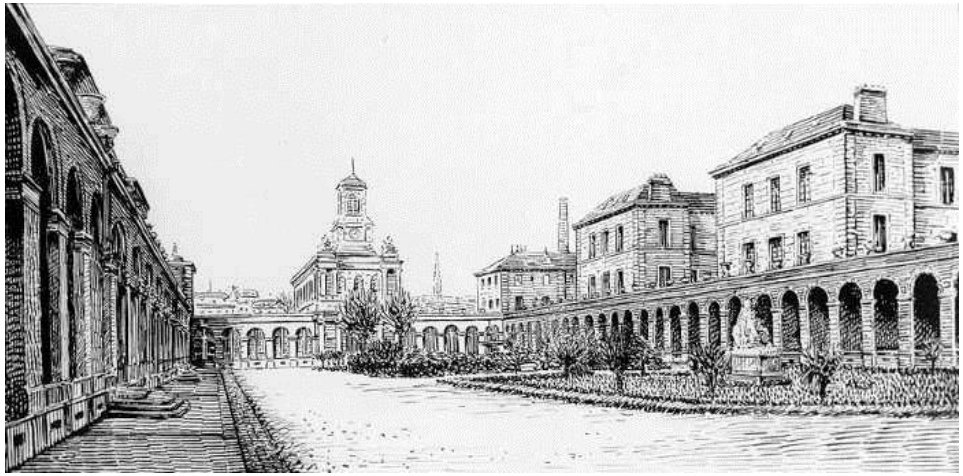
Insuffisance cardiaque aiguë : place des vasodilatateurs



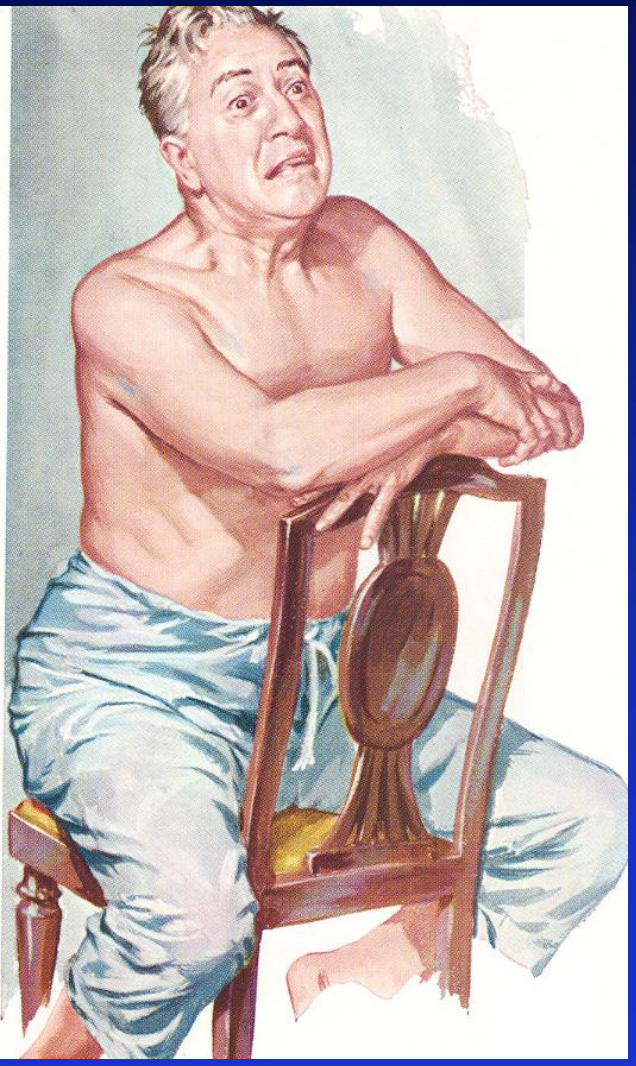
Alexandre Mebazaa

Département d'Anesthésie-Réanimation-SMUR

Hôpitaux Universitaires Saint Louis – Lariboisière

Université Paris 7; INSERM – UMR 942

ED: Dyspnea and/or Other Signs of Congestion + Elevated SBP (> 150 mmHg)



Acute pulmonary edema

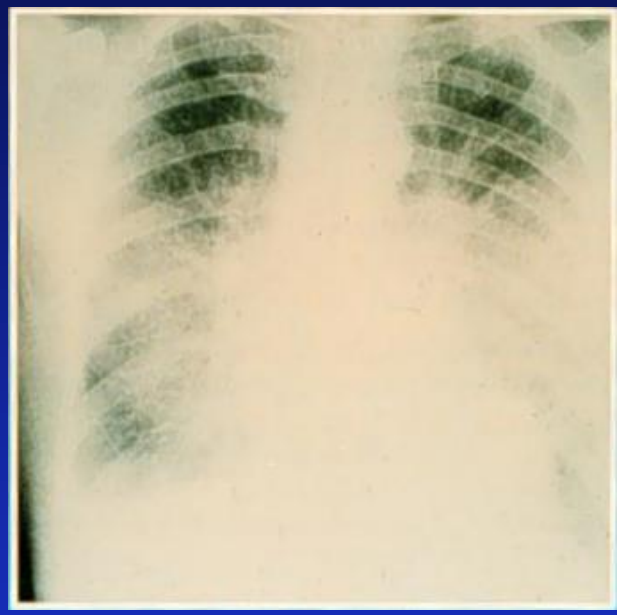
+

- Dyspnea develops abruptly
- Diffuse pulmonary edema
- Minimal systemic edema

It is a <u>vascular</u> illness

+ Warning !
Patient is very often
normovolemic
or hypovolemic

always

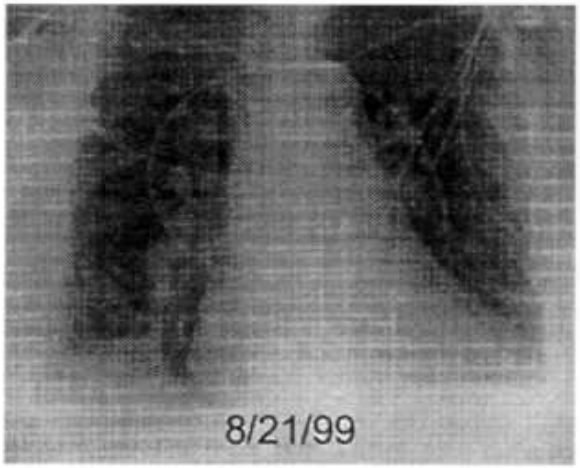


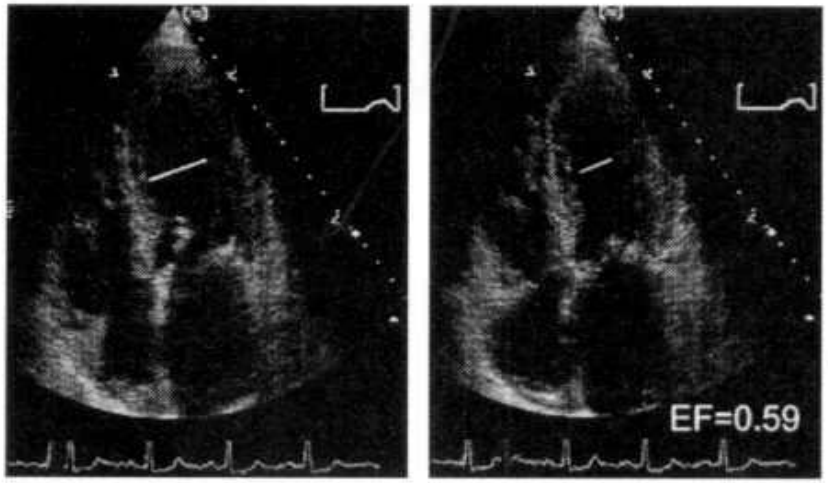
During Acute Pulmonary Edema

Blood pressure, 240/144 mm Hg

After Treatment

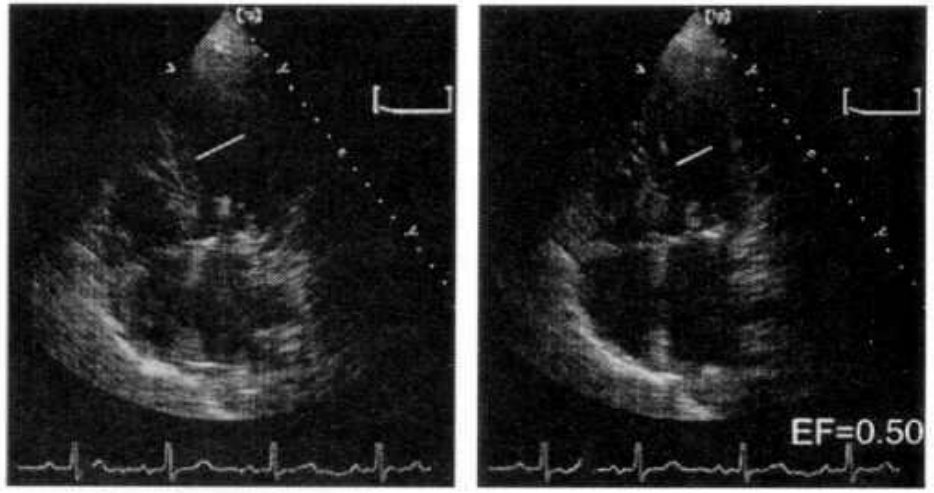
Blood pressure, 149/75 mm Hg





End Diastole

End Systole

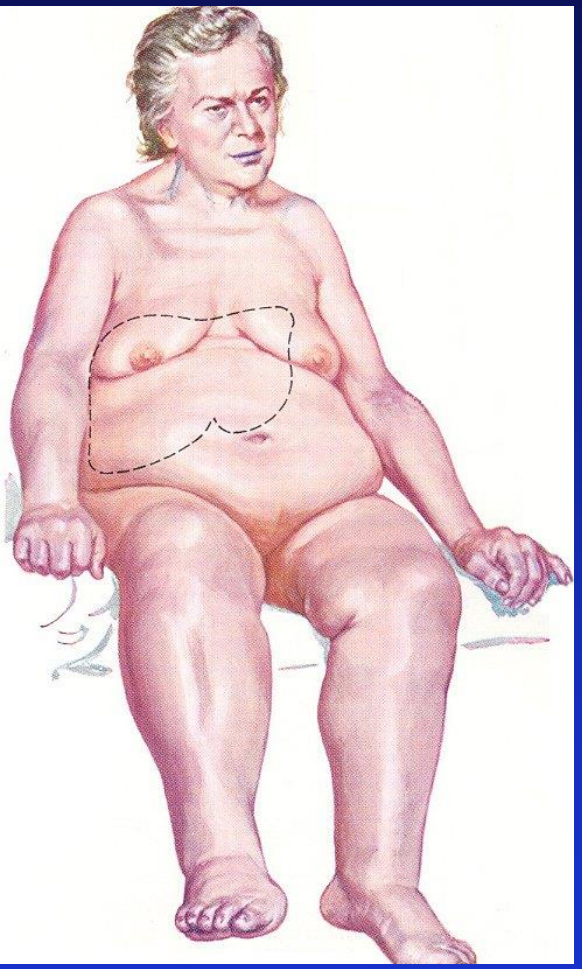


End Diastole

End Systole

SK Ghandi, NEJM 2001, 344: 17-22

CCU: Dyspnea + SBP 110 – 150 mmHg



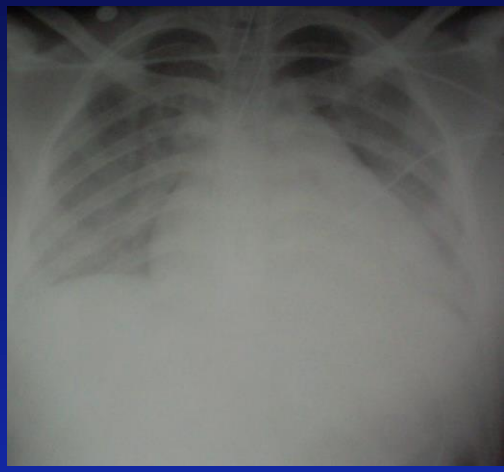
Decompensated chronic heart failure

+

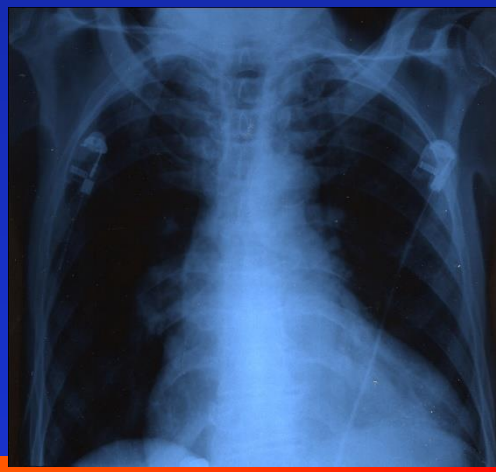
- Dyspnea develops gradually
- Gradual increase in body weight
- Systemic edema
- Minimal pulmonary edema

