5th iHEF CARD

The 5th Indonesian Symposium on Heart Failure and Cardiometabolic Disease

Indonesian Working Group on Heart Failure and Cardiometabolic Disease

WHFS World Heart Failure Society

HEART FAILURE SOCIETY (SINGAPORE)

Dilator-Diuretic Dilemma in Acute Heart Failure

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Sheraton Grand Jakarta Gandaria City, Jakarta, Indonesia

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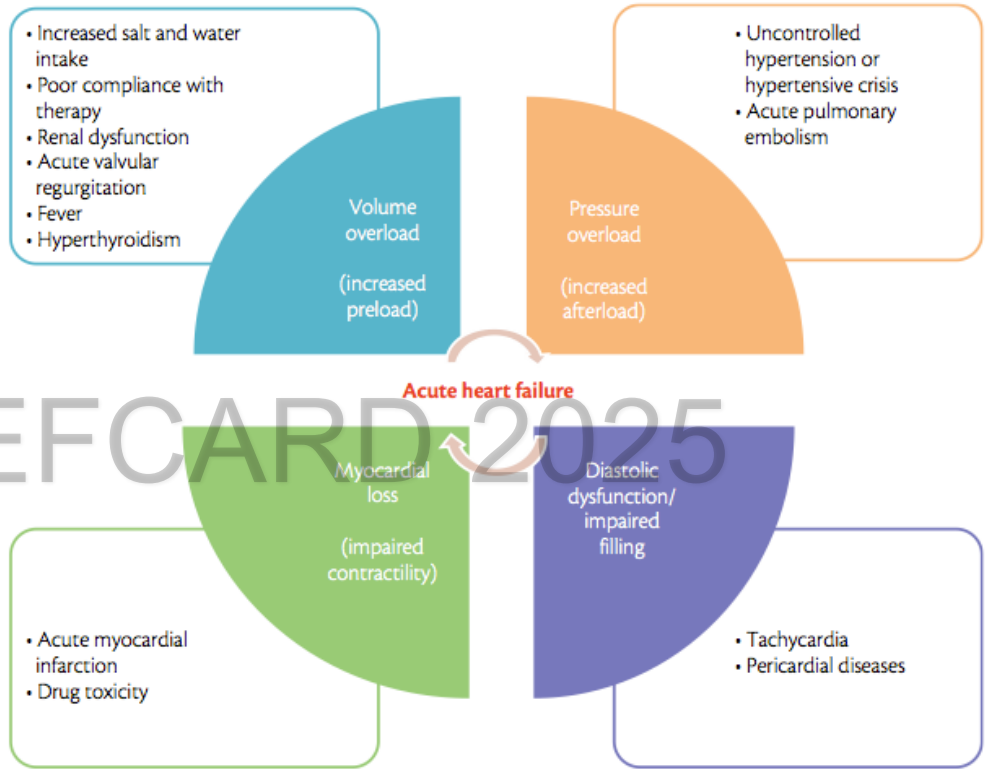
Introduction

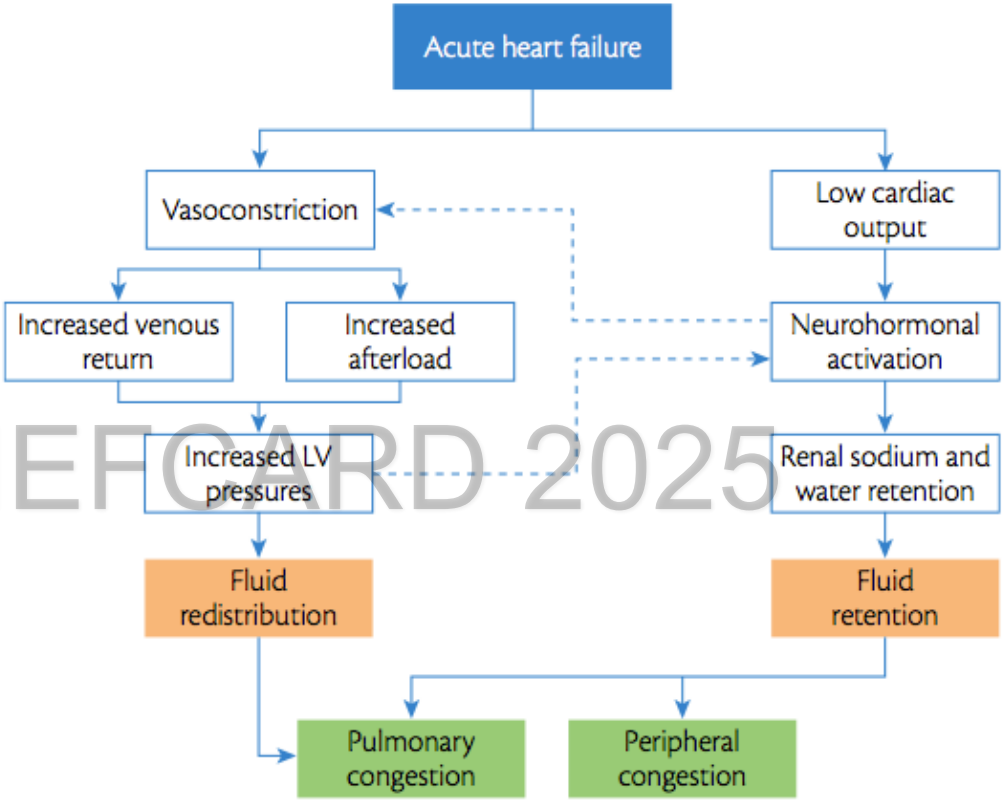
- Acute heart failure (AHF) : rapid development or change of symptoms and signs of heart failure that requires urgent medical attention
- Congestion and fluid retention are the hallmarks of decompensated heart failure and the major reason for the hospitalization of patients with heart failure
- The two main mechanisms leading to congestion is fluid retention and fluid redistribution→ 'Cardiac' versus 'vascular' failure
- Despite the fact that the majority of patients with ADHF require care in the hospital, there is limited evidence evaluating the processes of care that are commonly provided in this setting. In some cases, therapies may be widely used despite limited evidence for effectiveness

Main Patho-Mechanisms Leading to AHF



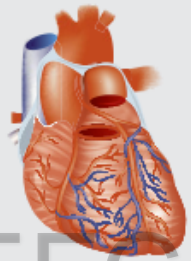
Arrigo M, et al. Eur Heart J. (2016) .11-18

