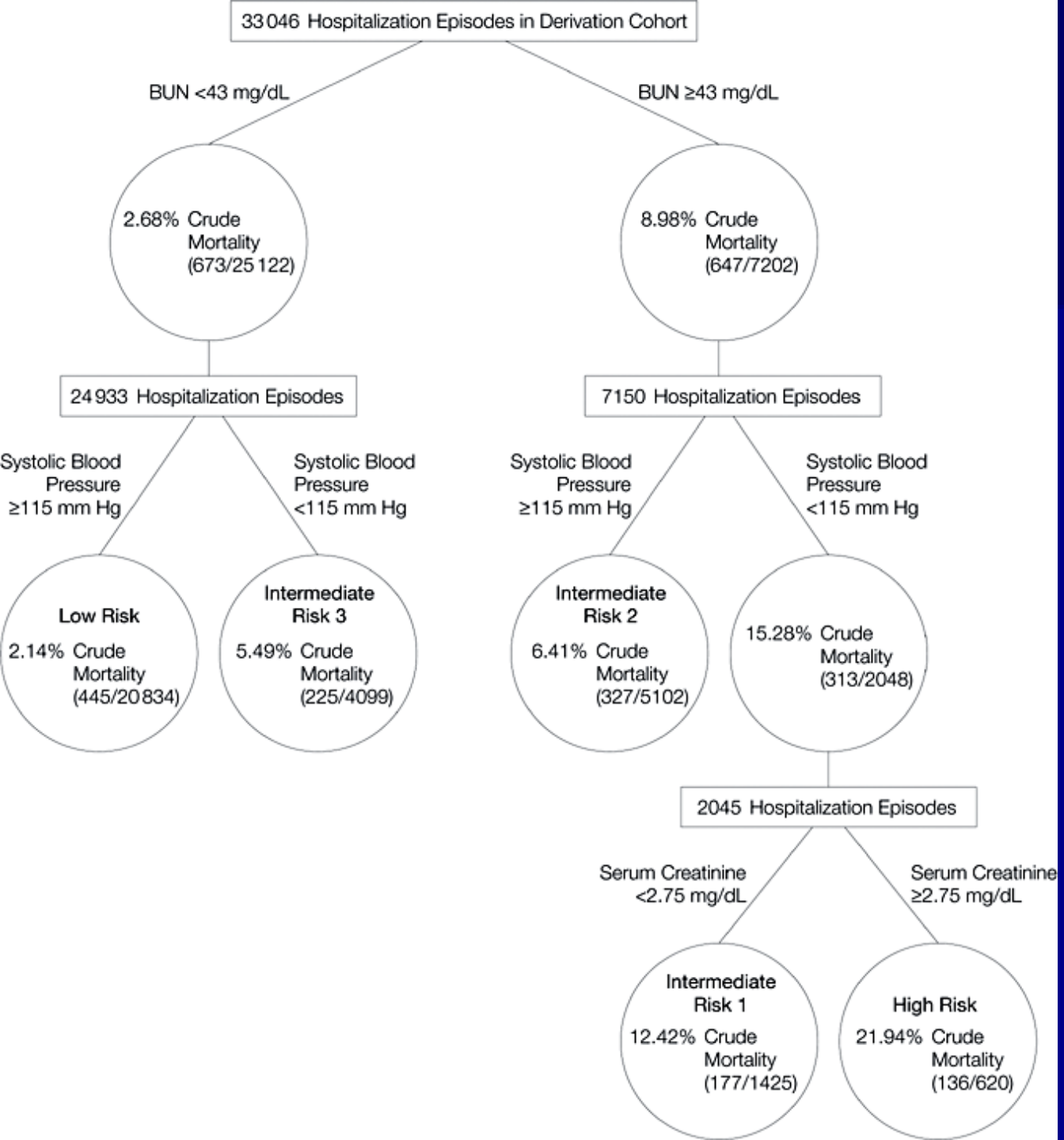






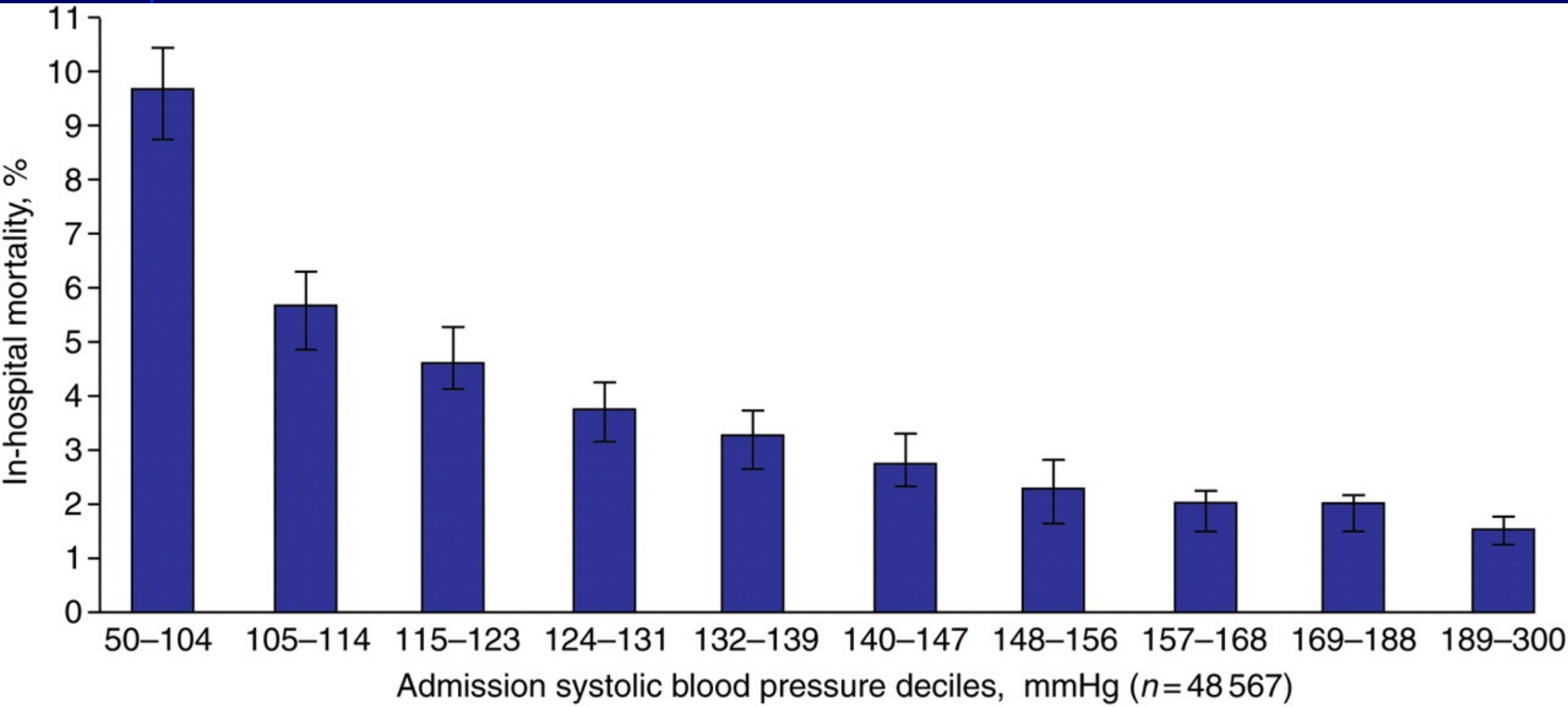
Neubauer S, NEJM 2007; 356:1140

Predictors of In-Hospital Mortality



Fonarow, G. C. et al. JAMA 2005;293:572-580.

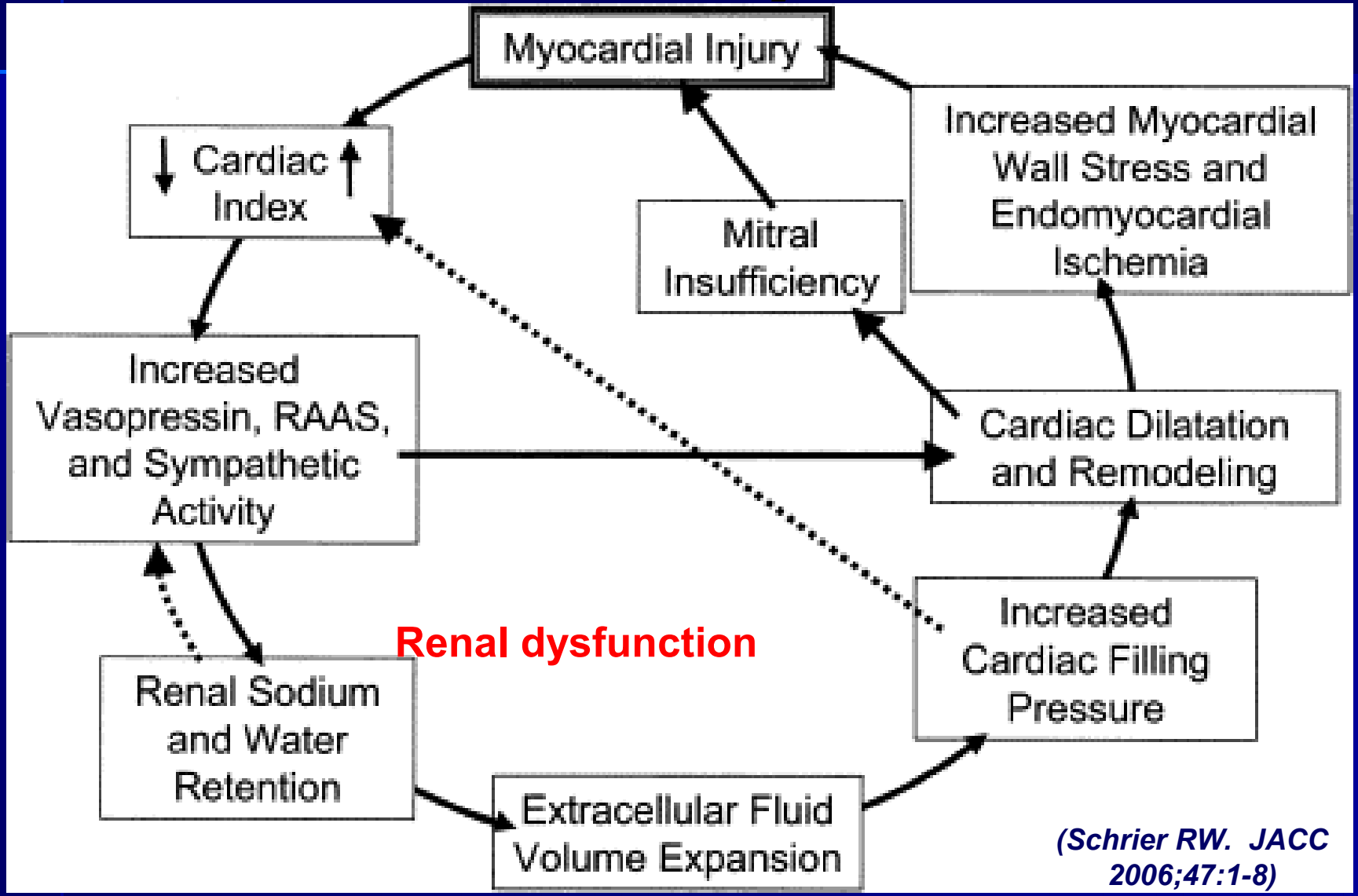
In-hospital mortality rates by admission systolic blood pressure deciles (n = 48 567).