It is a systemic illness:

- Possible Renal dysfunction
- Anemia
- Low albumin
- Increased Pulmonary Congestion
- Systemic Congestion



or



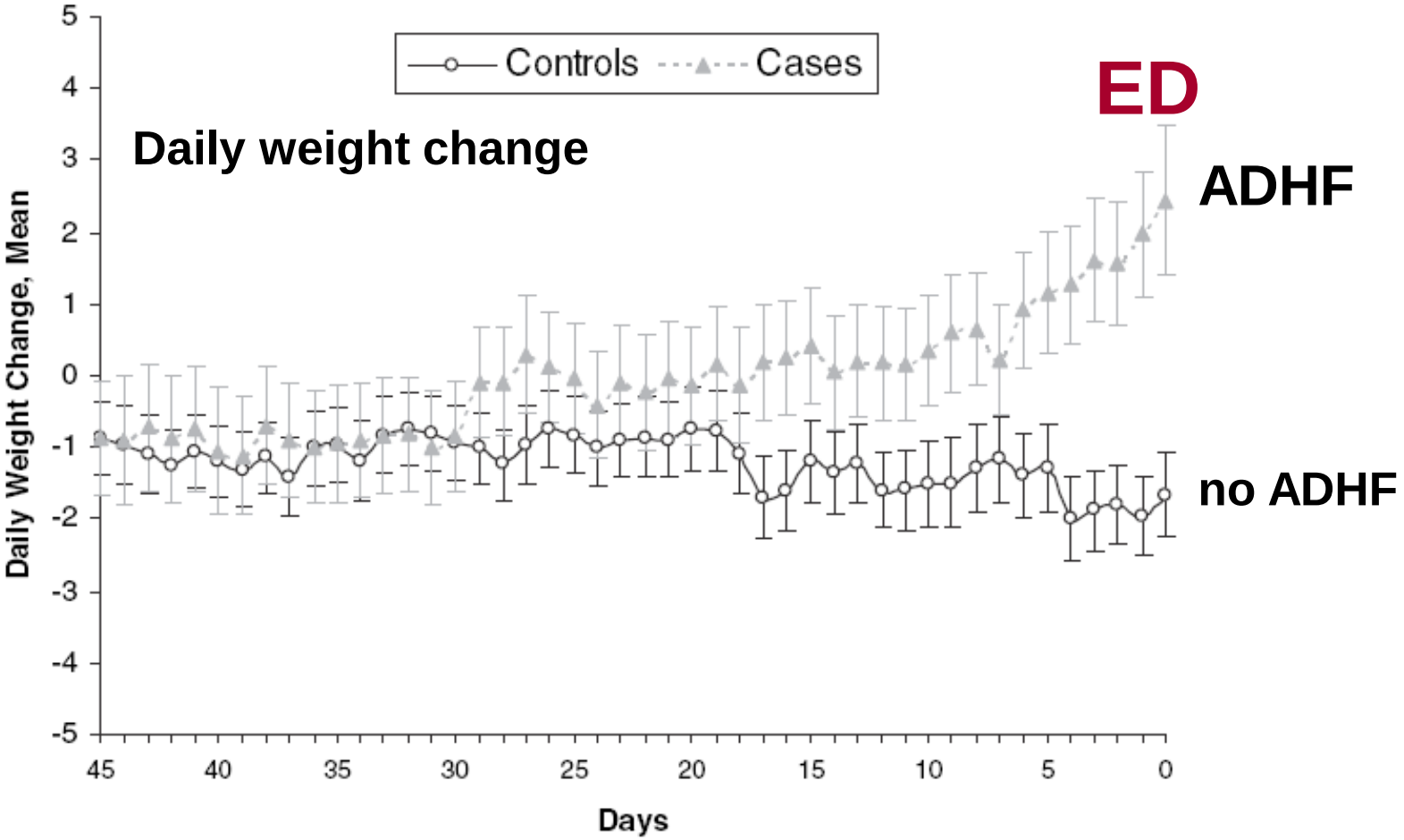


Figure 1. Daily weight change before heart failure hospitalization: cases vs controls. n=268. "Days" on the x-axis denotes days before hospital admission in case patients. The difference in daily weight changes between case and control patients within 30 days before (case) hospitalization was statistically significant ($P<0.001$) on the basis of a generalized linear model with daily weight change as the dependent variable.

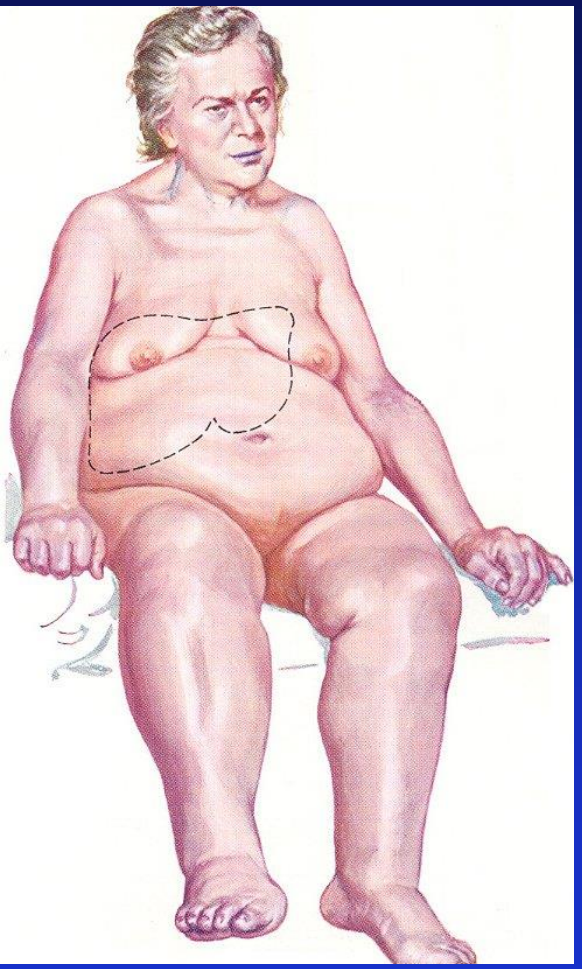
Chaudhry E al. Circulation 2007; 116: 1549-15

ICU: Cardiogenic Shock: EFICA study
Symptoms on Admission

	All patients	Cardiogenic shock		p^a
	($n=581$)	Yes ($n=166$)	No ($n=415$)	
Symptoms on admission (%)				
Cardiogenic shock	29	100	0	<0.0001
Pulmonary oedema	82	60	91	<0.0001
Peripheral oedema	27	20	30	0.02
Angina	14	17	13	0.29
Hepatomegaly	20	24	18	0.09
Syncope	4	9	2	0.0002
Arrhythmia	23	26	21	0.17
Stroke	1	1	1	1.00
SBP mmHg	**126**	**93**	**139**	**<0.0001**
DBP mmHg	**71**	**54**	**77**	**<0.0001**

Zannad F, Mebazaa A, et al. Eur J Heart Fail. 2006

CCU: Dyspnea + SBP 110 – 150 mmHg



Decompensated chronic heart failure

+

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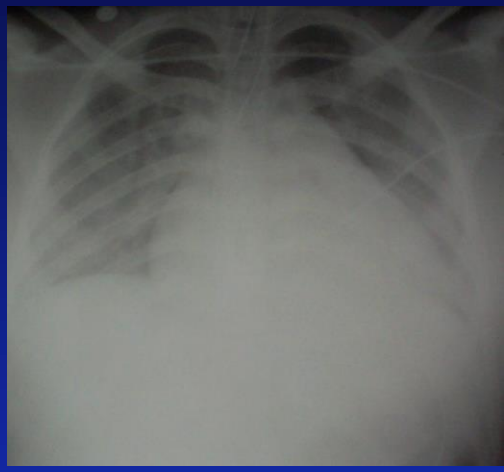
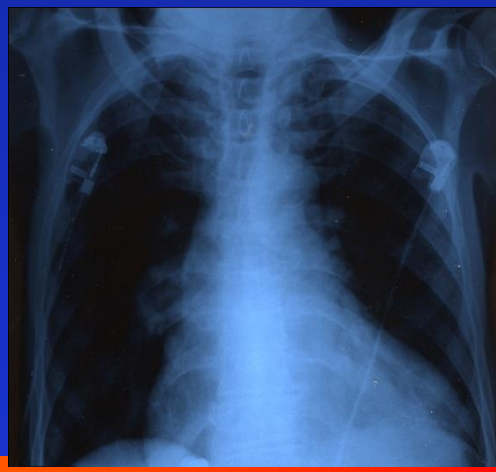


or



Assessing and grading congestion in acute heart failure: a scientific statement from the Acute Heart Failure Committee of the Heart Failure Association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine

Mihai Gheorghiade[1], Ferenc Follath[2], Piotr Ponikowski[3], Jeffrey H. Barsuk[4], John E.A. Blair[5], John G. Cleland[6], Kenneth Dickstein[7,8], Mark H. Drazner[9], Gregg C. Fonarow[10], Tiny Jaarsma[11], Guillaume Jondeau[12], Jose Lopez Sendon[13], Alexander Mebazaa[14,15], Marco Metra[16], Markku Nieminen[17], Peter S. Pang[18], Petar Seferovic[19], Lynne W. Stevenson[20], Dirk J. van Veldhuisen[21], Faiez Zannad[22], Stefan D. Anker[22], Andrew Rhodes[23], John J.V. McMurray[24], and Gerasimos Filippatos[25]*

Gheorghiade et al. Eur J Heart F 2010

Abstract of the review

Patients with acute heart failure (AHF) require urgent in-hospital treatment for relief of symptoms. The main reason for hospitalization is congestion, rather than low cardiac output. Although congestion is associated with a poor prognosis, many patients are discharged with persistent signs and symptoms of congestion and/or a high left ventricular filling pressure. Available data suggest that a pre-discharge clinical assessment of congestion is often not performed, and even when it is performed, it is not done systematically because no method to assess congestion prior to discharge has been validated. Grading congestion would be helpful for initiating and following response to therapy. We have reviewed a variety of strategies to assess congestion which should be considered in the care of patients admitted with HF. We propose a combination of available measurements of congestion. Key elements in the measurement of congestion include bedside assessment, laboratory analysis, and dynamic manoeuvres. These strategies expand by suggesting a routine assessment of congestion and a pre-discharge scoring system. A point system is used to quantify the degree of congestion. This score offers a new instrument to direct both current and investigational therapies designed to optimize volume status during and after hospitalization. In conclusion, this document reviews the available methods of evaluating congestion, provides suggestions on how to properly perform these measurements, and proposes a method to quantify the amount of congestion present.

« The main reason for hospitalization for acute heart failure is CONGESTION, rather than low cardiac output ».