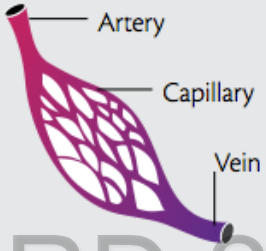
Pathophysiology of Congestion in AHF



Ponikowski P, et al. Eur Heart J (2016) , 43-55

Clinical Profile and Pathophysiology of AHF: ‘Cardiac’ VS ‘Vascular’ Failure



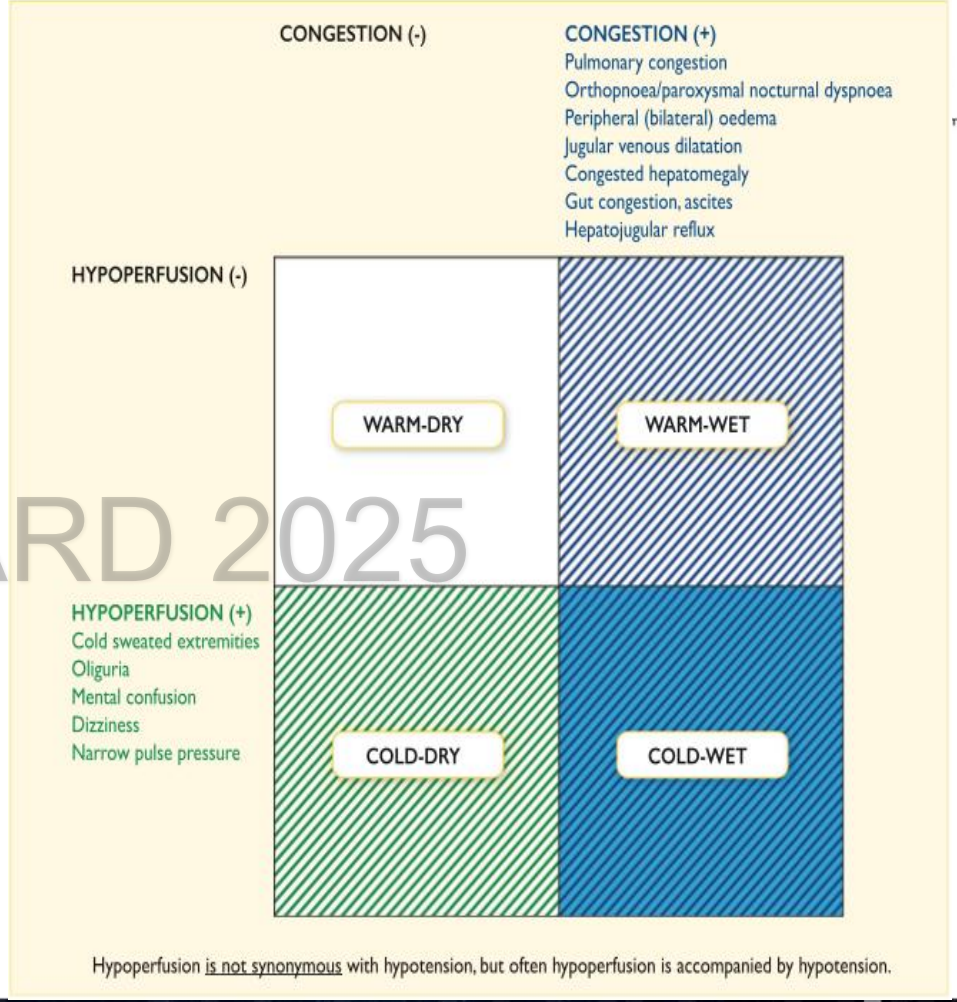


	‘Cardiac’ failure	‘Vascular’ failure
- Mechanism	- Fluid retention	- Fluid redistribution
- Heart failure type	- ADCHF	- *De novo*
- Onset	- Gradual	- Rapid
- Signs	- Peripheral and pulmonary congestion	- Pulmonary congestion
- Blood pressure	- Normal or low	- Normal or increased
- LV ejection fraction	- Reduced	- Preserved
- Filling pressures	- Lower*	- High
- Cardiac output	- Low	- Higher*
- Main therapy	- Diuretics	- Vasodilators
- Mortality rate	- High	- Lower*
- Rehospitalization rate	- High	- High

Ponikowski P, et al. Eur Heart J (2016) , 43-55

Classification of AHF

In practice the most useful classifications →
based on clinical presentation at admission



Ponikowski P, et al. Eur Heart J (2016) ,

The overall aims of pharmacological interventions in managing AHF

Immediate aims:

To relieve symptoms and optimize the fluid volume status

To restore the respiratory function, gas exchange, and systemic oxygenation

To improve the haemodynamics and end-organ function

To address any underlying cause or precipitant (e.g. myocardial ischaemia, arrhythmia, infection, anaemia, iatrogenic, etc.)

Further aims:

To identify patients who may benefit from further non-pharmacological therapy in the short term (e.g. invasive ventilation, ultrafiltration, percutaneous coronary intervention (PCI), mechanical circulatory support) and medium term (e.g. cardiac resynchronization therapy, transplantation)

To optimize oral therapy for chronic heart failure (ACE-Is or ARNIs, β-blockers, and mineralocorticoid receptor antagonists), once stable and prior to discharge

European Heart Journal (2003) **24**, 464–474

ELSEVIER

EUROPEAN SOCIETY OF CARDIOLOGY

The EuroHeart Failure Survey programme—a survey on the quality of care among patients with heart failure in Europe

Part 2: treatment

National surveys suggest that treatment of heart failure in daily practice differs from guidelines and is characterized by underuse of recommended medications

Diuretics and particularly loop diuretics were by far the most commonly used heart failure medications

Table 1 Rate of prescription of the major heart failure medication in the overall population (n=11 016)

	(%)
ACE inhibitors	61.8 (40–85.1)
Angiotensin II receptor antagonists	4.5 (1.9–14)
Antithrombotic therapy (any)	77.6 (57.7–92.7)
Aspirin	29.1 (27.1–73)
Beta-Blockers	36.9 (10–65.8)
Calcium channel blockers	21.2 (9.8–33.4)
Cardiac glycosides	35.7 (17.3–53.5)
Diuretics	86.9 (64.2–96.4)
IV inotropic agents	7.2 (0.5–19.5)
Nitrates	32.1 (6.3–70.6)
Spironolactone	20.5 (5.7–58.5)

European Heart Journal (2003) 24, 464–474

ESC European Society of Cardiology
European Journal of Heart Failure (2019) 21, 1338–1352
doi:10.1002/ejhf.1492
RESEARCH ARTICLE

Acute heart failure congestion and perfusion status – impact of the clinical classification on in-hospital and long-term outcomes; insights from the ESC-EORP-HFA Heart Failure Long-Term Registry

Ovidiu Chioncel[1*], Alexandre Mebazaa[2], Aldo P. Maggioni[3,4], Veli-Pekka Harjola[5], Giuseppe Rosano[6], Cecile Laroche[7], Massimo F. Piepoli[8], Maria G. Crespo-Leiro[9], Mitja Lainscak[10], Piotr Ponikowski[11,12], Gerasimos Filippatos[13,14], Frank Ruschitzka[15], Petar Seferovic[16], Andrew J.S. Coats[17], and Lars H. Lund[18,19], on behalf of the ESC-EORP-HFA Heart Failure Long-Term Registry Investigators[†]

