SCHOOL OF MEDICINE
EMERGENCY MEDICINE

Acute Heart Failure

Peter S. Pang MD MS
Rolly McGrath Professor & Chair

Disclosures

- Editorial Board: JACC-HF, and JCF
- Research Grants: AHA, AHRQ
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- Industry: Consulting: many in the past, none in the last 18 months
- Data Safety Monitoring Board: Heart Initiative
- No speakers bureaus
- IU as clinical trial site, I am the Site PI or investigator: Beckman-Coulter, NIH, DoD, AHRQ, AHA, IU Values grant funding, Abbott, OrthoDiagnostics, Momentum study

Why ?

5-year Mortality Compared To Cancer

50% HF

33% All Cancers

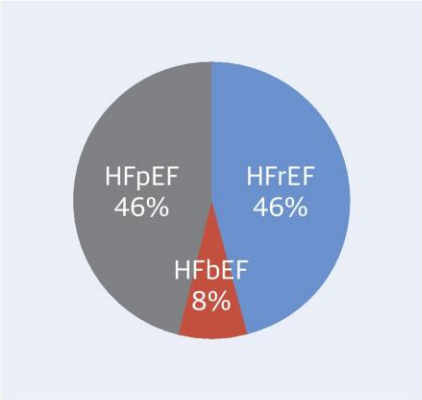
Maron Circ 2017;135:2317-19

N=39,982
254 hospitals

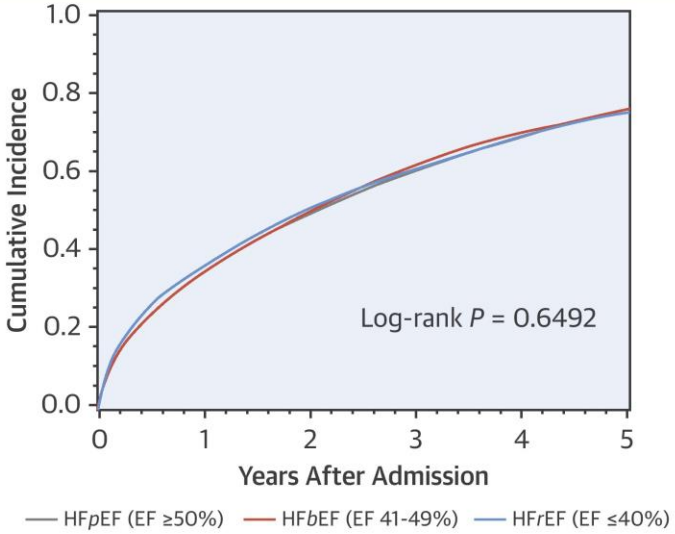
75%
5-year
mortality

CENTRAL ILLUSTRATION: 5-Year Outcomes in Patients Hospitalized With HF With Preserved, Borderline, and Reduced EF

Heart Failure



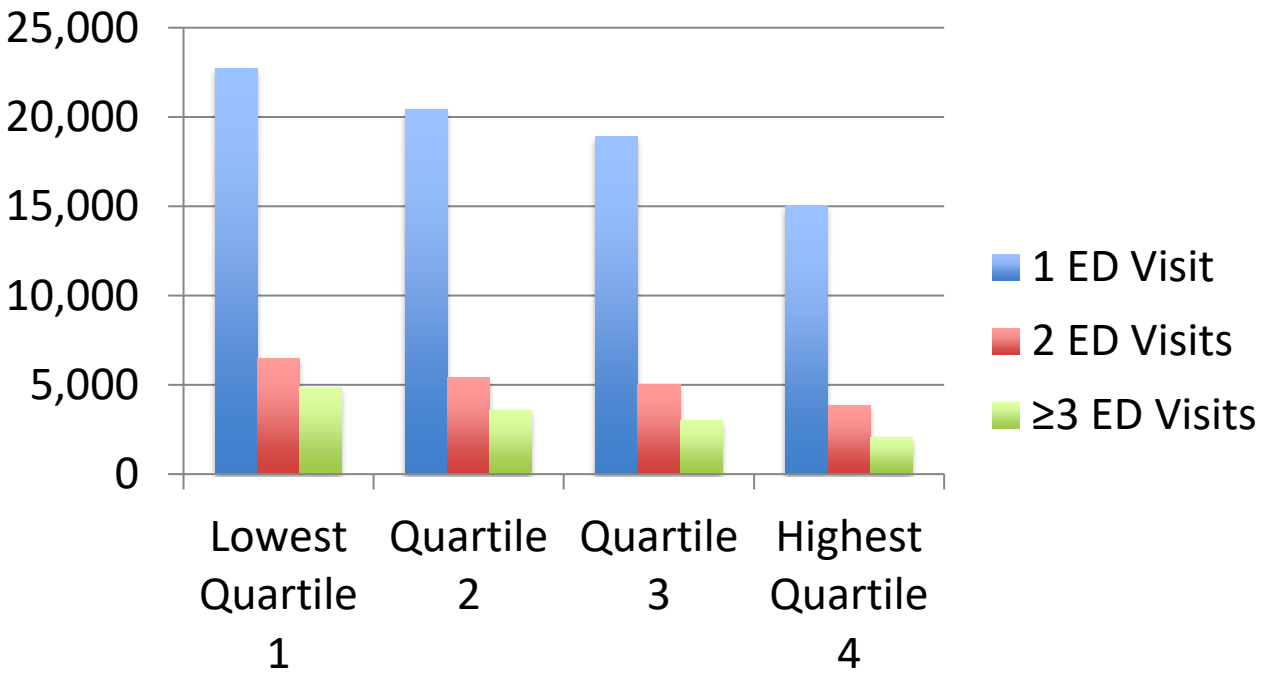
5-Year Mortality



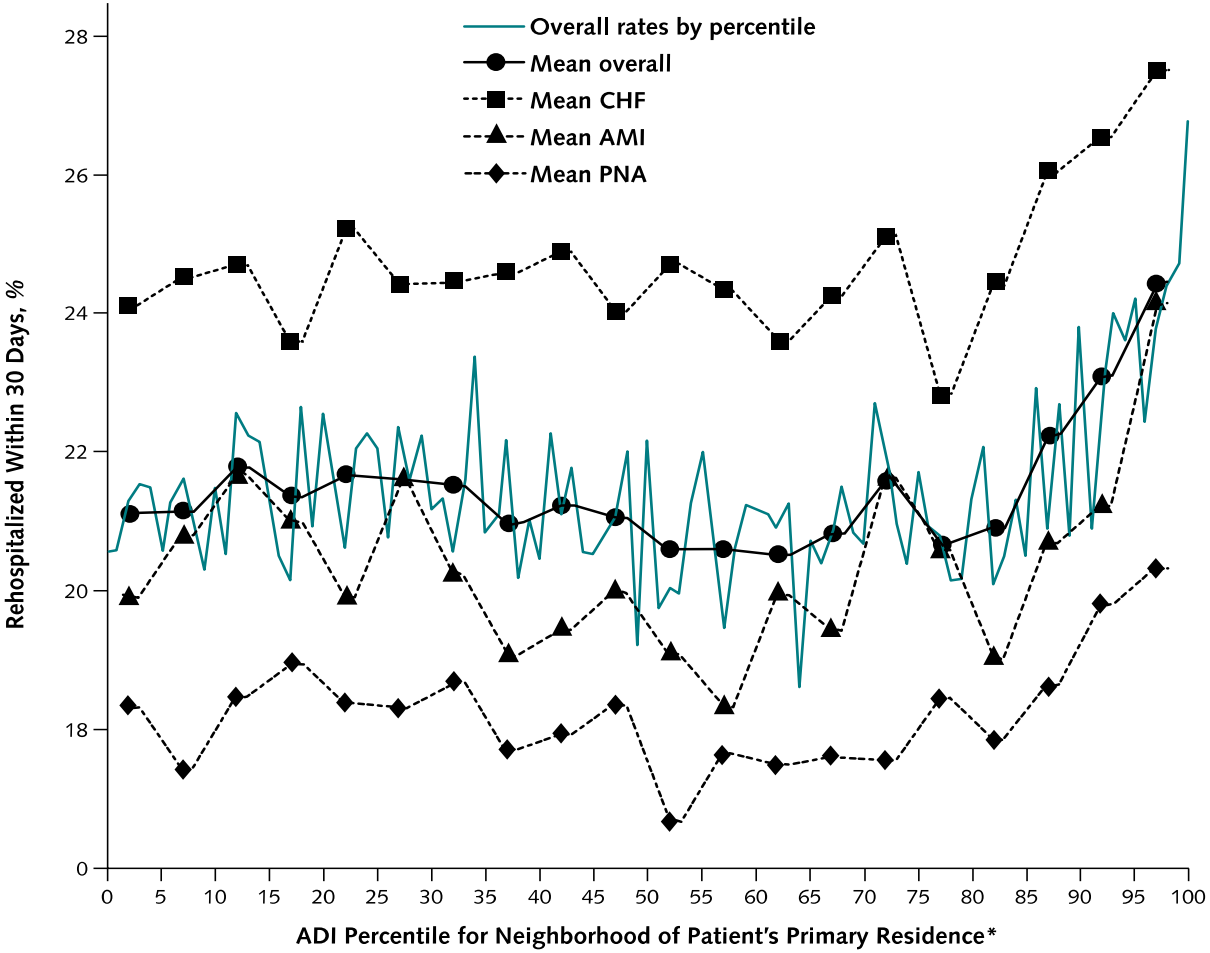
Outcomes – 5-Year Event Rates (%)					
	Mortality	Readmission	CV Readmission	HF Readmission	Mortality/Readmission
HFrEF	75.3	82.2	63.9	48.5	96.4
HFbEF	75.7	85.7	63.3	45.2	97.2
HFpEF	75.7	84.0	58.9	40.5	97.3

Shah, K.S. et al. J Am Coll Cardiol. 2017;70(20):2476-86.