Gheorghiade et al. Eur J Heart F 2010

RELAX trial: patients have preserved CI but a high RAP and very high PCWP

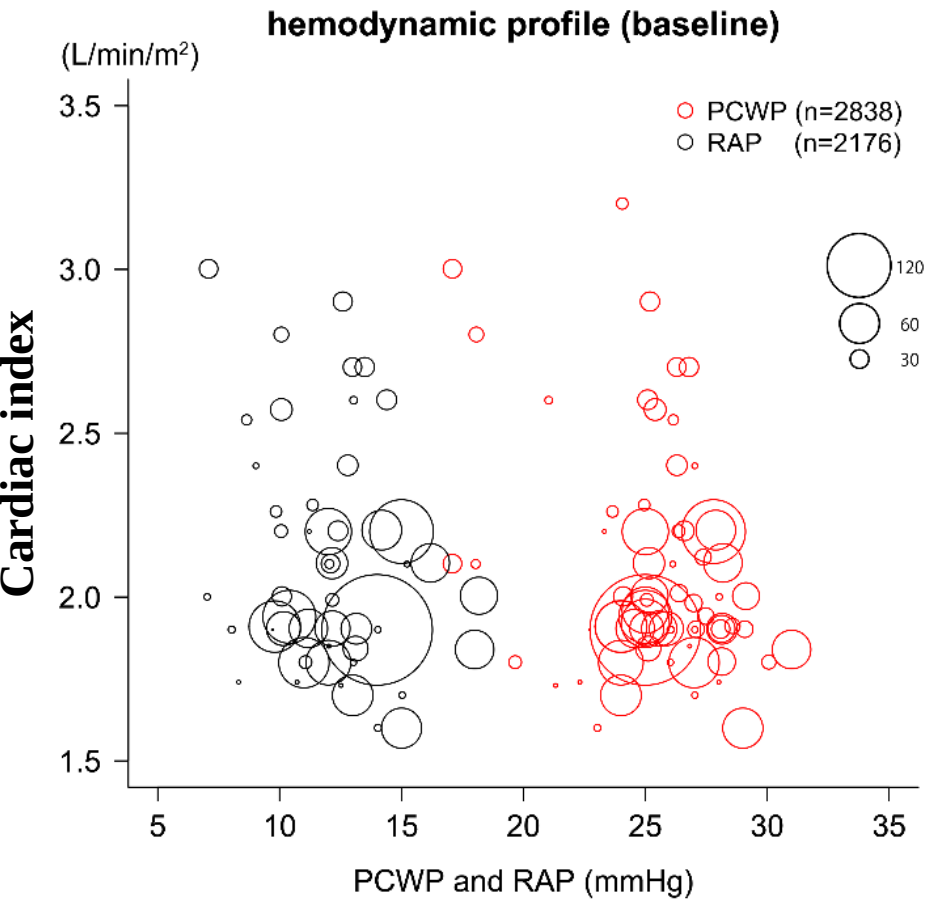
Pulmonary edema

Baseline haemodynamic parameters[d]	Normal values	Serelaxin (n=34)	Placebo (n=37)
PCWP (mmHg)	**3 - 5**	26.2 (5.9)	26.5 (5.2)
CI (L/min/m^2)	**2.5 – 3.0**	2.4 (0.7)	2.2 (0.6)
Systolic PAP (mmHg)		56.1 (13.0)	58.0 (13.8)
Diastolic PAP (mmHg)		27.3 (6.2)	28.8 (6.9)
Mean PAP (mmHg)		36.9 (7.9)	38.5 (8.1)
RAP (mmHg)	**0 - 2**	12.7 (5.9)	12.3 (5.5)
SVR (dynes × s/cm^5)		1530 (462)	1720 (607)
PVR (dynes × s/cm^5)		210 (161)	243 (166)

Kidney & liver dysfunction

Ponikowski et al Eur Heart J 2014 in press

Invasive hemodynamics at baseline and after treatment in AHF: results of a meta-analysis



Ishihara et al.

EUROPEAN SOCIETY OF CARDIOLOGY®

European Heart Journal (2010) **31**, 703–711
doi:10.1093/eurheartj/ehp507

CLINICAL RESEARCH
Heart failure/cardiomyopath

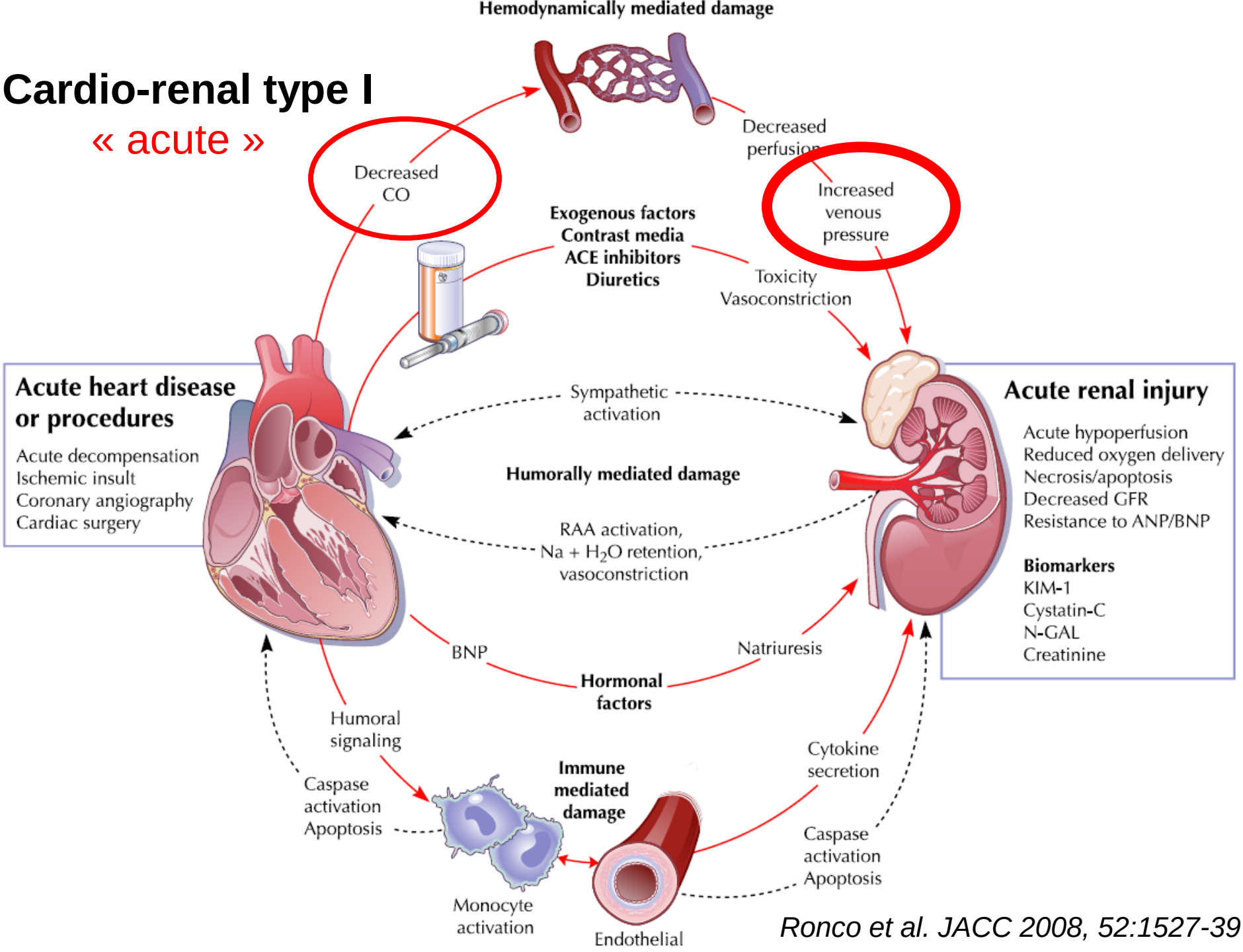
Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative

Claudio Ronco[1,2*], Peter McCullough[3], Stefan D. Anker[4,5], Inder Anand[6], Nadia Aspromonte[7], Sean M. Bagshaw[8], Rinaldo Bellomo[9], Tomas Berl[10], Ilona Bobek[1], Dinna N. Cruz[1,2], Luciano Daliento[11], Andrew Davenport[12], Mikko Haapio[13], Hans Hillege[14], Andrew A. House[15], Nevin Katz[16], Alan Maisel[17], Sunil Mankad[18], Pierluigi Zanco[19], Alexandre Mebazaa[20], Alberto Palazzuoli[21], Federico Ronco[11], Andrew Shaw[22], Geoff Sheinfeld[23], Sachin Soni[1,24], Giorgio Vescovo[25], Nereo Zamperetti[26], and Piotr Ponikowski[27] for the Acute Dialysis Quality Initiative (ADQI) consensus group

Ronco et al. Eur Heart Journal 2010

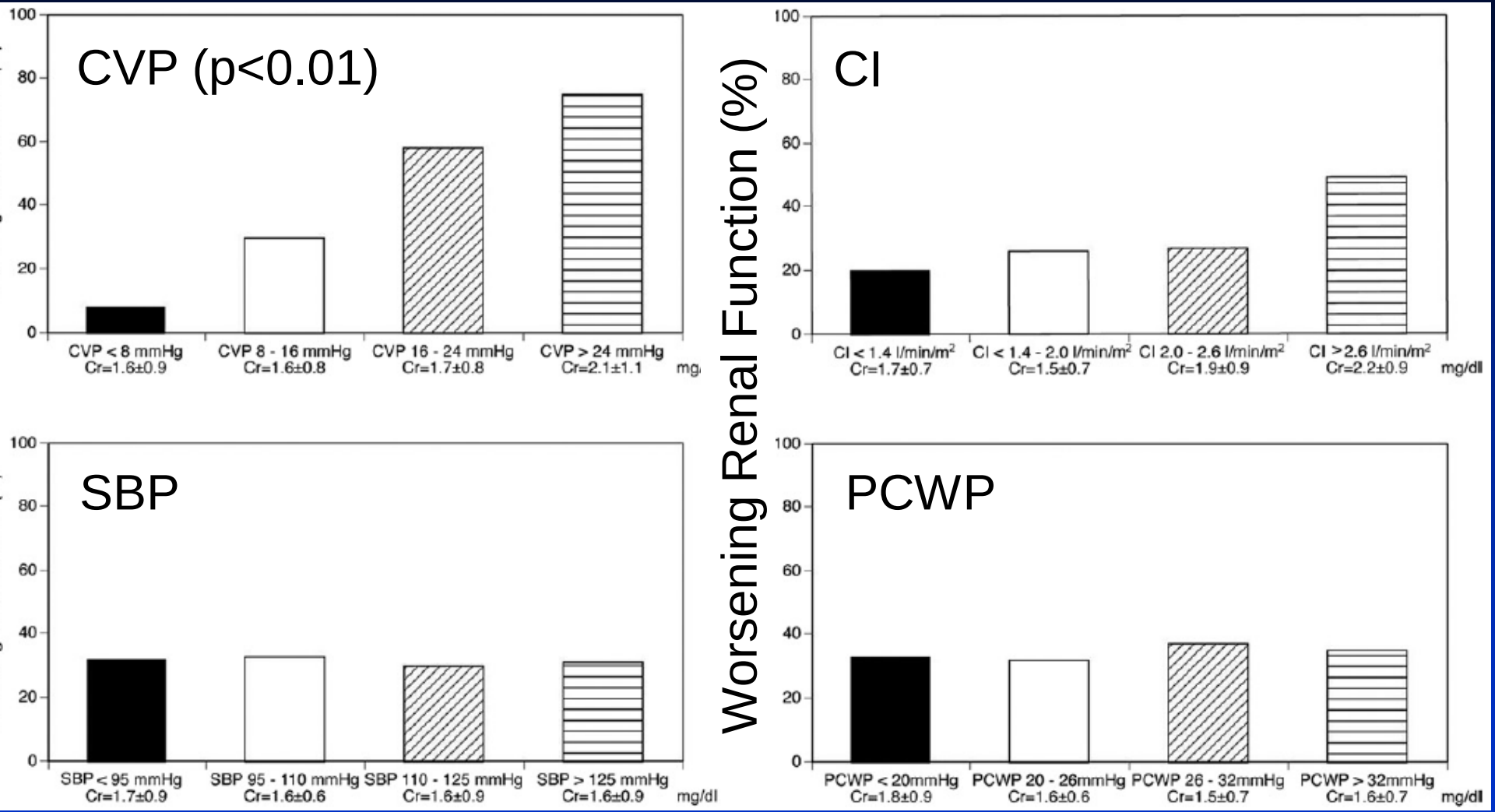
Cardio-renal type I

« acute »