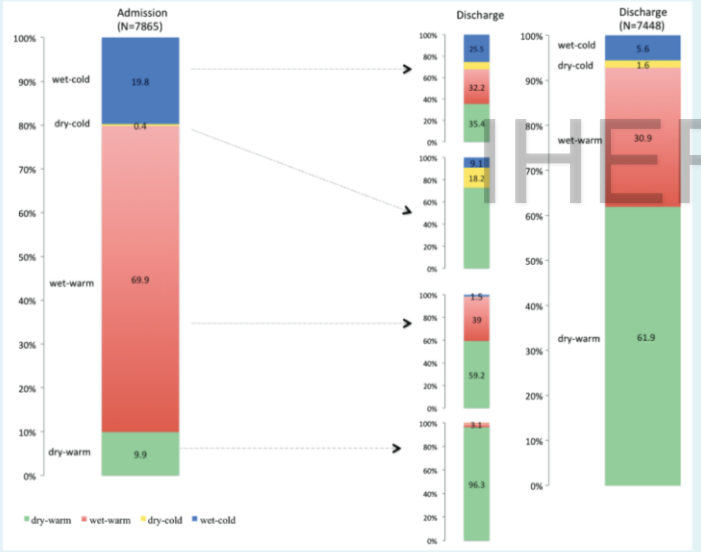


Figure 1 Classification based on congestion/hypoperfusion status assessed by clinical examination performed at admission and discharge. Classification at discharge was used in 7448 patients discharged alive.

Table 2 Intravenous vasoactive therapies, interventions and cardiovascular oral therapies during hospitalization according to profile at admission

	Overall (*n* = 7865)	Dry-warm (*n* = 785)	Wet-warm (*n* = 5492)	Dry-cold (*n* = 33)	Wet-cold (*n* = 1555)	*P*-value
Intravenous therapies						
Inotropes	11.7	5.0	8.2	9.1	27.8	<0.001
Vasodilators	19.3	7.0	20.6	28.1	20.7	<0.001
Diuretics	81.1	30.5	87.7	54.5	83.8	<0.001
Interventions						
Coronary angiography	21.7	41.5	20.2	15.2	17.0	<0.001
PCI/CABG	10.1	17.9	9.3	12.1	8.6	<0.001
EPS	0.6	1.2	0.6	0.0	0.2	0.029
Transcatheter ablation	0.7	1.5	0.6	0.0	0.3	0.006
Right heart catheterization	1.9	2.5	1.9	0.0	1.9	0.610
IABP	0.9	1.2	0.7	6.1	1.4	0.001
CRT	3.8	5.4	3.2	3.0	4.9	0.001
ICD	6.4	11.9	5.3	0.0	7.5	<0.001
Oral CV therapies						
BB admission	72.4	82.8	71.8	60.6	69.8	<0.001
BB discharge	73.9	84.6	74.0	63.6	68.2	<0.001
ACEi/ARB admission	77.7	84.5	78.7	75.8	71.3	<0.001
ACEi/ARB discharge	79.1	84.6	78.7	69.7	69.5	<0.001
MRA admission	55.9	53.0	57.2	27.3	53.6	<0.001
MRA discharge	54.7	53.9	56.1	27.3	50.8	<0.001
Ivabradine admission	3.2	1.3	3.2	3.0	4.0	0.05
Ivabradine discharge	3.1	1.4	3.3	3.0	3.4	0.033
Diuretics admission	80.3	71.6	81.9	54.5	79.8	<0.001
Diuretics discharge	83.2	73.1	86.3	54.5	77.8	<0.001
Digoxin admission	25.9	16.8	25.6	15.2	31.5	<0.001
Digoxin discharge	23.7	15.7	24.3	18.2	25.7	<0.001

Ovidiu Chioncel. European Journal of Heart Failure (2019) 21, 1338–1352

CLINICAL PRESENTATION ACUTE HEART FAILURE

	Acute decompensated heart failure	Acute pulmonary oedema	Isolated right ventricular failure	Cardiogenic shock
Main mechanisms	LV dysfunction Sodium and water renal retention	Increased afterload and/or predominant LV diastolic dysfunction Valvular heart disease	RV dysfunction and/or pre-capillary pulmonary hypertension	Severe cardiac dysfunction
Main cause of symptoms	Fluid accumulation, increased intraventricular pressure	Fluid redistribution to the lungs and acute respiratory failure	Increased central venous pressure and often systemic hypoperfusion	Systemic hypoperfusion
Onset	Gradual (days)	Rapid (hours)	Gradual or rapid	Gradual or rapid
Main haemodynamic abnormalities	Increased LVEDP and PCWP[a] Low or normal cardiac output Normal to low SBP	Increased LVEDP and PCWP[a] Normal cardiac output Normal to high SBP	Increased RVEDP Low cardiac output Low SBP	Increased LVEDP and PCWP[a] Low cardiac output Low SBP
Main clinical presentations[1,446]	Wet and warm OR Dry and cold	Wet and warm[b]	Dry and cold OR Wet and cold	Wet and cold
Main treatment	Diuretics Inotropic agents/vasopressors (if peripheral hypoperfusion/hypotension) Short-term MCS or RRT if needed	Diuretics Vasodilators[b]	Diuretics for peripheral congestion Inotropic agents/vasopressors (if peripheral hypoperfusion/hypotension) Short-term MCS or RRT if needed	Inotropic agents/vasopressors Short-term MCS RRT

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

11.3.3 Diuretics

Intravenous diuretics are the cornerstone of AHF treatment. They increase renal excretion of salt and water and are indicated for the treatment of fluid overload and congestion in the vast majority of AHF patients.

Loop diuretics are commonly used due to their rapid onset of action and efficacy. Data defining their optimal dosing, timing, and method of administration are limited. No difference in the primary efficacy outcome of patients' symptoms global assessment was shown with a high-dose regimen, compared with a low-dose regimen, in the DOSE trial. However, there was a greater relief of dyspnoea, change in weight and net fluid loss (with no prognostic role for increases in serum creatinine) in the higher-dose regimen.[460–462] High diuretic doses may cause greater neurohormonal activation and electrolyte abnormalities and are often associated with poorer outcomes, although a cause and effect relation cannot be proven by these retrospective analyses.[463–466] Based on these observations, it may be appropriate, when starting i.v. diuretic treatment, to use low doses, to assess the diuretic response and increase the dose when that is insufficient.