Median Income Quartiles for Number of ED AHF Visits



Hasegawa et.al. Circ: HF 2014



Kind et.al. Archives of IM, 2014

Which of the following AHF therapies has a Level I, Class A Guideline Recommendation?

A. IV loop diuretics (i.e. furosemide)
B. Nitroglycerin
C. Nesiritide
D. Dobutamine
E. ACE-I
F. All of the above
G. None of the above

- Sit the patient upright
- Oxygen
- Positive Pressure Ventilation
- Morphine
- Diuretics
- Nitrates
- Digoxin
- IABP
- **Inotropes**
- **Nesiritide**

- Sit the patient upright
- Oxygen
- Positive Pressure Ventilation
- Morphine
- Diuretics
- Nitrates
- Digoxin
- IABP
- Phlebotomy
- Rotating Tourniquets

IABP=intra-aortic balloon pump

Ramirez, Abelmann NEJM 1974

2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020,…

- Sit the patient upright
- Oxygen
- Positive Pressure Ventilation
- Morphine
- Diuretics
- Nitrates
- Digoxin
- IABP
- **Inotropes**
- **Nesiritide**

1974

- Sit the patient upright
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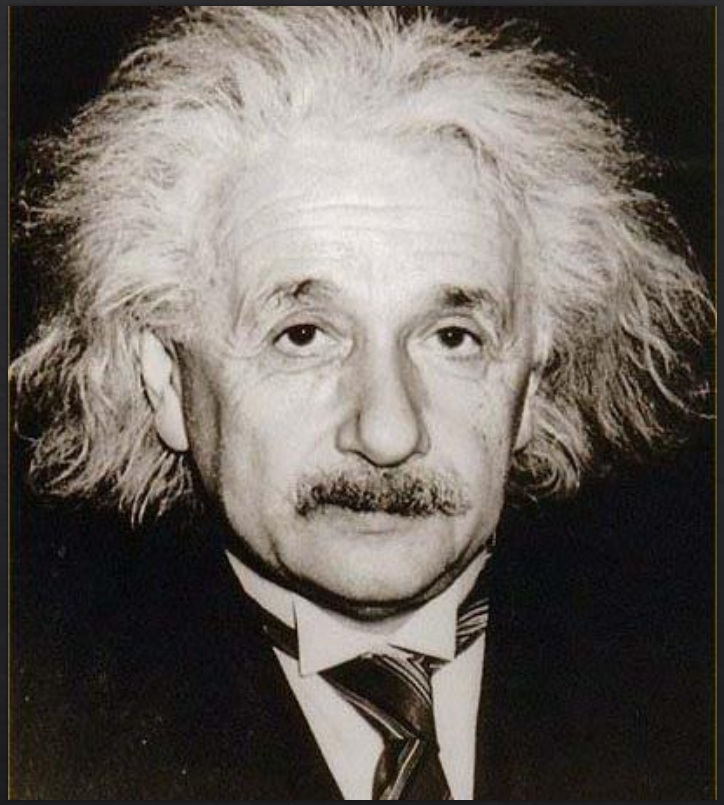


"**Insanity**: Doing the same thing over and over again and expecting different results."

- Albert Einstein

Initial Approach

1. Treat the life threat
2. Establish the diagnosis
3. Determine clinical profile (Volume or Vascular?)
4. **Identify and manage the precipitant**
5. Alleviate symptoms (e.g. dyspnea)
6. Risk stratification and disposition

Pang et.al. Expert Reviews 2013

SAEM
Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

EVIDENCE-BASED DIAGNOSTICS

Diagnosing Acute Heart Failure in the Emergency Department: A Systematic Review and Meta-analysis

Jennifer L. Martindale, MD, Abel Wakai, MD, Sean P. Collins, MD, MSc, Phil Levy, MD, Deborah Diercks, MD, Brian C. Hiestand, MD, Gregory J. Fermann, MD, Ian deSouza, MD, and Richard Sinert, DO

Diagnosing Acute Heart Failure in the ED: A Systematic Review and Meta-Analysis

	No. of Studies	No. of Patients	% AHF (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	LR+ (95% CI)	LR– (95% CI)
Lung ultrasound							
Positive B-line scan	8	1914	48.2 (46.0-50.5)	85.3 (82.8-87.5)	92.7 (90.9-94.3)	7.4 (4.2-12.8)	0.16 (0.05-0.51)

BNP Value (pg/mL)	Interval LR	N (%)	NT-proBNP (pg/mL)	Interval LR	N (%)
0-100	0.14 (0.12-0.18)	617 (28)	0-100	0.09 (0.05-0.17)	150 (7.5)
100-200	0.29 (0.23-0.38)	308 (14)	100-300	0.23 (0.16-0.33)	205 (10.2)
200-300	0.89 (0.67-1.17)	188 (9)	300-600	0.28 (0.20-0.39)	212 (10.5)
1500-2500	8.33 (4.60-15.12)	105 (5)	15,000-30,000	2.93 (1.95-4.39)	111 (5.5)
2500-5001	8.91 (4.09-19.43)	65 (3)	30,000-200,000	3.30 (2.05-5.31)	86 (4.3)
		2202 (100)			2013 (100)

Take home message:

Lung Ultrasound to rule in

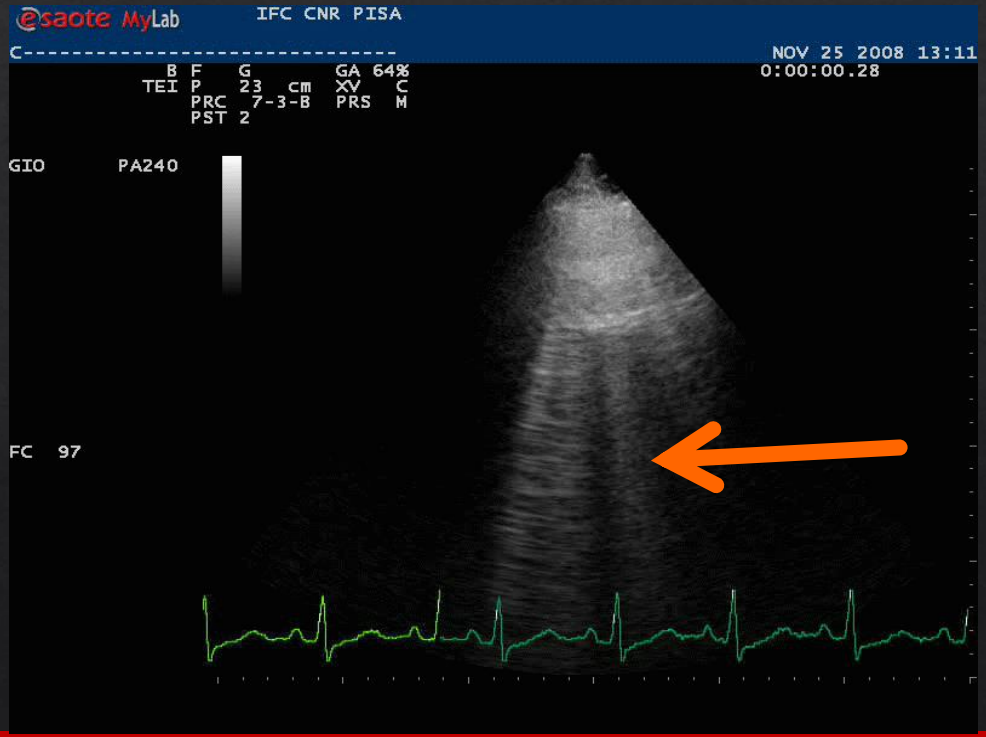
Natriuretic peptides to rule out

AHF, acute heart failure; LR+, likelihood ratio of a positive test; LR–, likelihood ratio of a negative test; LV, left ventricle.

