Acute Heart Failure 2010: update and guidelines

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Demographics and past history

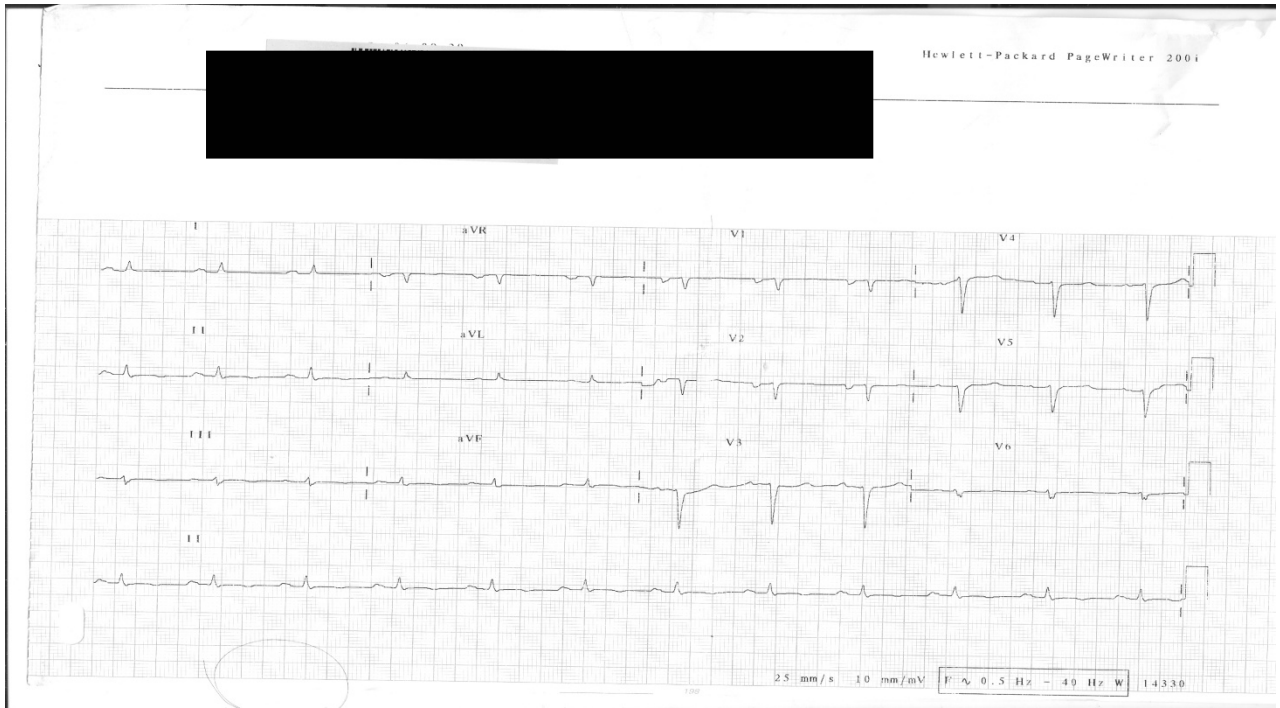
- C.G, a 48 y old male, married+4, until recently non-sedentary lifestyle
- *2000*- left temporal intracranial bleeding D/T AV malformation, treated by embolization and radiation. No neurological deficit. Impaired short-term memory and mood fluctuations.
- *Risk factors* : Dyslipidemia treated with statins, past history of smoking (18 years ago). No significant family history for IHD or CMP

Current event

- Fatigue over recent months.
- A month before admission “common cold” w/o fever.
- Progressive symptoms of fatigue, extreme weakness, effort dyspnea, epigastric pain,vomiting and weight loss.
- Admission to another hospital. Echo demonstrated dilated left ventricle with estimated LVEF of 20% and antero-apical dyskinesis
- Coronary angiography revealed anatomically normal coronary arteries.
- A diagnosis of **non-ischemic CMP (M/P post myocarditis**) was made and the patient was discharged under treatment of B.blockers, ACE inhibitors and diuretics.

Current event- contd’

- Due to further clinical deterioration (NYHA 3) the patient was admitted to a second hospital with signs of low CO state with secondary “shock liver” and acute renal failure.



- Echo at that time: LVEDD 62 mm, EF 15%, moderate MR, mild pulmonary HTN, severe RV dysfunction
- TDI- no evidence of intraventricular disynchrony.

Complicated situation !

Definition

Acute heart failure (AHF) is defined as a rapid onset or change in the signs and symptoms of HF, resulting in the need for urgent therapy. ***AHF may be either new HF or worsening of pre-existing chronic HF.*** Patients may present as a medical emergency

ACS is the most frequent cause of acute new onset HF.

Table 26 Causes and precipitating factors of acute heart failure

Ischaemic heart disease
- Acute coronary syndromes
- Mechanical complications of acute MI
- Right ventricular infarction

Valvular
- Valve stenosis
- Valvular regurgitation
- Endocarditis
- Aortic dissection

Myopathies
- Postpartum cardiomyopathy
- Acute myocarditis

Hypertension/arrhythmia
- Hypertension
- Acute arrhythmia

Circulatory failure
- Septicaemia
- Thyrotoxicosis
- Anaemia
- Shunts
- Tamponade
- Pulmonary embolism

Decompensation of pre-existing chronic HF
- Lack of adherence
- Volume overload
- Infections, especially pneumonia
- Cerebrovascular insult
- Surgery
- Renal dysfunction
- Asthma, COPD
- Drug abuse
- Alcohol abuse

ESC Guidelines

Clinical classification

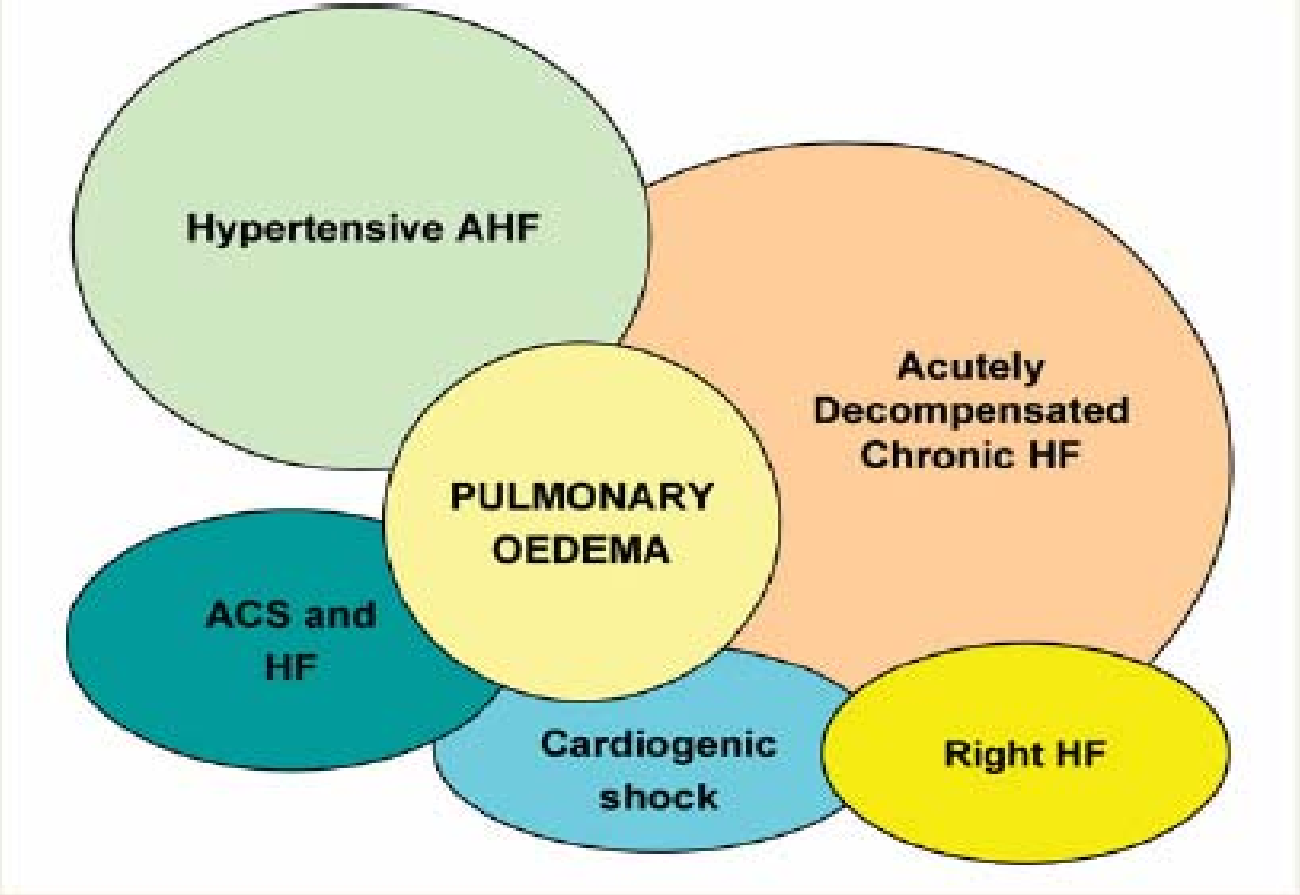
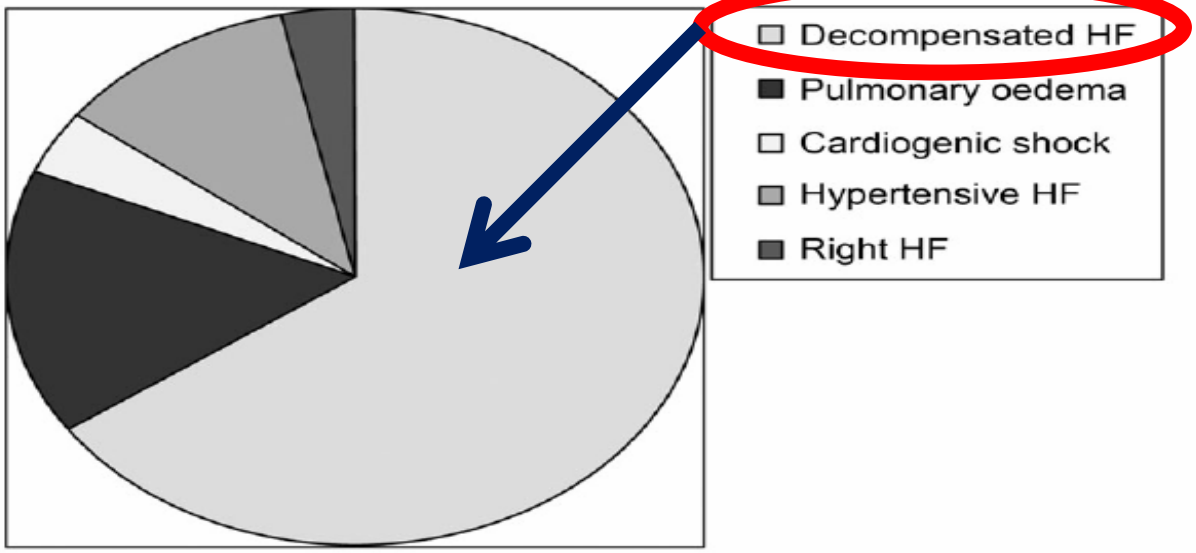


Figure 3 Clinical classification of acute heart failure. Modified from reference 205.

European Heart Journal (2006) 27, 2725–2736
doi:10.1093/eurheartj/ehl193

EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population



Classification of AHF %	All	*De novo* AHF	ADCHF
Decompensated HF	65.4	52.4	73.0***
Pulmonary oedema	16.2	26.0	10.4***
Cardiogenic shock	3.9	6.8	2.2***
Hypertensive HF	11.4	11.4	11.3
Right HF	3.2	3.4	3.0

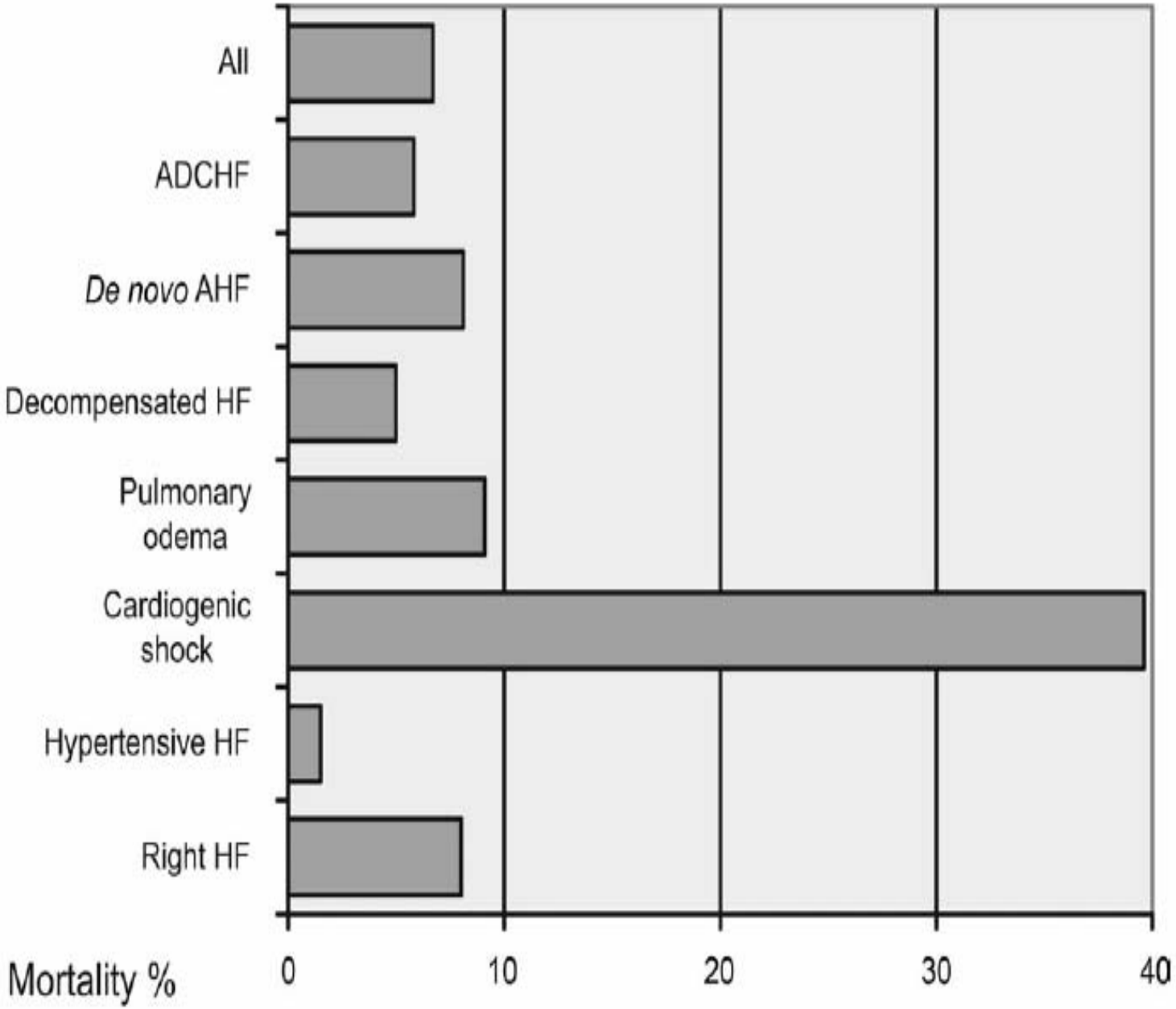


Figure 4 In-hospital mortality in EHFS II by history of HF and clinical class.