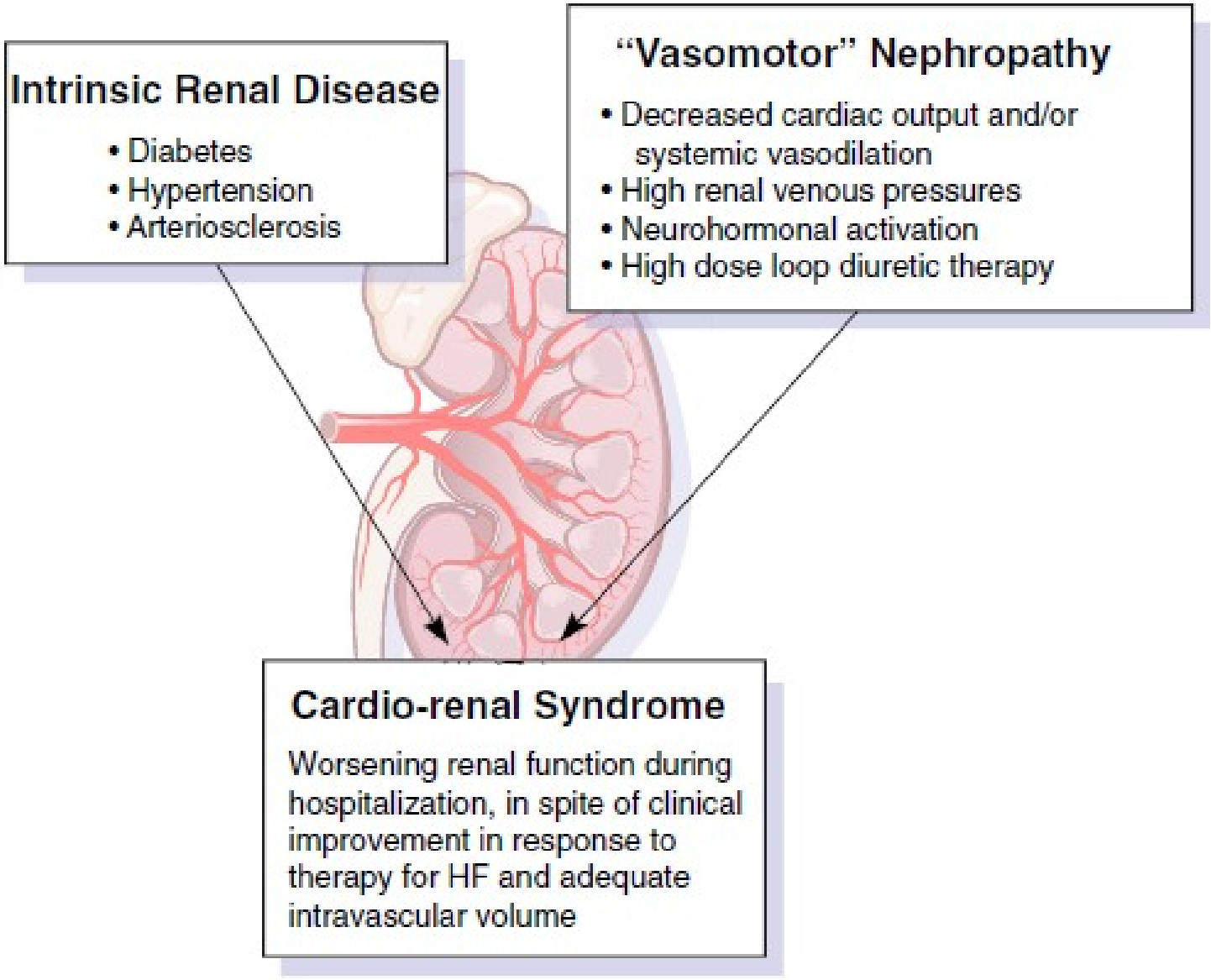
Pang P S et al. Eur Heart J 2010;31:784-793

European Heart Journal

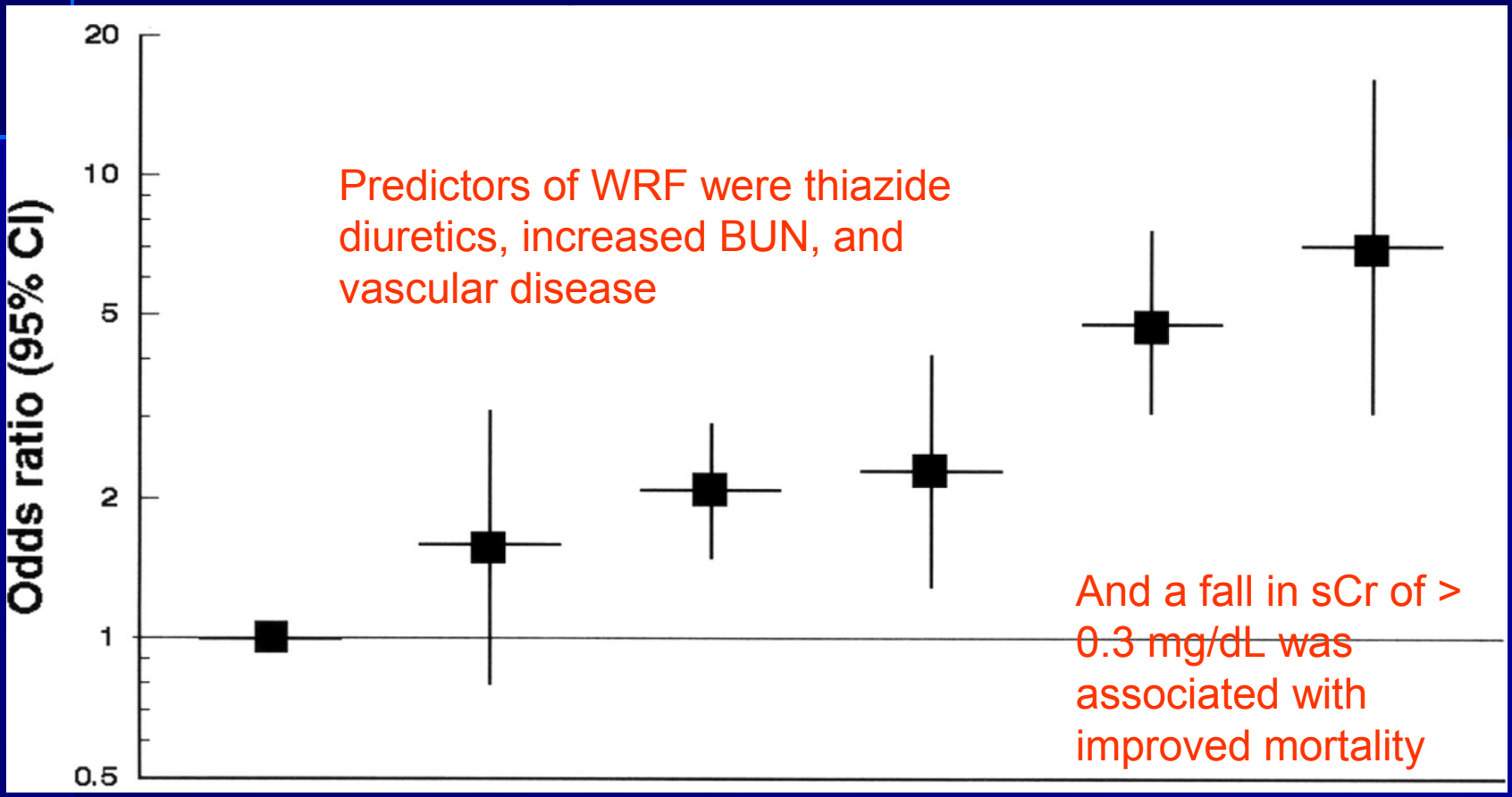
Mechanism of Worsening HF with Renal Dysfunction



(Schrier RW. JACC 2006;47:1-8)


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

Baseline Renal Dysfunction and Worsening Renal Function (WRF) are Additive in Predicting Mortality in HF Patients



sCreatinine	≤1.2	1.2-2.0	≥2.0	≤1.2	1.2-2.0	≥2.0
WRF (>0.3mg/dL)	no	no	no	yes	yes	yes

(de Silva, R. et al. Eur Heart J 2006 27:569-581)

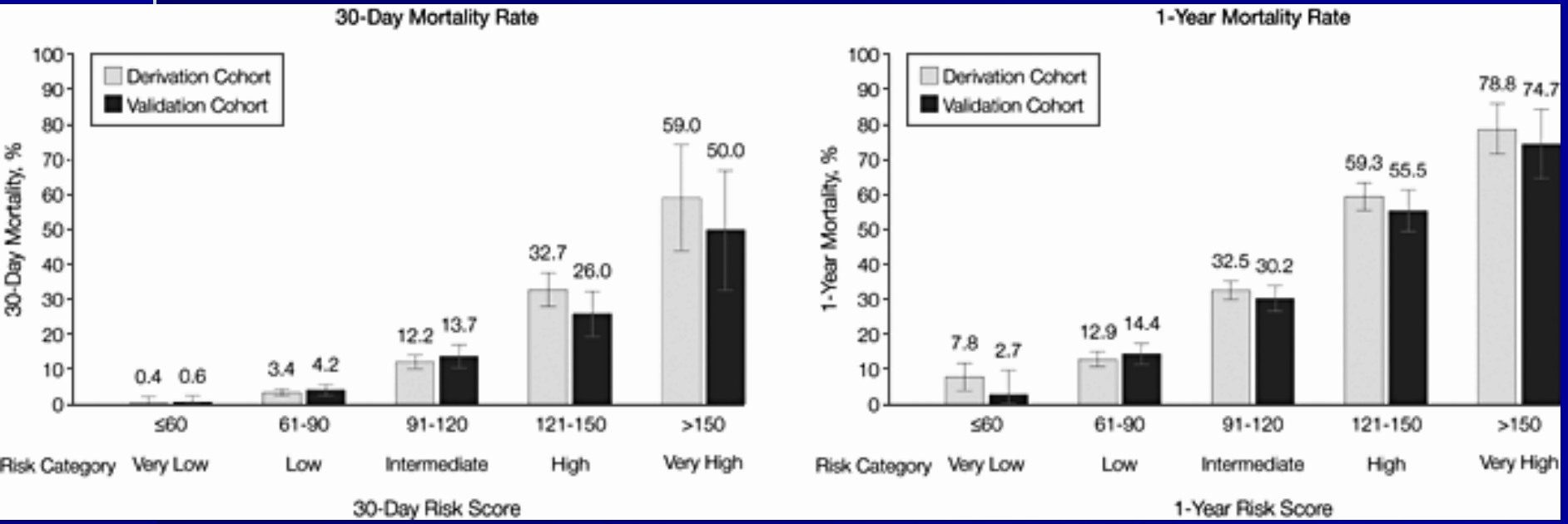
Heart Failure Risk Scoring System

Table 4. Heart Failure Risk Scoring System*

Variable	No. of Points	
	30-Day Score†	1-Year Score‡
Age, y	+Age (in years)	+Age (in years)
Respiratory rate, min (minimal 20; maximum 45)§	+Rate (in breaths/min)	+Rate (in breaths/min)
Systolic blood pressure, mm Hg‖		
≥180	−60	−50
160-179	−55	−45
140-159	−50	−40
120-139	−45	−35
100-119	−40	−30
90-99	−35	−25
<90	−30	−20
Urea nitrogen (maximum, 60 mg/dL)§¶	+Level (in mg/dL)	+Level (in mg/dL)
Sodium concentration <136 mEq/L	+10	+10
Cerebrovascular disease	+10	+10
Dementia	+20	+15
Chronic obstructive pulmonary disease	+10	+10
Hepatic cirrhosis	+25	+35
Cancer	+15	+15
Hemoglobin <10.0 g/dL (<100 g/L)	NA	+10