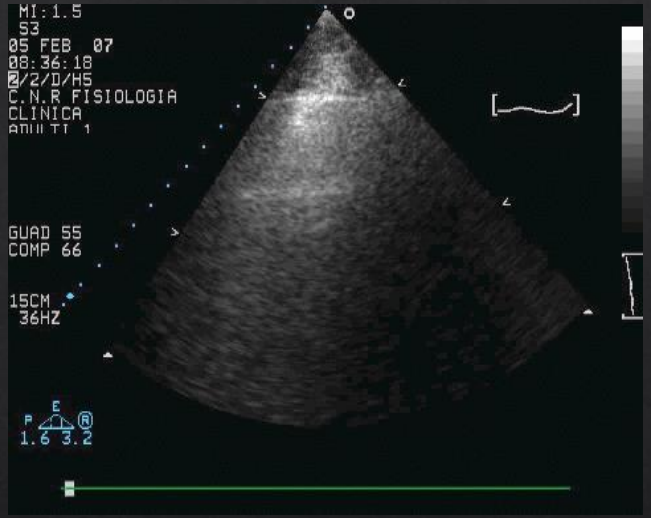
Martindale JL. *Acad Emerg Med*.2016;23:223-242.

B-lines: definition

Discrete laser-like vertical hyperechoic reverberation artifacts, that arise from the pleural line.



Acute dyspnea



COPD exacerbation

Acute pulmonary oedema

Universal Law of Biomarkers

“Biomarkers help good clinicians practice better medicine.”

Corollary to the Universal Law:

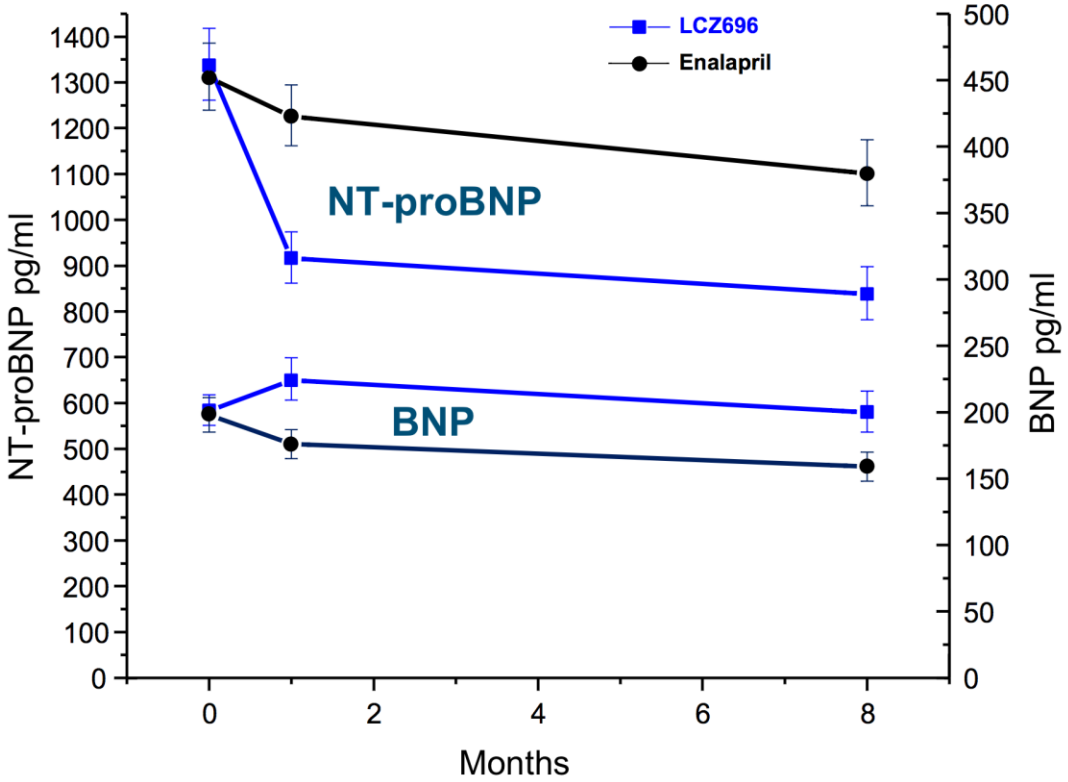
“Biomarkers can’t fix poor clinical judgment.”

Crenner et.al. Annals of IM, 1988

"Physicians throughout the 19th century had taught that careful palpation of the radial pulse revealed valuable information about the force of blood flow."

The new blood pressure cuff offered a way to replace this expert, subjective assessment of the pulse with a simple number…

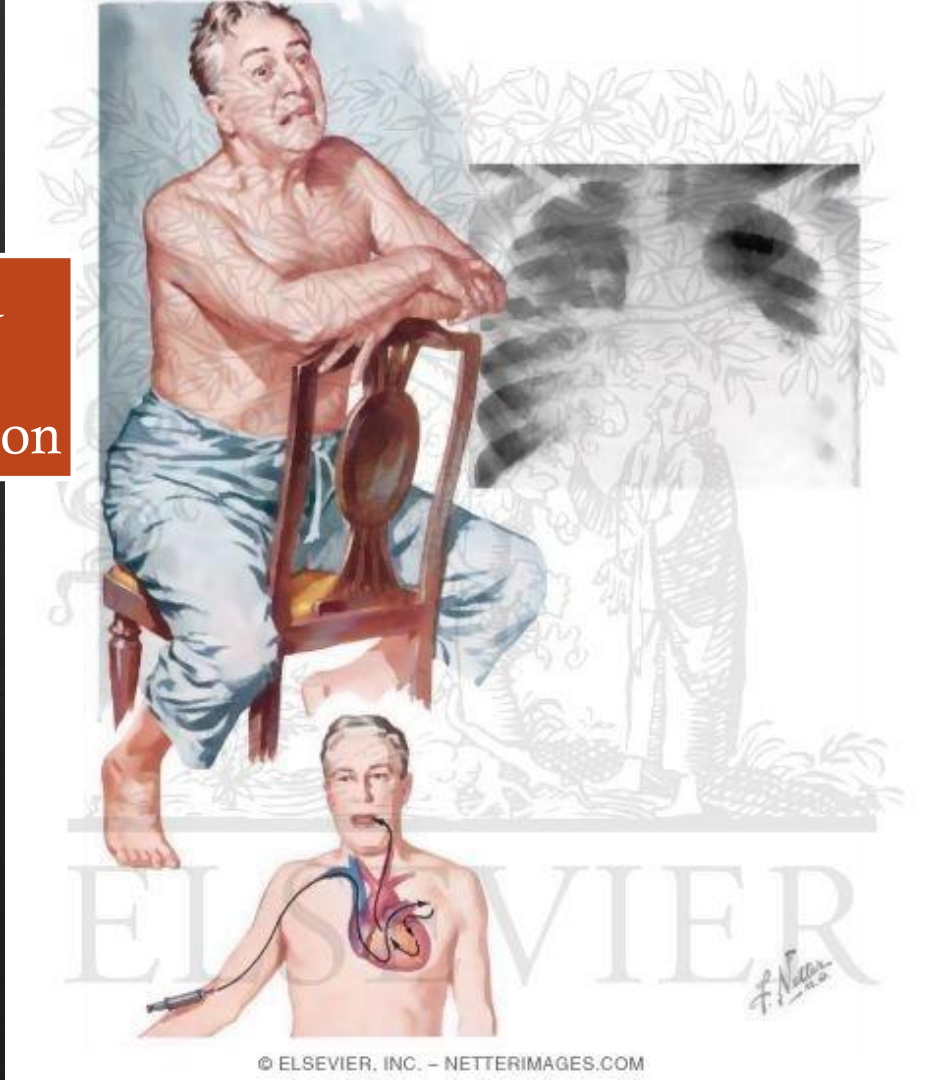
PARADIGM-HF: NT-proBNP and BNP



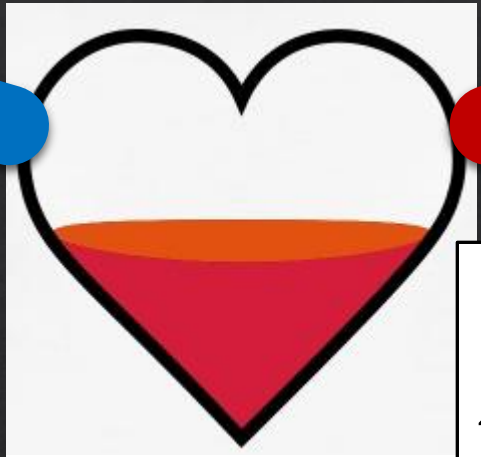
From Jhund PS, adapted from Packer et.al. Circulation 2015