Clinical Conditions

Acute decompensation of CHF: Signs and symptoms are mild

- Heart rate +/-
- SBP +/-
- CI +/-
- PCWP +
- Diuresis +
- Hypoperfusion +/-

AHF with pulmonary oedema: severe respiratory distress with rales over the lungs

- Heart rate +
- SBP +/-
- CI -
- PCWP ++
- Diuresis +
- Hypoperfusion +/-

Clinical Conditions
Cardiogenic shock

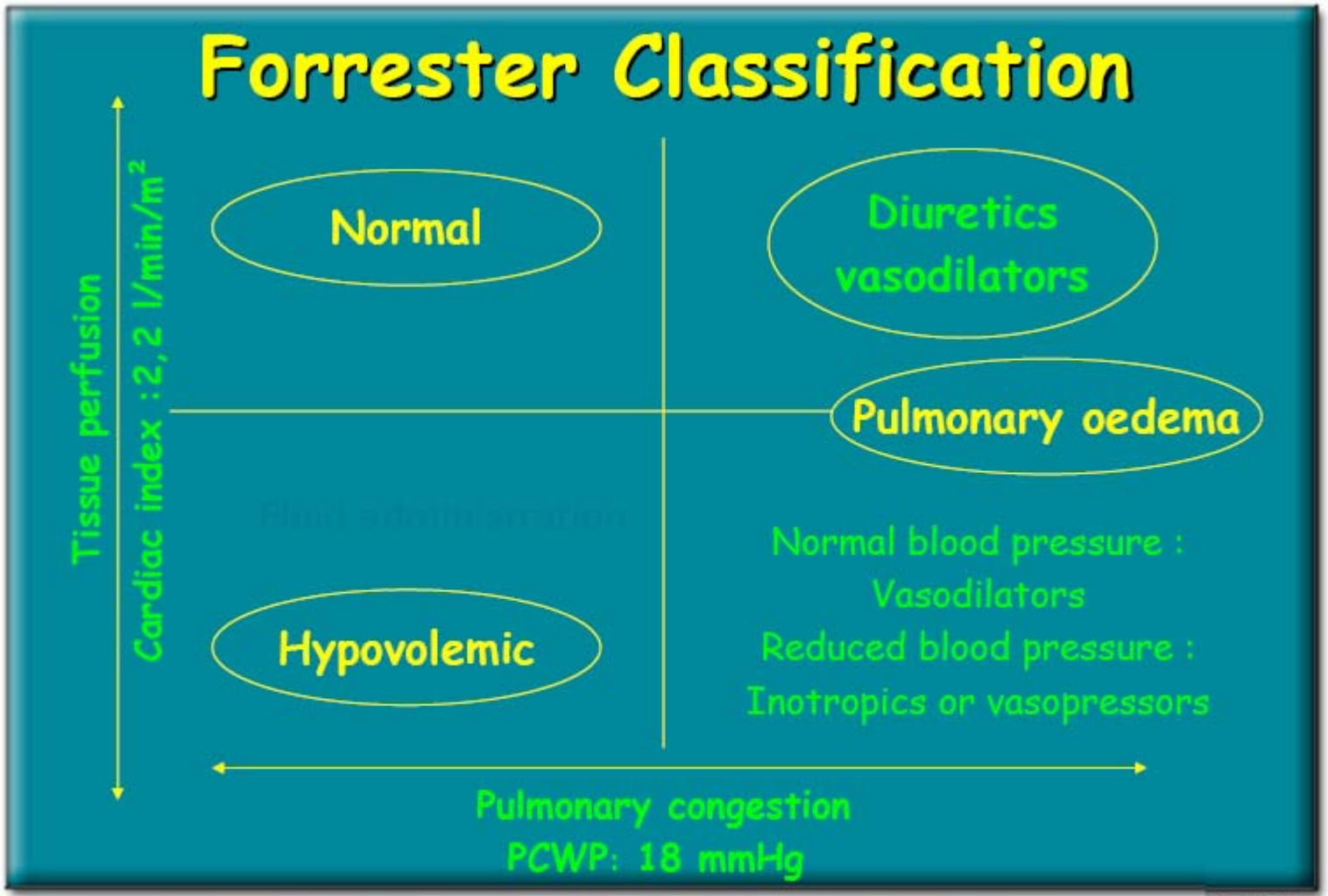
Low output syndrome: reduced BP, low urine output, tissue hypoperfusion

- Heart rate +
- SBP -
- CI -
- PCWP +
- Diuresis -
- Hypoperfusion +

Severe Cardiogenic shock: low BP, organ hypoperfusion, anuria

- Heart rate ++
- SBP --
- CI --
- PCWP ++
- Diuresis --
- Hypoperfusion ++

Forrester Classification



Initial evaluation

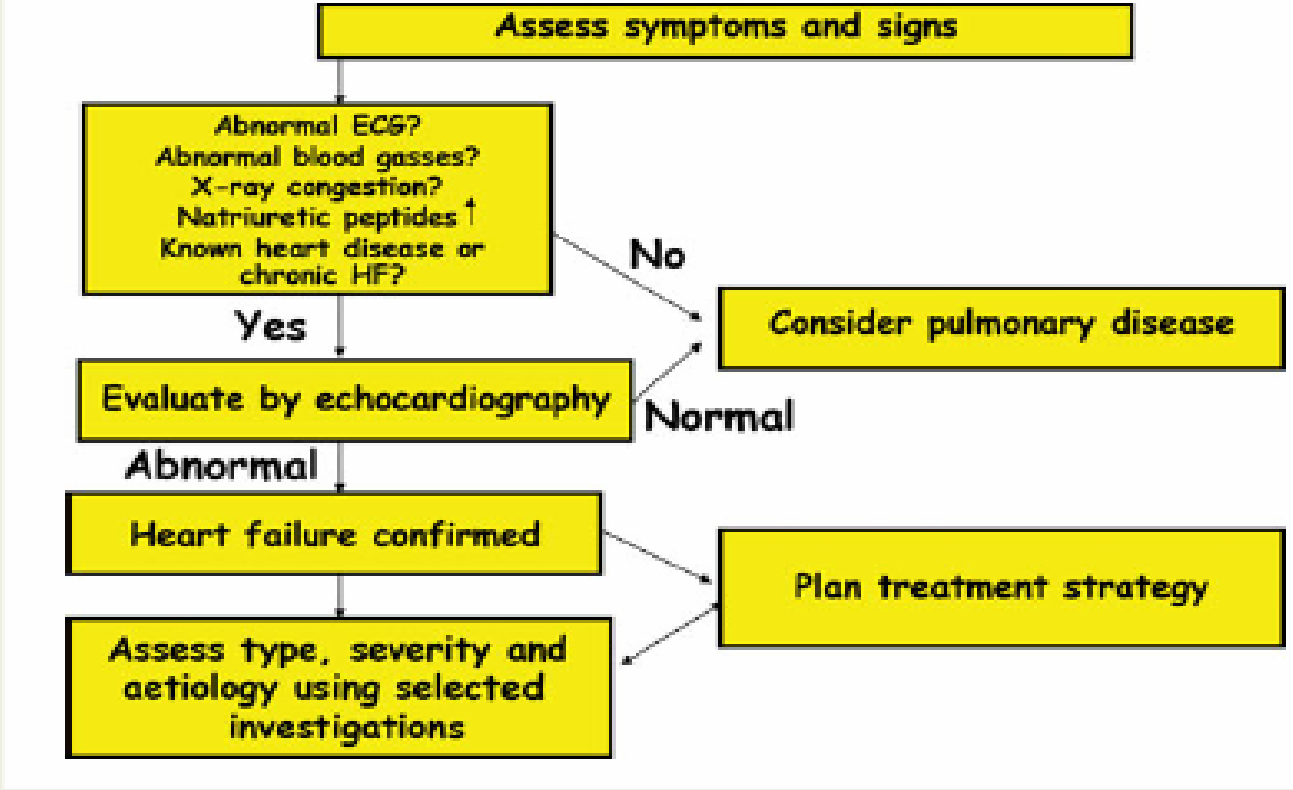


Figure 5 Evaluation of patients with suspected AHF.

the recommendations largely represent
expert consensus opinion without adequate documented
evidence. Class of recommendation I, level of evidence C

To BNP or not...?

- “There is no consensus regarding BNP or NT-proBNP reference values in AHF”.
- During ‘flash’ pulmonary edema or acute MR, natriuretic peptide levels may remain normal at the time of admission.
- **Increased BNP and NT-pro BNP levels on admission and before discharge carry important prognostic information”**

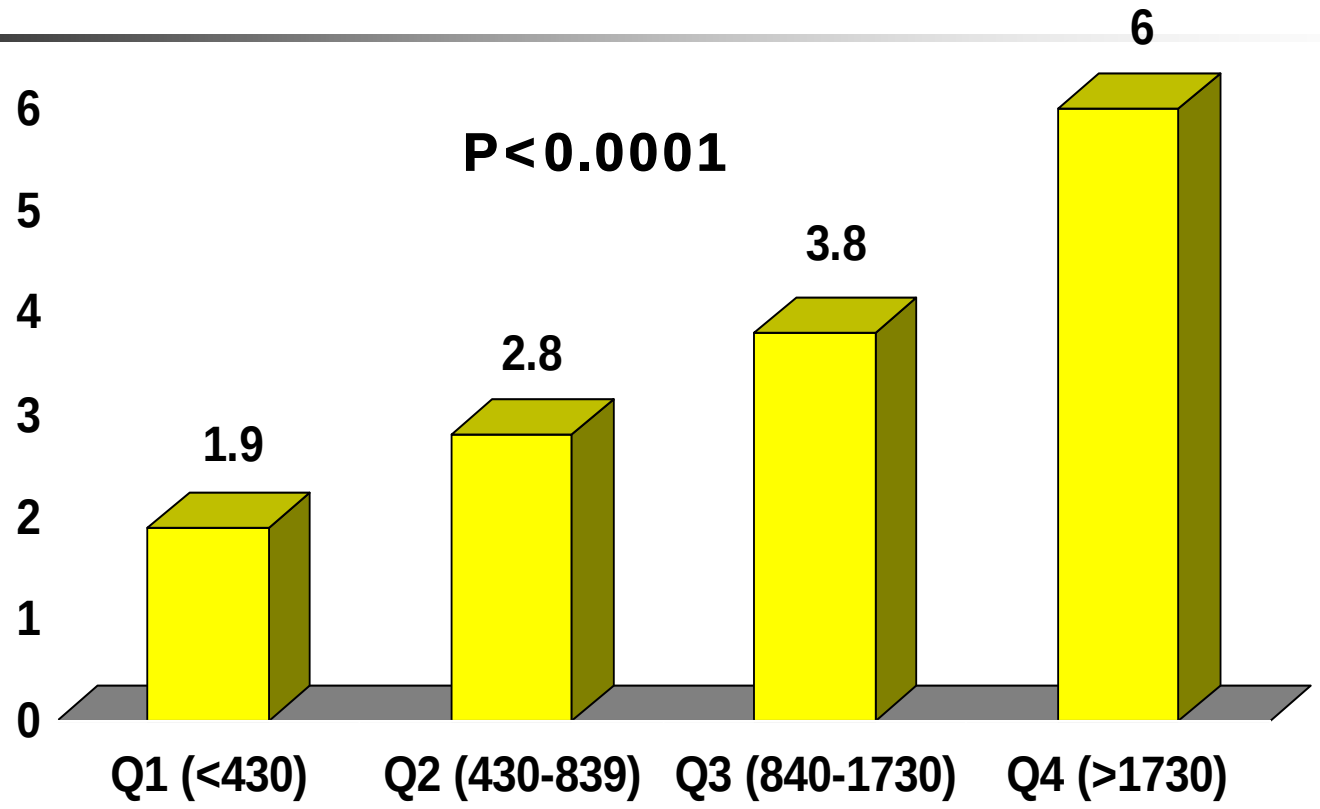
ESC guidelines 2008

Admission B-Type Natriuretic Peptide Levels and In-Hospital Mortality in Acute Decompensated Haeart Failure-**Adhere**

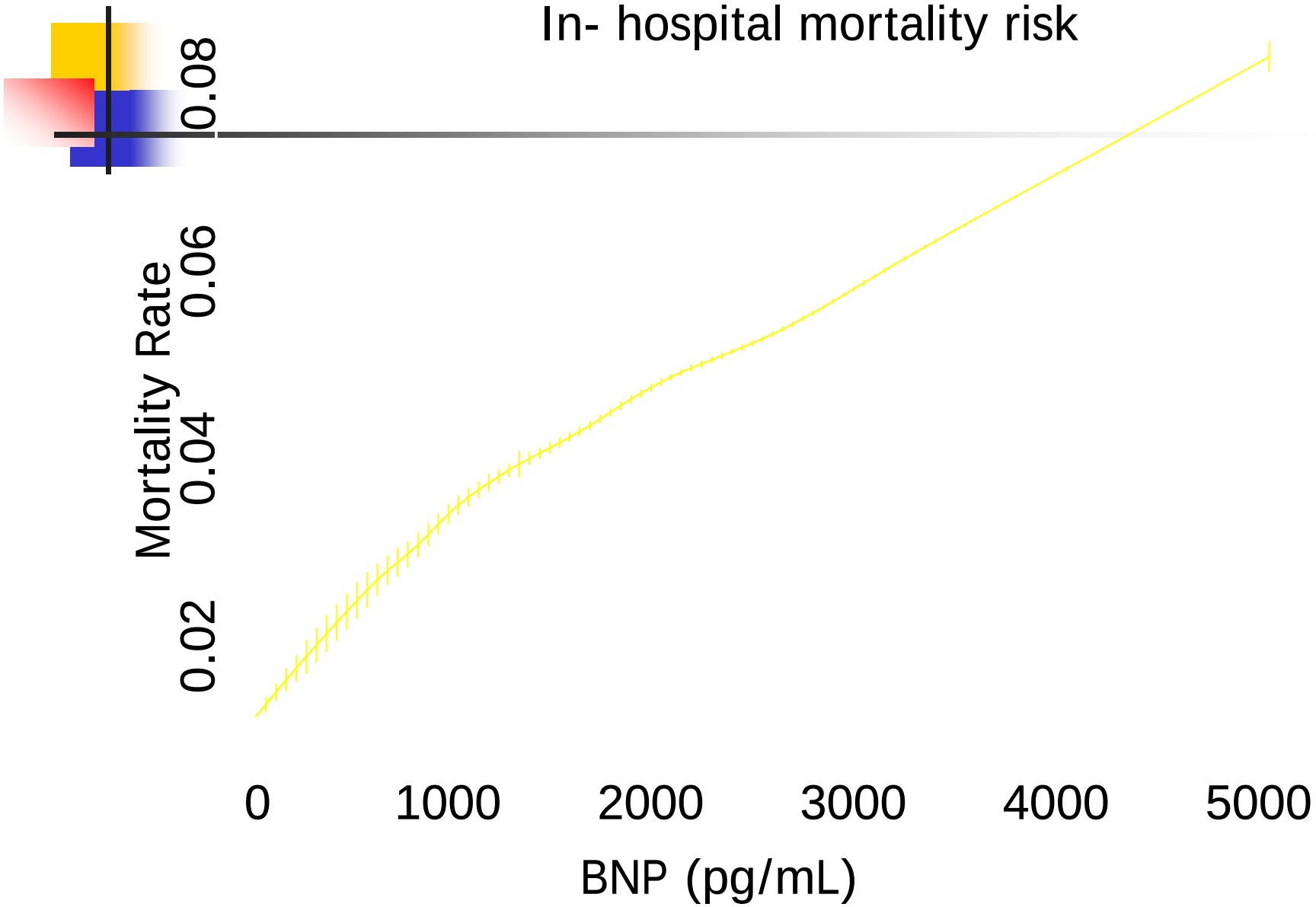
Gregg C. Fonarow MD, FACC, William F. Peacock MD, Christopher O. Phillips MD, MPH, Michael M. Givertz MD, FACC, Margarita Lopatin MS and ADHERE Scientific Advisory Committee and Investigators

Fonarow GC et al. J Am Coll Cardiol 2007; 49(19):1943-1950

In-Hospital Mortality Risk by Initial BNP Levels in the ADHERE Registry



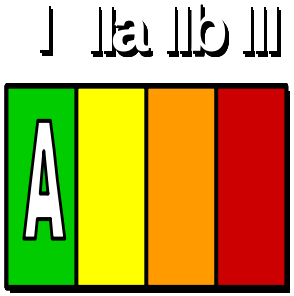
Fonarow GC et al. J Am Coll Cardiol 2007; 49(19):1943-1950