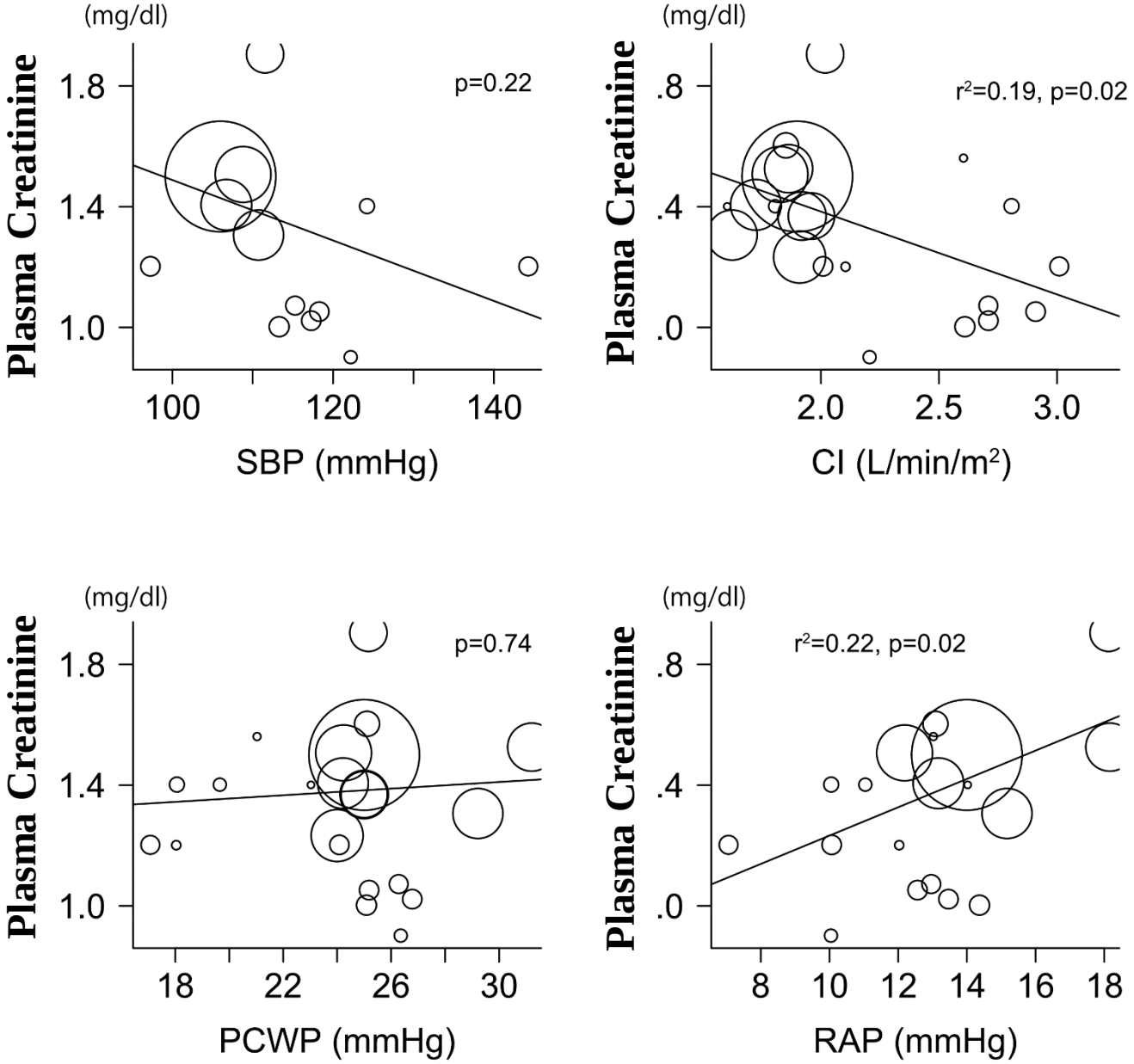
Ronco et al. JACC 2008, 52:1527-39

Effects of CVP, CI, SBP and PcwP on worsening renal function in Acute Heart Failure patients



Mullens et al. JACC 2009, 53:589-596

Association between baseline creatinine level and invasive hemodynamics in AHF: results of a meta-analysis



Ishihara et al.

European Heart Journal Advance Access published October 22, 2012

European Heart Journal
doi:10.1093/eurheartj/ehs332

CLINICAL RESEARCH

Liver function abnormalities, clinical profile, and outcome in acute decompensated heart failure

Maria Nikolaou[1,2,3], John Parissis[3], M. Birhan Yilmaz[1,15], Marie-France Seronde[1,2,4], Matti Kivikko[5,6], Said Laribi[1,2,7], Catherine Paugam-Burtz[2,8], Danlin Cai[9], Pasi Pohjanjousi[6], Pierre-François Laterre[10], Nicolas Deye[1,11], Pentti Poder[12], Alain Cohen Solal[1,2,13], and Alexandre Mebazaa[1,2,14]*

[1]UMRS 942 Inserm, F-75010 Paris, France; [2]Univ Paris Diderot, Sorbonne Paris Cité, F-75205 Paris, France; [3]Heart Failure Unit, 2nd Cardiology Department, Attikon University Hospital, University of Athens, Athens, Greece; [4]Department of Cardiology, University Hospital Jean-Minjoz, Besançon, France; [5]Department of Cardiology, Helsinki University Central Hospital, Helsinki, Finland; [6]Orion Pharma, Kuopio, Finland; [7]AP-HP, Department of Emergency Medicine, Hôpital Lariboisière, F-75475 Paris Cedex 10, France; [8]AP-HP, Department of Anesthesiology and Critical Medicine, Hôpital Beaujon, F-92110 Clichy, France; [9]Abbott Laboratories, Abbott Park, IL, USA; [10]Department of Critical Care Medicine, Saint-Luc University Hospital, Université Catholique de Louvain, Brussels, Belgium; [11]AP-HP, Medical ICU, Hôpital Lariboisière, F-75475 Paris Cedex 10, France; [12]First Department of Cardiology, North Estonia Medical Center, 12419 Tallinn, Estonia; [13]AP-HP, Department of Cardiology, Hôpital Lariboisière, F-75475 Paris Cedex 10, France; [14]AP-HP, Department of Anesthesiology and Critical Care Medicine, Hôpital Lariboisière, 2 Rue A Paré F-75475 Paris Cedex 10, France; and [15]Cumhuriyet University School of Medicine, Department of Cardiology, Sivas, Turkey

Received 14 March 2012; revised 21 August 2012; accepted 12 September 2012

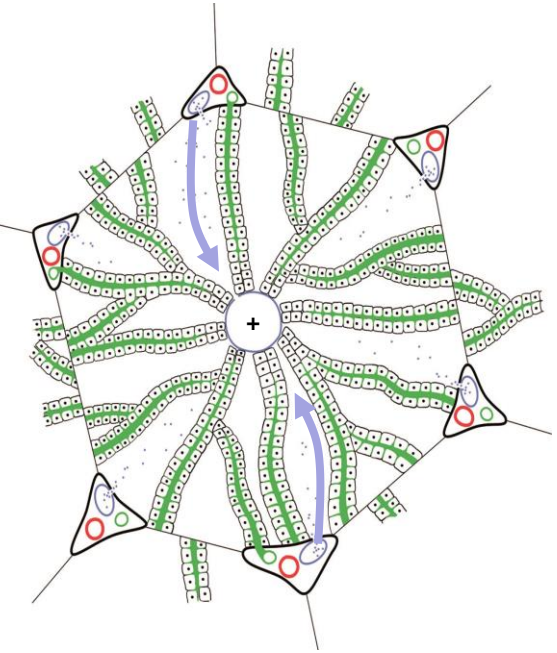
Liver dysfunction in AHF:

Clinical characteristics

	Alk Phosphatase			***Transaminases***		
	normal	abnormal		normal	abnormal	
N	944	261 **(22%)**		740	427 **(37%)**	
Clinical signs at baseline						
SBP (mmHg)	117	114	0.013	117	114	0.012
DBP (mmHg)	71	69	0.073	70	71	NS
HR (bpm)	83	83	NS	81	87	<0.001
Peripheral edema (%)	65.8	79.3	<0.001	70.0	63.7	0.023
Ascites **(%)**	16.9	31.0	<0.001	22.0	17.1	0.049
Cold extremities (%)	20.8	26.1	0.076	19.6	25.5	0.022
Biological parameters at baseline						
BNP (pg/mL)	1465.1	2250.9	<0.001	1464	1918	<0.001
Initial hospitalization characteristics (%)						
Acute MI	19.0	10.7	0.002	11.1	30.1	<0.001
LVEF	24.0	23.3	0.071	24.1	23.5	0.048
Tricuspid regurgitation	45.8	52.9	0.04	51.6	40.8	<0.001
All-cause mortality (%)						
at 31 d	11.1	14.6	NS	8.4	17.6	<0.001
at 180 d	23.5	34.9	0.001	22.4	31.6	<0.001

Nikolaou et al Eur Heart Journal 2013

Normal liver lobule

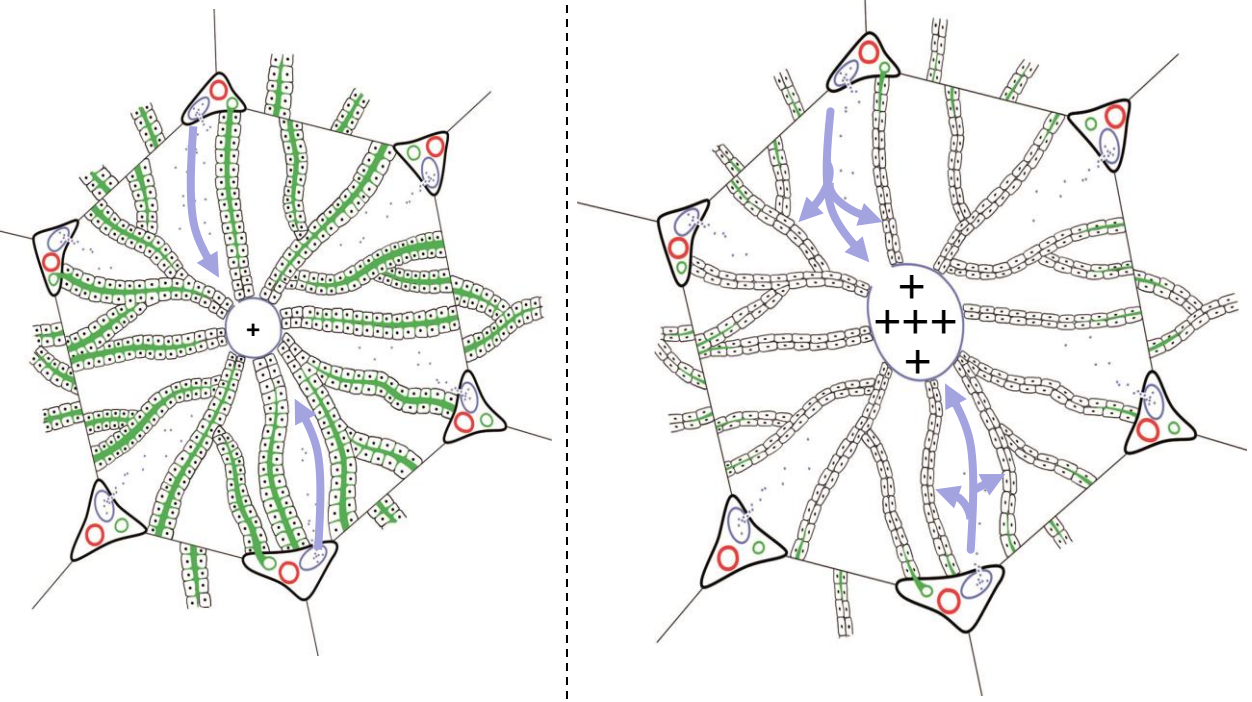


Nikolaou et al Eur Heart Journal 2013

AHF-induced liver congestion
(increased BNP)

Normal liver lobule

bile duct compression
(increased AP)



Nikolaou et al Eur Heart Journal 2013

Intensive Care Med (2011) 37:619–626
DOI 10.1007/s00134-010-2113-0

ORIGINAL

F. Follath
M. B. Yilmaz
J. F. Delgado
J. T. Parissis
R. Porcher
E. Gayat
Nigel Burrows
A. Mclean
F. Vilas-Boas
A. Mebazaa