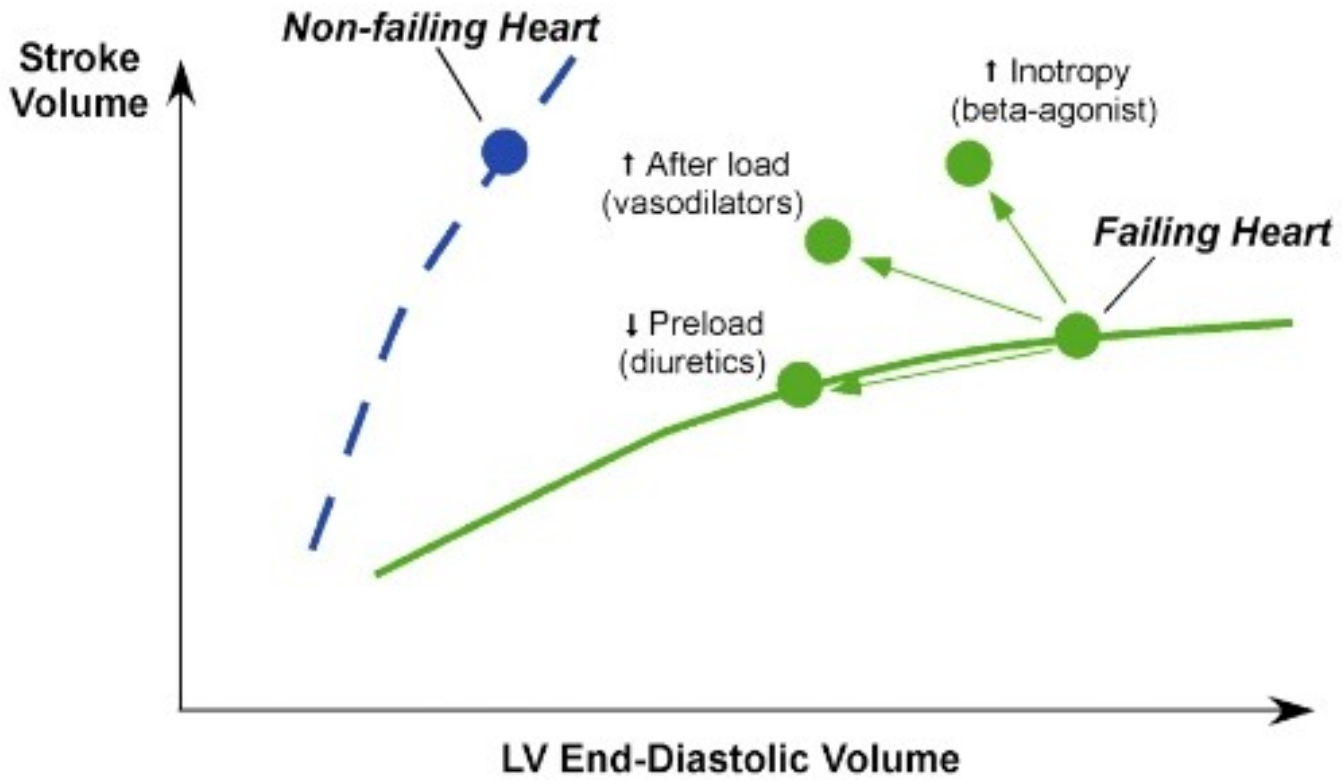
JAMA. 2003;289:2541-2547

Mortality Rates in Acutely Decompensated Heart Failure by Risk Score



JAMA. 2003;290:2581-2587.

Frank-Starling Relationship



Клиничен профил на ХСН

Застой в покой

Ниска перфузия в покой	НЕ	ДА
НЕ	Топли и сухи	Топли и влажни
ДА	Студени и сухи	Студени и влажни

Признаци на застой:

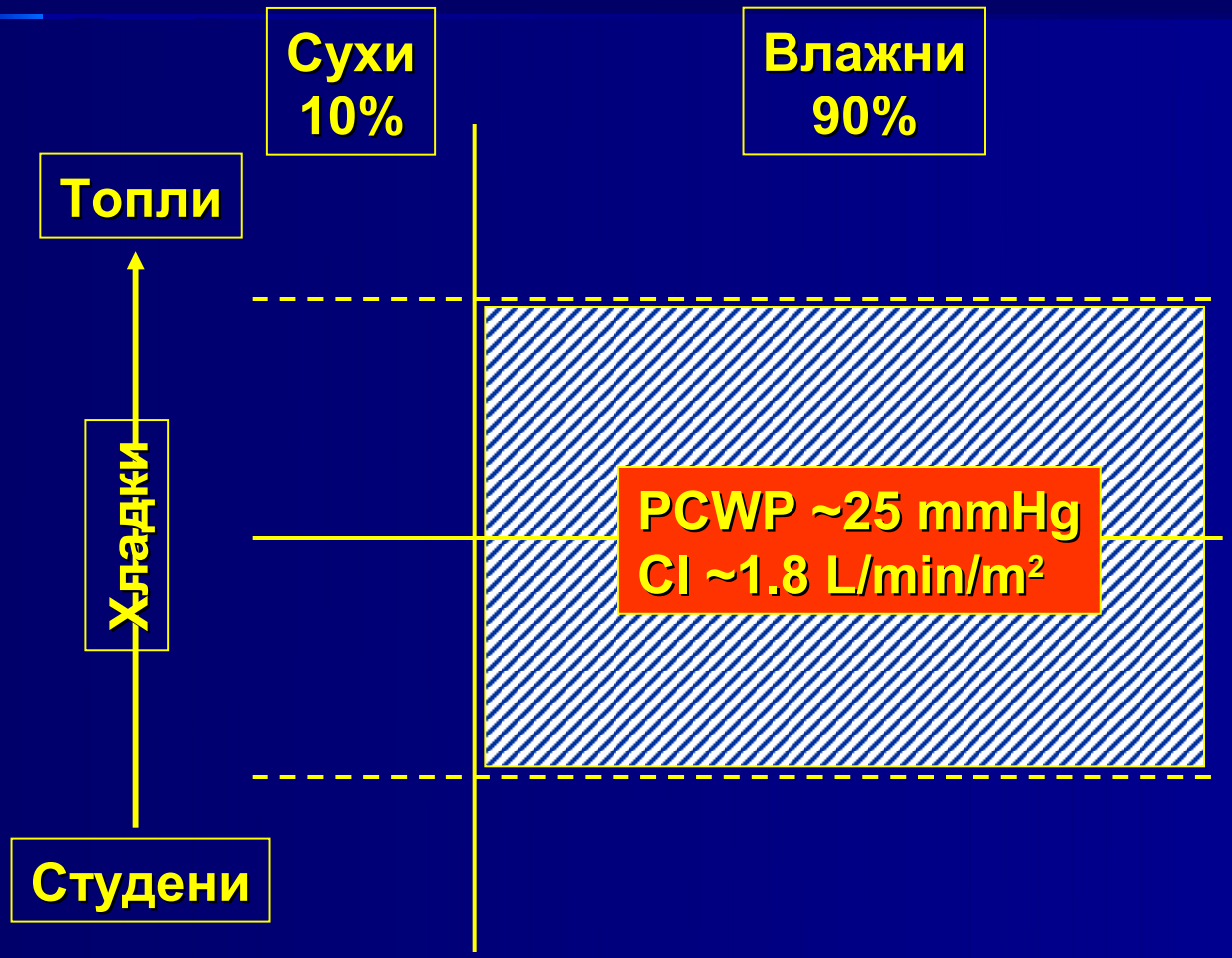
- Ортопнея
- Астма кардиале
- Шиен венозен застой
- Т3
- Хепатомегалия
- Отоци
- Хрипове
- Хепато-югуларен рефлукс

Клинични белези за хипоперфузия:

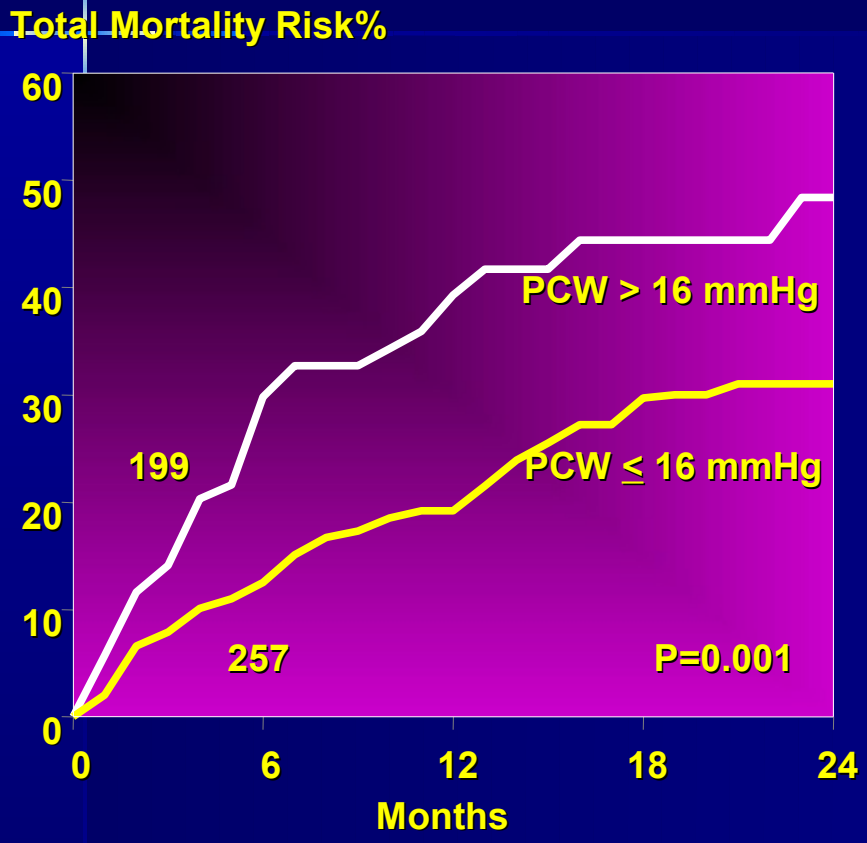
- Ниско пулсово налягане
- Сънливост
- Нисък серумен Na
- Студени крайници
- Хипотония при ACE инхибитор
- Бъбречна/чернодробна дисфункция

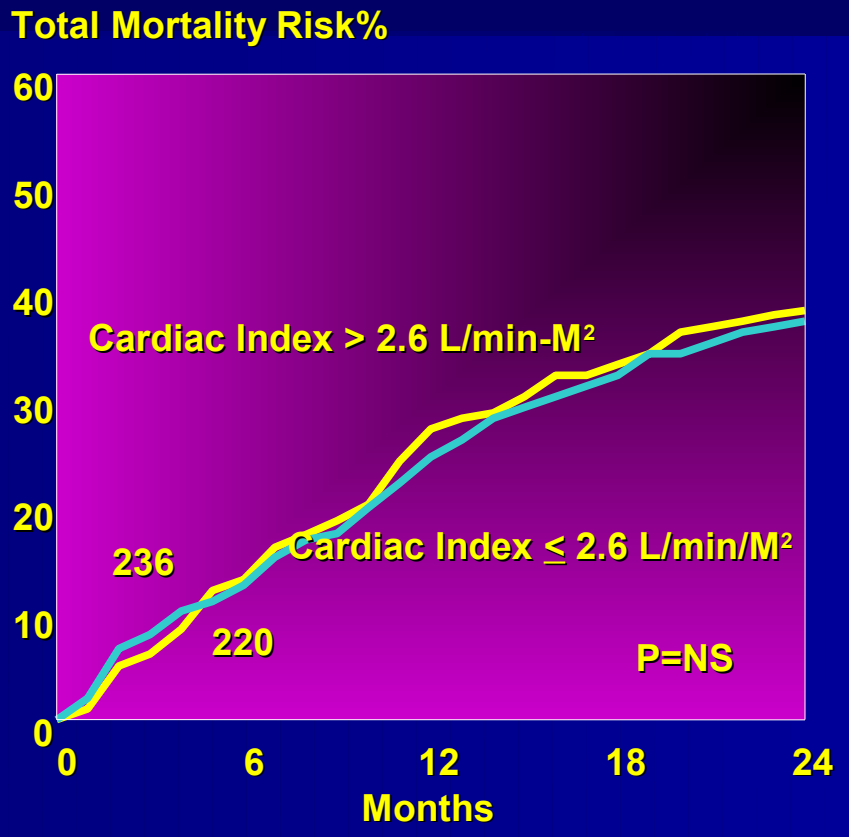
По Warner Stevenson

Клиничен профил на болните с ХСН



Early Response of PCW but not CI Predicts Subsequent Mortality in Advanced Heart Failure