Fonarow GC et al. J Am Coll Cardiol 2007; 49(19):1943-1950

- 2009 update- The Hospitalized Patient

Patients Being Evaluated for Dyspnea



Concentrations of BNP or NT-proBNP *should be measured* in patients being evaluated for dyspnea in which the contribution of HF is not known. Final diagnosis requires interpreting these results in the context of all available clinical data and ought not to be considered a stand-alone test

New

Invasive monitoring

- **Arterial line-** ?
- **CVP**- Class of recommendation IIa, level of evidence C
- **Pulmonary artery catheter** -?
- **Coronary angiography** -Class of recommendation I, level of evidence B

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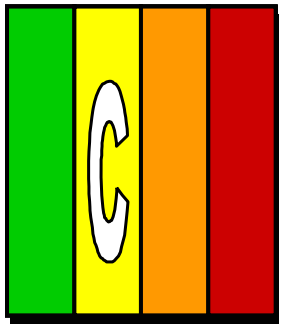
Invasive Hemodynamic Monitoring

IIa



Invasive hemodynamic monitoring *can be useful for carefully selected patients* with acute HF who have persistent symptoms despite empiric adjustment of standard therapies, and

a. whose fluid status, perfusion, or systemic or pulmonary vascular resistances are uncertain;

b. whose systolic pressure remains low, pr is associated with symptoms, despite initial therapy;

c. whose renal function is worsening with therapy;

d. who require parenteral vasoactive agents; or

e. who may need consideration for advanced device therapy or transplantation

New

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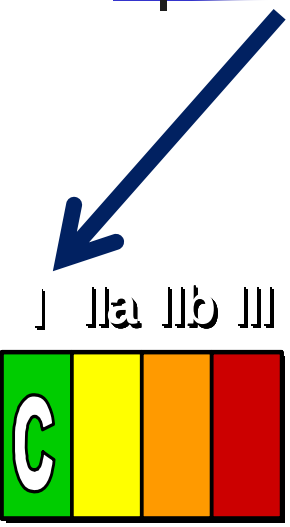
Preserving End-Organ Performance

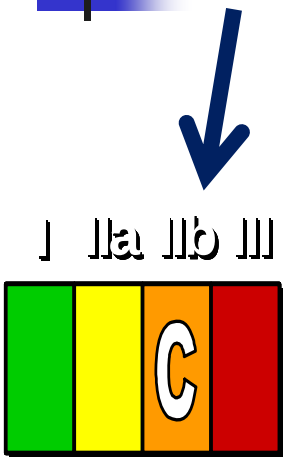


Invasive hemodynamic monitoring *should be performed to guide therapy in patients who are in respiratory distress or with clinical evidence of impaired perfusion in* whom the adequacy or excess of intracardiac filling pressures cannot be determined from clinical

New

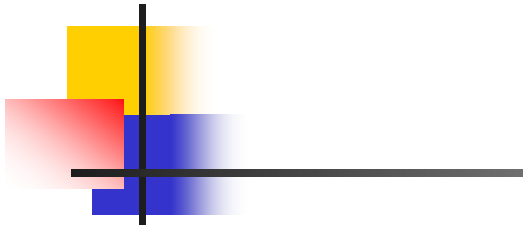
Patients With Refractory End-Stage Heart Failure (Stage D)

Pulmonary Artery Catheter Placement



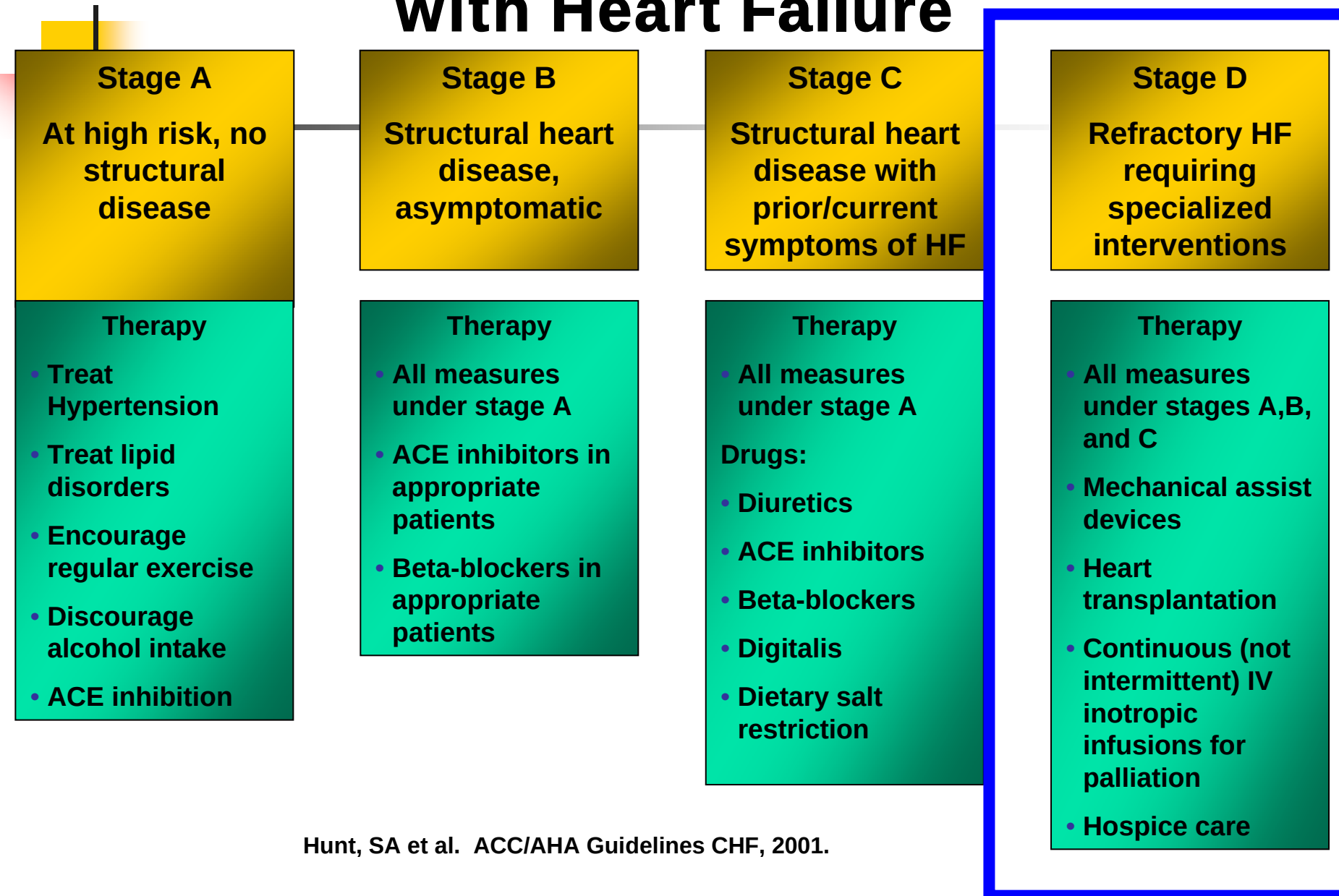
Pulmonary artery catheter placement may be reasonable to guide therapy in patients with refractory end-stage HF and persistently severe symptoms.

NO CHANGE from 2005 guidelines



What can we do?

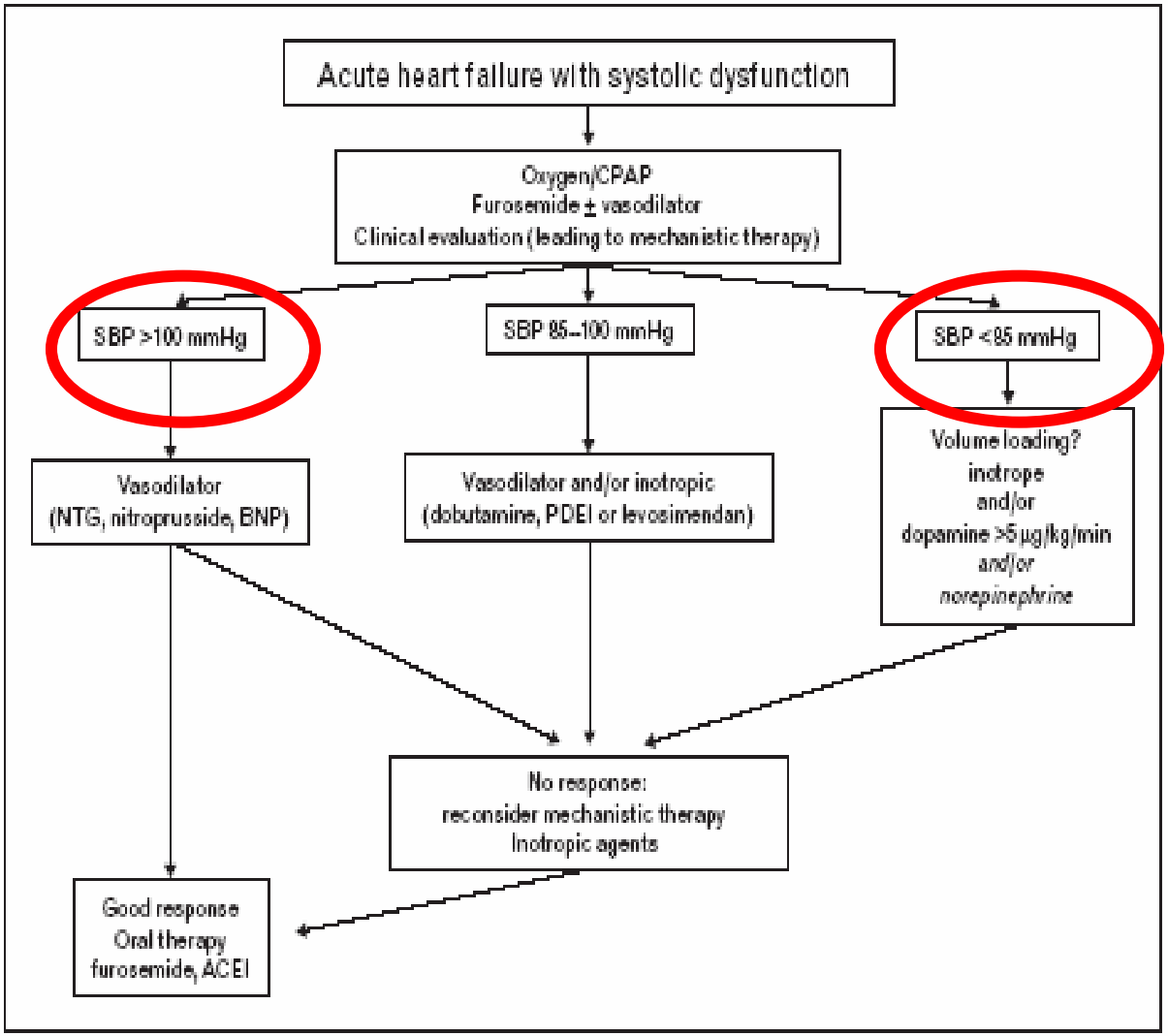
Treatment Approach for the Patient with Heart Failure



Hunt, SA et al. ACC/AHA Guidelines CHF, 2001.

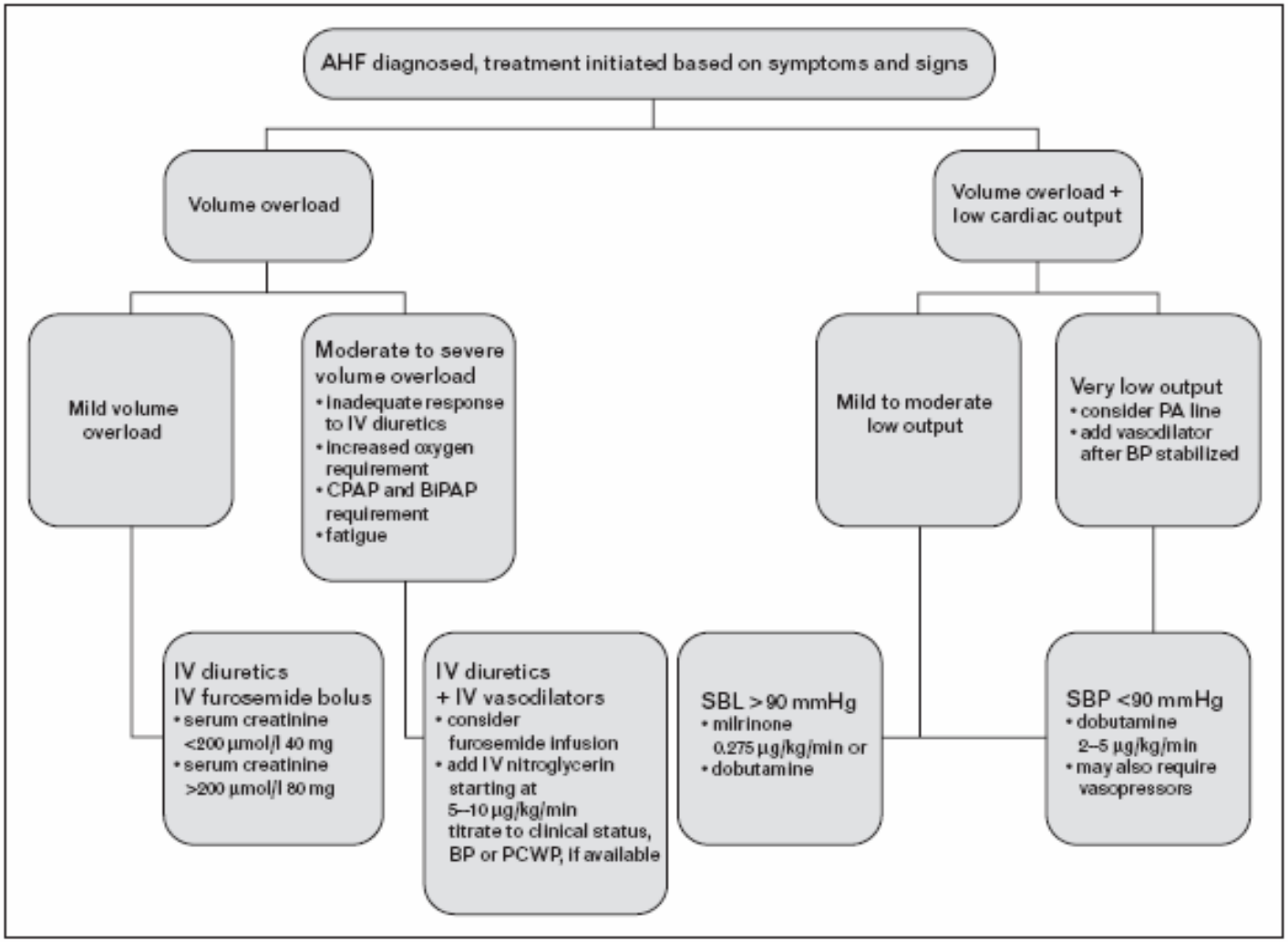
Figure 1 Immediate goals in treatment of the patients with acute heart failure [13]

ACEI, angiotensin-converting-enzyme inhibitor; BNP, brain natriuretic peptide; CPAP, continuous positive airway pressure; NTG, nitroglycerine; PDEI, phosphodiesterase inhibitors; SBP, systolic blood pressure.

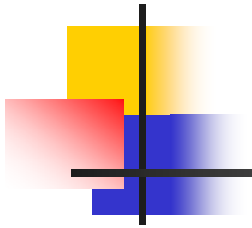


Current Opinion in Cardiology 2008, 23:134

Figure 2 Algorithm for acute heart failure treatment, data from Canadian Cardiovascular Society guidelines on the management of acute decompensated heart failure [14]



AHF, acute heart failure; BiPAP, bilevel positive airway pressure; BP, blood pressure; CPAP, continuous positive airway pressure; IV, intravenous; PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure; SBP, systolic blood pressure.