Acute Heart Failure Management

Diuretics

- Loop diuretics are commonly used due to their rapid onset of action
- No difference in efficacy outcome of patients symptoms global assessment between high dose and low dose
- Greater relief of dyspnea, change in weight, and net fluid loss in high dose
- If diuretic response remains inadequate after doubling loop diuretic use (<100 mL hourly) concomitant administration of other diuretic agent may be considered

Diuretics		
Intravenous loop diuretics are recommended for all patients with AHF admitted with signs/symptoms of fluid overload to improve symptoms.[145]	I	C
Combination of a loop diuretic with thiazide-type diuretic should be considered in patients with resistant oedema who do not respond to an increase in loop diuretic doses.[145]	IIa	B

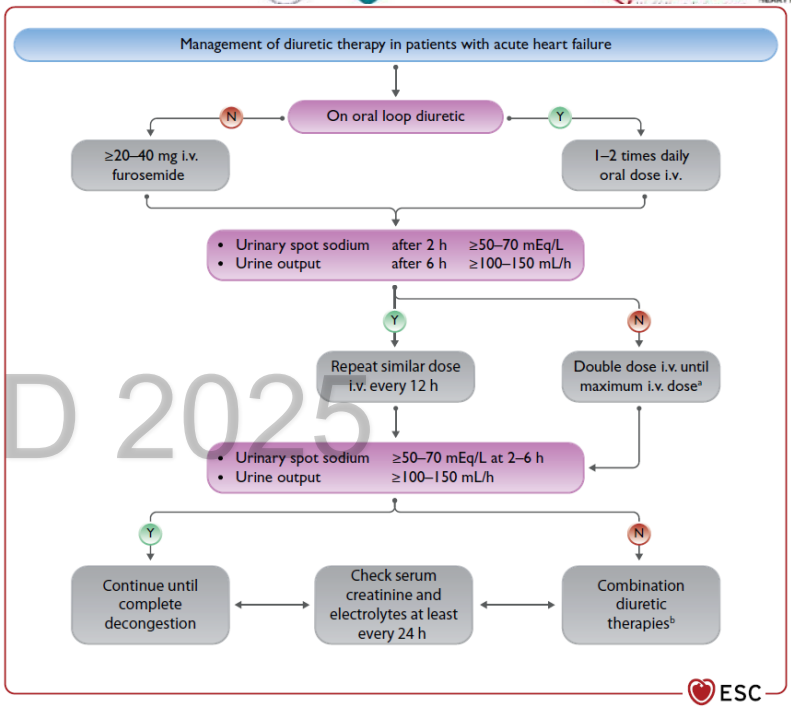


Figure 13 Diuretic therapy (furosemide) in acute heart failure. i.v. = intravenous. [a]The maximal daily dose for i.v. loop diuretics is generally considered furosemide 400–600 mg though up to 1000 mg may be considered in patients with severely impaired kidney function. [b]Combination therapy is the addition to the loop diuretic of a diuretic with a different site of action, e.g. thiazides or metolazone or acetazolamide. Modified from [145].

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

COR	LOE	Recommendations
1	B-NR	1. Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to improve symptoms and reduce morbidity.[1]
1	B-NR	2. For patients hospitalized with HF, therapy with diuretics and other guideline-directed medications should be titrated with a goal to resolve clinical evidence of congestion to reduce symptoms and rehospitalizations.[1–6]
1	B-NR	3. For patients requiring diuretic treatment during hospitalization for HF, the discharge regimen should include a plan for adjustment of diuretics to decrease rehospitalizations.[7]
2a	B-NR	4. In patients hospitalized with HF when diuresis is inadequate to relieve symptoms and signs of congestion, it is reasonable to intensify the diuretic regimen using either: a. higher doses of intravenous loop diuretics.[1,3]); or b. addition of a second diuretic.[3]

Protocols for recent trials of other medications in patients hospitalized with HF have all included intravenous diuretic therapy as background therapy

No RCTs for hospitalized patients comparing intravenous loop diuretics to placebo

ORIGINAL ARTICLE

Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome

Authors: Bradley A. Bart, M.D., Steven R. Goldsmith, M.D., Kerry L. Lee, Ph.D., Michael M. Givertz, M.D., Christopher M. O'Connor, M.D., David A. Bull, M.D., Margaret M. Redfield, M.D., +15, for the Heart Failure Clinical Research Network Author Info & Affiliations

Published December 13, 2012 | N Engl J Med 2012;367:2296-2304 | DOI: 10.1056/NEJMoa1210357

CARRESS-HF TRIAL:
RCT that compared ultrafiltration with a strategy of diuretic-based stepped pharmacologic therapy

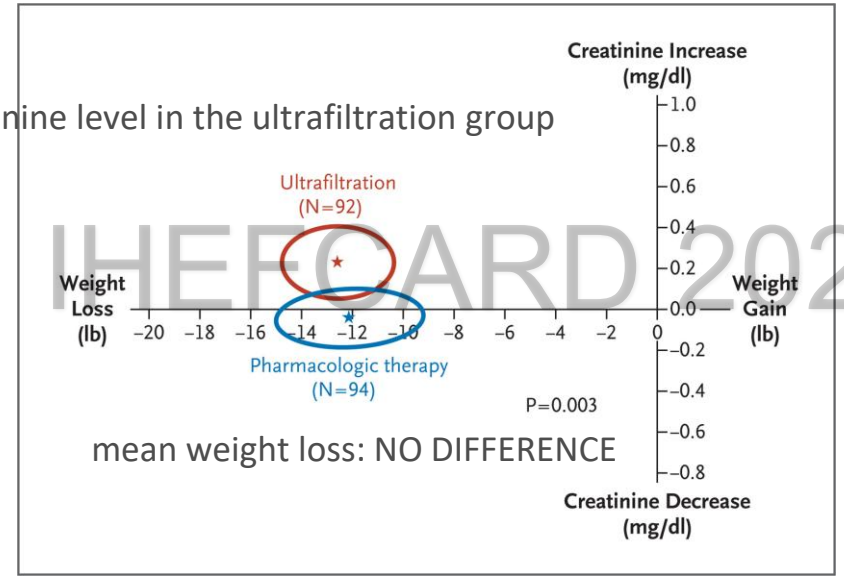
CONCLUSIONS

In a randomized trial involving patients hospitalized for acute decompensated heart failure, worsened renal function, and persistent congestion, the use of a stepped pharmacologic-therapy algorithm was superior to a strategy of ultrafiltration for the preservation of renal function at 96 hours, with a similar amount of weight loss with the two approaches. Ultrafiltration was associated with a higher rate of adverse events. (Funded by the National Heart, Lung, and Blood Institute; ClinicalTrials.gov number, NCT00608491.)