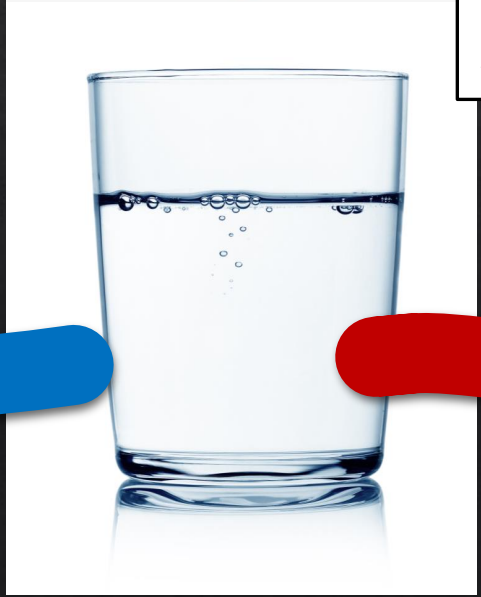
An approach …

Volume overload
vs.
Volume redistribution

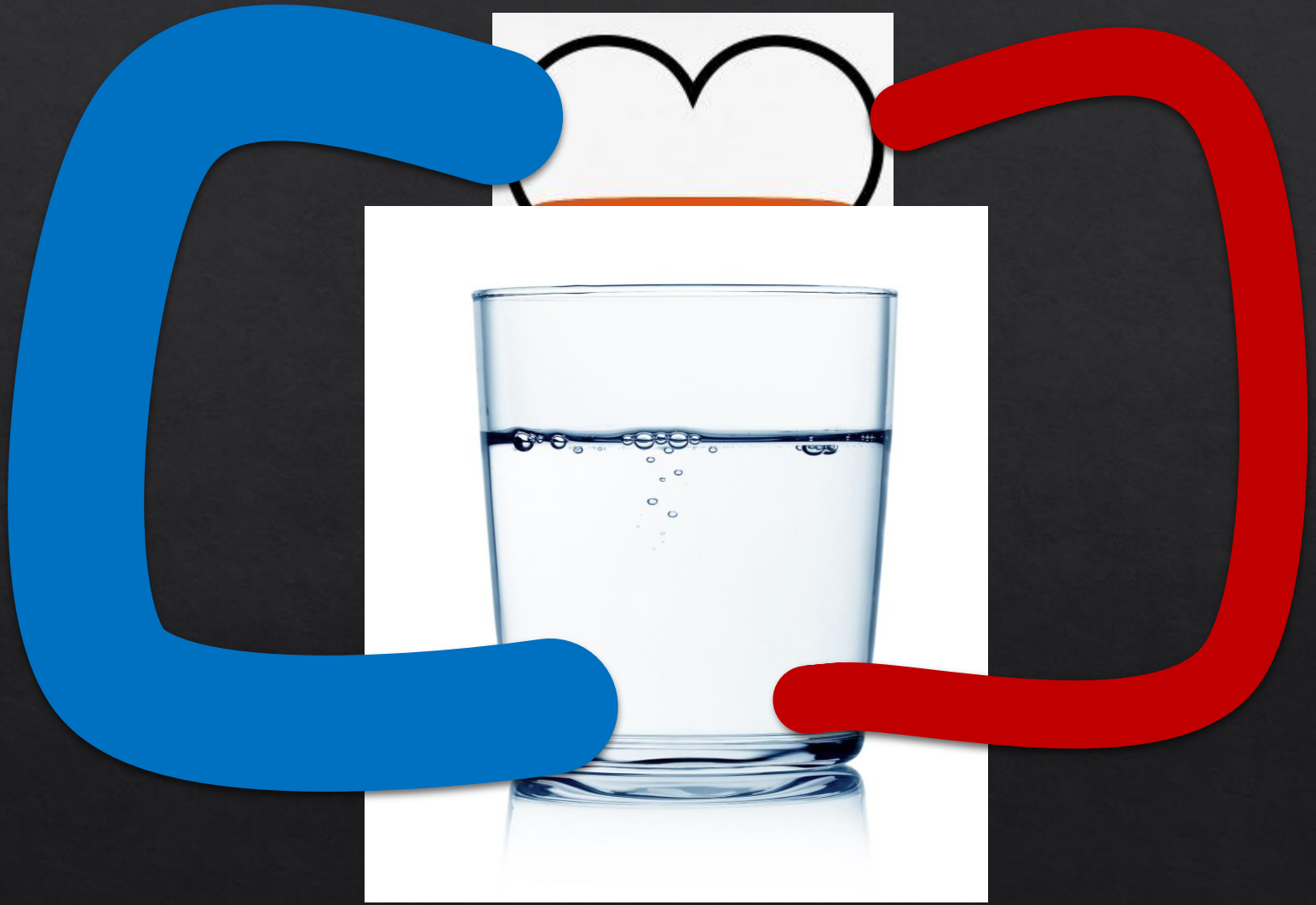


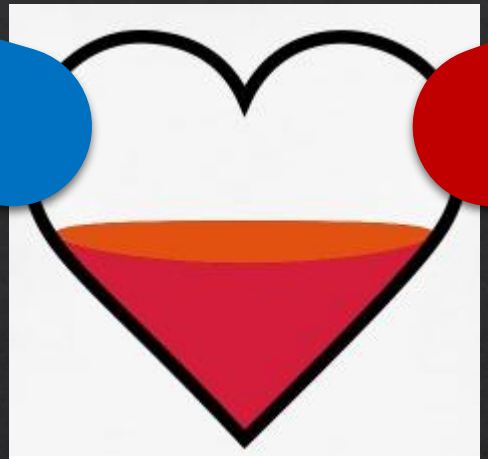
Cotter et.al. AJC 2008
Fallick et.al. Circ HF 2011

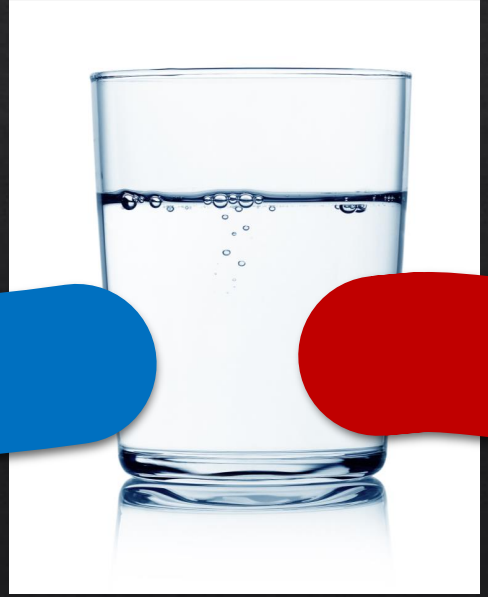




1. Pump
2. Volume
3. Tone







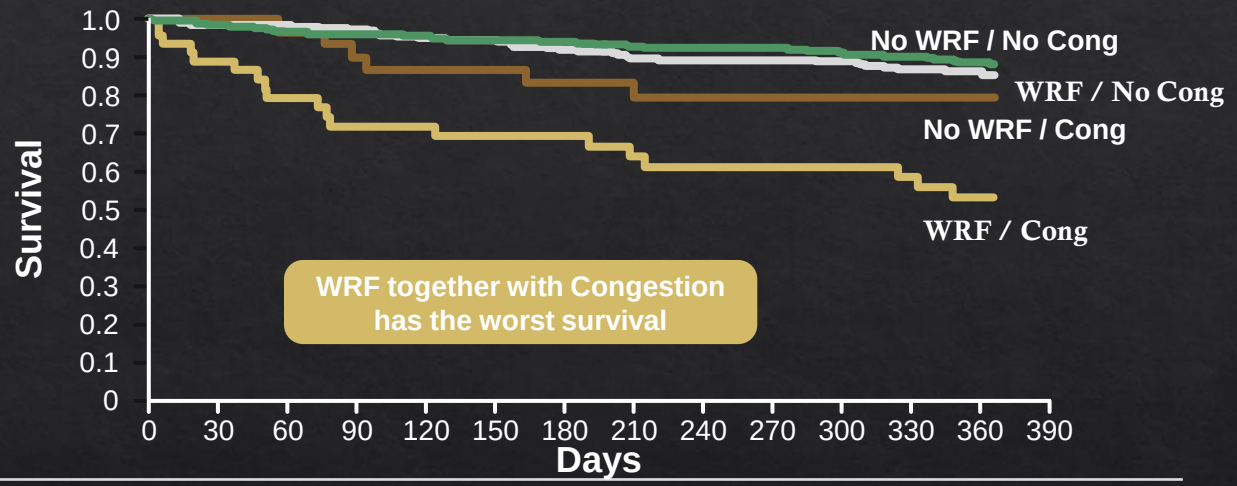
Congestion

How to remove congestion

DIURETICS

Diuretics are evil….