Medical treatment

Euro heart survey

Table 5 Acute cardiac care by clinical class

Treatment % performed	Total	Decomp. HF	Pulmonary oedema	Cardiogenic shock	Hypert. HF	Right HF
Ventilatory support[a]	13.9	8.1	31.5	56.1	7.4	14.2
Invasive mechanical ventilation	5.1	2.3	11.0	36.7	1.7	4.4
Diuretic	92.9	94.6	97.6	77.5	82.8	88.5
Oral	8.6	10.3	3.6	0.0	8.7	8.0
Iv bolus	72.1	71.7	81.9	58.7	68.6	58.4
Infusion	12.3	12.6	12.1	18.8	5.5	22.1
Beta-blocker	10.1	10.4	8.3	9.4	11.1	10.6
Opioids	19.4	13.5	38.3	49.3	18.2	10.7
Iv nitrate	37.8	30.4	70.6	36.5	39.7	8.6
Iv nitroprusside	0.9	0.5	2.1	2.2	1.2	0.0
Iv inotrope						
Adrenaline	1.8	1.2	2.6	15.8	0.0	1.8
Dobutamine	10.2	8.6	13.3	44.6	2.0	14.2
Dopamine	11.3	8.5	15.8	65.5	2.2	12.4
Levosimendan	3.9	4.4	3.8	7.9	0.2	0.9
Noradrenaline	2.6	1.2	4.5	24.5	0.7	2.7

Diuretics

Table 1 Systemic effects associated with acute high-dose diuretic administration

- ↑ RAAS stimulation
- ↑ AVP levels
- ↑ HR
- ↑ Norepinephrine levels
- ↓ GFR
- ↑ SVR

RAAS-renin-angiotensin-aldostrerone-system; AVP-arginine vasopressin; HR-heart rate; GFR-glomerular filtration rate; SVR-systemic vascular resistance

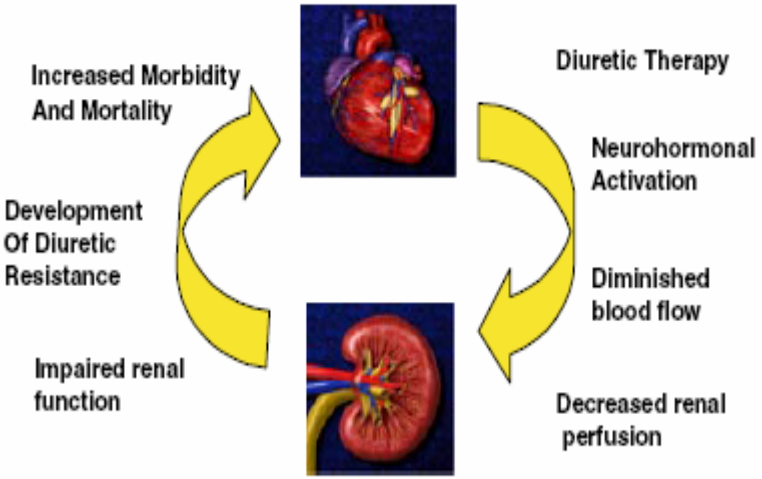


Fig. 1 The ''latrogenic'' cardio-renal syndrome of heart failure

- The use of diuretics for the treatment of patients with ADHF represents an area of medicine with a paucity of rigorous clinical trials.
- The acceptance of diuretics into the HF treatment paradigm is largely based on clinical and anecdotal experience over the last forty years without the benefit of large, multi-center randomized trials.

Class of recommendation I, level of evidence B

There is evidence that low-dose furosemide in combination with vasodilators may enhance diuresis with less adverse effects than high-dose boluses.

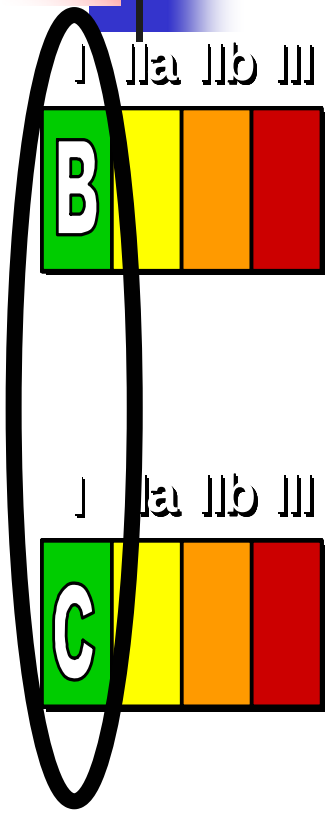
23. Cotter G, Metzkor E, Kaluski E et al (1998) Randomized trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary edema. Lancet 351:389–393

- A recently performed Cochrane database review found that based on the data from the limited studies available, that an increased diuretic effect and a better safety profile was observed with a **continuous infusion of loop diuretics when compared to bolus dosing for patients in NYHA III-IV HF .**
- However, the currently available existing data still does not allow definitive recommendations for clinical practice.

- ***Heart Fail Rev (2007) 12:125–130***

2009 update- The Hospitalized Patient

Treatment With Intravenous Loop Diuretics



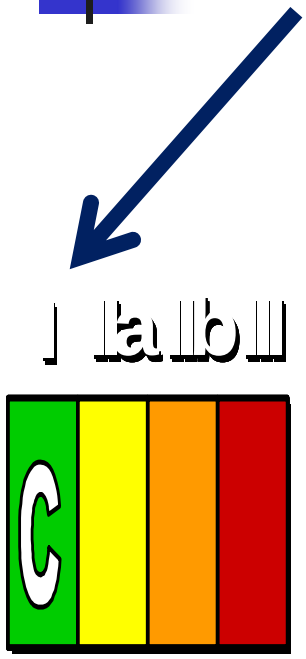
Patients admitted with HF and with evidence of significant fluid overload should be treated with intravenous loop diuretics. Therapy should begin in the emergency department or outpatient clinic without delay, as early intervention may be associated with better outcomes for patients hospitalized with decompensated HF ***(Level of Evidence: B).***

If patients are already receiving loop diuretic therapy, the initial intravenous dose should equal or exceed their chronic oral daily dose. Urine output and signs and symptoms of congestion should be serially assessed, and diuretic dose should be titrated accordingly to relieve symptoms and to reduce extracellular fluid volume excess. ***(Level of Evidence: C).***

New

UPDATE 2009 The Hospitalized Patient

Intensifying the Diuretic Regimen



When diuresis is inadequate to relieve congestion, as evidence by clinical evaluation, the diuretic regimen should be intensified using either:

New

a. higher doses of loop diuretics;
b. addition of a second diuretic (such as metolazone, spironolactone or intravenous chlorthiazide) or
c. Continuous infusion of a loop diuretic.

Inotropes

Class of recommendation IIa, level of evidence B

Table 2 Classification and mechanisms of agents which improve contractility and their concomitant clinical effects

	Mechanism			
	Incr. i Ca	PDEi	SV	Vasodilation
Inotropic agents				
Dobutamine	++		+	
Dopamine	++		+	
Milrinone	++	++	+	++
Enoximone	++	++	+	++
Cardiac enhancers				
Levosimendan	+ –	+	+	++
Pimobendan	+ –	+	+	+

Incr. I Ca: increasing of intracellular calcium; PDEi: Phosphodiesterase inhibitors; SV: stroke volume

Table 30 Dosing of positive inotropic agents in acute heart failure

	Bolus	Infusion rate
Dobutamine	No Class of recommendation IIa, level of evidence B	2–20 μg/kg/min (β+)
Dopamine	N Class of recommendation IIb, level of evidence C	3 μg/kg/min: renal effect (δ+) 3–5 μg/kg/min: inotropic (β+) >5 μg/kg/min: (β+), vasopressor (α+)
Milrinone	25–75 μg/kg over 10-20 min	0.375–0.75 μg/kg/min
Enoximone	0.25–0.75 mg/kg	1.25–7.5 μg/kg/min
Levosimendan*	12 μg/kg over 10 min (optional)**	0.1 μg/kg/min which can be decreased to 0.05 or increased to 0.2 μg/kg/min
Norepinephrine	No	0.2–1.0 μg/kg/min
Epinephrine	Bolus: 1 mg can be given i.v. during resuscitation, repeated every 3–5 min	0.05–0.5 μg/kg/min

*This agent also has vasodilator properties.

**In hypotensive patients (SBP <100 mmHg) initiation of therapy without a bolus is recommended.

Elkayam U, Tasissa G, Binanay C, Stevenson L. Use and impact of inotropes and vasodilator therapy in hospitalized patients with severe heart failure. ***Am Heart J 2007; 153:98–104.***

The ESCAPE trial published in 2007 revealed that inotropic agents such as dobutamine and milrinone in heart-failure patients with low ejection fraction and hypotension had higher 6-month mortality rates [hazard ratio (HR) 2.14, 95% CI 1.10– 4.15] than patients on vasodilators such as Nesiritide when compared with placebo (HR 1.39, 95% CI 0.64–3.0). **Inotropes in combination with vasodilators showed the highest mortality (HR 2.90, 95% CI 1.88–4.48)**

In-Hospital Mortality in Patients With Acute Decompensated Heart Failure Requiring Intravenous Vasoactive Medications An Analysis From the Acute Decompensated Heart Failure National Registry (ADHERE)

Table 3. Mortality Predictors Selected by Classification Tree Model

Parameter	Died (n = 2675)	Survived (n = 62,505)	OR of Death (95% CI)
Age (yrs)			
Mean ± SD	77.4 ± 12.2	72.3 ± 14.0	
Median (Q1, Q3)*	79.6 (71.3, 86.0)	74.9 (63.7, 82.5)	
Age >78 vs. ≤78			1.88 (1.74–2.04)
BUN (mg/dl)			
Mean ± SD	47.9 ± 29.7	31.2 ± 20.5	
Median (Q1, Q3)	40.0 (26.0, 61.0)	25.0 (17.0, 39.0)	
Median (Q1, Q3)	67 (55, 78)	76 (64, 90)	
DBP ≤55 vs. >55			2.87 (2.62–3.14)
Serum sodium (mmol/l)			
Mean ± SD	136.5 ± 6.2	138.2 ± 4.8	
Median (Q1, Q3)	137 (133, 140)	139 (136, 141)	
Sodium ≤134 vs. >134			2.26 (2.08–2.47)
HR (beats/min)			
Mean ± SD	90.7 ± 23.3	88.5 ± 21.8	
Median (Q1, Q3)	88 (74, 105)	86 (73, 101)	
HR >84 vs. ≤84			1.20 (1.11–1.30)
Dyspnea at rest, n (%)	1,220 (46%)	21,757 (35%)	1.57 (1.45–1.70)

Table 4. Mortality Odds Ratios in Pair-Wise Treatment Comparisons

Analysis*	NTG (n = 6,055) vs. MIL (n = 1,660)	NTG (n = 5,713) vs. DOB (n = 3,478)	NES (n = 4,663) vs. MIL (n = 1,534)	NES (n = 4,270) vs. DOB (n = 3,301)	NES (n = 4,402) vs. NTG (n = 5,668)	DOB (n = 3,656) vs. MIL (n = 1,496)
Unadjusted	0.34 (0.28–0.41)†	0.24 (0.20–0.28)†	0.53 (0.44–0.64)†	0.37 (0.32–0.44)†	1.64 (1.38–1.94)†	1.39 (1.15–1.68)†
Adjusted for covariates‖	0.69 (0.54–0.88)†	0.46 (0.38–0.57)†	0.59 (0.48–0.73)†	0.47 (0.39–0.56)†	0.95 (0.78–1.16)‡	1.27 (1.04–1.56)§
Adjusted for covariates and propensity score¶	0.69 (0.53–0.89)†	0.46 (0.37–0.57)†	0.59 (0.48–0.73)†	0.47 (0.39–0.56)†	0.94 (0.77–1.16)‡	1.24 (1.03–1.55)§

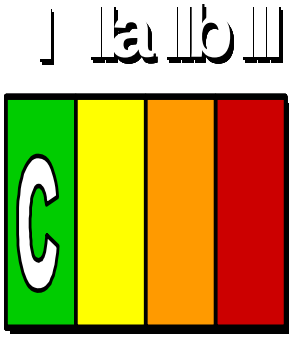
RESULTS Patients who received intravenous nitroglycerin or nesiritide had lower in-hospital mortality than those treated with dobutamine or milrinone. The risk factor and propensity score-adjusted ORs for nitroglycerin were 0.69 (95% confidence interval [CI] 0.53 to 0.89, $p \leq 0.005$) and 0.46 (94% CI 0.37 to 0.57, $p \leq 0.005$) compared with milrinone and dobutamine, respectively. The corresponding values for nesiritide compared with milrinone and dobutamine were 0.59 (95% CI 0.48 to 0.73, $p \leq 0.005$) and 0.47 (95% CI 0.39 to 0.56, $p \leq 0.005$), respectively. The adjusted OR for nesiritide compared with nitroglycerin was 0.94 (95% CI 0.77 to 1.16, $p = 0.58$).

(95% CI 0.77 to 1.16, p = 0.58).

CONCLUSIONS tide or vasodilator was associated with significantly lower in-hospital mortality than positive inotropic therapy in patients hospitalized with ADHF. The risk of in-hospital mortality was similar for nesiritide and nitroglycerin. (J Am Coll Cardiol 2005;46:57–64)

The Hospitalized Patient 2009 UPDATE

Preserving End-Organ Performance



patients with clinical evidence of hypotension associated with hypoperfusion and obvious evidence of elevated cardiac filling pressures (e.g., elevated jugular venous pressure; elevated pulmonary artery wedge pressure), intravenous inotropic or vasopressor drugs should be administered to maintain systemic perfusion and preserve end-organ performance while more definitive therapy is considered

New

Patients With Refractory End-Stage Heart Failure (Stage D) 2009 update

Continuous Intravenous Infusion of Positive Inotropic Agents

I IIa IIb III

C

Continuous intravenous infusion of a positive inotropic agent may be considered for palliation of symptoms in patients with refractory **end-stage** HF.

NO CHANGE

I IIa IIb III

A

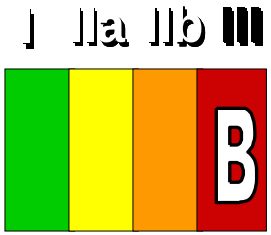
Routine intermittent infusions of vasoactive and positive inotropic agents are not recommended for patients with refractory end-stage HF.