Bradley A. Bart. **N Engl J Med 2012;367:2296-2304**

CARRESS-HF TRIAL:
RCT that compared ultrafiltration with a strategy of diuretic-based stepped pharmacologic therapy

increase in the serum creatinine level in the ultrafiltration group

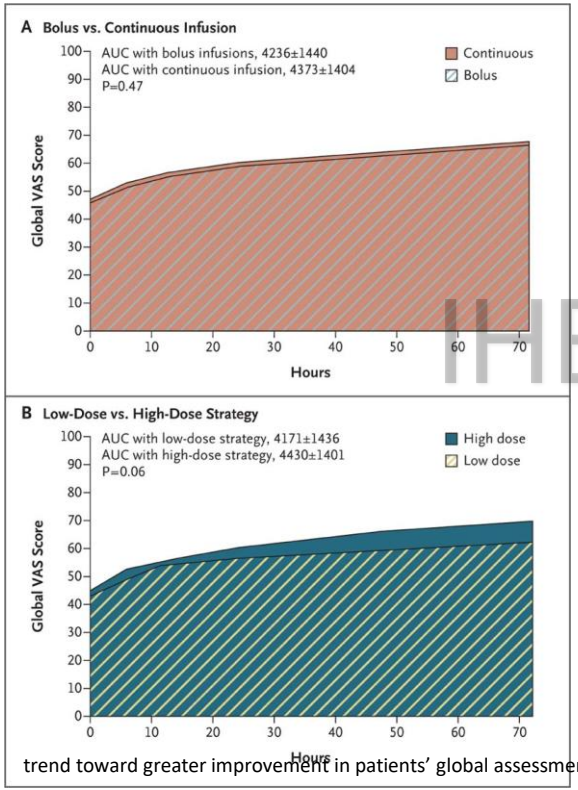


mean weight loss: NO DIFFERENCE

ANOTHER FINDINGS: no significant between-group differences in weight loss, mortality, or the rate of hospitalization for heart failure during the 60-day follow-up period

Bradley A. Bart. **N Engl J Med 2012;367:2296-2304**

DOSE TRIAL:
BOLUS VS CONTINUOUS INFUSION
HIGH VS LOW DOSE FUROSEMIDE



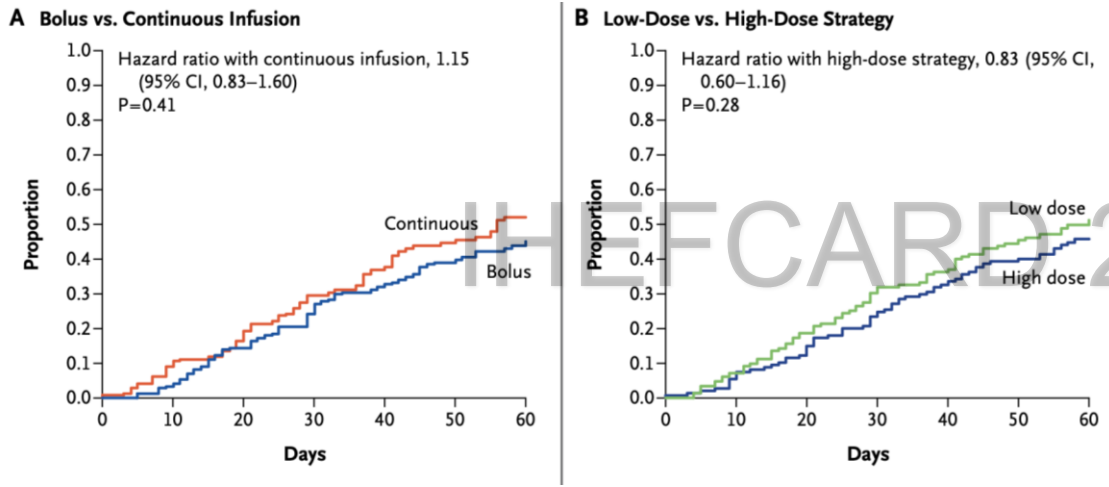
trend toward greater improvement in patients' global assessment of symptoms in the high-dose group

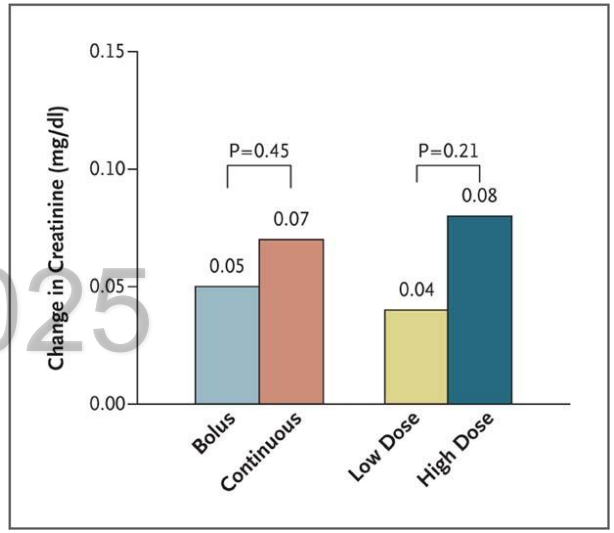
Table 2. Secondary End Points for Each Treatment Comparison.*

End Point	Bolus Every 12 Hr (N=156)	Continuous Infusion (N=152)	P Value	Low Dose (N=151)	High Dose (N=157)	P Value
AUC for dyspnea at 72 hr	4456±1468	4699±1573	0.36	4478±1550	4668±1496	0.04
Freedom from congestion at 72 hr — no./total no. (%)	22/153 (14)	22/144 (15)	0.78	16/143 (11)	28/154 (18)	0.09
Change in weight at 72 hr — lb	−6.8±7.8	−8.1±10.3	0.20	−6.1±9.5	−8.7±8.5	0.01
Net fluid loss at 72 hr — ml	4237±3208	4249±3104	0.89	3575±2635	4899±3479	0.001
Change in NT-proBNP at 72 hr — pg/ml	−1316±4364	−1773±3828	0.44	−1194±4094	−1882±4105	0.06
Worsening or persistent heart failure — no./total no. (%)	38/154 (25)	34/145 (23)	0.78	38/145 (26)	34/154 (22)	0.40
Treatment failure — no./total no. (%)†	59/155 (38)	57/147 (39)	0.88	54/147 (37)	62/155 (40)	0.56
Increase in creatinine of >0.3 mg/dl within 72 hr — no./total no. (%)	27/155 (17)	28/146 (19)	0.64	20/147 (14)	35/154 (23)	0.04
Length of stay in hospital — days			0.97			0.55
Median	5	5		6	5	
Interquartile range	3–9	3–8		4–9	3–8	
Alive and out of hospital — days			0.36			0.42
Median	51	51		50	52	
Interquartile range	42–55	38–55		39–54	42–56	

Felker GM et al. N Engl J Med 2011;364:797-805

DOSE TRIAL:
BOLUS VS CONTINUOUS INFUSION
HIGH VS LOW DOSE FUROSEMIDE





death, rehospitalization, or emergency department visit during the 60-day

Felker GM et al. N Engl J Med 2011;364:797-805

What guideline said about Nitrates on Acute Heart Failure?