Clinical presentation, management and outcomes in the Acute Heart Failure Global Survey of Standard Treatment (ALARM-HF)

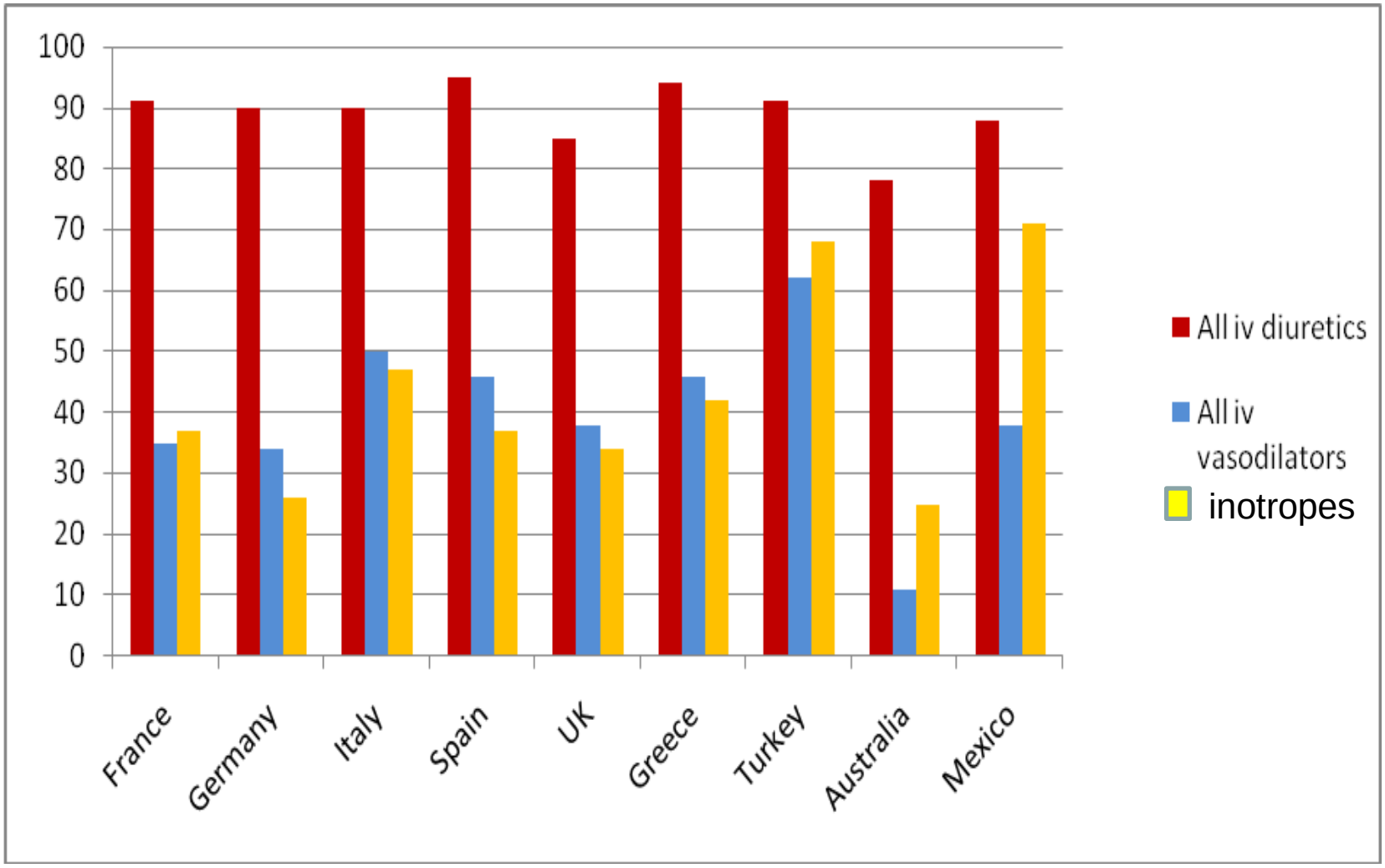
Intensive Care Med (2011) 37:290–301
DOI 10.1007/s00134-010-2073-4

ORIGINAL

Alexandre Mebazaa
John Parissis
Raphael Porcher
Etienne Gayat
Maria Nikolaou
Fabio Vilas Boas
J. F. Delgado
Ferenc Follath

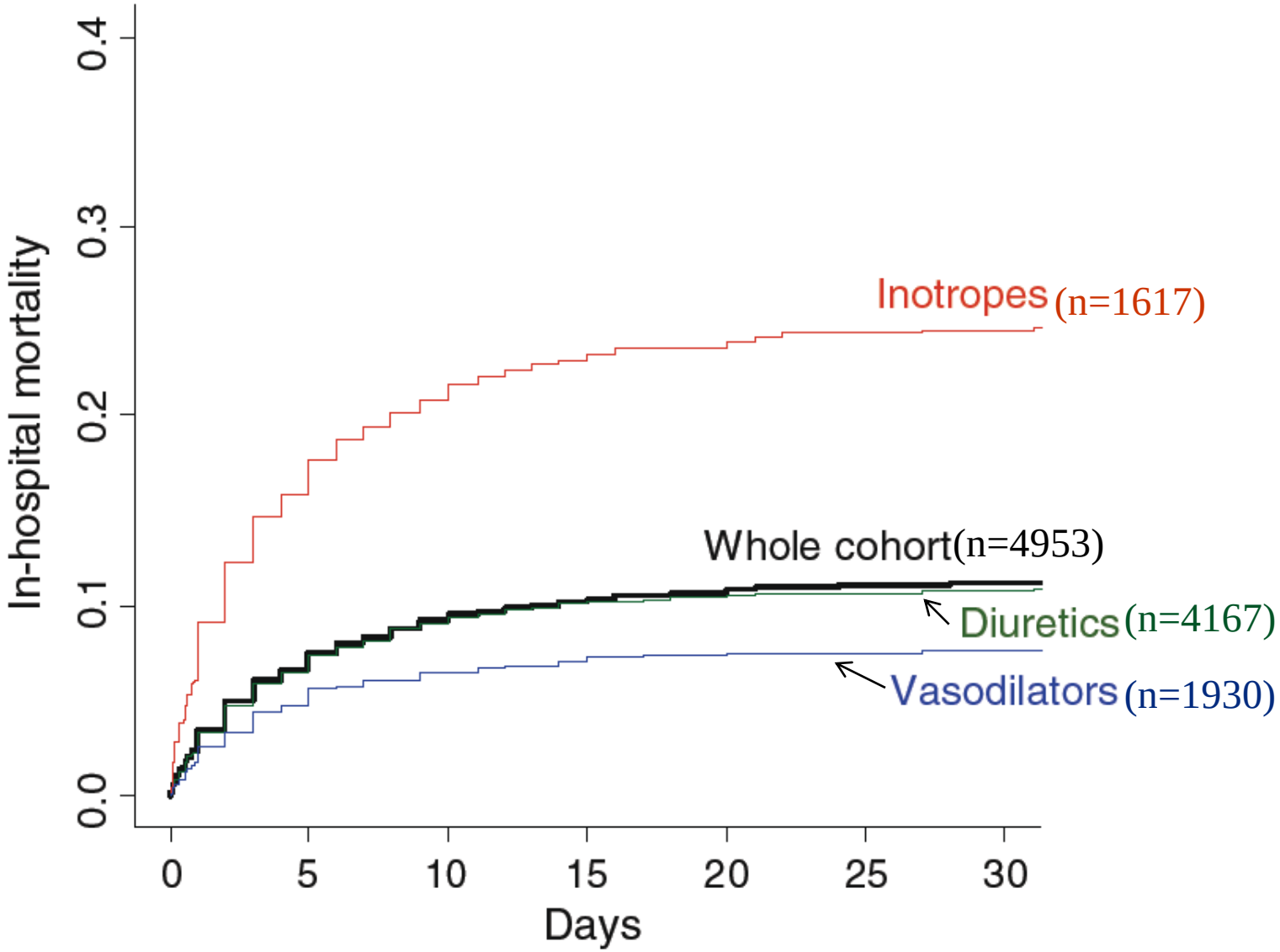
Short-term survival by treatment among patients hospitalized with acute heart failure: the global ALARM-HF registry using propensity scoring methods

ALARM-HF: IV treatment at admission

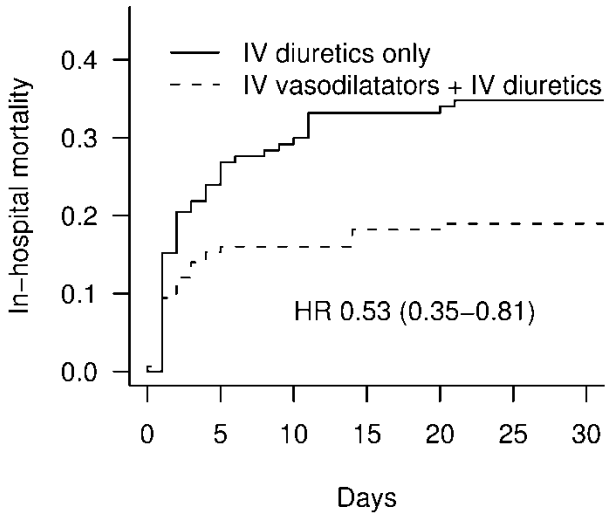


Mebazaa et al Intensive Care Medicine 2011

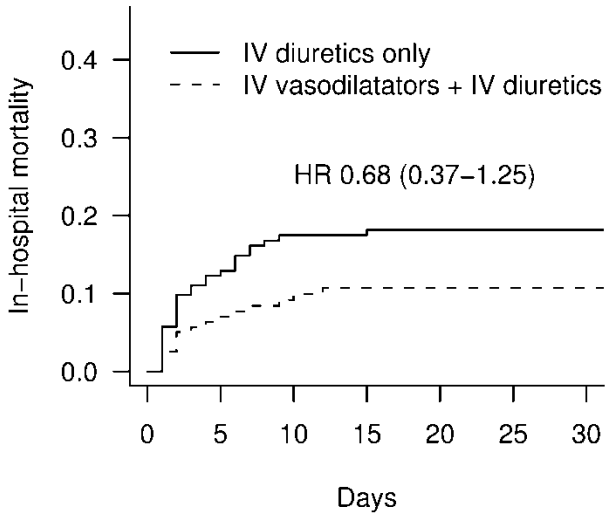
Effect of IV drugs given during the first 48 hours in AHF patients on in-hospital mortality



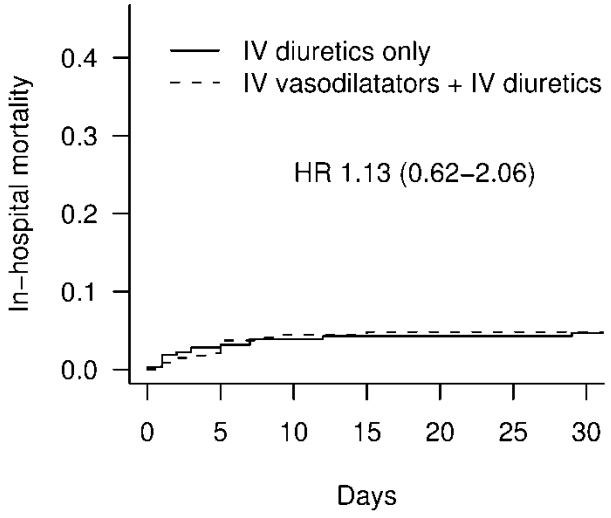
SBP < 100 mmHg (n=318)



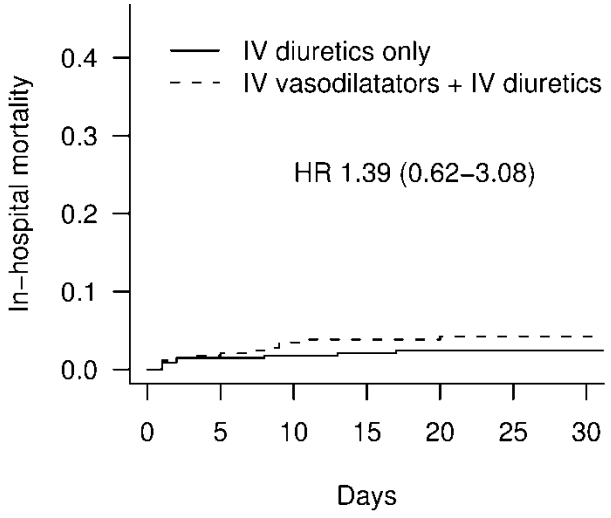
SBP 100-119 mmHg (n=334)