The Role of Congestion and Its Interaction with Worsened Renal Function (WRF)



WRF/Cong	45	40	32	29	28	26	26	24	23	23	23	22	20
No WRF/Cong	31	31	29	27	26	26	24	22	20	19	19	19	18
WRF/No Cong	253	247	243	235	218	216	204	196	189	188	186	178	170
No WRF/No Cong	266	259	249	244	237	229	227	223	217	214	208	202	197

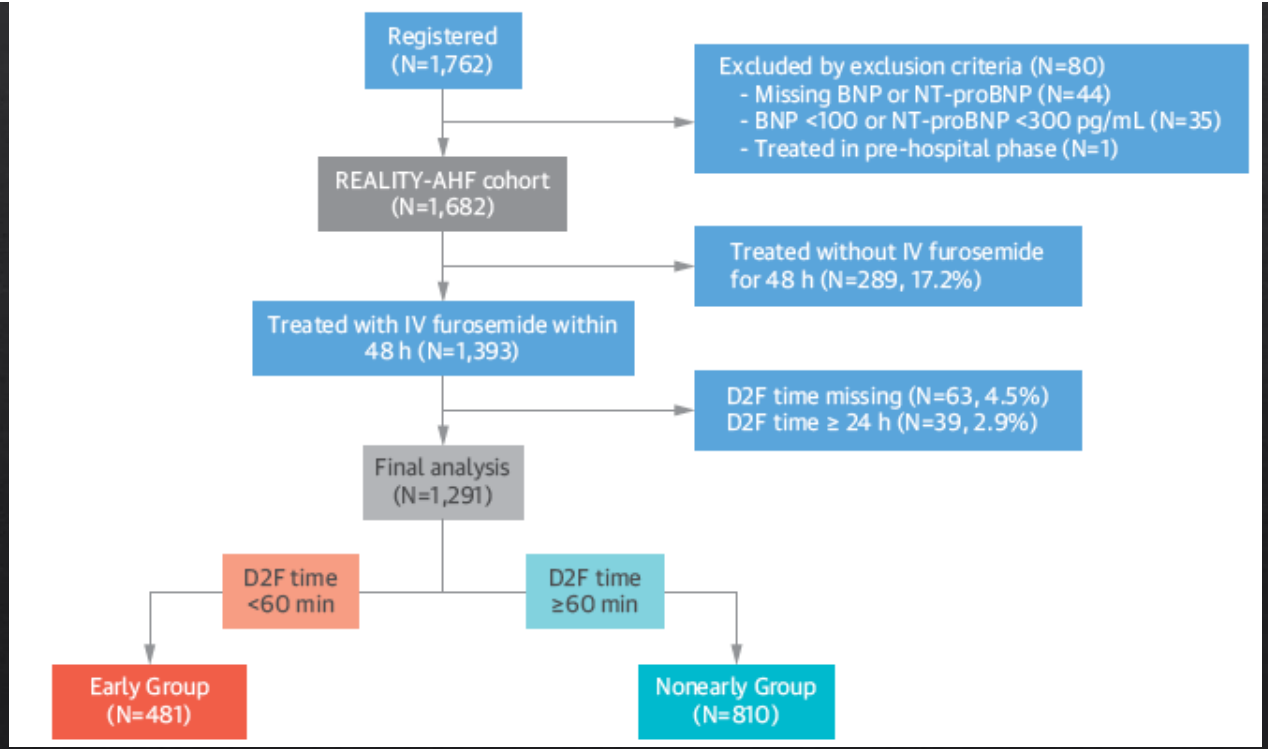
Cong = congestion.

Metra M, et al. *Circ Heart Fail*. 2012;5:54-62.

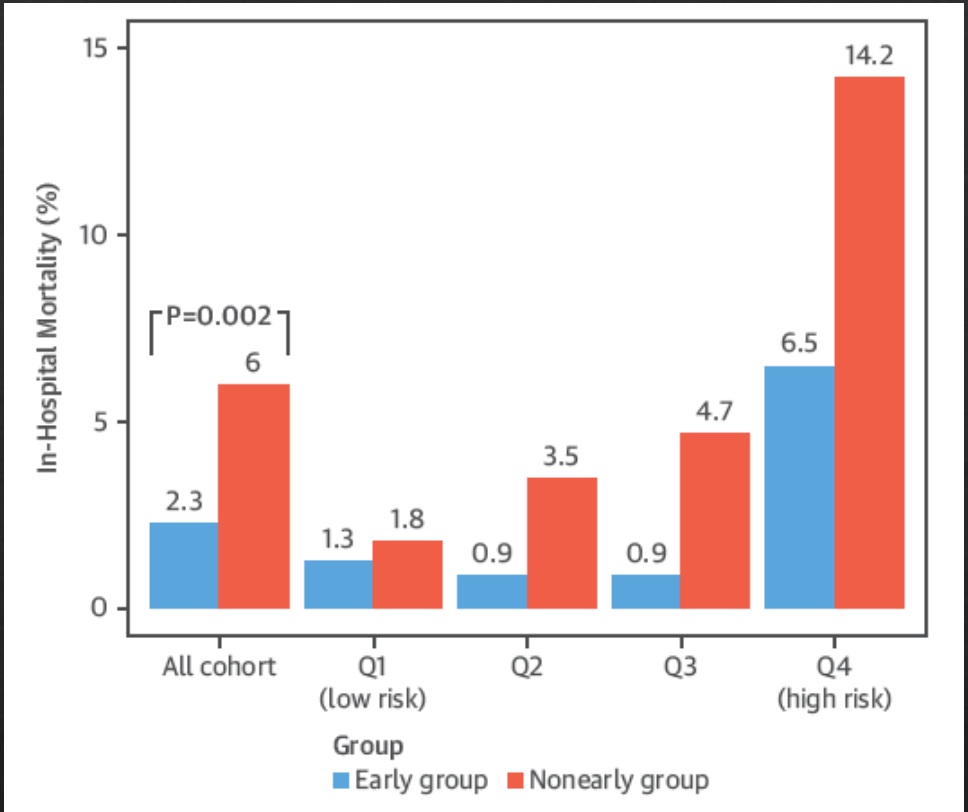
MISTAKES

IT COULD BE THAT THE PURPOSE OF YOUR LIFE IS
ONLY TO SERVE AS A WARNING TO OTHERS.

Time-to-Furosemide Treatment and Mortality in Patients Hospitalized With Acute Heart Failure



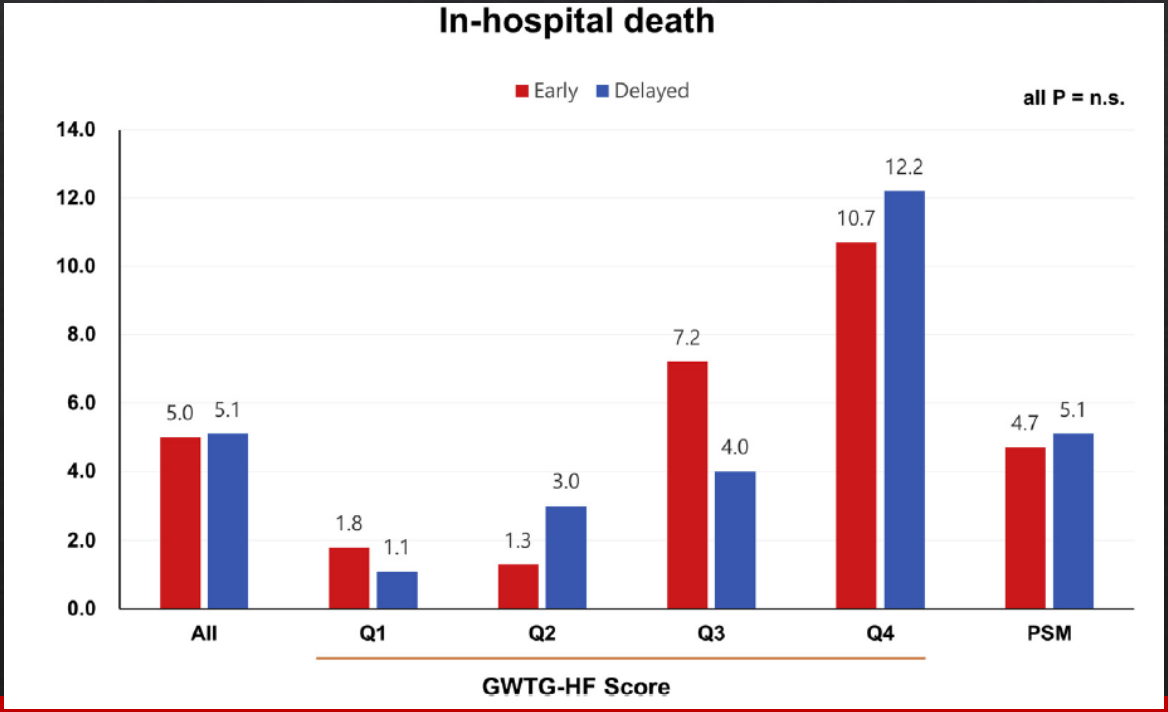
Matsue et al. J Am Coll Cardiol 2017;69:3042-