Guidelines recommend the use of nitrate therapy in ADHF

Canadian Cardiovascular Society: The use of nitrates is strongly recommended
European Society of Cardiology : class IIb recommendation
American Heart Association: class IIb recommendation

The evidence behind these recommendations is limited and based on small studies or consensus opinion of experts (moderate quality, level of evidence B and C)

Indeed, most large studies of vasodilators in ADHF did not study nitrates, but instead, were randomized controlled trials that often evaluated the effect of nesiritide, a recombinant brain natriuretic peptide

Vasodilators

- Dilate venous and arterial vessels → reduced venous return, less congestion, lower afterload, increased SVR, relief symptoms
- IV vasodilators may be considered to relieve AHF symptoms when SBP >110 mmHg

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Supplementary Table 21 Intravenous vasodilators for acute heart failure

Vasodilator	Dosing	Main side effects	Other
Nitroglycerine	Start with 10–20 μg/min, increase up to 200 μg/min	Hypotension, headache	Tolerance in continuous use
Isosorbide dinitrate	Start with 1 mg/h, increase up to 10 mg/h	Hypotension, headache	Tolerance in continuous use
Nitroprusside	Start with 0.3 μg/kg/min and increase up to 5 μg/kg/min	Hypotension, isocyanate toxicity	Light sensitivity

Vasodilators		
In patients with AHF and SBP >110 mmHg, i.v. vasodilators may be considered as initial therapy to improve symptoms and reduce congestion.[475–477,479,480]	IIb	B

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

11.3.4 Vasodilators

Intravenous vasodilators, namely nitrates or nitroprusside (*Supplementary Table 21*), dilate venous and arterial vessels leading to a reduction in venous return to the heart, less congestion, lower afterload, increased stroke volume and consequent relief of symptoms. Nitrates act mainly on peripheral veins whereas nitroprusside is more a balanced arterial and venous dilator.[474,475] Because of their mechanisms of action, i.v. vasodilators may be more effective than diuretics in those patients whose acute pulmonary oedema is caused by increased afterload and fluid redistribution to the lungs in the absence or with minimal fluid accumulation.[427,476–478] However, two recent randomized trials comparing usual care with early intensive and sustained vasodilation failed to show a beneficial effect of i.v. vasodilators vs. high-dose diuretics.[479,480] No recommendation favouring a regimen based on vasodilator treatment vs. usual care can thus be given, to date.

Intravenous vasodilators may be considered to relieve AHF symptoms when SBP is ≥110 mmHg. They may be started at low doses and uptitrated to achieve clinical improvement and BP control. Nitrates are generally administered with an initial bolus followed by continuous infusion. However, they may also be given as repeated boluses. Nitroglycerine can be given as 1–2 mg boluses in severely hypertensive patients with acute pulmonary oedema.[477] Care should be taken to avoid hypotension due to an excessive decrease in preload and afterload. For this reason, they should be used with extreme caution in patients with LVH and/or severe aortic stenosis. However, favorable effects were described in patients with LV systolic dysfunction and aortic stenosis when vasodilators were given with careful monitoring of haemodynamic parameters.[481]

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

COR	LOE	Recommendation
2b	B-NR	1. In patients who are admitted with decompensated HF, in the absence of systemic hypotension, intravenous nitroglycerin or nitroprusside may be considered as an adjuvant to diuretic therapy for relief of dyspnea.[1,2]

1. The role for directed vasodilators in acute decompensated HF remains uncertain. Part of the rationale for their use is targeting pulmonary congestion, while trying to avoid some potential adverse consequences of loop diuretics. Patients with hypertension, coronary ischemia, or significant MR may be suitable candidates for the use of intravenous nitroglycerin. However, tachyphylaxis may develop within 24 hours, and up to 20% of those with HF may develop resistance to even high doses.[3,4] Because of sodium nitroprusside's potential for producing marked hypotension, invasive hemodynamic blood pressure monitoring (eg, an arterial line) is typically required, and nitroprusside is usually used in the intensive care setting; longer infusions of the drug have been associated, albeit rarely, with thiocyanate and cyanide toxicity, particularly in the setting of renal insufficiency and significant hepatic disease. Nitroprusside is potentially of value in severely congested patients with hypertension or severe MV regurgitation complicating LV dysfunction.[5] Overall, there are no data that suggest that intravenous vasodilators improve outcomes in the patient hospitalized with HF; as such, use of intravenous vasodilators is limited to the relief of dyspnea in the hospitalized HF patient with intact or high blood pressure.[6,7]

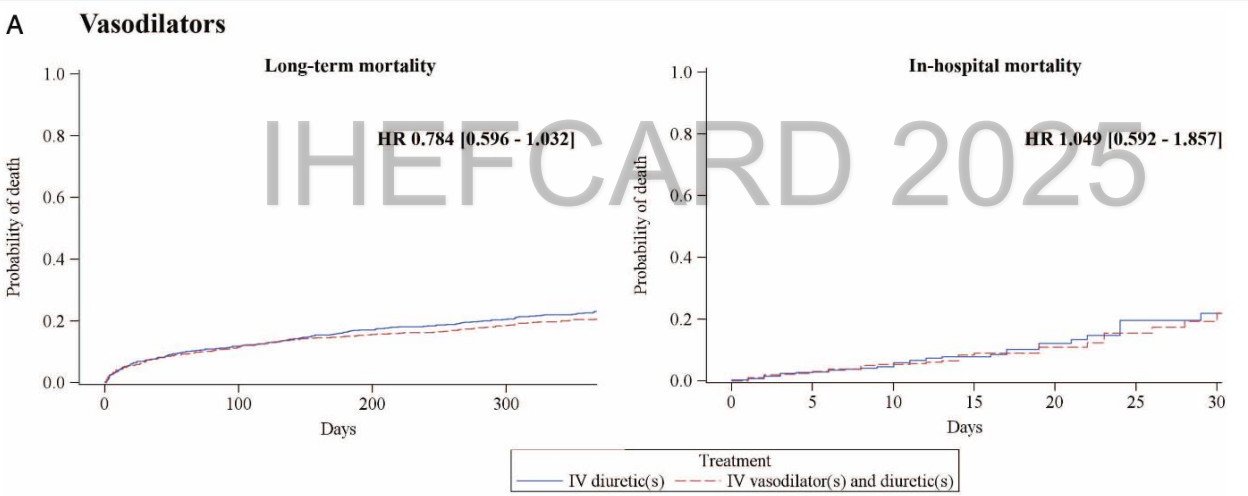
European Journal of Heart Failure (2018) 20, 332–341
doi:10.1002/ejhf.991

RESEARCH ARTICLE

Long-term safety of intravenous cardiovascular agents in acute heart failure: results from the European Society of Cardiology Heart Failure Long-Term Registry