SBP 120-159 mmHg (n=618)



SBP > 160 mmHg (n=694)



Mebazaa et al Intensive Care Medicine 2011

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Inserm
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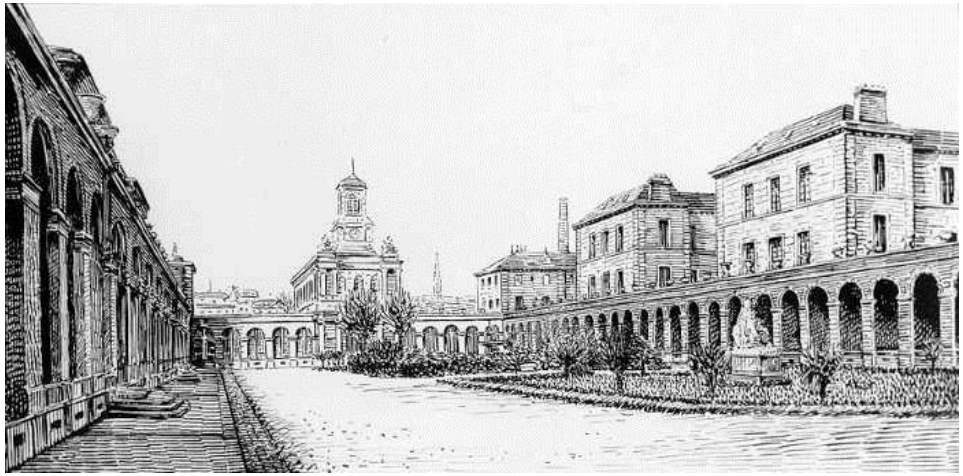
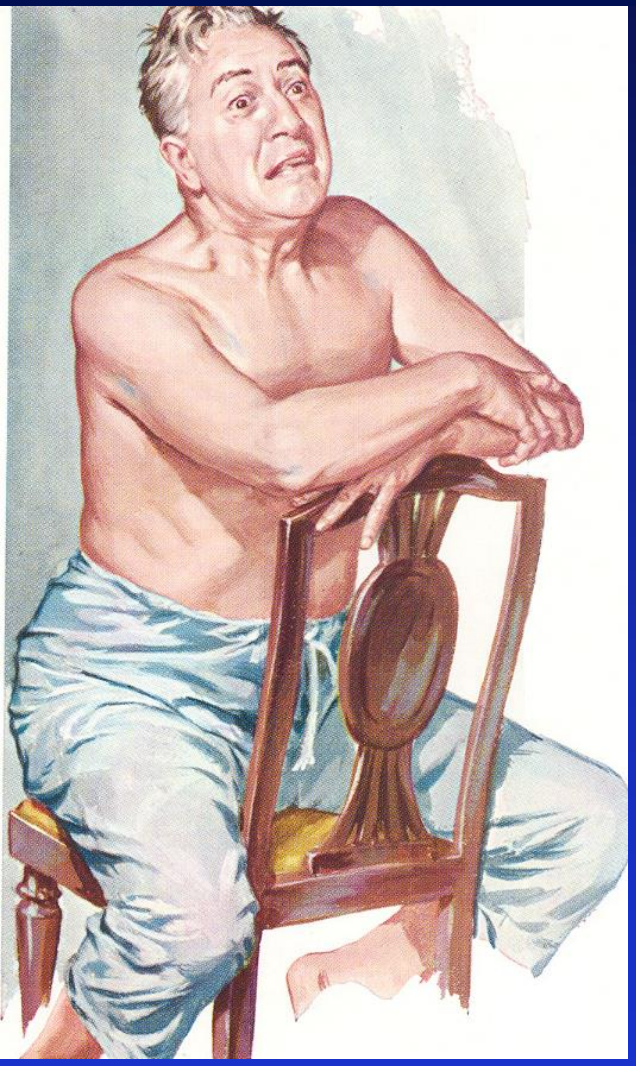
université PARIS DIDEROT PARIS 7

Perspectives thérapeutiques



ED: Dyspnea and/or Other Signs of Congestion + Elevated SBP (> 150 mmHg)



Acute pulmonary edema

+

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- Diffuse pulmonary edema
- Minimal systemic edema

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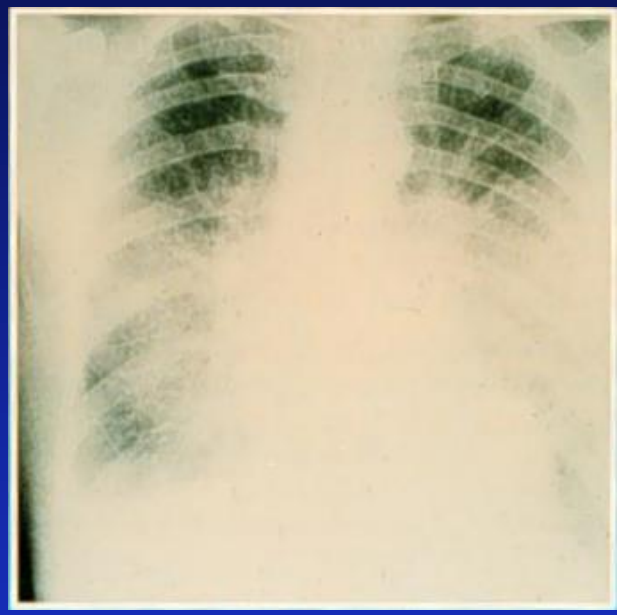
or hypovolemic

always



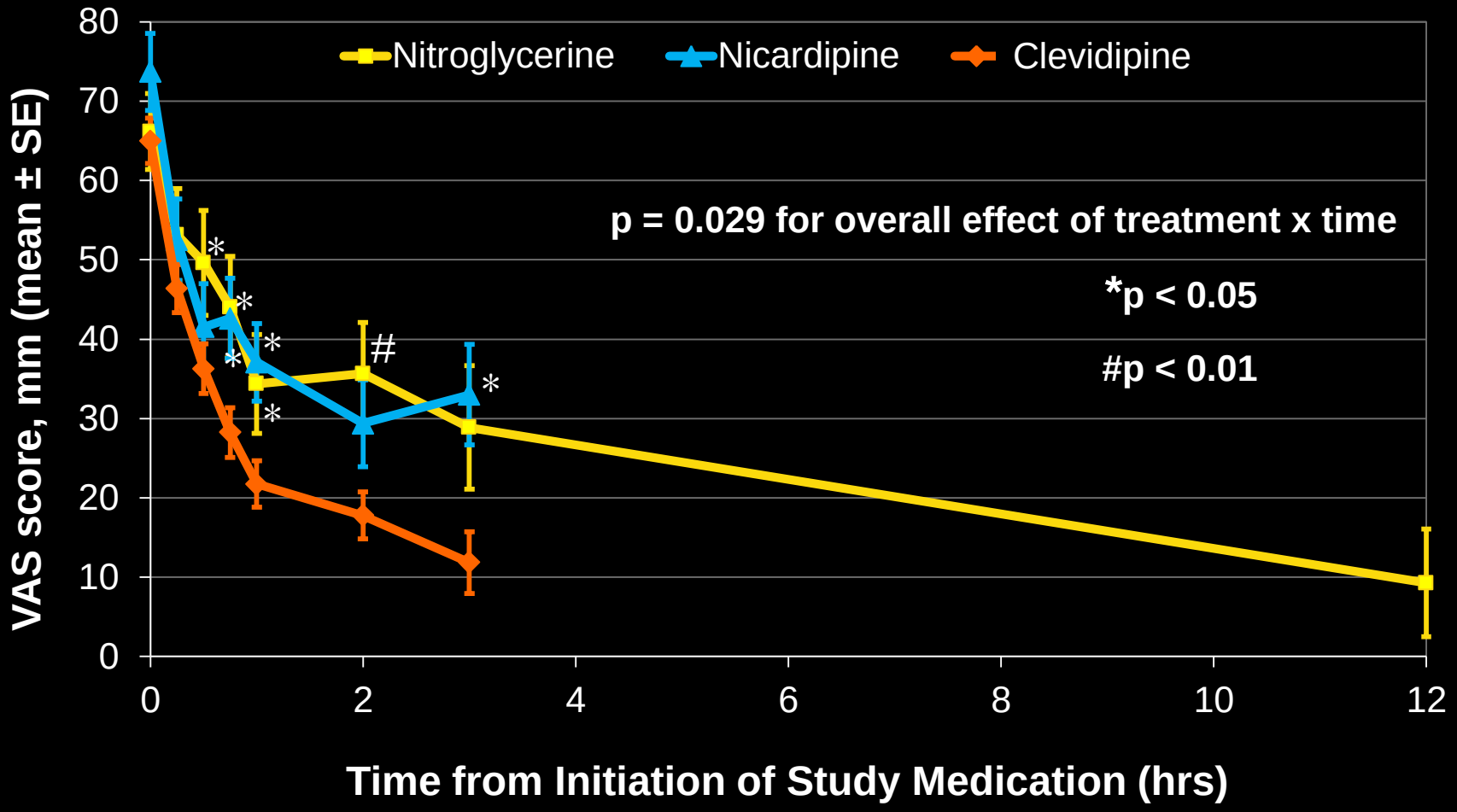
Clevidipine Improves Dyspnea in ED Acute Heart Failure: A Randomized, Open Label Study

Peacock WF, Baylor College of Medicine, Houston, TX
Chandra A, Kaiser Permanente, Sacramento, CA
Collins S, Vanderbilt University, Nashville, TN
Fonarow G, University of California LA, Los Angeles, CA
Garrison N, Drug Research & Analysis, Montgomery, AL
Mebazaa A, University Paris, Paris, France

Peacock et al Am Heart J 2014

DYSPNEA REDUCTION

VAS score over time (Confirmed AHF)



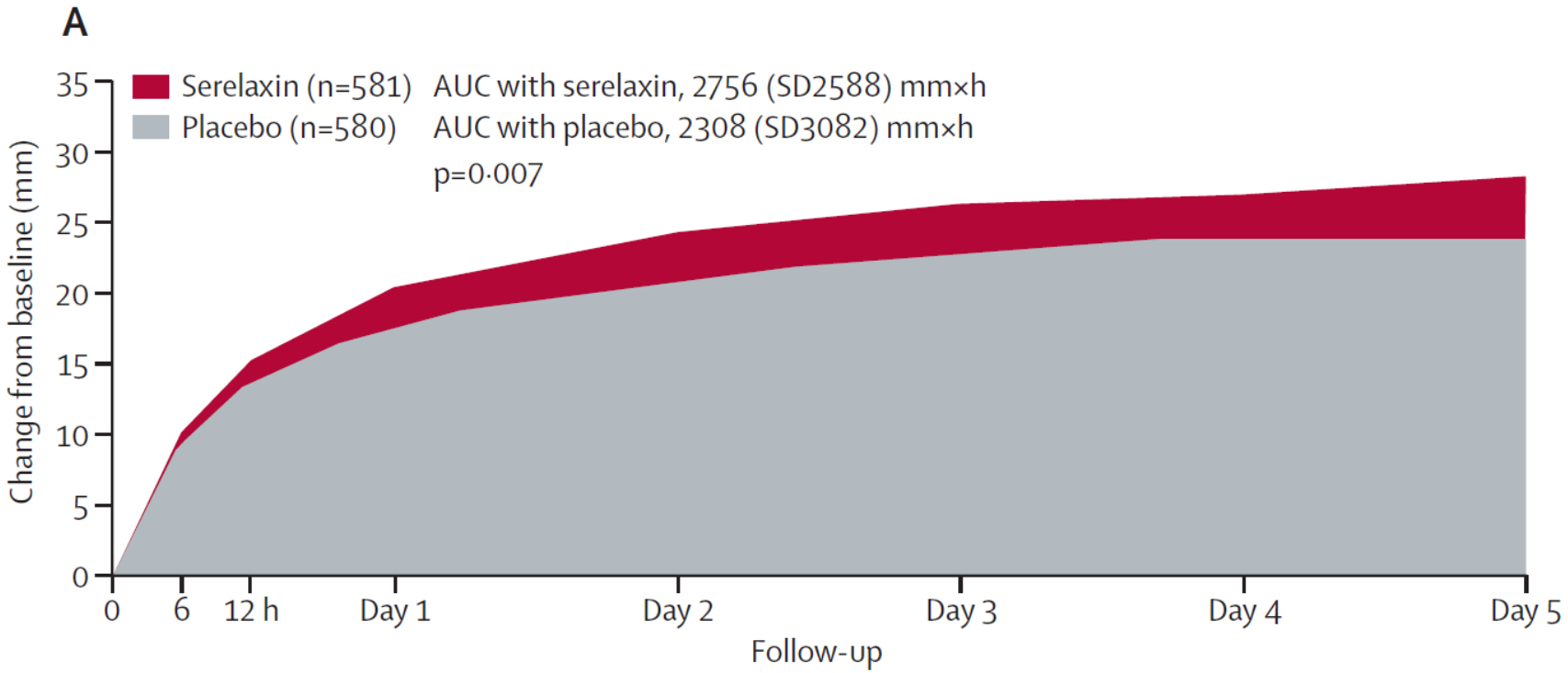
Peacock et al Am Heart J 2014

Serelaxin, recombinant human relaxin-2, for treatment of acute heart failure (RELAX-AHF): a randomised, placebo-controlled trial