Adjustment	In-Hospital Mortality			30-Day Mortality		
	OR	95% CI	p Value	OR	95% CI	p Value
Univariate	0.36	0.19–0.71	0.002	0.52	0.28–0.96	0.037
Adjusted for GWTG-HF risk score	0.39	0.20–0.76	0.006	0.56	0.13–1.0	0.072
Propensity score matching	0.41	0.18–0.89	0.030	0.49	0.22–1.05	0.067

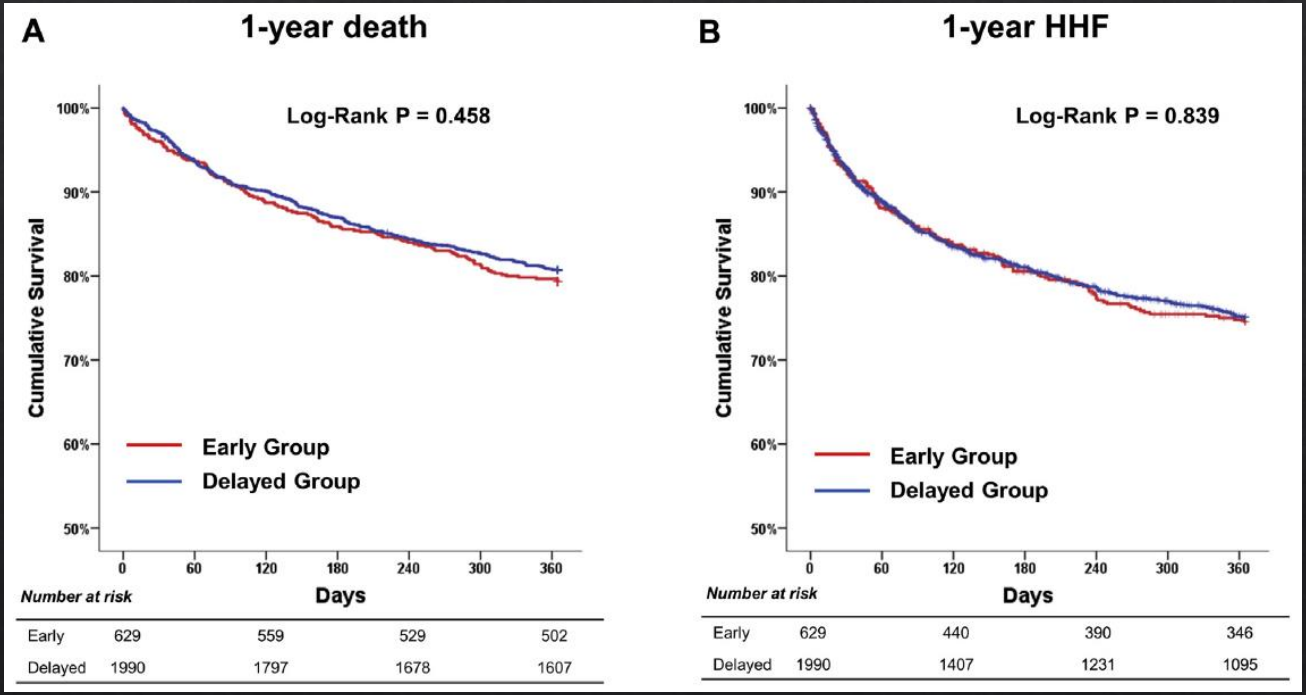
Matsue et al. J Am Coll Cardiol 2017;69:3042-

The Effect of Door-to-Diuretic Time on Clinical Outcomes in Patients With Acute Heart Failure



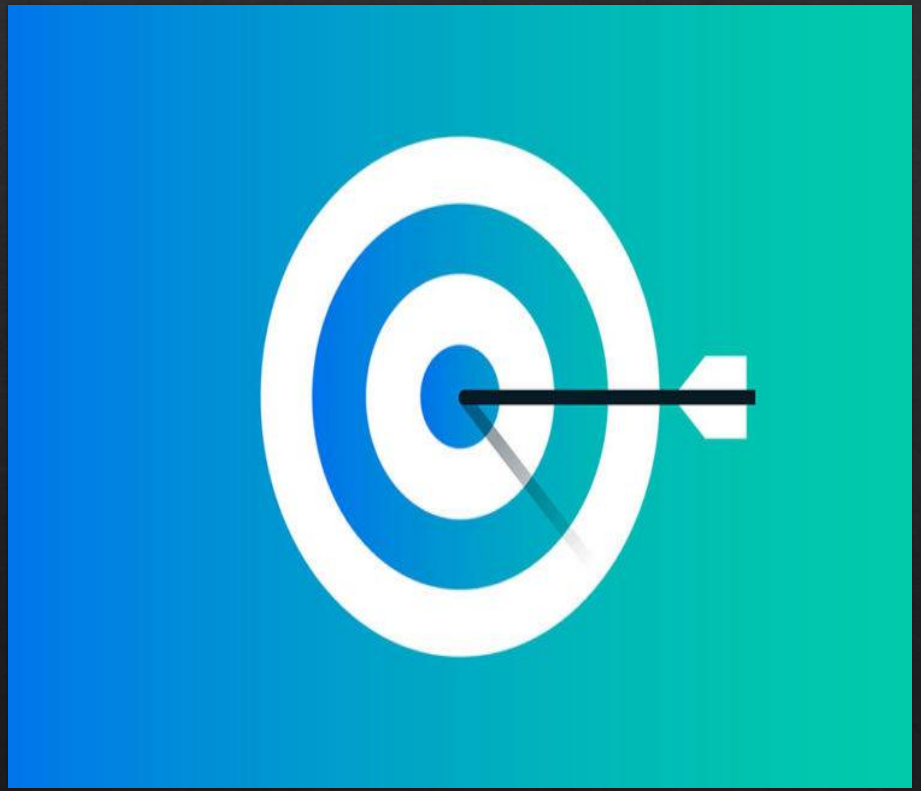
Park et al. JACC: Heart Failure 2018;6:286-94.

The Effect of Door-to-Diuretic Time on Clinical Outcomes in Patients With Acute Heart Failure



Park et al. JACC: Heart Failure 2018;6:286-94.

“You must unlearn what you have learned.”



- Dyspnea?
- Urine output?
- Weight loss?
- Natriuretic peptides?

CLINICAL RESEARCH

Natriuretic Response Is Highly Variable and Associated With 6-Month Survival

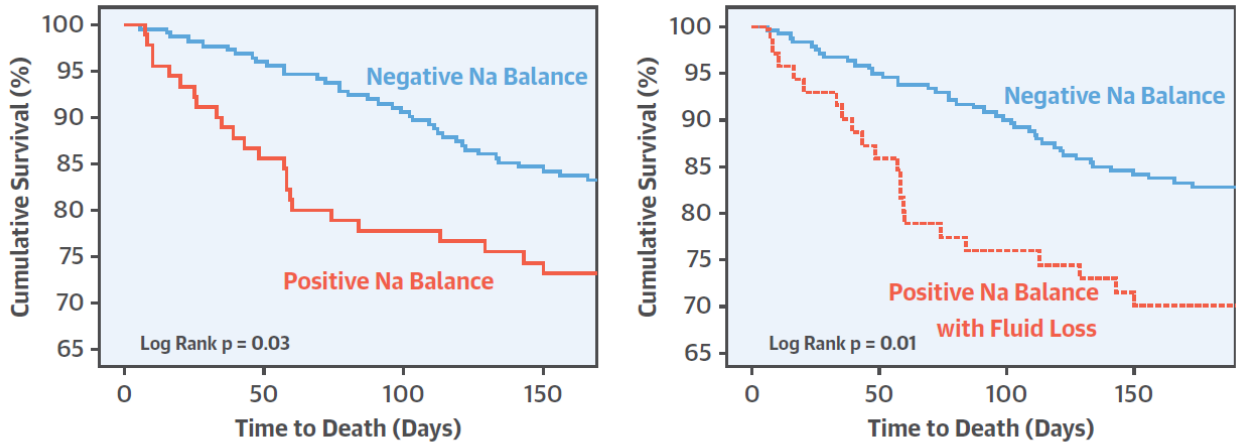
Insights From the ROSE-AHF Trial

Daniel Z. Hodson, BA,[a,*] Matthew Griffin, MD,[a,*] Devin Mahoney, BS,[a] Parinita Raghavendra, MS,[a] Tariq Ahmad, MD, MPH,[a] Jeffrey Turner, MD,[b] F. Perry Wilson, MD, MS,[b] W.H. Wilson Tang, MD,[c] Veena S. Rao, PhD,[a] Sean P. Collins, MD,[d] Wilfried Mullens, MD, PhD,[e] Jeffrey M. Testani, MD, MTR[a]