Alexandre Mebazaa[1,2,3]*, Justina Motiejunaite[1,2,4], Etienne Gayat[1,2,3],

The European Society of Cardiology Heart Failure Long-Term (ESC-HF-LT) registry



Did not confirm any harms or benefits of the use of vasodilators on long-term clinical outcomes

Treatment of severe decompensated heart failure with high-dose intravenous nitroglycerin: a feasibility and outcome analysis

Phillip Levy [1], Scott Compton, Robert Welch, George Delgado, Alison Jennett, Neelima Penugonda, Robert Dunne, Robert Zalenski

hypertension (systolic blood pressure ≥160 mm Hg or mean arterial pressure ≥120 mm Hg)
bolus of high-dose nitroglycerin (2 mg) repeated up to 10 doses

Conclusion

In this nonrandomized, open-label trial, high-dose nitroglycerin was associated with endotracheal intubation, BiPAP, and ICU admission less frequently than expected to occur without high-dose nitroglycerin, and adverse events were uncommon. Treatment of hypertensive, severely decompensated heart failure patients with high-dose nitroglycerin seems promising, but a randomized, blinded study is needed to more completely define its clinical utility. According to this trial, such a study seems feasible.

Phiilip Levi. Ann Emerg Med. 2007Aug;50(2):144-52

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High-Dose Intravenous Isosorbide-Dinitrate Is Safer and Better Than Bi-PAP Ventilation Combined With Conventional Treatment for Severe Pulmonary Edema

OBJECTIVE To determine the feasibility, safety and efficacy of bilevel positive airway ventilation (BiPAP) in the treatment of severe pulmonary edema compared to high dose nitrate therapy.

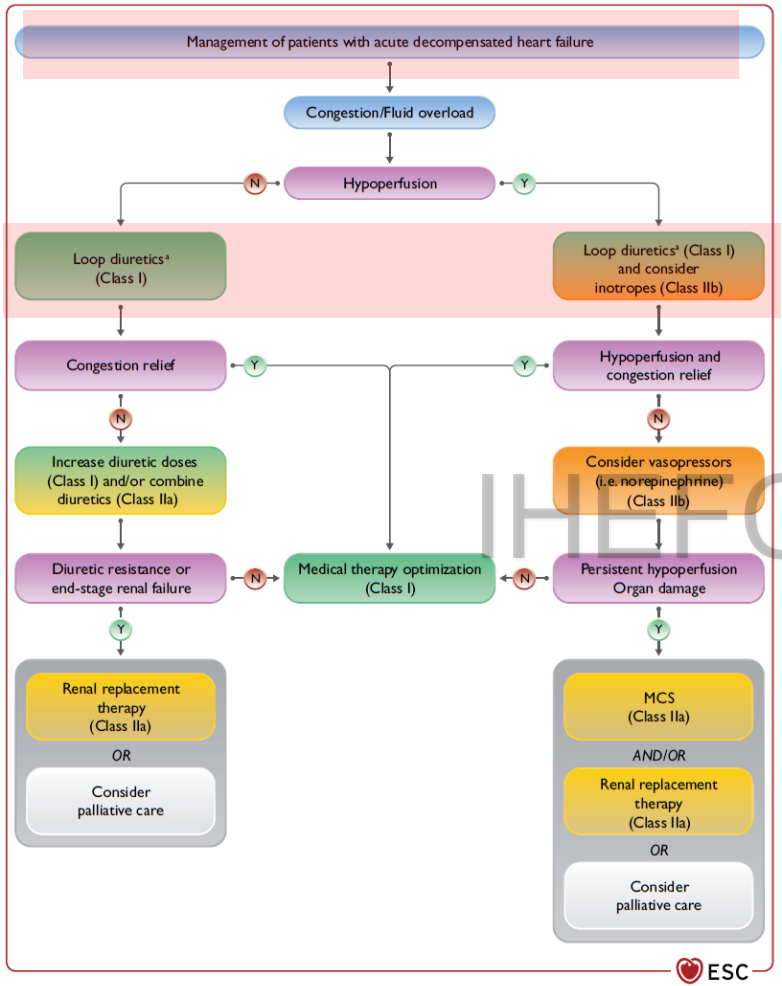
BACKGROUND Although noninvasive ventilation is increasingly used in the treatment of pulmonary edema, its efficacy has not been compared prospectively with newer treatment modalities.

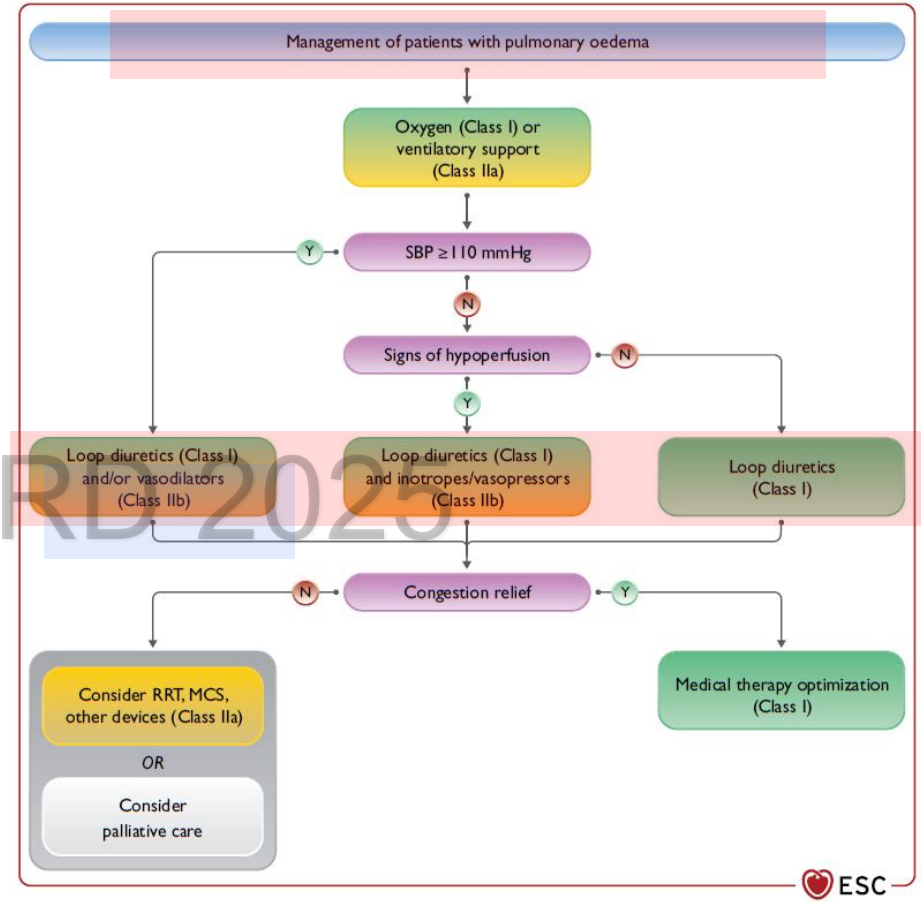
METHODS We enrolled 40 consecutive patients with severe pulmonary edema (oxygen saturation <90% on room air prior to treatment). All patients received oxygen at a rate of 10 liter/min, intravenous (IV) furosemide 80 mg and IV morphine 3 mg. Thereafter patients were