Modified

The Hospitalized Patient

Parenteral Inotropes

Use of parenteral inotropes in normotensive patients with acute decompensated HF without evidence of decreased organ perfusion is not recommended



New

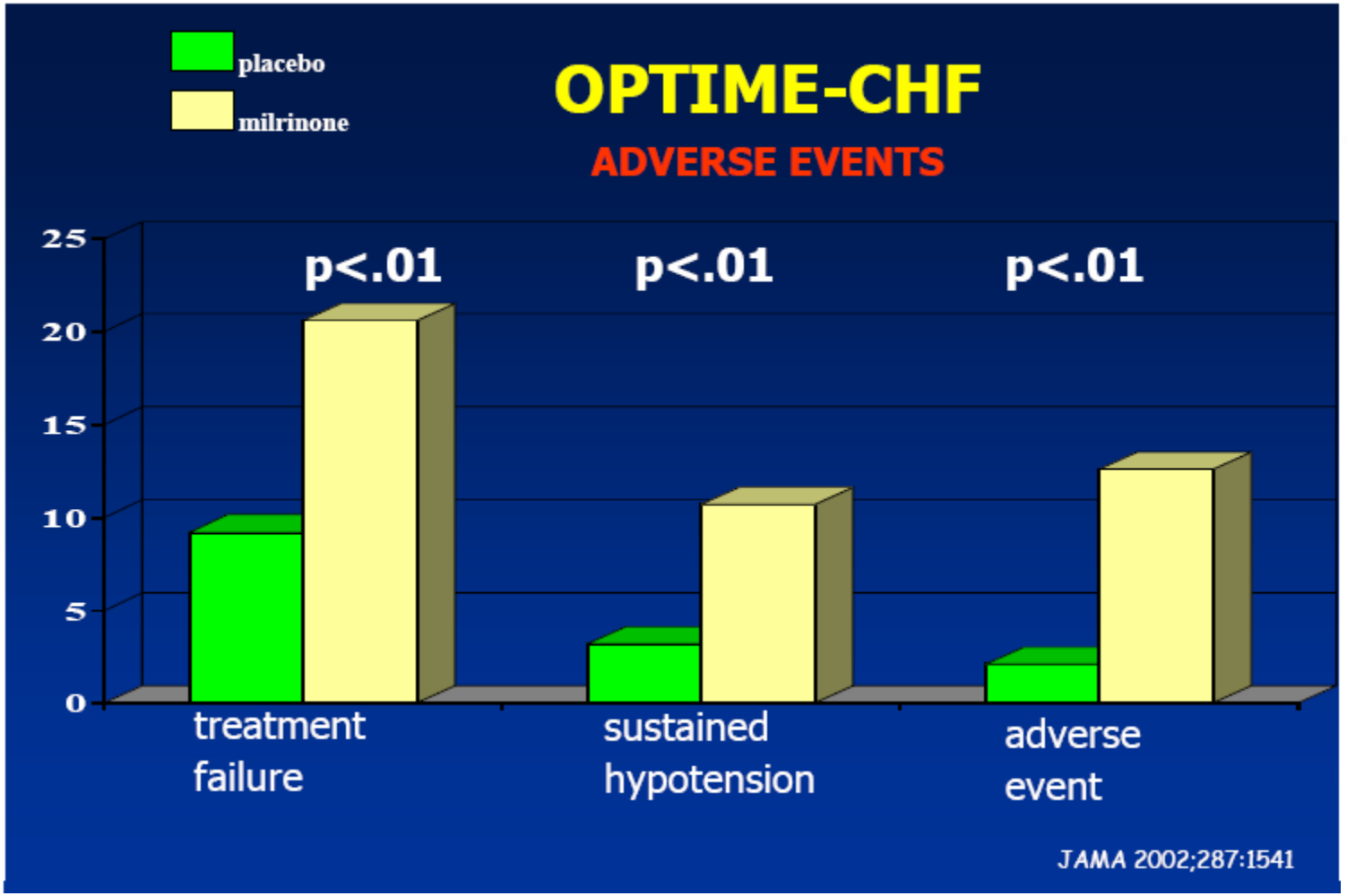
Phosphodiesterase inhibitors (Milrinone)

- Increases myocardial cAMP concentrations by selective inhibition of phospho-diesterase III, which leads to an increase in intracellular calcium, causing increased myocardial contractility, myocardial toxicity secondary to calcium overload, and relaxation of the endothelium.
- Intermediate effect between pure vasodilator to pure inotropic agent

OPTIME-CHF

OUTCOME	PLACEBO n 472	MILRINONE n 477	
1. Days of H for CV cause within 60 days (mean)	12.5	12.3	n.s.
2. Days of H from infusion to discharge (mean)	7.0	7.0	n.s.
3. Death/readmission within 60 days (%)	35.3	35.0	n.s.

JAMA 2002;287:1541


placebo
milrinone
OPTIME-CHF
ADVERSE EVENTS
25
20
15
10
5
0
p<.01
p<.01
p<.01
treatment failure
sustained hypotension
adverse event
JAMA 2002;287:1541

It can be used simultaneously with catecholaminergic agonists or antagonists.

Class of recommendation IIb, level of evidence B

Table 3 Drawbacks of dobutamine and milrinone

(A) *Dobutamine*

(i) Increased myocardial oxygen consumption

(ii) Myocardial injury

(iii) Tolerance/tachyphylaxis

(iv) Interaction with beta-blockers

(v) Arrhythmiogenesis

(vi) Increased mortality

(B) *Milrinone*

(i) Hypotension

(ii) Arrhythmiogenesis

(iii) Worsening prognosis in ischemic disease

Summary :

- Inotropes are indicated in the case of peripheral hypo perfusion with or without pulmonary edema

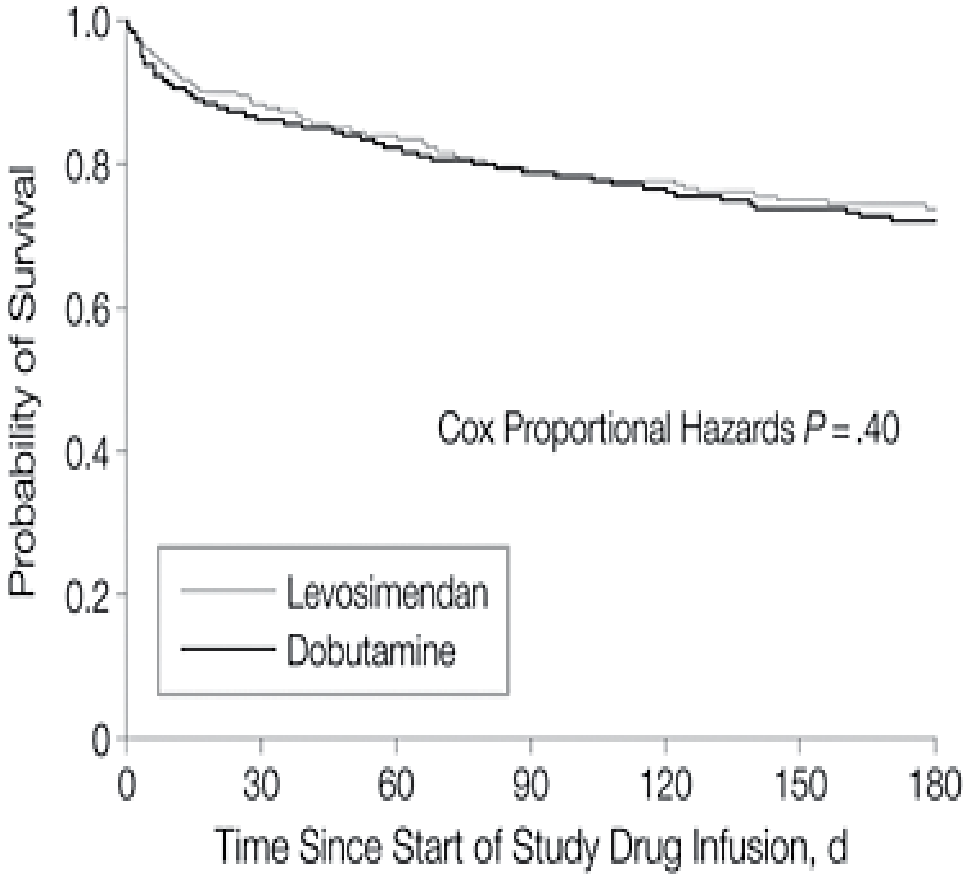
Levosimendan

- Levosimendan differs from conventional inotropic agents due to its vasodilator properties and positive inotropic effects achieved by enhancing myocyte sensitivity to calcium that is already in the cells rather than increasing calcium in the cell

Class of recommendation IIa, level of evidence B

- Two most recent trials, SURVIVE and REVIVE II, both support the symptomatic benefit of Levosimendan in comparison with placebo.
- **Mortelity** untill 180 days did not differ between levosimendan vs either inotropes or plcebo(survive),and was non- significantly increased at 90 days (Revive2)

In a meta-analysis of LIDO, CASINO and SURVIVE, mortality at 6months was lower in the Levosimendan group (relative risk 0.76, P¼0.032)

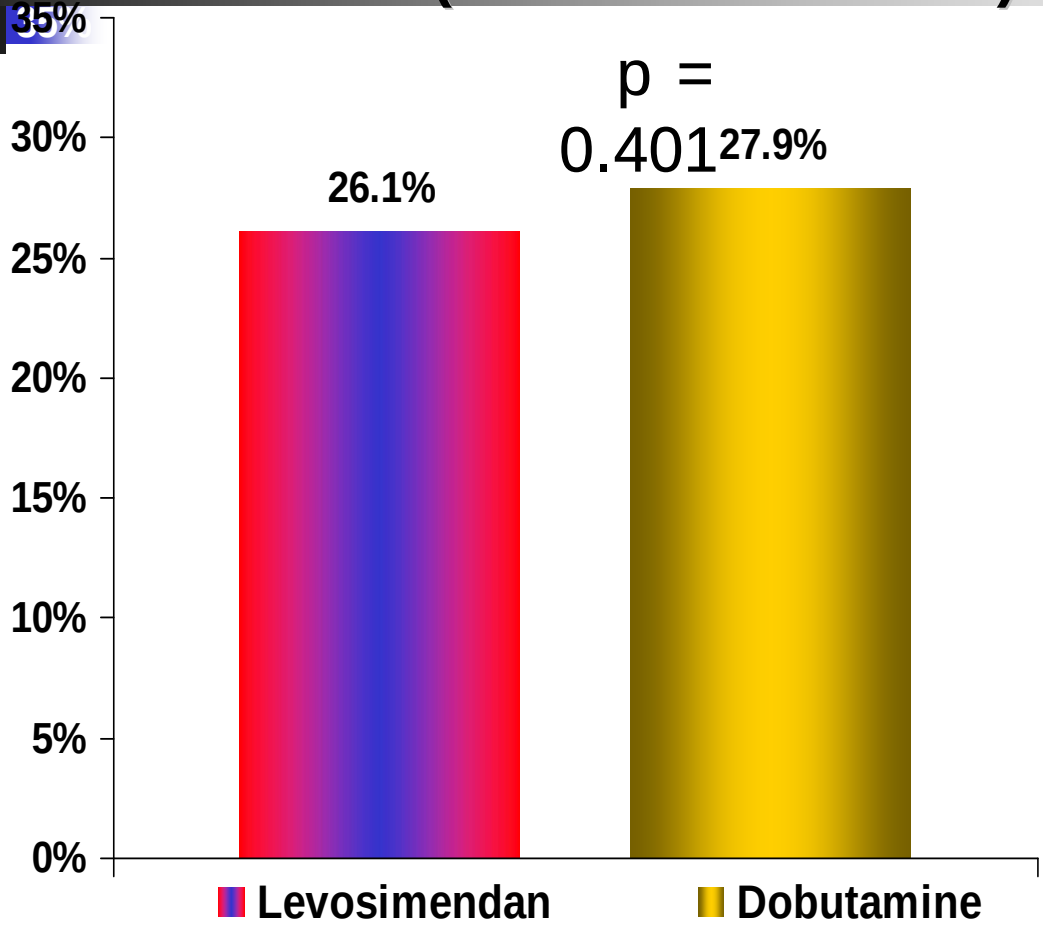


No. at Risk					
Levosimendan	664	608	586	525	462
Dobutamine	663	596	568	519	454

Table 4 Large-scale randomized clinical trials comparing the effects of levosimendan with dobutamine or placebo treatment in patients with acutely decompensated heart failure

Trial acronym	*N*	Treatment arms	Duration of therapy	Primary end-point	Survival
RUSSLAN	504	Levosimendan versus placebo in post-MI cardiac failure	Loading dose + 6-h infusion	Hypotension or myocardial ischemia	↓ Risk of death or worsening of heart failure at 6 and 24 h ↓ mortality at 14 days and at 180 days
LIDO	203	Levosimendan versus dobutamine in decompensated heart failure	Loading dose + 24-h infusion	Hemodynamic improvement	↓ Mortality at 180 days
REVIVE-1	100	Levosimendan versus placebo in decompensated heart failure	10-min loading dose + 50-min infusion + 23-h infusion (if well-tolerated)	Clinical outcome	↓ ''Worsening'' (including death) at 24 h and at 5 days
REVIVE-2	600	Levosimendan versus placebo in decompensated heart failure	Loading dose (6–12 mcg/kg) + 24-h infusion (0.1–0.2 mcg/kg/min)	A composite of clinical signs and symptoms of acute decompensated heart failure over 5 days	Neutral effects on mortality at 90 days (secondary end-point); improvement of primary-end-point and length of hospitalization; reduction of BNP
SURVIVE	1,327	Levosimendan versus dobutamine in decompensated heart failure	Loading dose (12 mcg/kg) + 24-h infusion (0.1–0.2 mcg/kg/min)	Survival at 5, 15, 30 and 180 days	No significantly different effects compared with dobutamine on mortality; greater reduction of BNP than dobutamine (secondary end-point)

SURVIVE-W: Primary endpoint



- There was no significant difference in the primary endpoint of all-cause mortality between the levosimendan and dobutamine groups

Nieminen MS, Bohm M, Cowie MR et al (2005) ESC committee for practice guideline. Executive summary of the guidelines on the diagnosis and treatment of acute heart failure: the task force on acute heart failure of the European society of cardiology. Eur Heart J 26:384–416

Table 5 Dosing schedules, recommendation classes and levels of evidence for positive inotropic agents in acute heart failure syndromes (modified from ref. [11])

Agent	Intravenous bolus dose	Intravenous infusion rate	Recommendation class	Level of evidence
Dobutamine	–	2–20 μg/kg/min	IIa	C
Dopamine	–	≤ 2 μg/kg/min: renal effect, 2–5 μg/kg/min: inotropic effect, >5 μg/kg/min: vasoconstriction	IIb	C
Milrinone	25–75 mg/kg	0.375–0.75 μg/kg/min	IIb	C
Enoximone	0.25–0.75 mg/kg	1.25–7.5 μg/kg/min	IIb	C
Levosimendan	12–24 mg/kg	0.05–0.2 μg/kg/min	IIa	B

Vasopressors

- Vasopressors (norepinephrine) are not recommended as first-line agents and are only indicated in cardiogenic shock when the combination of an inotropic agent and fluid challenge fails to restore SBP .90 mmHg, with inadequate organ perfusion, despite an improvement in cardiac output. Patients with sepsis complicating AHF may require a vasopressor.

- ***Class of recommendation IIb, level of evidence C***

Vasodilators

- **Nitroglycerin**
- **Nitropruside**
- **Nesiritide**

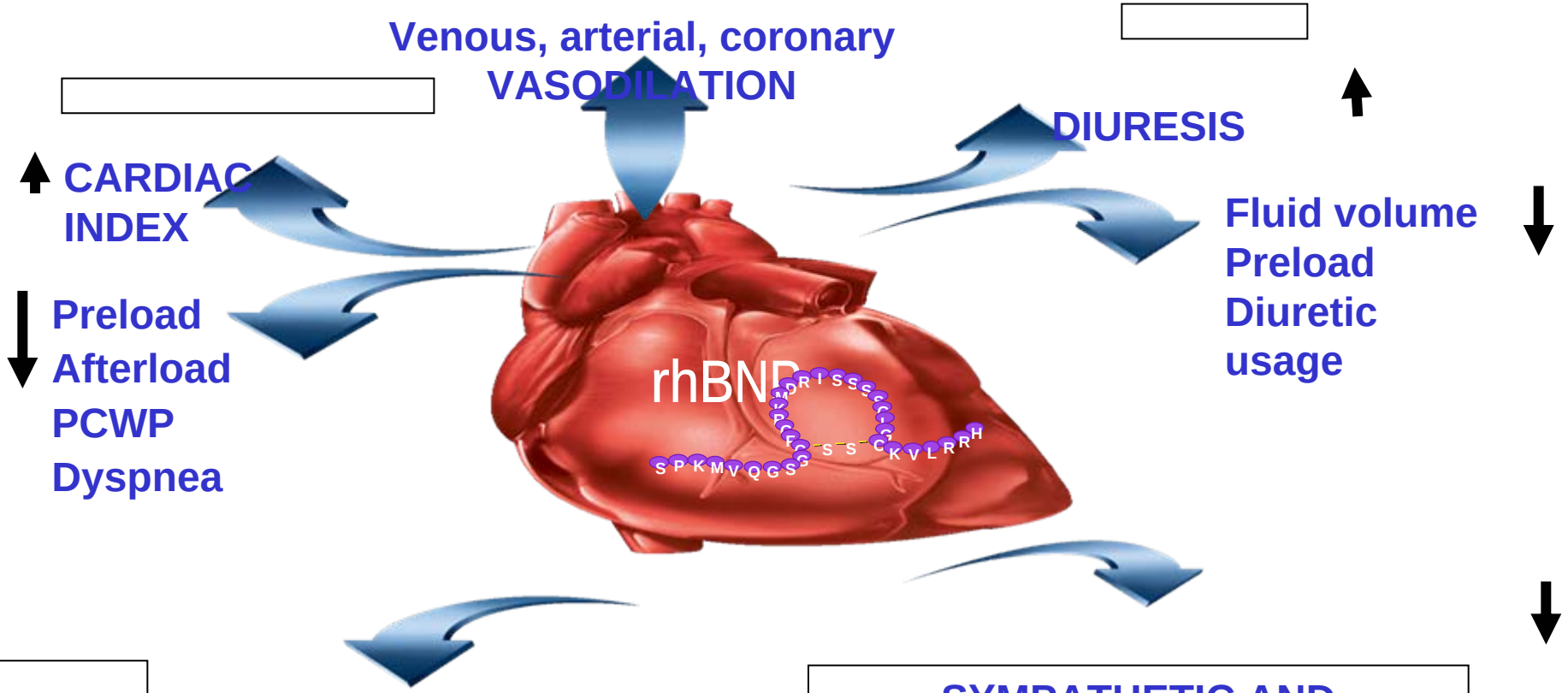
Class of recommendation I, level of evidence B

Table 29 Indications and dosing of i.v.vasodilators in acute heart failure

Vasodilator	Indication	Dosing	Main side-effects	Other
Nitroglycerine	Pulmonary congestion/oedema BP >90 mmHg	Start 10–20 µg/min, increase up to 200 µg/min	Hypotension, headache	Tolerance on continuous use
Isosorbide dinitrate	Pulmonary congestion/oedema BP >90 mmHg	Start with 1 mg/h, increase up to 10 mg/h	Hypotension, headache	Tolerance on continuous use
Nitroprusside	Hypertensive HF congestion/ oedema BP >90 mmHg	Start with 0.3 µg/kg/min and increase up to 5 µg/kg/min	Hypotension, isocyanate toxicity	Light sensitive
Nesiritide*	Pulmonary congestion/oedema BP >90 mmHg	Bolus 2 µg/kg + infusion 0.015–0.03 µg/kg/min	Hypotension	

*Not available in many ESC countries.