- 316 patients in ROSE trial
- 24-hour urinary sodium excretion:
- Highly variable and NOT associated with diuretic dose
- Highly predictive of 6-month outcomes

Hodson JACC HF 2019 7:383-91

FLUID LOSS DID NOT MATTER



Hodson, D.Z. et al. J Am Coll Cardiol HF. 2019;7(5):383-91.

Even if you had fluid loss- if you did not lose sodium you died sooner

Hodson JACC HF 2019 7:383-91

The use
congest
Heart F
Society

Wilfried Mull
Hans-Peter B
W.H. Wilson
Gerasimos Fi
and Andrew J

n the
an

Mebazaa[5],

[11],

A

Congestion with volume overload

Acute treatment phase

Within 1 hour of admission

Loop diuretic naive?

No: Starting dose =1-2 times 24-hours oral home dose intravenously + ask to empty bladder

Yes: Starting dose ≥ 20-40 furosemide equivalents intravenously & + ask to empty bladder

Early evaluation phase

First 6 hours after loop diuretic administration

Start urine collection

EARLY EVALUATION OF TREATMENT
After 2 hours: spot urinary sodium analysis
- After 6 hours: assess average urine output

Urine spot sodium > 50-70 meq/L
6-hours urine output > 100-150ml/hours

Early response phase

ning time of first 24 hours

Yes: Persistent congestion? → No*
Yes: Repeat similar dose of IV loop diuretics every 12-hours #

No: Double dose IV loop diuretics
Assess within 6 hours
< 50-70meq/L sodium
< 100mL / hourly diureses
Yes: Repeat until maximal dose loop diuretics°

Parallel interventions: (1) continue guideline directed medical therapy, (2) consider early use of mineralocorticoid receptor antagonists in case of low potassium, (3) salt and water restriction, (4) IV potassium and magnesium if necessary

Parallel evaluation: Standard non-invasive monitoring of heart rate, rhythm, respiratory rate, oxygen saturation and blood pressure. Check for signs of hypoperfusion. Consider invasive BP measurement in case of hypotension. Clearly register baseline weight before diuretics.

Mullens EJHF 2019

Insufficient Natriuretic Response to Continuous Intravenous Furosemide Is Associated With Poor Long-Term Outcomes in Acute Decompensated Heart Failure

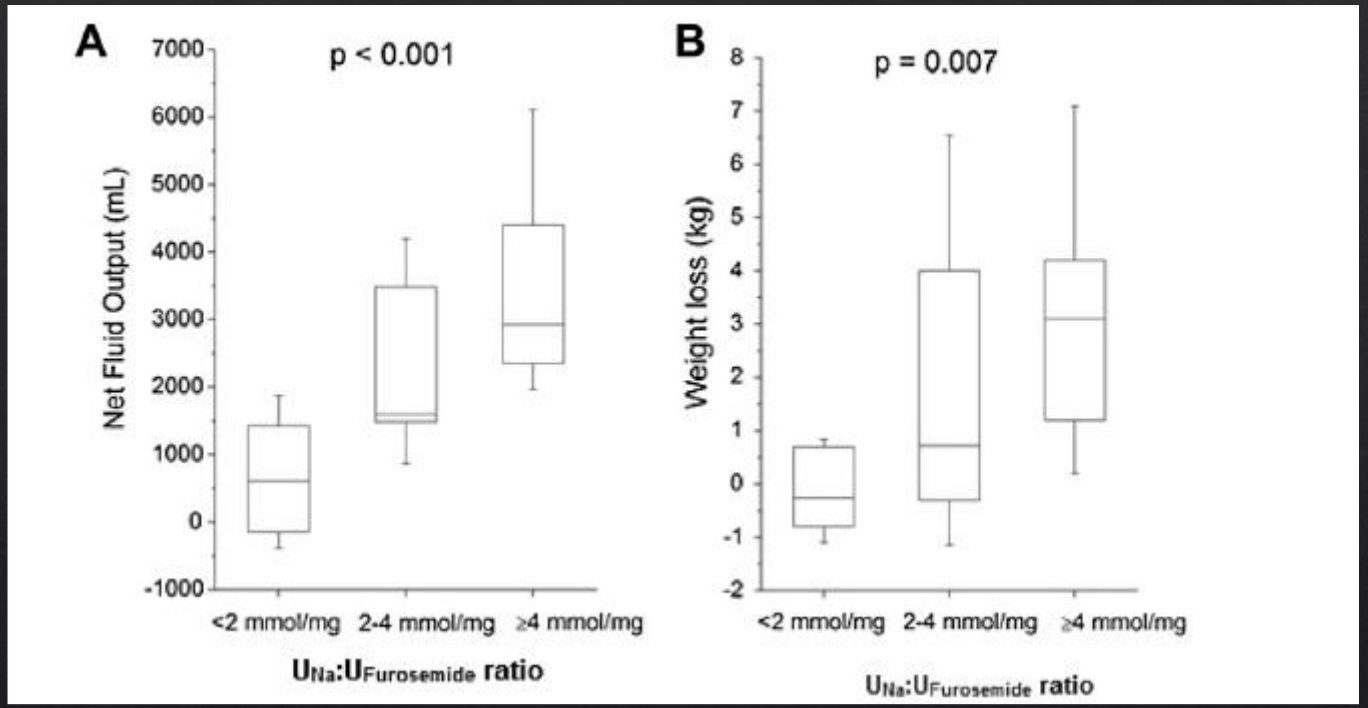
DHSSRAJ SINGH, MD,[1] KEVIN SHRESTHA, MD,[2] JEFFREY M. TESTANI, MD, MTR,[3] FREDERIK H. VERBRUGGE, MD,[4,5] MATTHIAS DUPONT, MD,[4] WILFRIED MULLENS, MD, PhD,[4,5] AND W.H. WILSON TANG, MD[2]

Kansas City, Kansas; Cleveland, Ohio; New Haven, Connecticut; Genk and Diepenbeek, Belgium

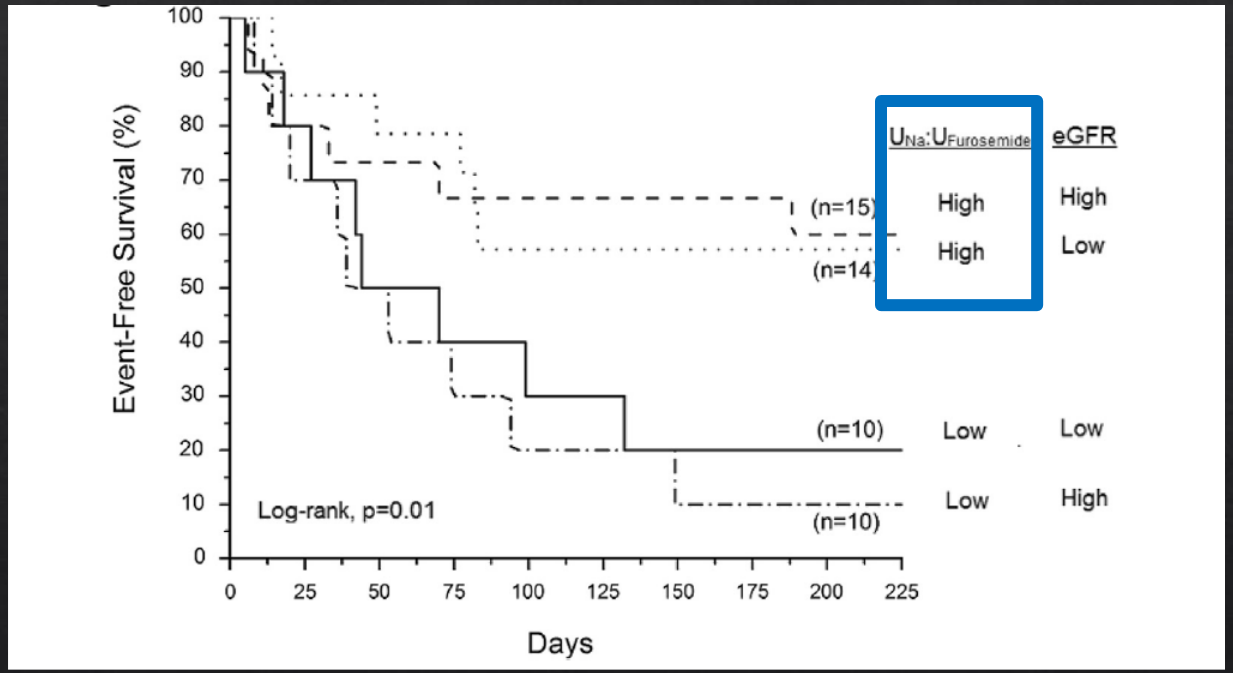
- **Diuretic efficiency** – maximal natriuretic response to IV diuretic
- Low urine sodium after diuretic = POOR response = POOR prognosis
  - It's not just urine output – it's what's in the urine
- Measure UNa immediately
- Don't wait for bad stuff to happen……