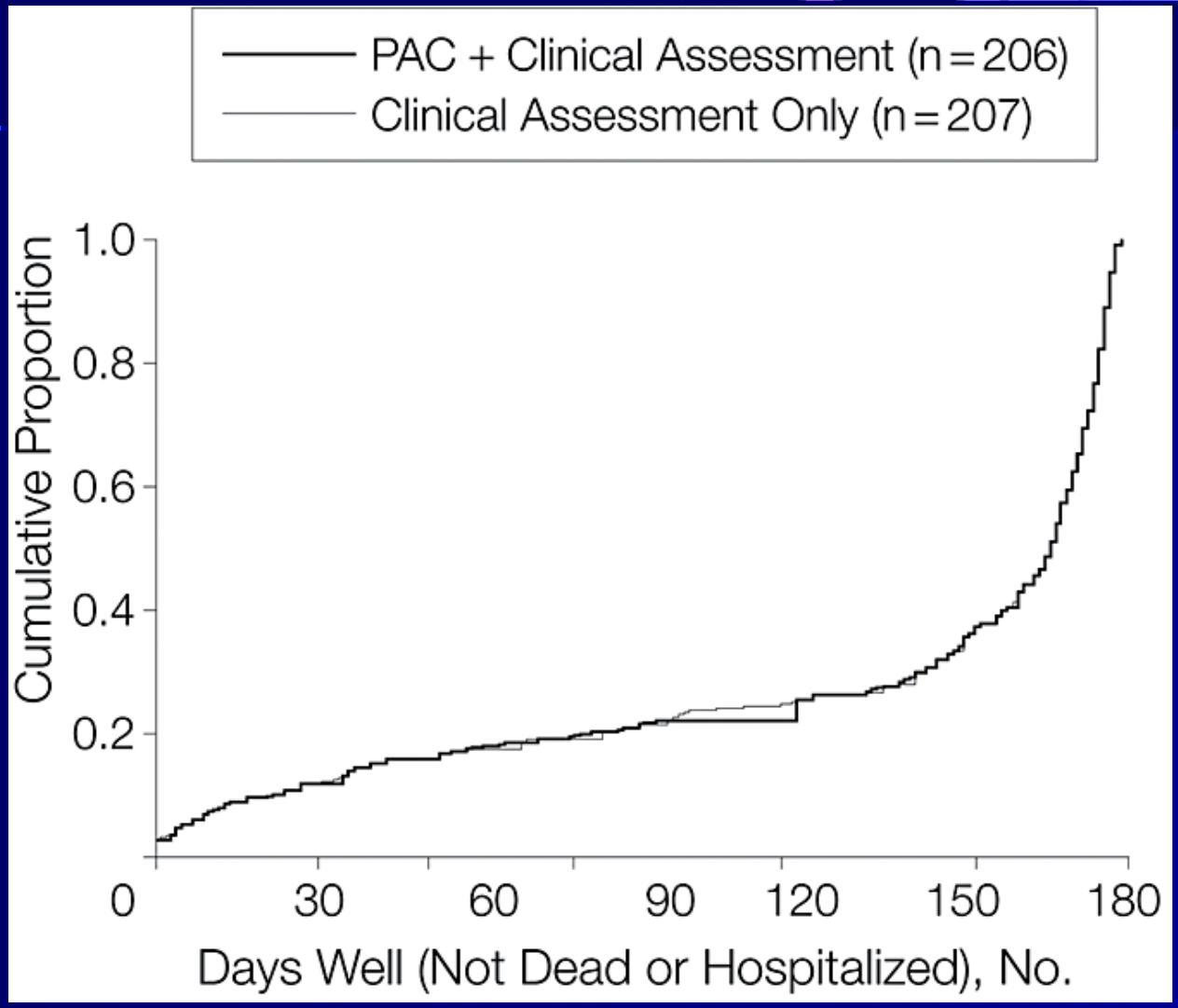




Final hemodynamic measurement in 456 advanced HF patients after tailored vasodilator therapy

(Fonarow G Circulation 1994;90:I-488)

Is the Swan-Ganz Catheter Useful in the Patient with Acute Decompensated HF?



(Stevenson, et al. JAMA 2005;294:1625-1633)

Table 5 Ideal properties for an acute heart failure syndromes therapy

1. Improve signs and symptoms (e.g. dyspnoea)
2. Improve haemodynamics without adversely effecting heart rate and blood pressure
3. Improve the neurohumoral profile
4. Do not cause myocardial and/or kidney damage
5. Be effective in the context of current evidence-based therapy such as ACE-I and beta-blockers
6. Demonstrate efficacy in both the acute and chronic setting
7. Be affordable
8. Reduce both in-hospital and post-discharge morbidity and mortality.

Утвърдени и експериментални медикаменти за лечение на остра сърдечна недостатъчност

	Утвърдени медикаменти	Експериментални медикаменти
СН при нормално – високо САН	1. Диуретици 2. Вазодилататори Нитроглицерин Нитропрусид Несиритид 3. АСЕ инхибитори	1. Антагонисти на вазопресин 2. Антагонисти на аденозин 3. Антагонисти на ендотелин 4. Уларитид
СН при нормално – ниско САН	1. Левосимендан 2. Добутамин 3. Допамин 4. Милринон 5. Дигоксин	1. Активатори на миозина 2. Метаболитни модулатори 3. Истароксим

Table 3 Initial therapeutic management

Target	Therapeutic example	Mechanism of action	Side effects
Alleviate congestion	IV furosemide	Water and sodium excretion	Electrolyte abnormalities
Reduce elevated LV filling pressures	IV nitrates	Direct relaxation of vascular smooth muscle cells through various mechanisms	Hypotension, decreased coronary perfusion pressure
Poor cardiac performance	Inotropes	Activate camp or calcium sensitization resulting in improved contractility; also powerful vasodilators: in effect, inodilators	Hypotension, arrhythmias, myocardial damage, association with increased morbid events
Tachycardia and increased systemic blood pressure (i.e. in cases of excessive sympathetic tone)	Beta-blockers: IV esmolol may be used when HF is related to AF with RVR and/or severe hypertension	Blockade of beta-1 and beta-2 receptors	Bradycardia, hypotension, negative inotropy; however given short half-life of esmolol, these side effects should be short lived

Adopted and reproduced with permission from Khan *et al.*[67]

Comprehensive assessment

Potential targets	*Method of assessment*
Congestion	JVP, body weight, peripheral oedema
High blood pressure	Blood pressure measurement
LV function, valvular disease, wall motion abnormalities, aneurysm	ECHO Doppler, MRI, nuclear imaging
Ischaemia	Pharmacological or exercise testing with imaging
CAD	Cardiac catheterization and angiography
Ventricular dyssynchrony (wide QRS)	Electrocardiogram
Viable but dysfunctional myocardium	Low-dose dobutamine ECHO, MRI

Cardiac reconstruction
(five overarching thematic targets—myocardium, coronary arteries, electrical system, pericardium, valves)

Myocardium

LV dysfunction #
- ACE-I or ARB
- Beta-blockers
- Aldosterone antagonist*
- Hydral/ISDN*
- Digoxin*
- Macronutrients**
- Micronutrients**
- Metabolic modulators**

Coronary arteries

CAD
- Anti-platelet*
- Statins*
- Revascularization*
- Other ESC guideline recommended therapy for secondary prevention

Electrical system

Sudden cardiac death
- ICD
- Beta-blockers
- Aldosterone antagonists

Ventricular dyssynchrony
- CRT +/– ICD*

Atrial fibrillation
- Rate control*
  - Digoxin
  - Beta-blocker
  - Non-dihydropyridine calcium channel blockers*
- Warfarin*
- Rhythm control*
- MAZE procedure

Valves
- Surgery*
- Procedural*
- Statins
- Per ESC guidelines

Pericardium

Congestion – (salt restriction, diuretics, ultrafiltration*, vasopressin antagonists**

Hypertension (ACE-I or ARB, beta-blockers, diuretics, others per ESC guidelines)

Enhance Adherence (education, disease management, performance improvement systems)

Pang P S et al. Eur Heart J 2010;31:784-793

Panel 1: **Indications and contraindications for NIV in acute care**

Indications

Bedside observations

- Increased dyspnoea—moderate to severe
- Tachypnoea (>24 breaths per min in obstructive, >30 per min in restrictive)
- Signs of increased work of breathing, accessory muscle use, and abdominal paradox

Gas exchange

- Acute or acute on chronic ventilatory failure (best indication), $PaCO_2$>45 mm Hg, pH<7·35
- Hypoxaemia (use with caution), PaO_2/F_IO_2 ratio<200

Contraindications

Absolute

- Respiratory arrest
- Unable to fit mask

Relative

- Medically unstable—hypotensive shock, uncontrolled cardiac ischaemia or arrhythmia, uncontrolled copious upper gastrointestinal bleeding
- Agitated, uncooperative
- Unable to protect airway
- Swallowing impairment
- Excessive secretions not managed by secretion clearance techniques
- Multiple (ie, two or more) organ failure
- Recent upper airway or upper gastrointestinal surgery

NIV=non-invasive ventilation; $PaCO_2$=arterial partial pressure of carbon dioxide; PaO_2=arterial partial pressure of oxygen; F_IO_2=fraction of inspired oxygen.