Nesiritide



Not proarrhythmic

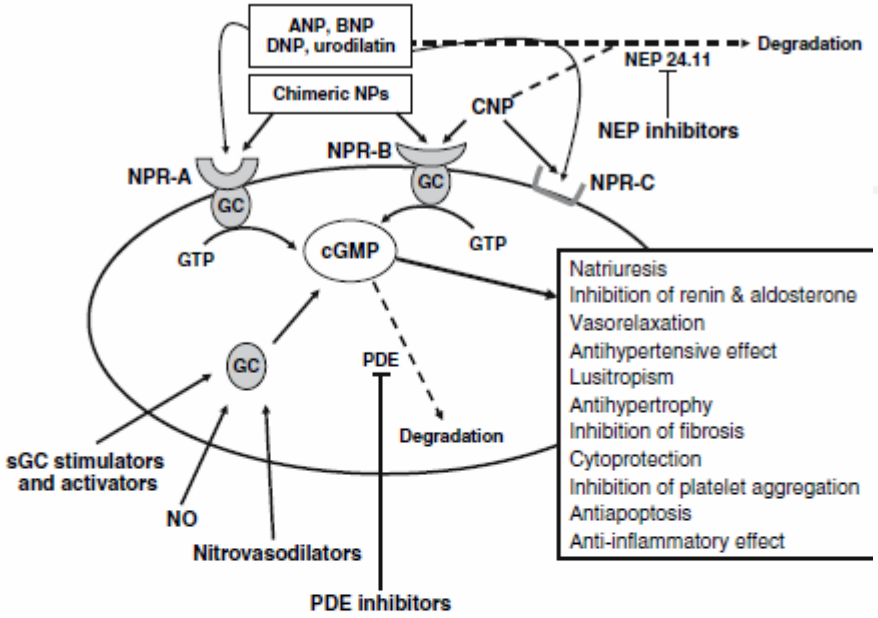


Fig. 2 Schematic illustration of the signal transduction pathways
the natriuretic peptide/nitric oxide system and therapeutic targets f
potentiation of cGMP effects [4, 7, 77]. ANP = A-type natriuret
peptide, BNP = B-type natriuretic peptide, CNP = C-type natriuret
peptide, DNP = *Dendroaspis* natriuretic peptide, GC = guanyla
cyclase, sGC = soluble guanylate cyclase, cGMP = cyclic guanosi
monophosphate, GTP = guanosine triphosphate, NEP = neutral end
peptidase, NO = nitric oxide, NPs = natriuretic peptides, NPI
A = natriuretic peptide receptor-A, NPR-B = natriuretic peptic
receptor-B, NPR-C = natriuretic peptide receptor-C, PDE = pho
phodiesterase

Short-term Risk of Death After Treatment With Nesiritide for Decompensated Heart Failure

A Pooled Analysis of Randomized Controlled Trials

Jonathan D. Sackner-Bernstein, MD
Marcin Kowalski, MD
Marshal Fox, MD
Keith Aaronson, MD, MS

Context Nesiritide improves symptoms in patients with acutely decompensated heart failure compared with placebo and appears to be safer than dobutamine. Its short-term safety relative to standard diuretic and vasodilator therapies is less clear.

Objective To investigate the safety of nesiritide relative to noninotrope-based control therapies, primarily consisting of diuretics or vasodilators.

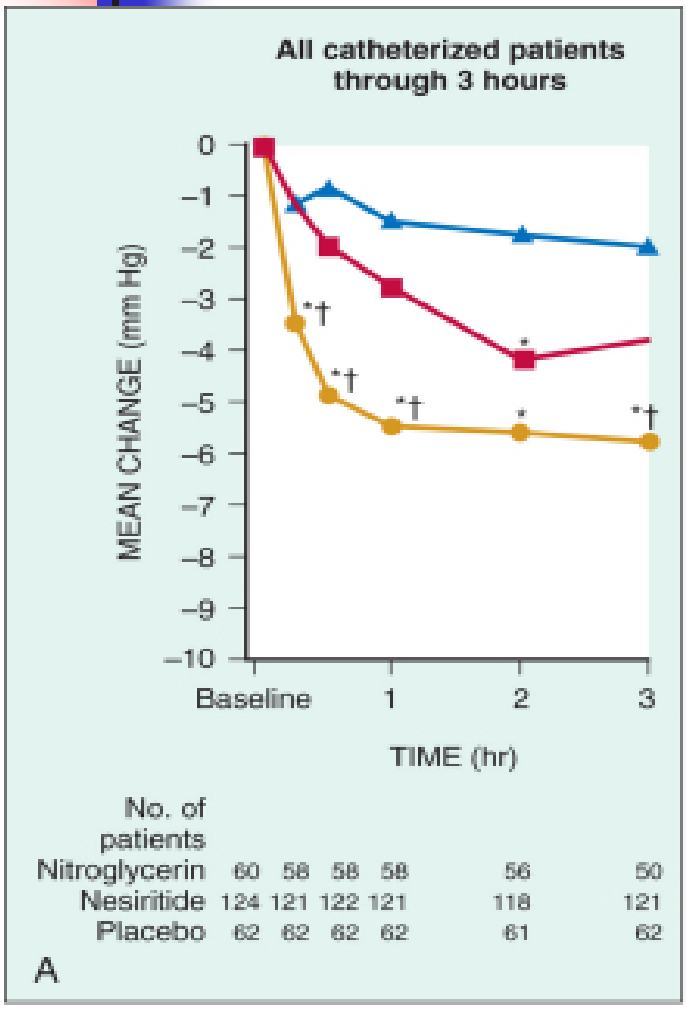
Table 2. Mortality Within 30 Days of Treatment Associated With Nesiritide or Control Therapy With Overall Risk Ratio Calculated by Mantel-Haenszel Test Using a Fixed-Effects Model

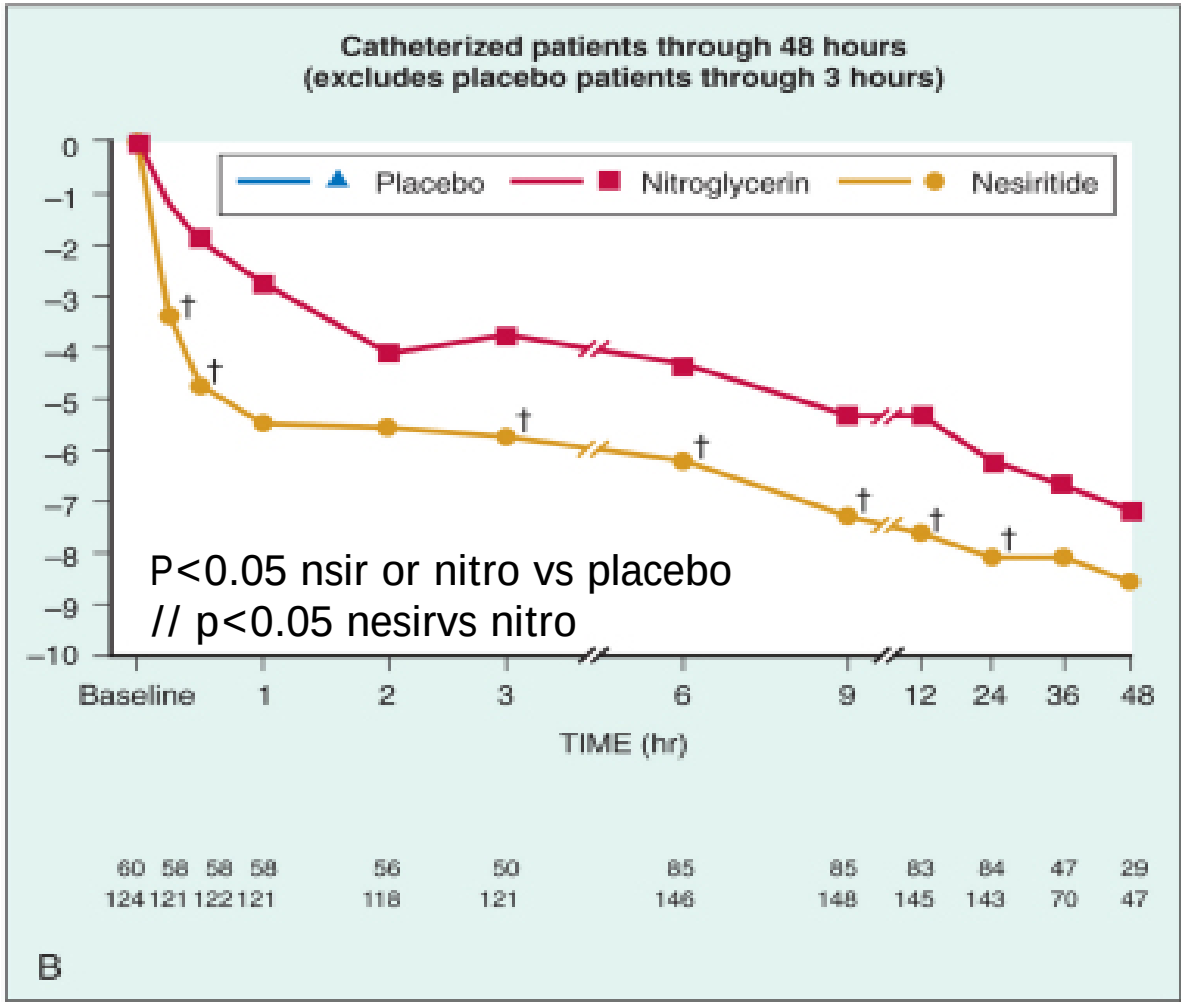
Study	No. of Deaths/Total No. (%) of Patients		Risk Ratio (95% CI)	*P* Value
	Nesiritide Therapy	Control Therapy		
NSGET	6/85 (7.1)	2/42 (4.8)	1.48 (0.31-7.03)	ND
VMAC	24/280 (8.6)	12/218 (5.5)	1.56 (0.80-3.04)	ND
PROACTION	5/120 (4.2)	1/117 (0.9)	4.88 (0.58-41.1)	ND
Total	35/485 (7.2)	15/377 (4.0)	1.74 (0.97-3.12)	.059

Abbreviations: CI, confidence interval; ND, not determined; NSGET, Nesiritide Study Group Efficacy Trial; PROACTION, Prospective Randomized Outcomes Study of Acutely Decompensated Congestive Heart Failure Treated Initially in Outpatients with Natrecor; VMAC, Vasodilation in the Management of Acute Congestive heart failure.

VMAC investigators *JAMA2002 287:1531*

*(*acute heart failure+RHC*)*





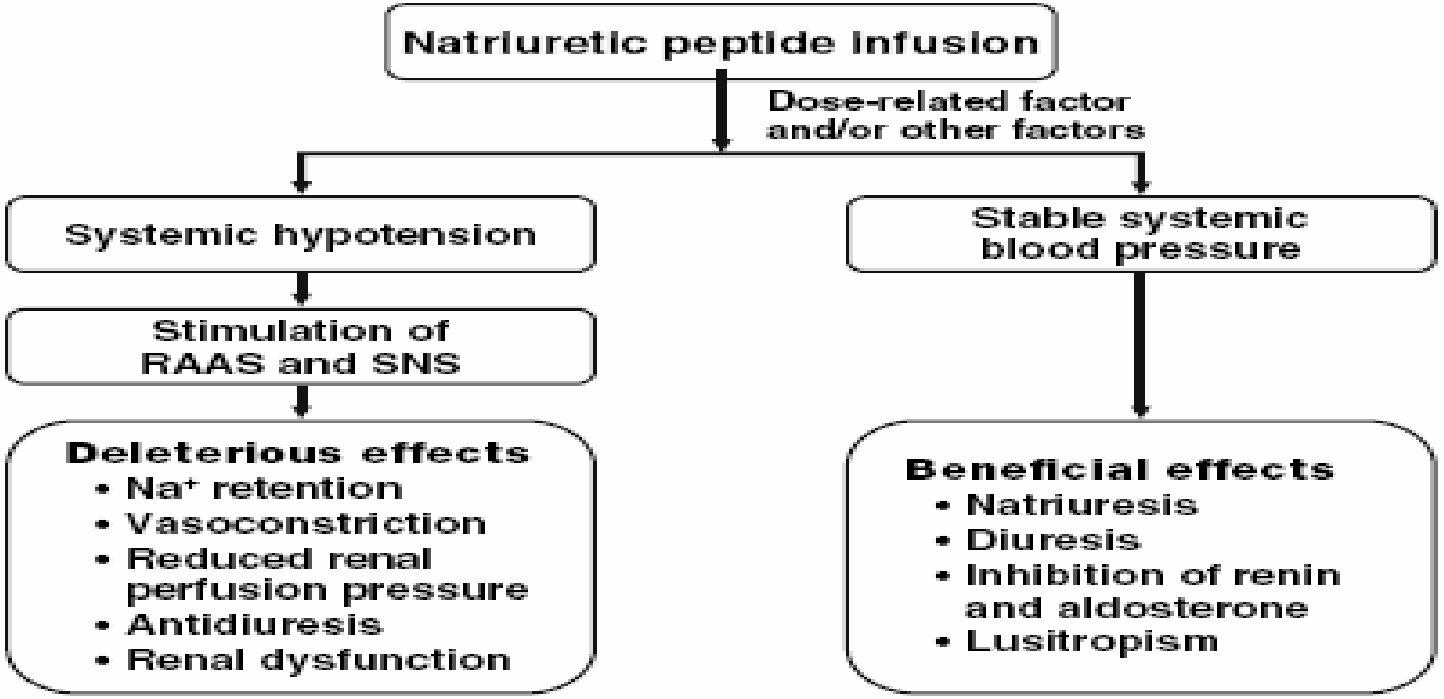
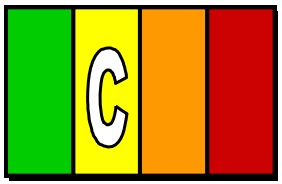


Fig. 3 Proposed mechanisms for differential renal effects mediated by natriuretic peptides [3, 68]. NPs = natriuretic peptides RAAS = -renin-angiotensin-aldosterone system SNS = sympathetic nervous system

2009 UPDATE The Hospitalized Patient

Severe Symptomatic Fluid Overload

IIa



In patients with evidence of severely symptomatic fluid overload in the absence of systemic hypotension, vasodilators such as intravenous nitroglycerin, nitroprusside or neseritide can be beneficial when added to diuretics and/or in those who do not respond to diuretics alone

New

Non-pharmacological therapies

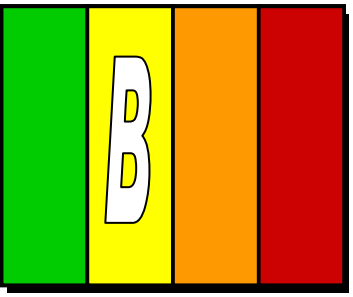
- Small randomized trials have shown that continuous positive airway pressure ***(CPAP)*** and other noninvasive ventilation decreased the need for endotracheal intubation in cardiogenic shock without a significant impact in mortality.
- ***Ultrafiltration***- small trials revealed its potential benefit for relief of pulmonary edema, ascites,and peripheral edema

Costanzo MR, Guglin M, Saltzberg M, et al. ***UNLOAD*** Trial Investigators, ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. *J Am Coll Cardiol 2007; 49:675–683*.