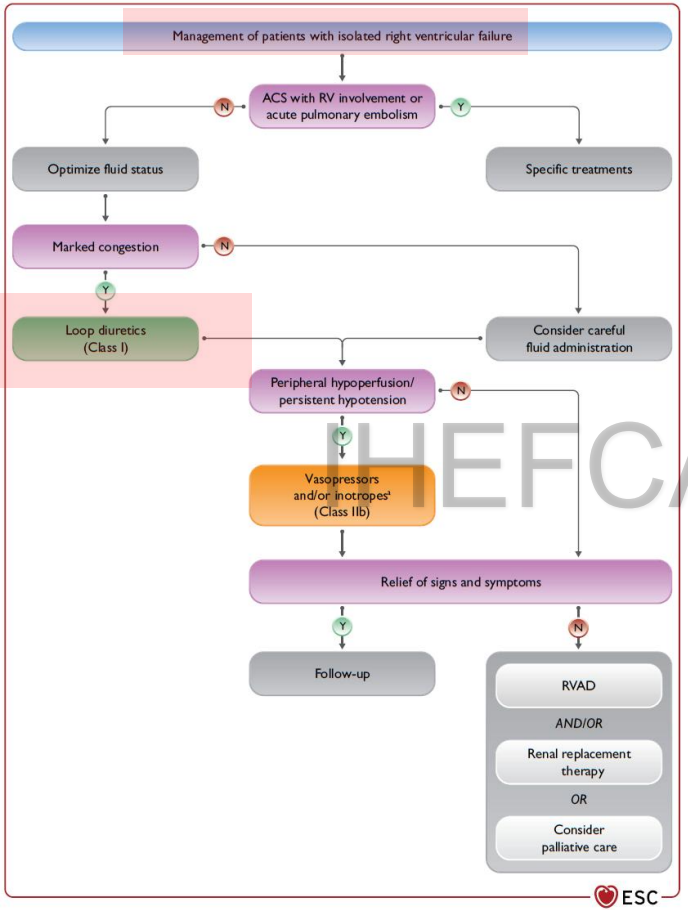
High-dose nitrate patients had fewer intubations (20 versus 80 %; P<0.0004), higher oxygenation at 1 hour (96 versus 89 %; P<0.017) and a lower rate of the combined endpoint of death, MI and endotracheal intubation (25 versus 85 %; P<0.0003)

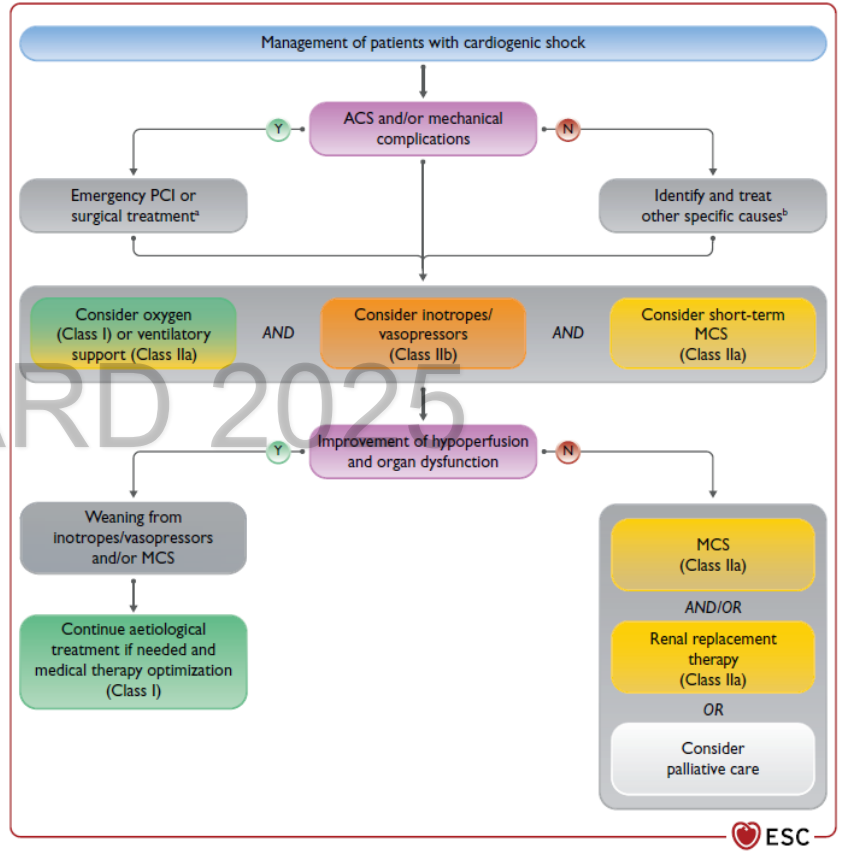
RESULTS Patients treated by BiPAP had significantly more adverse events. Two BiPAP treated patients died versus zero in the high dose ISDN group. Sixteen BiPAP treated patients (80%) required intubation and mechanical ventilation compared to four (20%) in the high dose ISDN group ($p = 0.0004$). Myocardial infarction (MI) occurred in 11 (55%) and 2 (10%) patients, respectively ($p = 0.006$). The combined primary end point (death, mechanical ventilation or MI) was observed in 17 (85%) versus 5 (25%) patients, respectively ($p = 0.0003$). After 1 h of treatment, oxygen saturation increased to 96 ± 4% in the high dose ISDN group as compared to 89 ± 7% in the BiPAP group ($p = 0.017$). Due to the significant deterioration observed in patients enrolled in the BiPAP arm, the study was prematurely terminated by the safety committee.

CONCLUSIONS High dose ISDN is safer and better than BiPAP ventilation combined with conventional therapy in patients with severe pulmonary edema. (J Am Coll Cardiol 2000;36:832–7) © 2000 by the American College of Cardiology









TAKE HOME MESSAGES

- Acute heart failure (AHF) is a frequent reason for hospitalization worldwide and effective treatment options are limited
- The primary therapeutic objective during AHF hospitalization is decongestion →whilst avoiding the complications of hypotension and worsening renal function (WRF)
- Loop diuretic is universally recommended in international guidelines
- Nitrates appear to be a safe and effective in the absence of systemic hypotension
- While nitrates have been used in AHF for many years, the lack of well-powered studies to support their use has lead to large practice variations

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