Level 1 evidence

Systematic reviews (with homogeneity) of RCTs and individual RCTs (with narrow CIs)

Evidence of use (favourable)

- COPD exacerbations
- Facilitation of weaning/extubation in patients with COPD
- Cardiogenic pulmonary oedema
- Immunosuppressed patients

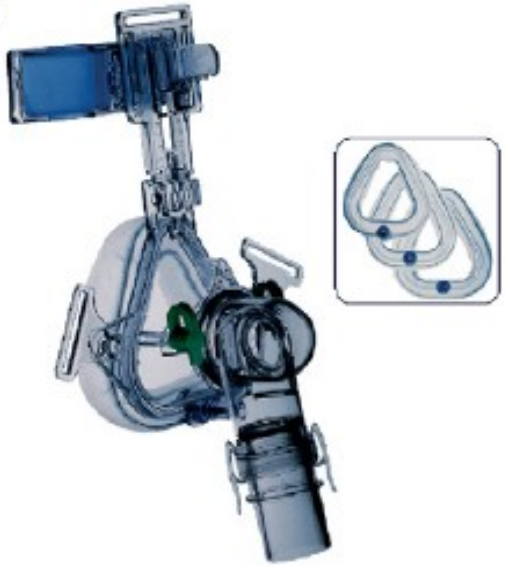
Evidence of use (caution)

- None

A

Full face mask

C



Nasal mask

Nava S et al., Lancet2009;374: 250

National Heart Lung and Blood Institute
People Science Health

HEART FAILURE NETWORK

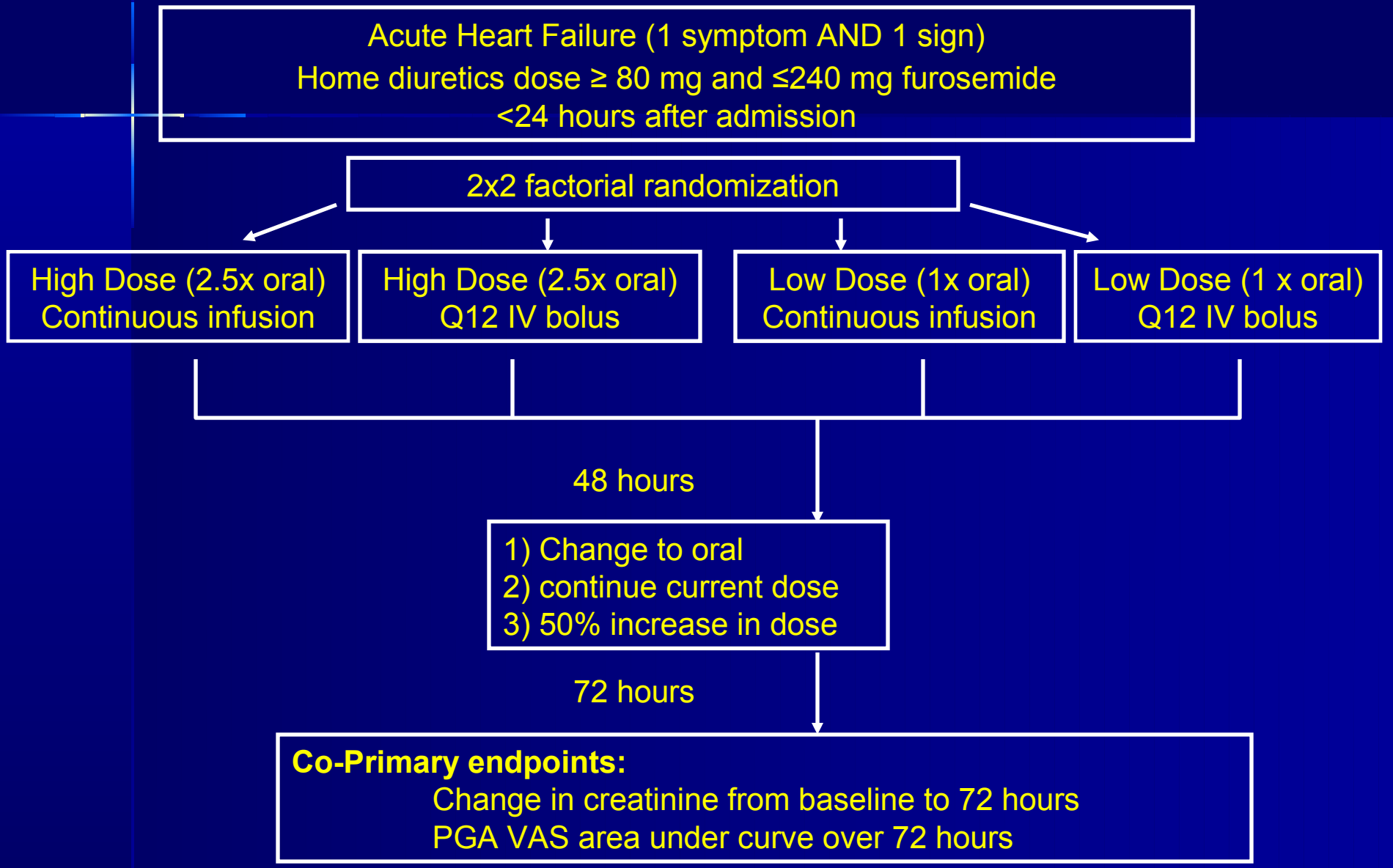
Diuretic Optimization Strategies Evaluation in Acute Heart Failure (DOSE)

G. Michael Felker, MD, MHS, FACC
Christopher M. O'Connor, MD, FACC

on behalf of the

NHLBI Heart Failure Clinical Research Network

Study Design



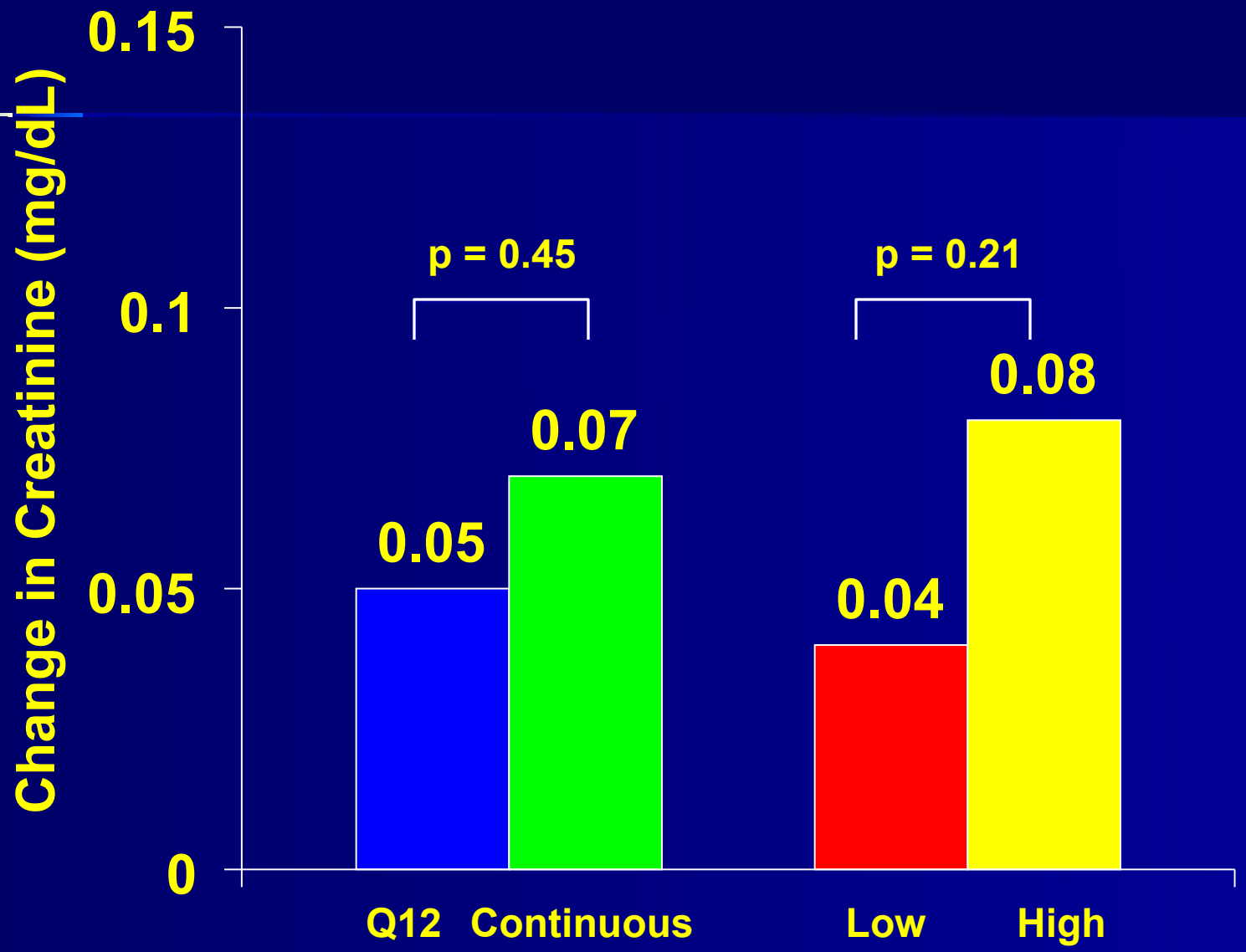
Baseline Characteristics (1)

Characteristic	N = 308
Age, yrs (mean, SD)	66 (13.6)
Male, % (N)	73% (226)
Race, % white, (N)	72% (222)
Baseline furosemide dose, mg/day, mean (SD)	130.6 (51.7)
Ejection fraction, %, mean (SD)	35 (18)
Prior HF hosp in last 12 mos, % (N)	74% (225)
Ischemic etiology, % (N)	57% (176)
Atrial fibrillation or flutter, % (N)	53% (162)
Diabetes mellitus, % (N)	51% (158)

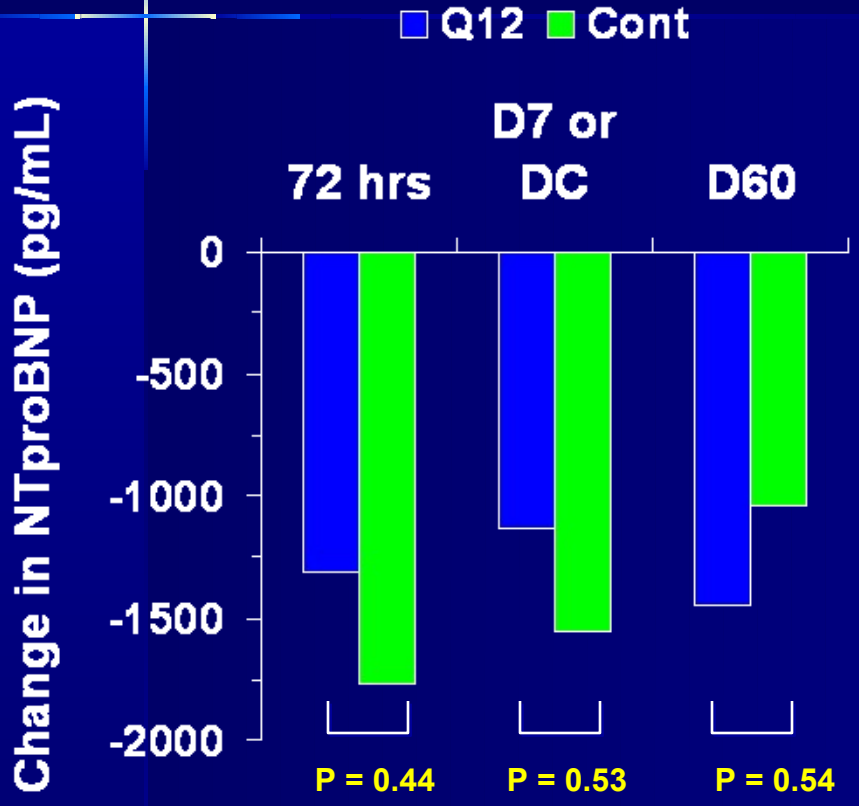
Baseline Characteristics (2)

Characteristic	N = 308
ACE or ARB, %, (N)	64% (197)
Beta blocker, % (N)	83% (256)
Aldosterone antagonist % (N)	28% (86)
Systolic blood pressure, mg, mean (SD)	119 (20)
Heart rate, beats/min, mean (SD)	78 (16)
Jugular venous pulse > 8 cm H20, % (N)	91% (267)
Rales, % (N)	58% (178)
Sodium, mg/dL, mean (SD)	138 (4)
Creatinine, mg/dL, mean (SD)	1.6 (0.5)
NT-proBNP, pg/mL, mean (SD)	7439 (7319)