2009 UPDATE The Hospitalized Patient

Ultrafiltration

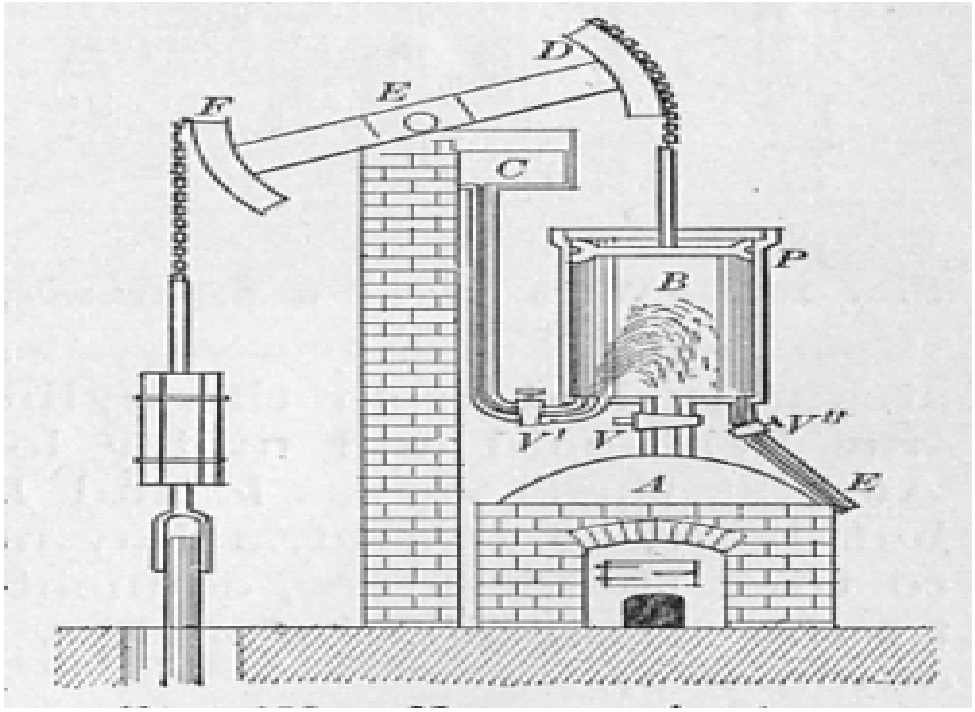
I IIa IIb III



refractory congestion not responding to medical therapy.

New

Mechanical assistance



IABP

- Recommended in acute decompensated states, as an urgent measure of cardiac support, to stabilize the patient and maintain organ perfusion until transplantation is done.

Class I B

What can we do more?

Assist device!!!

Rationale of assist device use

- Restoration of normal hemodynamics and vital organ perfusion.
- Reduction of ventricular strain and improving remodeling

Assist devices

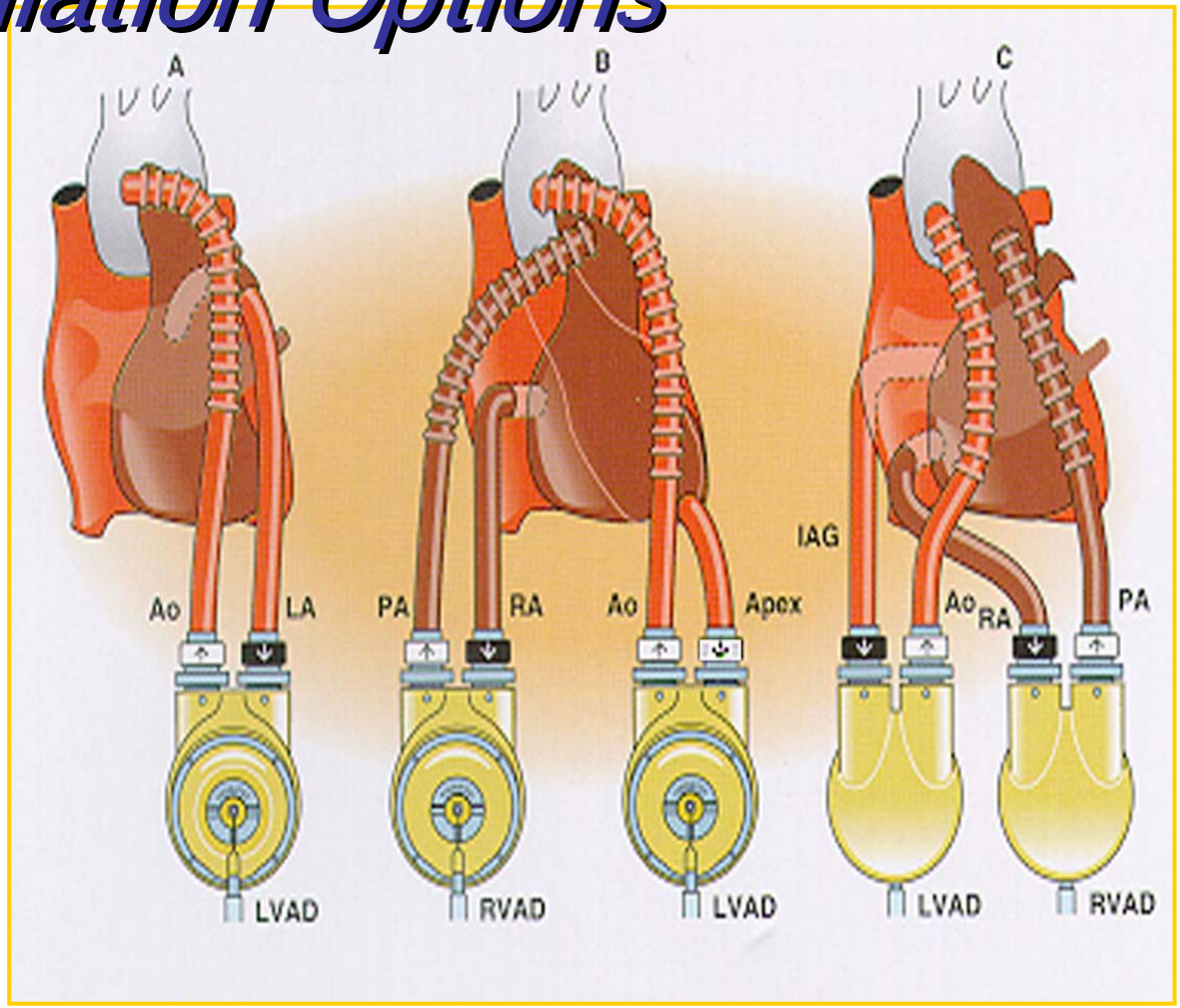
- A a bridge to recovery or to heart transplantation

Class IIa B

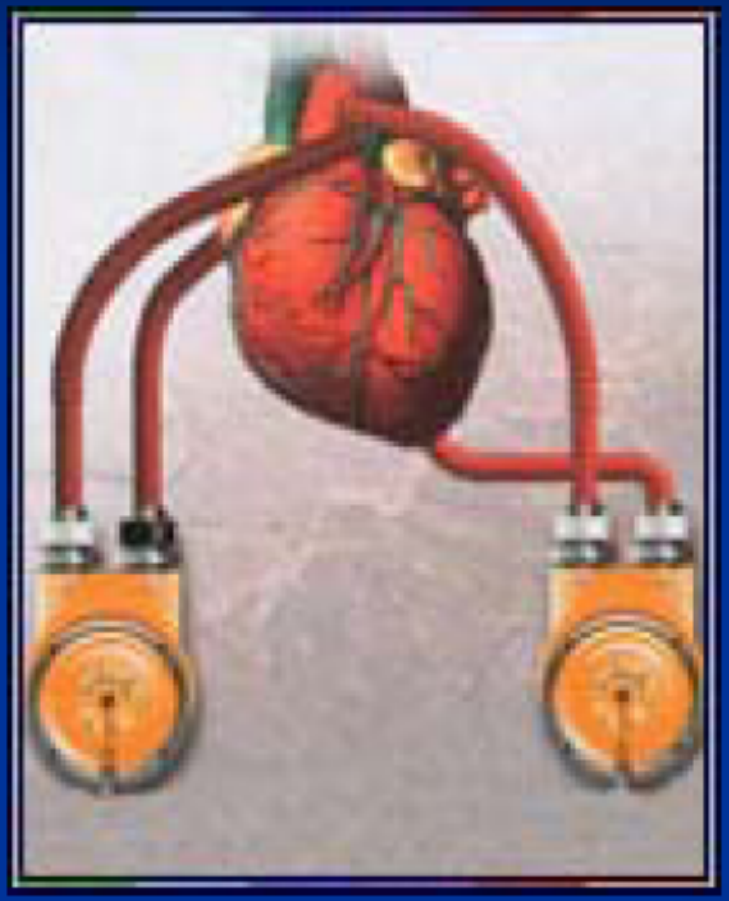
Oxygenator- ecmo	Short term
Thoratec	LV+RV
Heartmate I/II/ Heartware	long term, destination
Total artificial heart	