John R Teerlink, Gad Cotter, Beth A Davison, G Michael Felker, Gerasimos Filippatos, Barry H Greenberg, Piotr Ponikowski, Elaine Unemori, Adriaan A Voors, Kirkwood F Adams Jr, Maria I Dorobantu, Liliana R Grinfeld, Guillaume Jondeau, Alon Marmor, Josep Masip, Peter S Pang, Karl Werdan, Sam L Teichman, Angelo Trapani, Christopher A Bush, Rajnish Saini, Christoph Schumacher, Thomas M Severin, Marco Metra, for the RELAXin in Acute Heart Failure (RELAX-AHF) Investigators

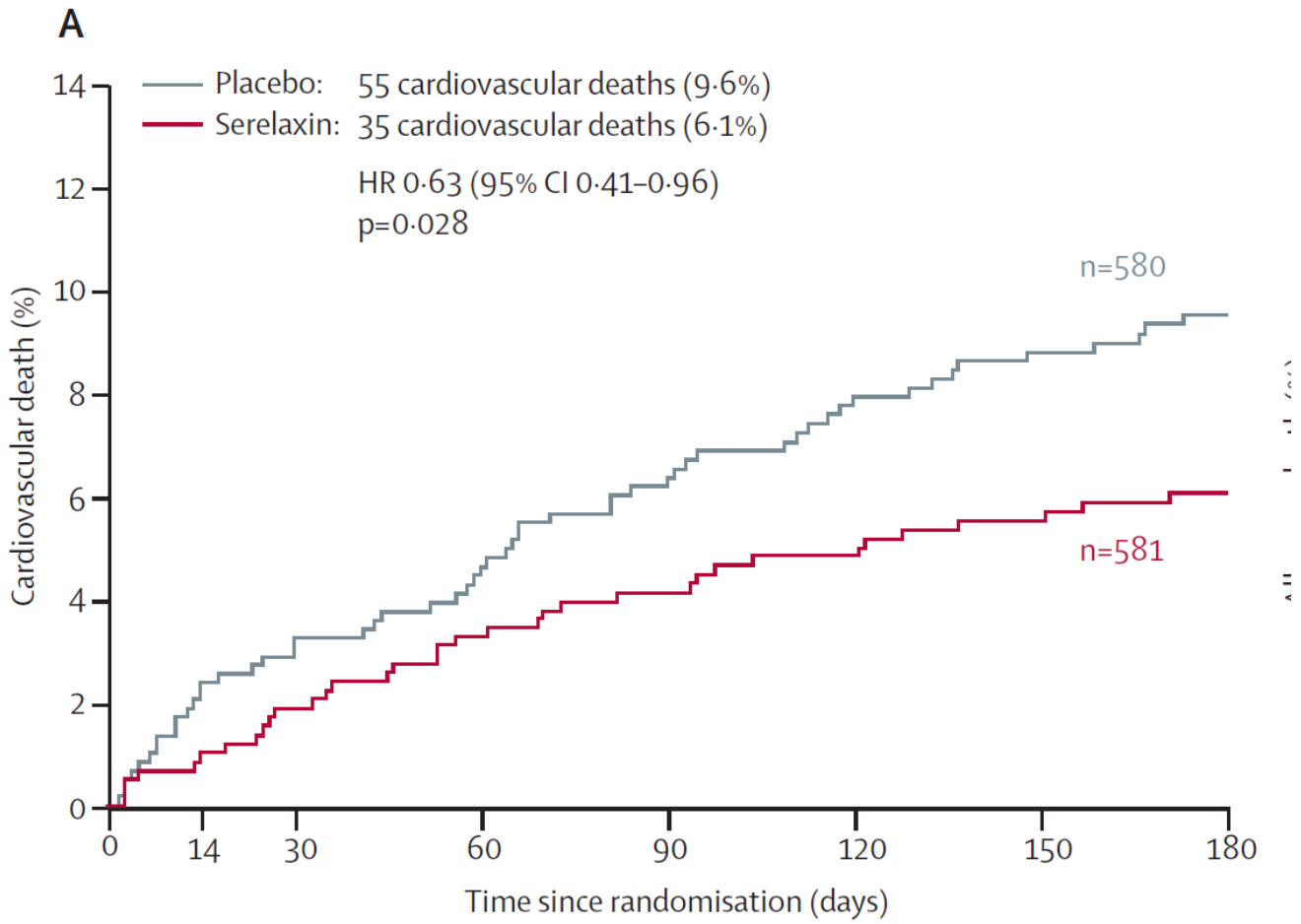
Teerlink et al, Lancet 2012

Improvement in dyspnea



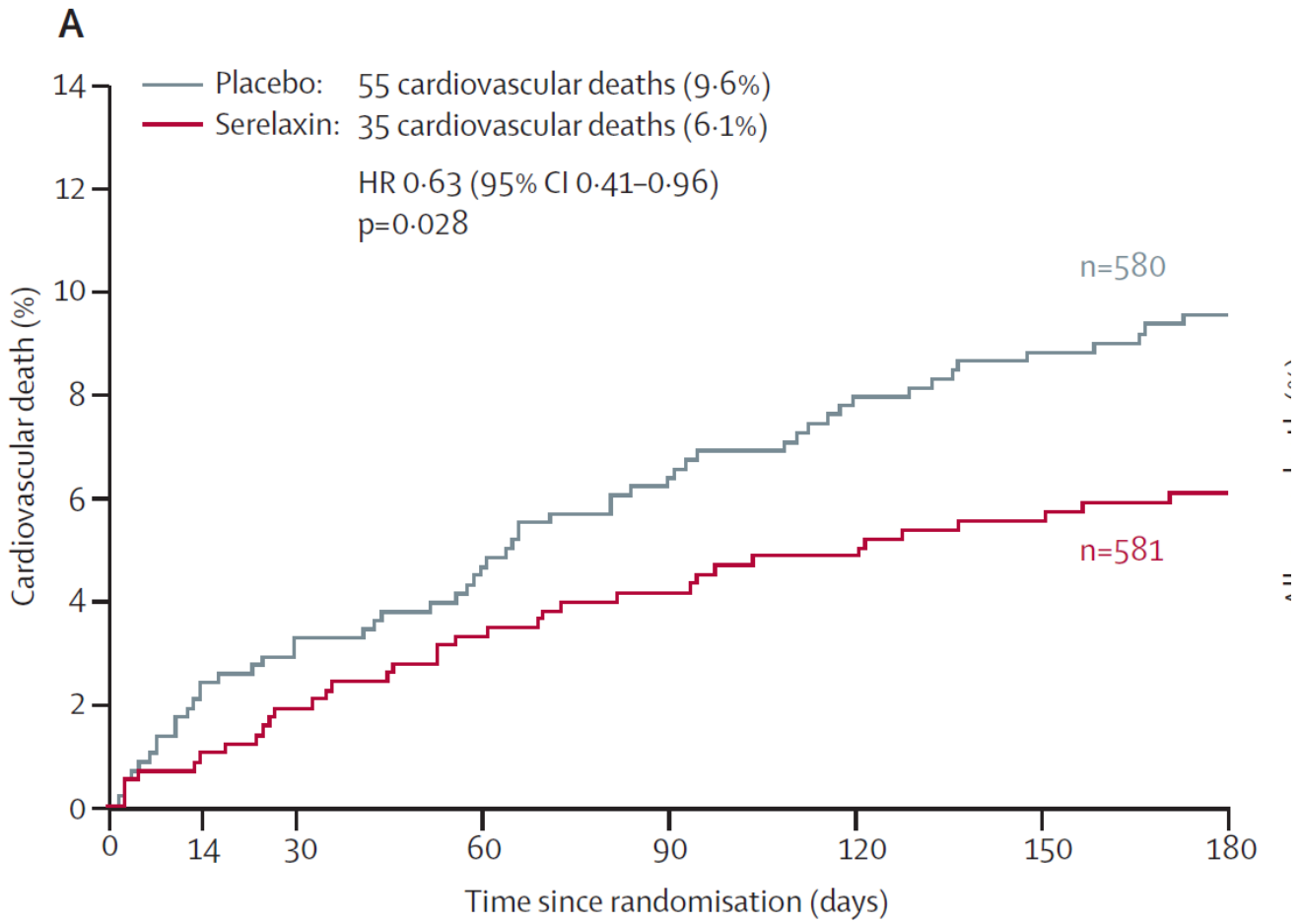
Teerlink et al, Lancet 2012

Improvement in 180-d cardiovascular mortality



Teerlink et al, Lancet 2012

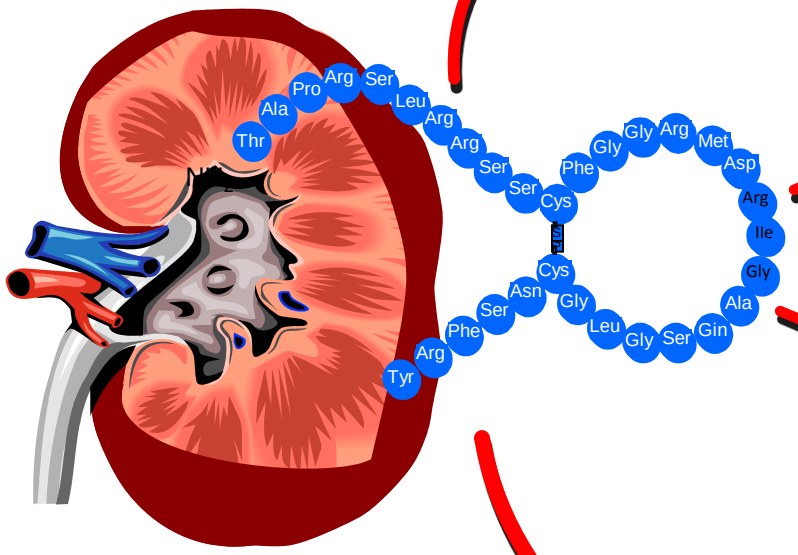
Improvement in 180-d cardiovascular mortality



Teerlink et al, Lancet 2012

Summary of the Pharmacological Effects of Ularitide

CARDIORENTIS



Hemodynamic (vasodilation)