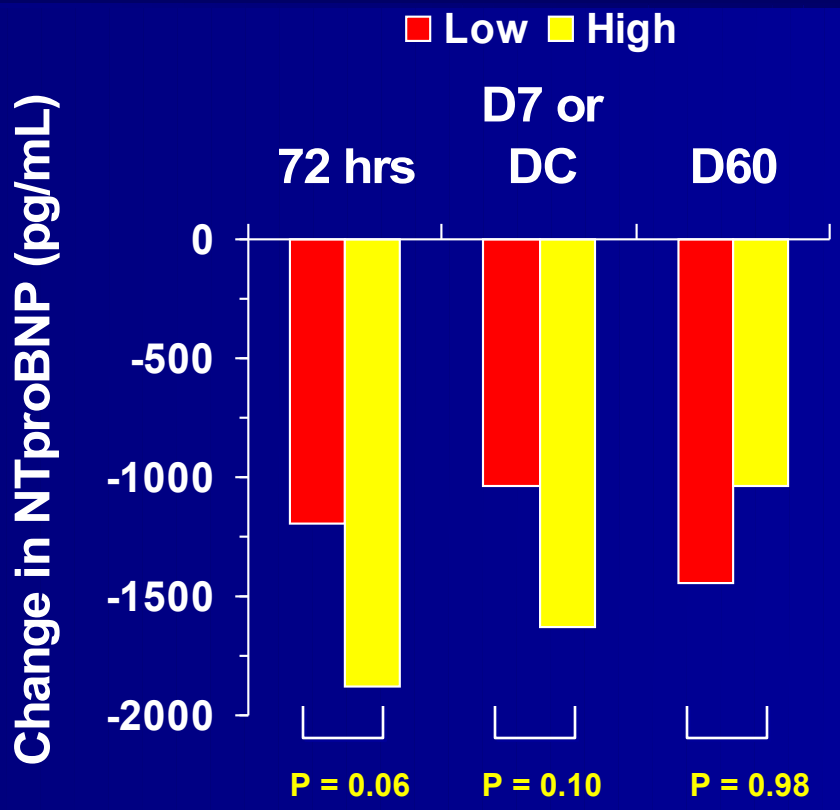
Change in Creatinine at 72 hours



Changes in NTproBNP

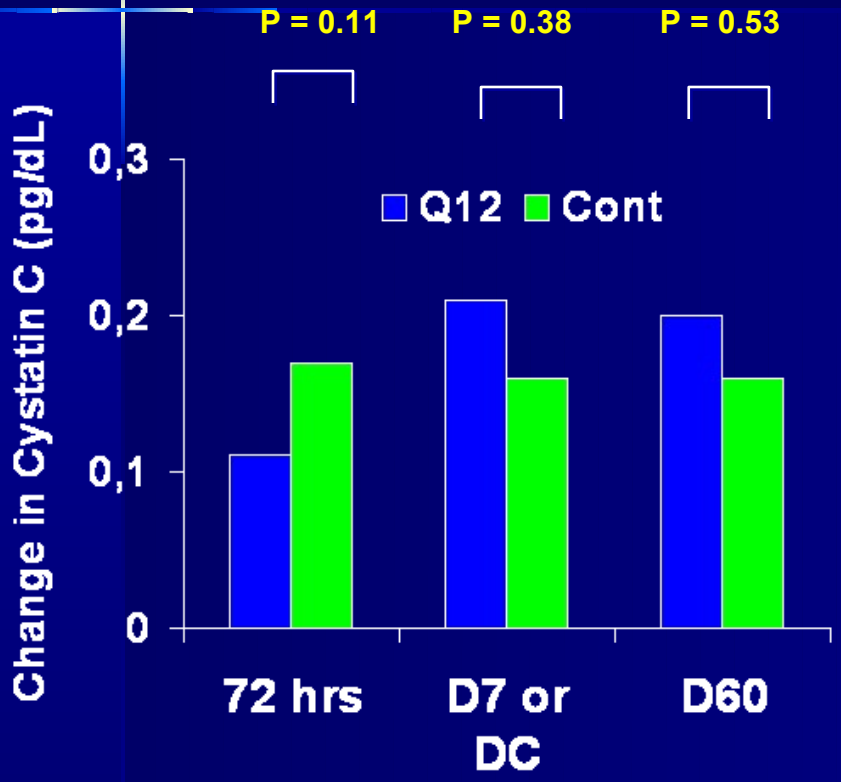


Q12 vs. Continuous

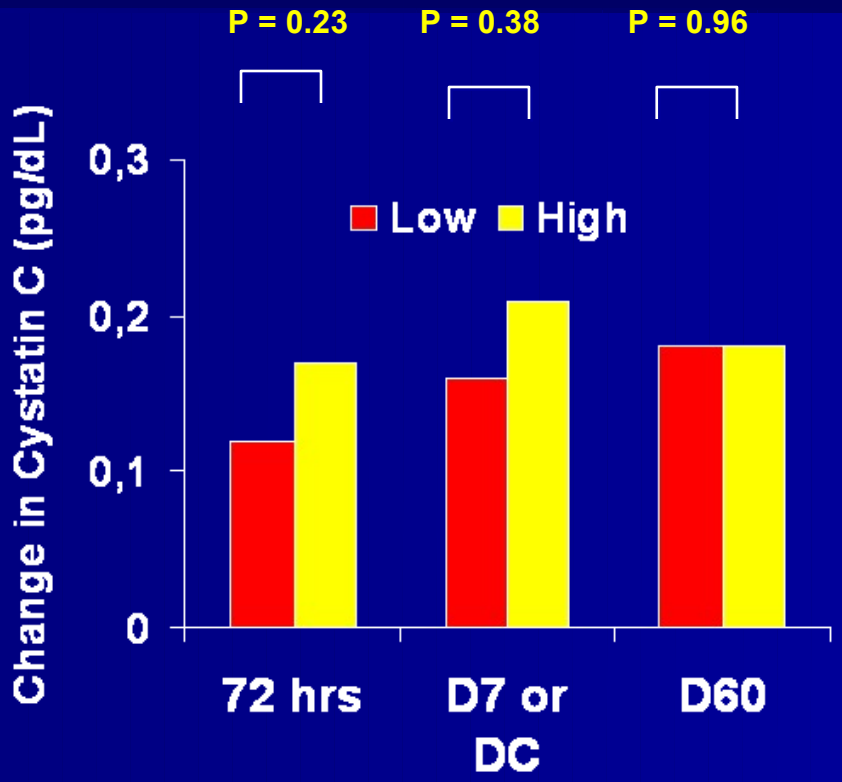


Low vs. High

Changes in Cystatin C

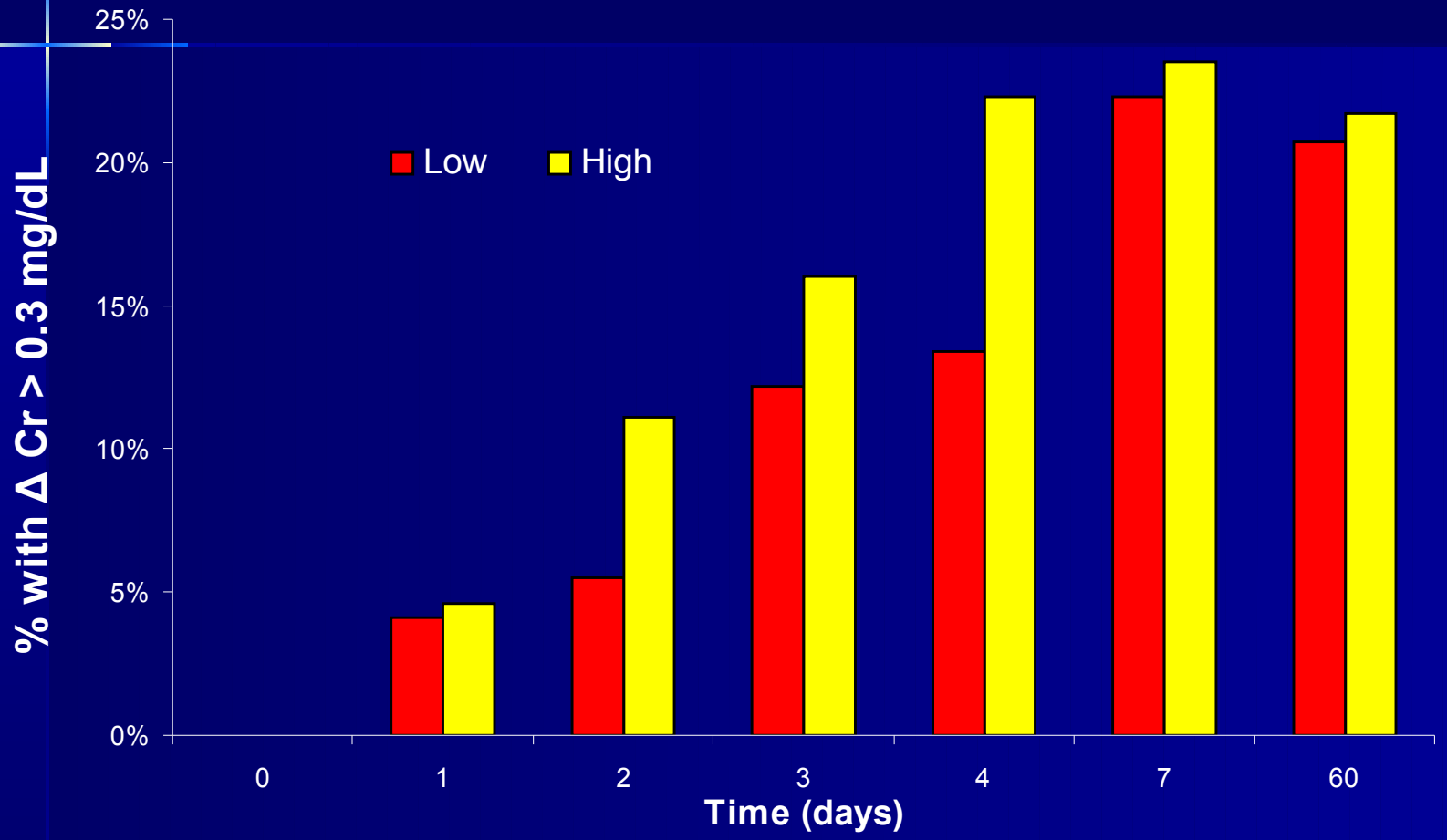


Q12 vs. Continuous



Low vs. High

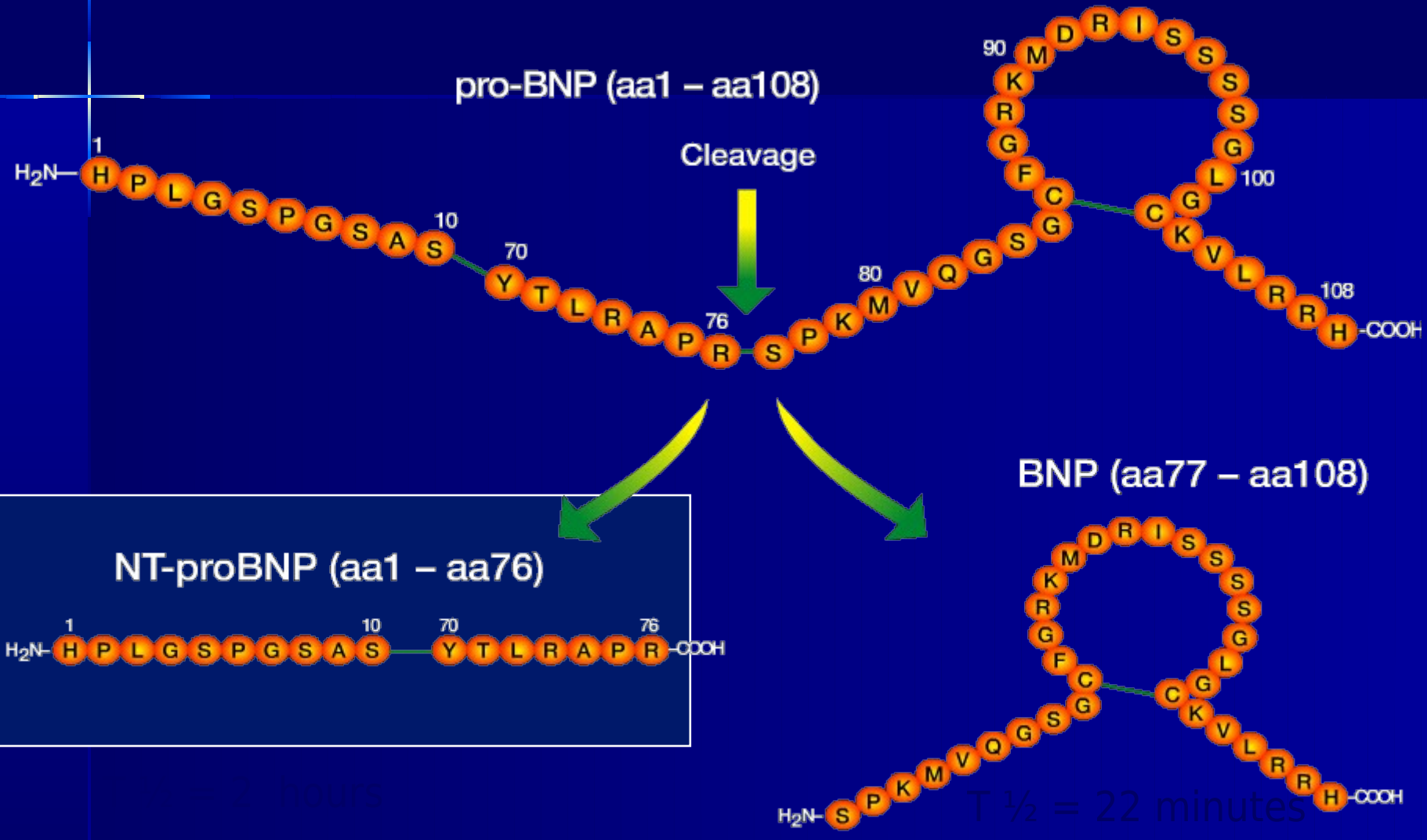
Proportion with Worsening Renal Function: High vs. Low