Thoratec® Implant Versatility

Cannulation Options

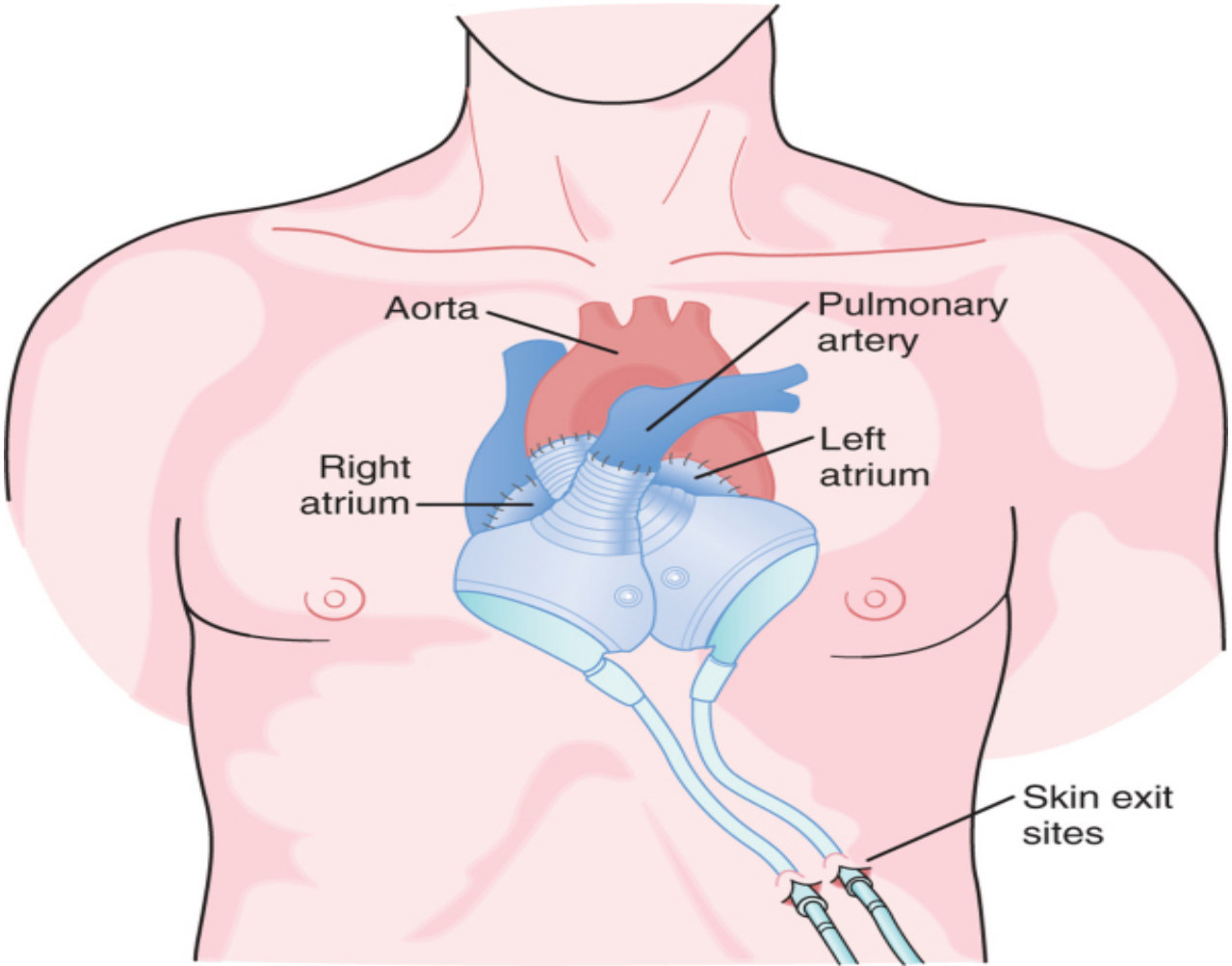


BIVAD

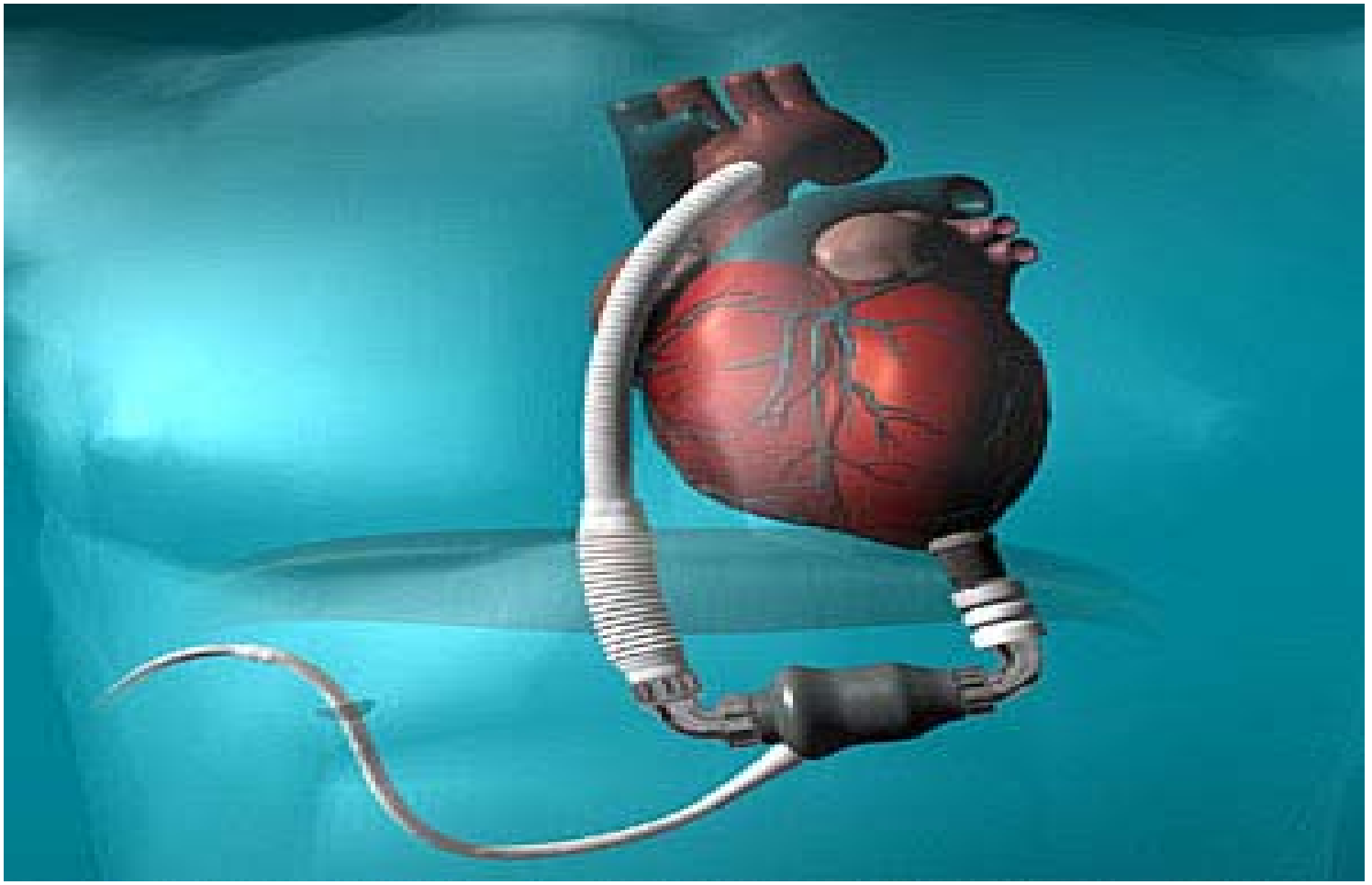


- support of RV and LV

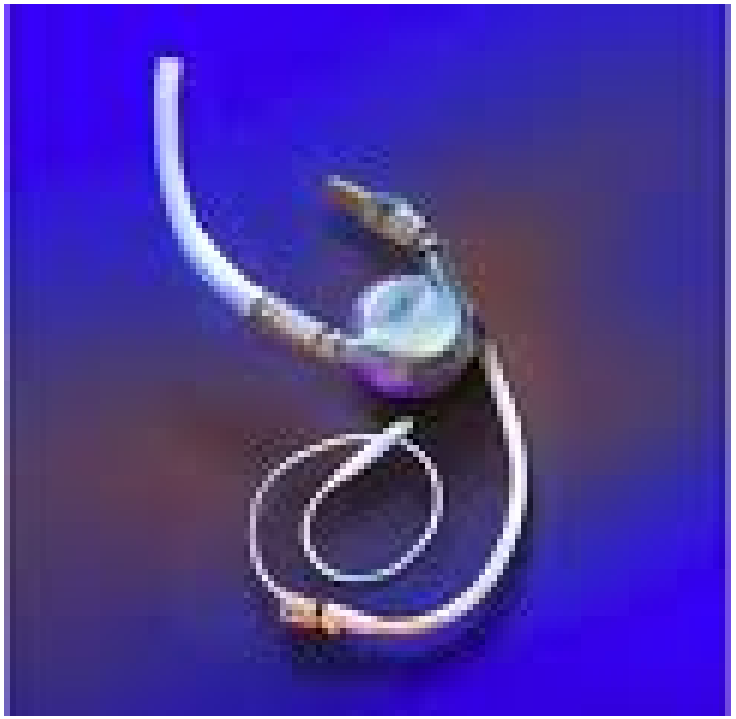
Total artificial heart - abiocor



Heartmate II



Heart ware



Indications

- May be indicated to patients not responding to conventional Rx, when there is a potential for recovery or as a bridge to transplant

There is therefore no consensus concerning LVAD indications or the most appropriate patient population

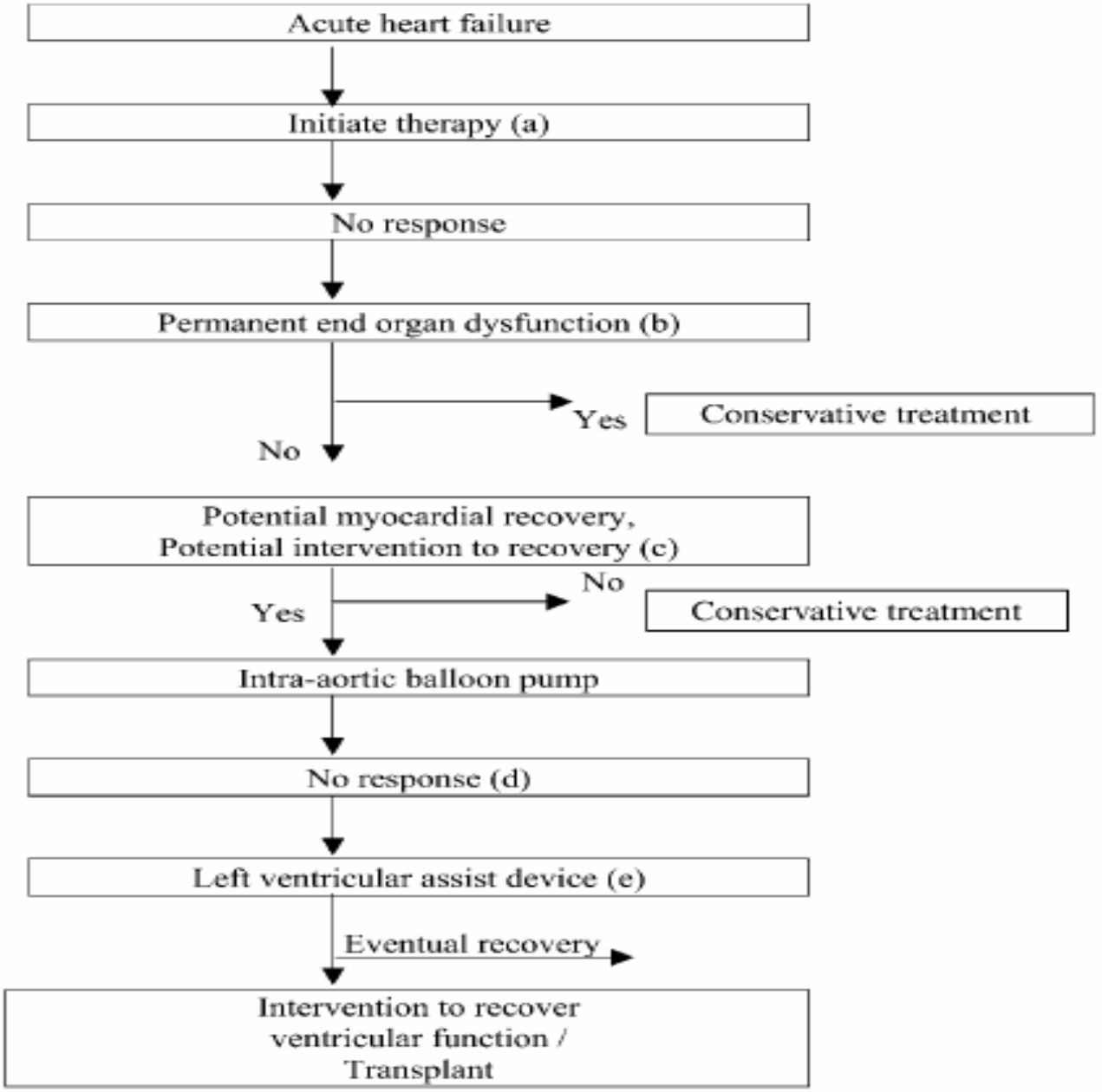
† Current indications for LVADs and artificial hearts include bridging to transplantation and managing patients with acute, severe myocarditis.

Class of recommendation IIa, level of evidence C

† Although experience is limited, these devices may be considered for long-term use when no definitive procedure is planned.

Class of recommendation IIb, level of evidence C

Who should get an assist device?

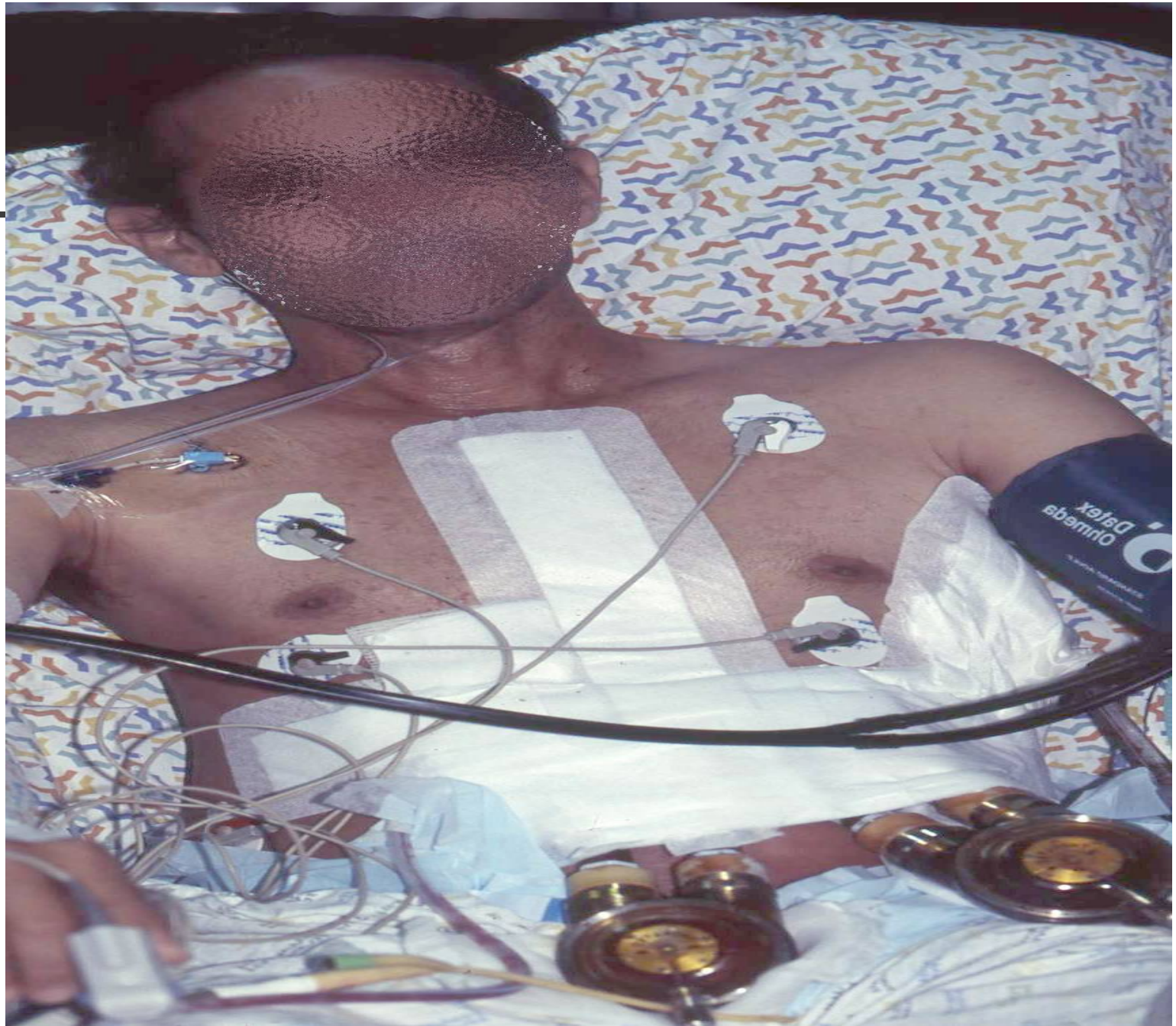


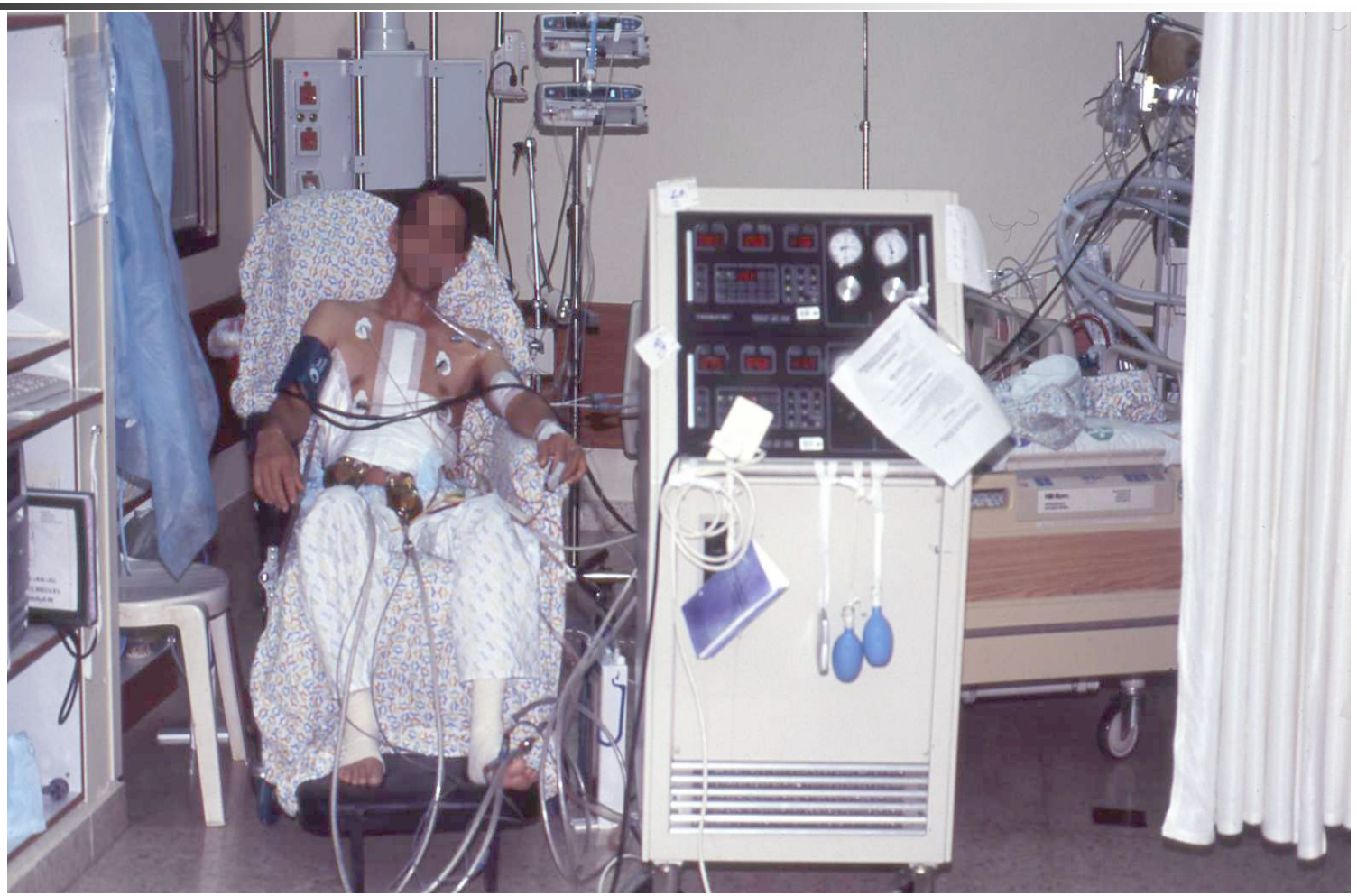
Major complications of assist device

- Bleeding
- Infection
- Neurologic events

Univentricular vs. Biventricular Assist Device Support

- ***Indications for Biventricular Support***
  - Signs of Right Heart Failure
  - Intractable Arrhythmias
  - RV/Septal Infarction
  - Elevated PVR
  - Secondary Organ Involvement
  - Prolonged Cardiogenic Shock “Sicker Patients”


Dalex
Ormeda



There is always an option for patients with severe decompensated heart failure

- Patients with acute decompensated heart failure should receive all evidence –based treatments (medical and mechanical) in order to maintain vital organ function
- After stabilization, patients should be transferred to tertiary centers specializing in assist device implantation and orthotropic heart transplantation

FIN

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