- veins
- arteries

Bronchodilation

- Tracheal smooth muscle relaxation

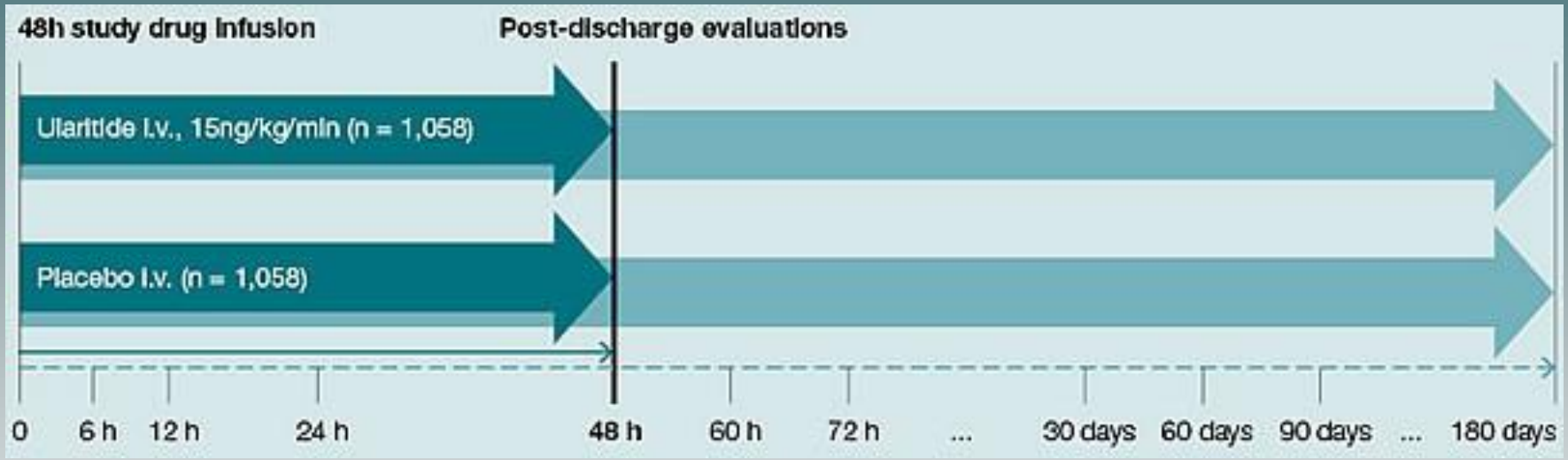
Neurohumoral

↓ renin
↓ angiotensin
↓ aldosterone
↓ endothelin

Renal

↑ diuresis
↑ natriuresis

TRUE-AHF: Study design

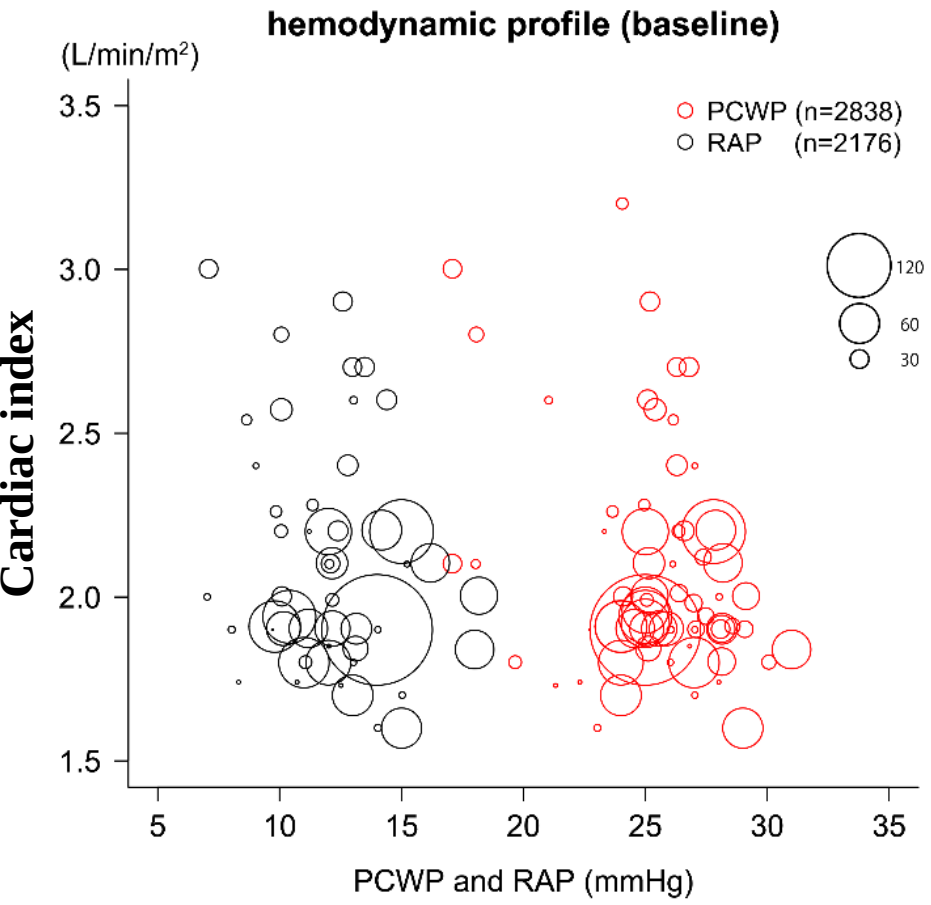


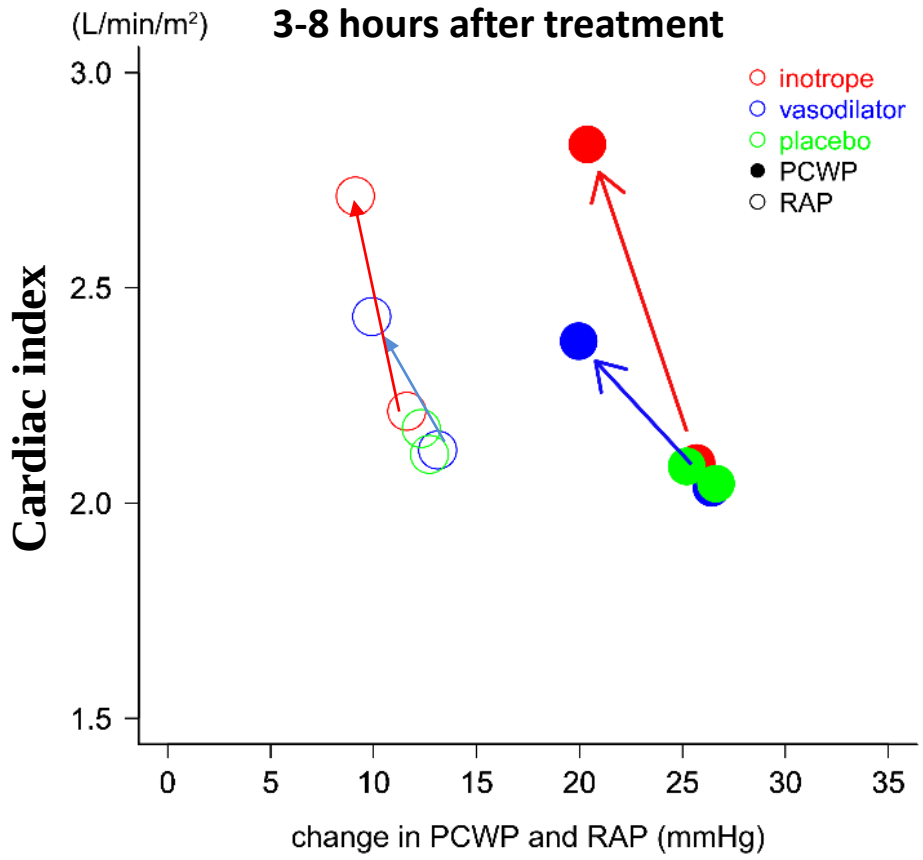
- **Multicenter, randomized, double blind, placebo-controlled trial, to evaluate the efficacy and safety of intravenous (IV) ularitide in patients suffering from AHF**
- **Patient enrolment has started across approximately 190 centres in the US, Europe and Canada**
- **Minimum 2,152 patients with AHF will be randomised to receive placebo or ularitide for 48 hours in addition to standard care**
  - **The trial maybe enlarged in size after a planned interim analysis (up to 4,000 patients)**

Vasodilateurs versus inotropes

Quelle classe a les meilleurs effets sur l'OAP ou sur la congestion des organes ?

Invasive hemodynamics at baseline and after treatment in AHF: results of a meta-analysis





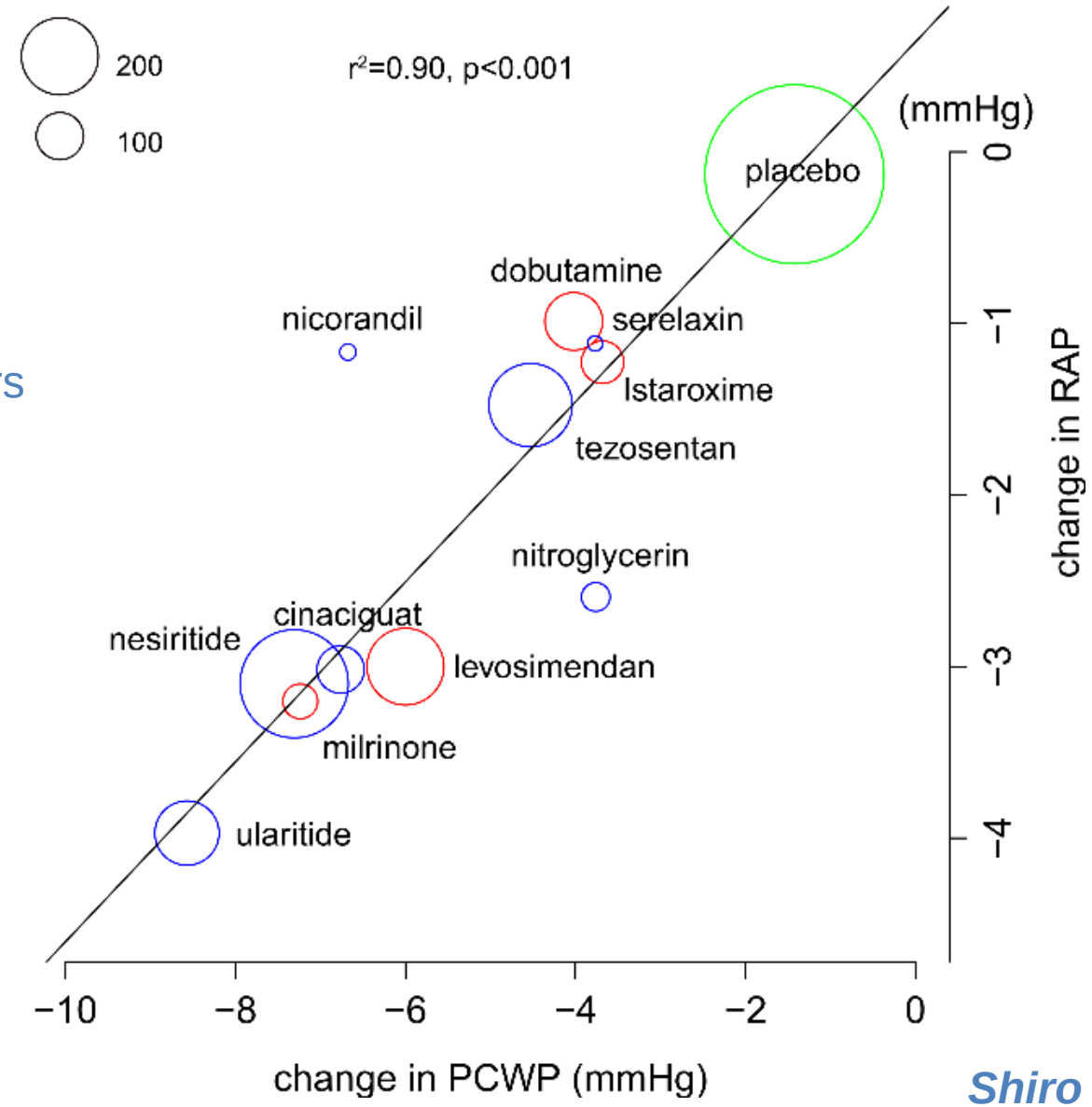
Ishihara et al.

Vasodilateurs versus inotropes

Ont-ils des effets différents sur le VD et le VG?

Vasodilators does as well as inotropes on congestion: results of a meta-analysis

Green: placebo
Red: Inotropes
Blue: vasodilators



Shiro Ishihara et al.

En résumé,

- L'ICA est une pathologie globale du cœur touchant très souvent le VD **et** le VG

- Les vasodilatateurs

  – sont encore sous-utilisés
  – agissent sur le VD et le VG
  – offrent de nouvelles perspectives