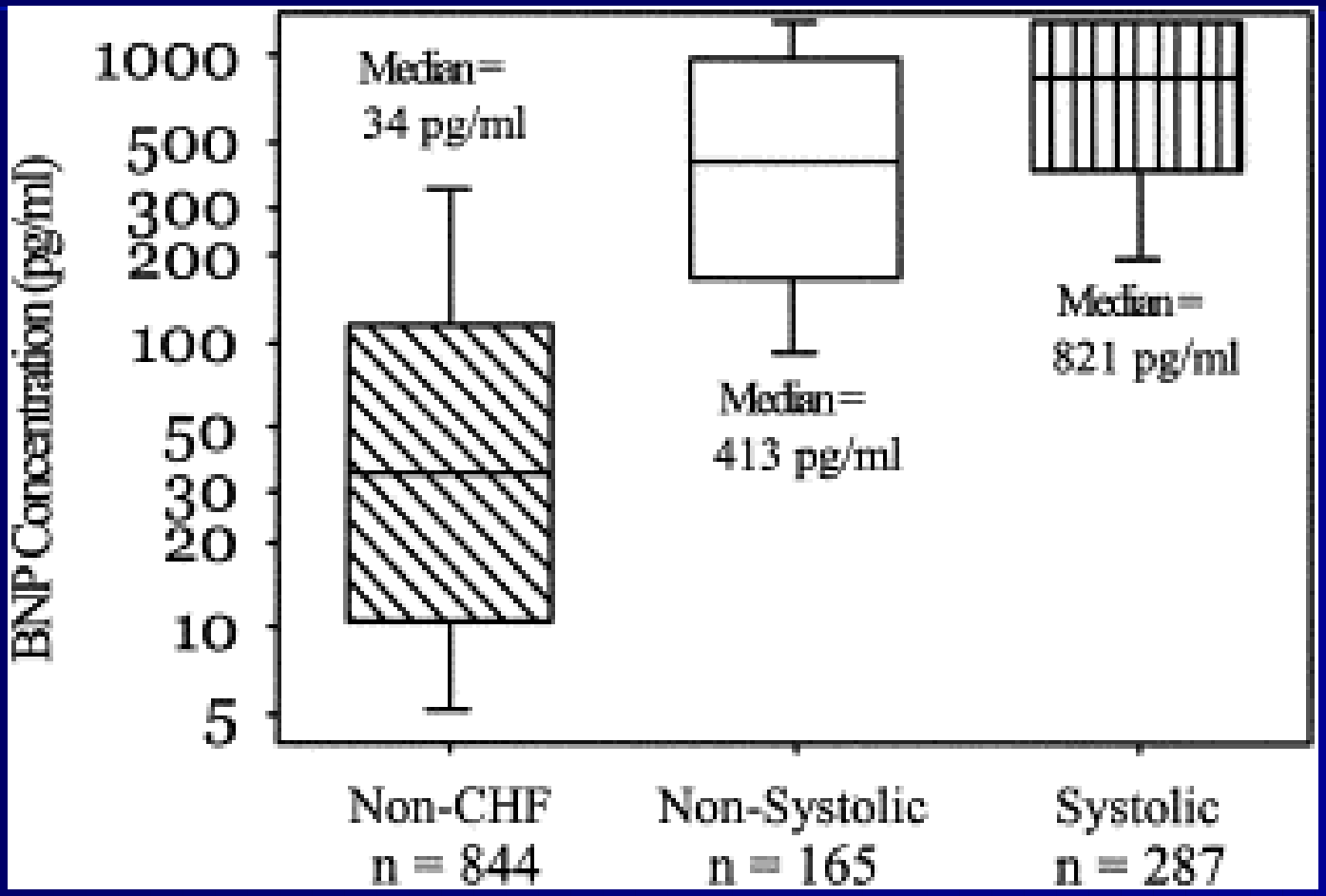
Conclusions

- There was no statistically significant difference in global symptom relief or change in renal function at 72 hours for either:
  - Intermittent bolus vs. continuous infusion
  - Low intensification vs. high intensification

Structure and Cleavage of proBNP

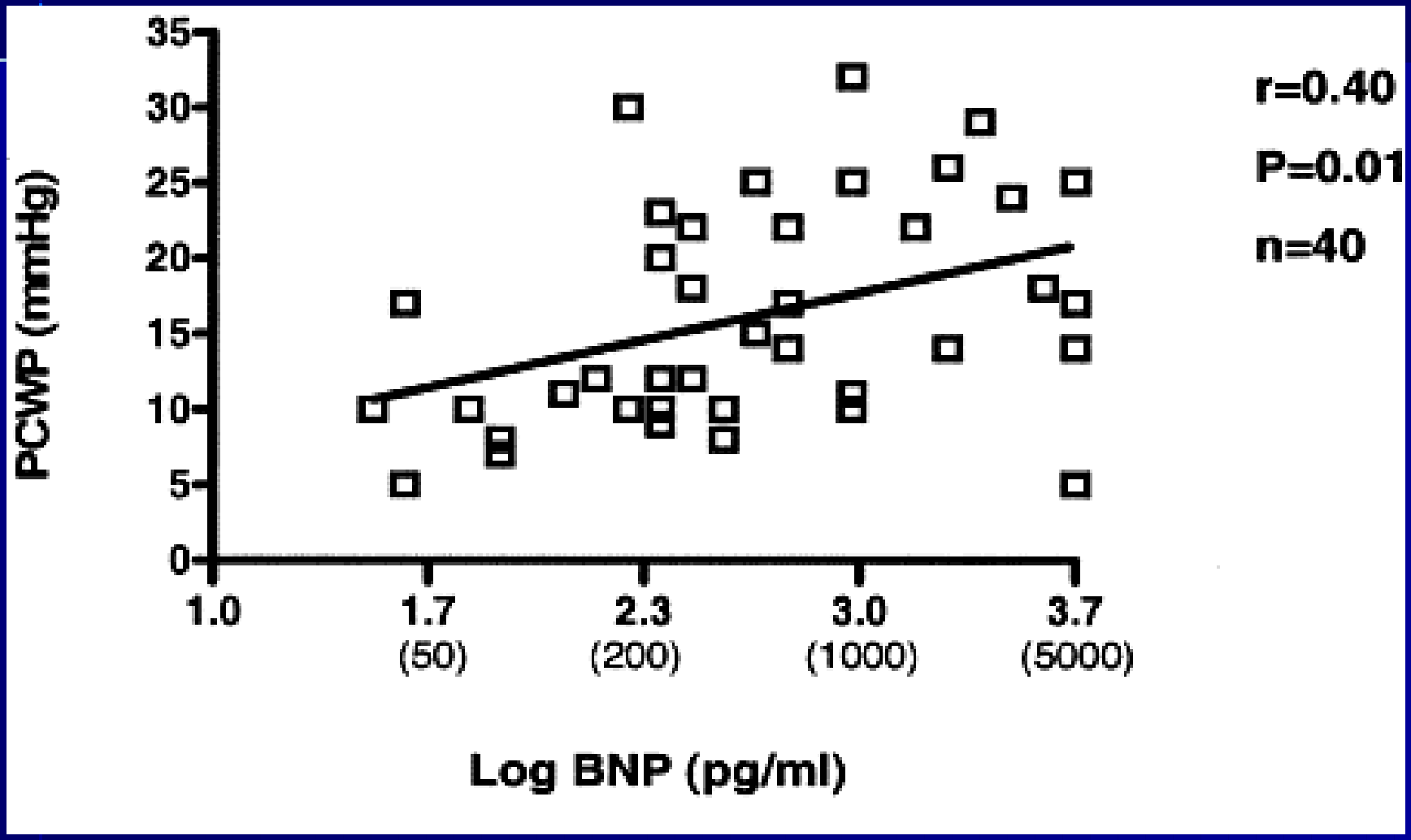


BNP is Increased with HF and Systolic or Diastolic Dysfunction



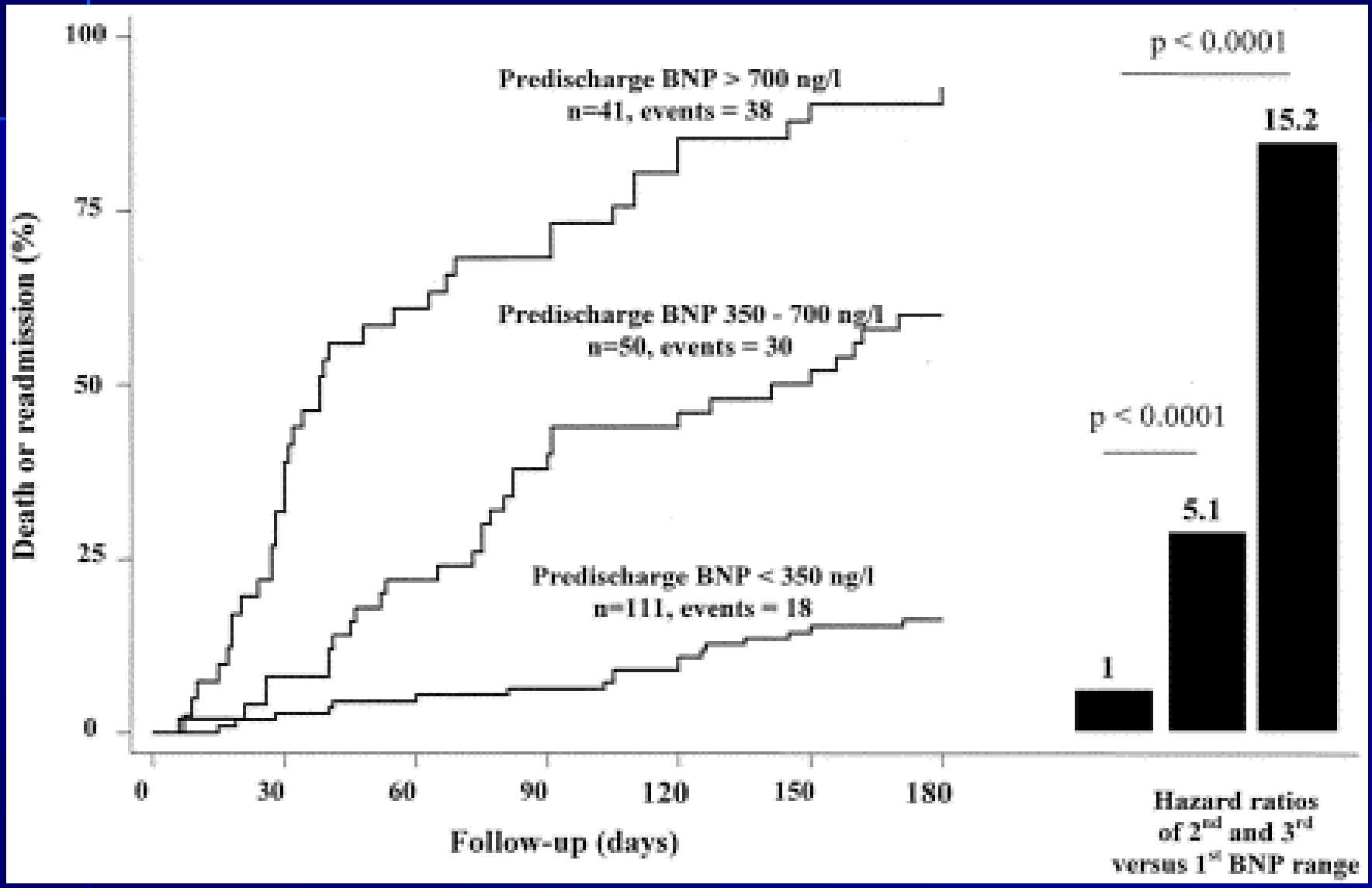
Maisel AS, et al. JACC 2003;41:2010

BNP on admission is a poor predictor of PCW



(Forfia PR, et al. J Am Cardiol 2005;45:1667-71)

BNP Levels Pre-discharge Predict Mortality and Readmisssion



(Logeart D, et al. JACC 20042;40:976-82)

Table 4 Short- and long-term novel therapies for acute heart failure syndromes

Short term	Long term	Both
Cinaciguat	Direct renin inhibitors	Adenosine antagonists
CD-NP	Macronutrients	Vasopressin antagonists
Relaxin	Micronutrients	Digoxin
Adenosine regulating agents	CRT/AICD	
Stresscopin		
Istaroxime		
Cardiac myosin activators		

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

EUROPEAN SOCIETY OF CARDIOLOGY®

Recommendations for the treatment of patients with acute heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
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	213
High-flow oxygen is recommended in patients with a capillary oxygen saturation <90% or PaO_2 <60 mmHg (8.0 kPa) to correct hypoxaemia.	I	C	–
Thrombo-embolism prophylaxis (e.g. with LMWH) is recommended in patients not already anticoagulated and with no contraindication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism.	I	A	214–216
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 systolic blood pressure <85 mmHg (and blood pressure should be monitored regularly when this treatment is used).	IIa	B	217
An i.v. opiate (along with an antiemetic) should be considered in particularly anxious, restless, or distressed patients to relieve these symptoms and improve breathlessness. Alertness and ventilatory effort should be monitored frequently after administration because opiates can depress respiration.	IIa	C	–
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	218, 219
An i.v. infusion of sodium nitroprusside may 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. Caution is recommended in patients with acute myocardial infarction. Nitroprusside may also relieve dyspnoea and congestion. Symptoms and blood pressure should be monitored frequently during administration of i.v. nitroprusside.	IIb	B	220
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	–

15.6 Acute heart failure

The treatment of acute heart failure remains largely opinion-based with little good evidence to guide therapy.

Intravenous nitrates—efficacy and safety still uncertain.

Levosimendan—efficacy and safety still uncertain.

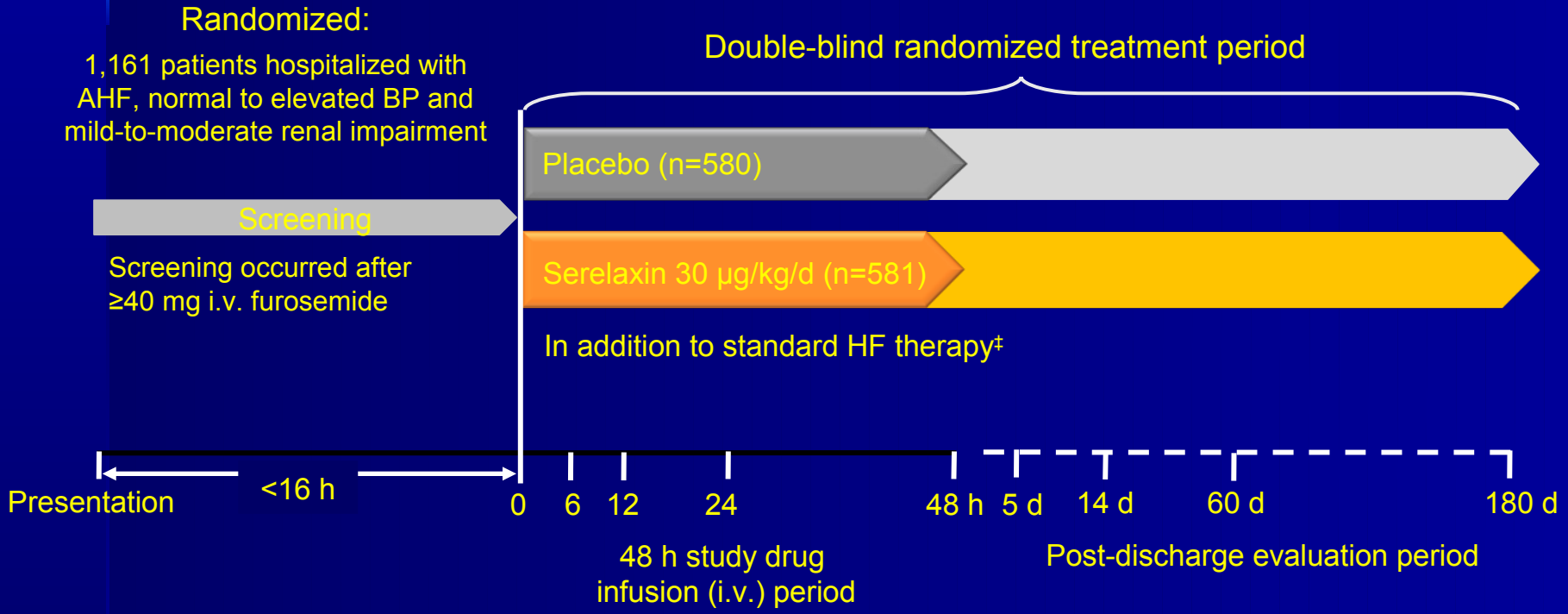
Omecamtiv mecarbil—is it effective and safe?

Ultrafiltration—efficacy and safety unknown.

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

RELAX-AHF: study design

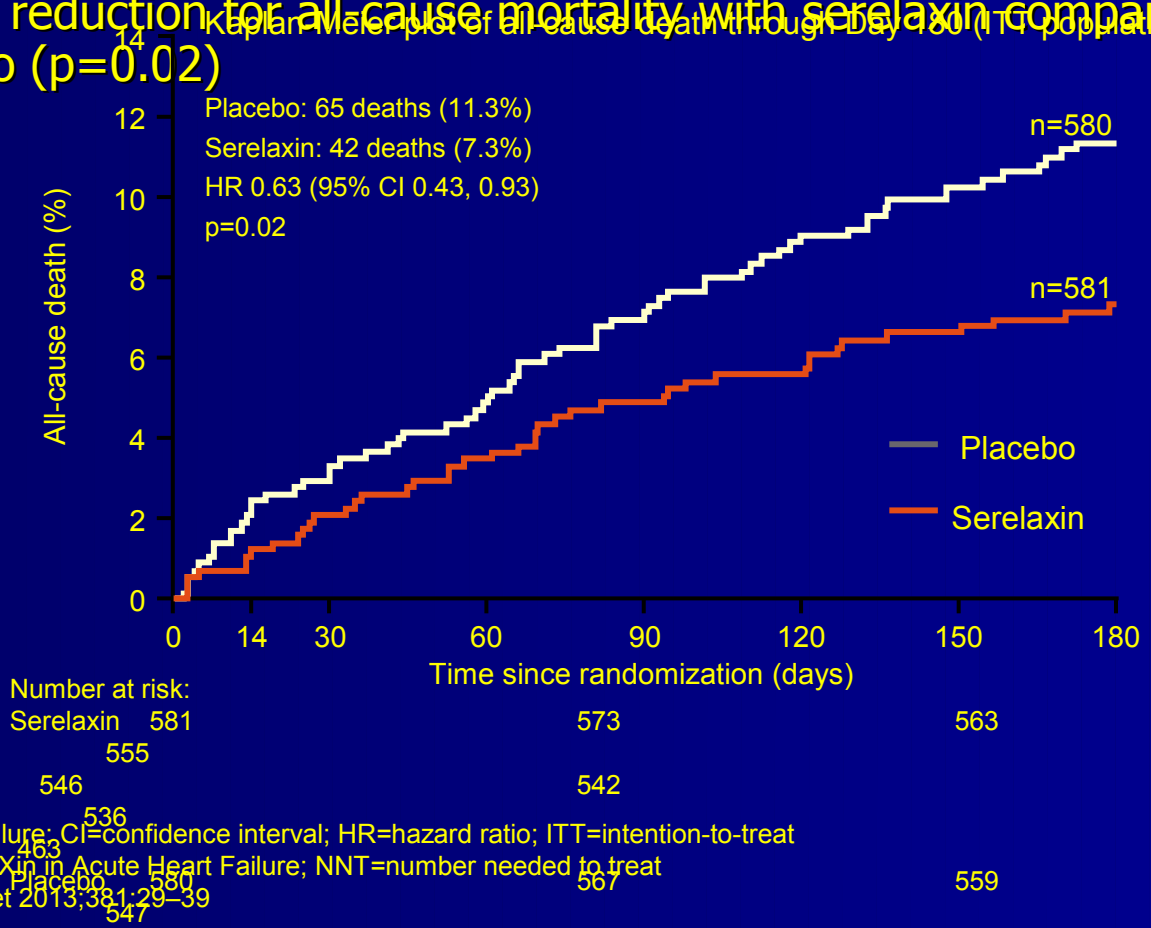
A Phase III, multicenter, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of serelaxin, in addition to standard therapy, in subjects hospitalized for AHF



‡Standard HF therapy permitted at physician's discretion
AHF=acute heart failure; BP=blood pressure; d=day; h=hour; i.v.=intravenous; RELAX-AHF=RELAXin in Acute Heart Failure
Teerlink et al. Lancet 2013;381:29–39; Ponikowski et al. Am Heart J 2012;163:149–55.e1

RELAX-AHF: significant reduction in all-cause mortality with serelaxin vs. placebo at 180 days in patients with AHF

- In the pre-specified safety analysis, serelaxin treatment was associated with a significant reduction in all-cause mortality at Day 180 (p=0.02; NNT=25)
- A *post-hoc* sensitivity analysis in the ITT population demonstrated a 37% hazard reduction for all-cause mortality with serelaxin compared with placebo (p=0.02)



AHF=acute heart failure; CI=confidence interval; HR=hazard ratio; ITT=intention-to-treat
RELAX-AHF=RELAXin in Acute Heart Failure; NNT=number needed to treat
Teerlink et al. Lancet 2013;381:29–39

Before I came here I was confused about this subject. Having listened to your lecture I am still confused. But on a higher level.

-Enrico Fermi