Singh J Card Fail 2014 20;6

And it predicts “response”



And bad things don't happen



Original Article

Rapid and Highly Accurate Prediction of Poor Loop Diuretic Natriuretic Response in Patients With Heart Failure

Jeffrey M. Testani, MD, MTR; Jennifer S. Hanberg, BA; Susan Cheng, MD; Veena Rao, PhD; Chukwuma Onyebeke, BS; Olga Laur, MS; Alexander Kula, MS; Michael Chen, MD; F. Perry Wilson, MD, MSCE; Andrew Darlington, DO; Lavanya Bellumkonda, MD; Daniel Jacoby, MD; W.H. Wilson Tang, MD; Chirag R. Parikh, MD, PhD

- Formula based on UNa and UCr/SCr
- Predicts subsequent natriuresis at 6 hours
- Only need spot urine sodium/creatinine after diuretic

Table 2. Correlations With Measured Sodium Output

Parameter	Correlation With Measured Cumulative Sodium Output: r	r^2	P Value
Predicted sodium output (2-h sample)	0.91	0.83	<0.001
Predicted sodium output (1-h sample)	0.85	0.72	<0.001
Clinically recorded net fluid balance from corresponding nursing shift*	0.66	0.44	<0.001
24-h clinically recorded net fluid balance	0.72	0.52	<0.001
24-h clinically recorded weight loss	0.41	0.17	0.006

Data is Accumulating……..

Long-term prognostic significance of urinary sodium concentration in patients with acute heart failure

Early urine electrolyte patterns in patients with acute heart failure

Sean P. Collins[1*], Cathy A. Jenkins[2], Adrienne Baughman[1], Karen F. Miller[1], Alan B. Storrow[1], Jin H. Han[1], Nancy J. Brown[3,4], Dandan Liu[2], James M. Luther[4,5,6], Candace D. McNaughton[1], Wesley H. Self[1], Dungeng Peng[5], Jeffrey M. Testani[7] and JoAnn Lindenfeld[8]

[1]Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, TN, USA; [2]Department of Biostatistics, Vanderbilt University Medical Center, Nashville, TN, USA; [3]Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, TN, USA; [4]Department of Pharmacology, Vanderbilt University Medical Center, Nashville, TN, USA; [5]Department of Internal Medicine, Division of Clinical Pharmacology, Vanderbilt University Medical Center, Nashville, TN, USA; [6]Department of Internal Medicine, Division of Nephrology, Vanderbilt University Medical Center, Nashville, TN, USA; [7]Department of Internal Medicine, Division of Cardiology, Yale University, New Haven, CT, USA; [8]Department of Internal Medicine, Division of Cardiology, Vanderbilt University Medical Center, Nashville, TN, USA

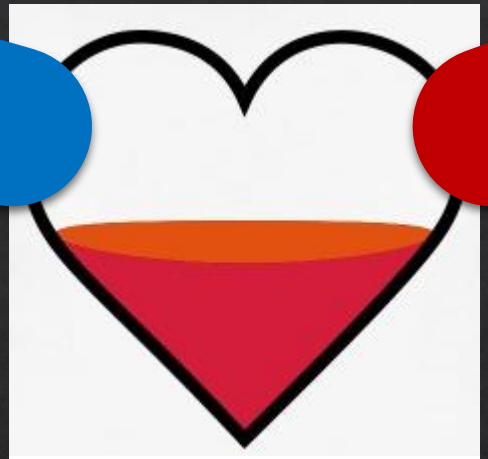
[d] *Lahey Hospital and Medical Center, Burlington, MA*
[e] *Vanderbilt University Medical Center, Nashville, TN*

Spot UNa < 50 mmol/L?

Table 2: Studies to date that have investigated urinary sodium (U_{Na}) measurements as a predictor of clinical outcomes and natriuretic responsiveness

Study	Time point of measurement of urine sample	N	Measurements	Predictive value/outcome
Singh, et al 2014	Spot sample at steady state during continuous loop diuretic infusion	52	U_{Na} < 50 mmol U_{Na}: urine furosemide ratio < 2 mmol/mg	Less weight loss and decreased net fluid output over 24 hours Above, and worse clinical outcomes
Ferreira, et al 2016	Spot sample on day 3 of therapy with loop diuretic +/- spironolactone	100	U_{Na} > 60 mmol/L and U_{Na}: urine potassium >	Fewer adverse clinical outcomes
Testani, et al 2016	1-2 hours after loop diuretic administration	50	U_{Na} < 60 mmol/L cumulative in 6 hours b equation	Worse cumulative 6-hour sodium output/poor natriuretic response
Luk, et al 2018	1st urine void after loop diuretic administration	103	U_{Na} < 60 mmol/L	More adverse clinical outcomes
Brinkley, et al 2018	1st urine void after loop diuretic administration	176	U_{Na} < 60 mmol/L	Greater rates of 30 day hospitalization or emergency room visit
Collins, et al 2018	1 hour after loop diuretic administration	61	U_{Na} < 35 mEq/L	Worsening heart failure

Gupta 2019 Current HF Reports *in press*



VASODILATORS

Nitrates for acute heart failure syndromes (Review)

Wakai A, McCabe A, Kidney R, Brooks SC, Seupaul RA, Diercks DB, Salter N, Fermann GJ, Pospisil C

THE COCHRANE COLLABORATION®

- **Objectives:** To quantify the effect of different nitrate preparations (isosorbide dinitrate and nitroglycerin) and the effect of route of administration of nitrates on clinical outcome, and to evaluate the safety and tolerability of nitrates in the management of AHF.

- **Selection criteria:** Randomised controlled trials comparing nitrates with alternative interventions in the management of AHF in adults aged 18 and over.

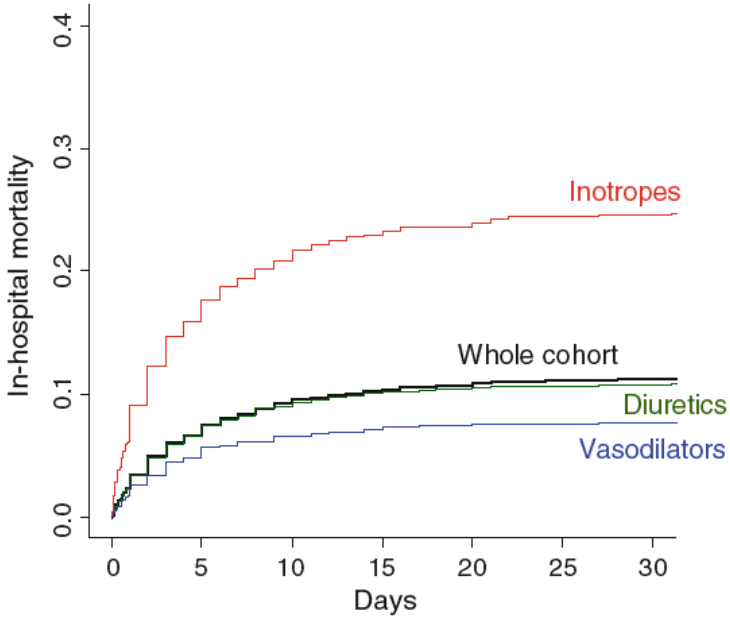
Results

- 4 studies (n=634)
- Two included ONLY post-MI
- One excluded MI
- One included both

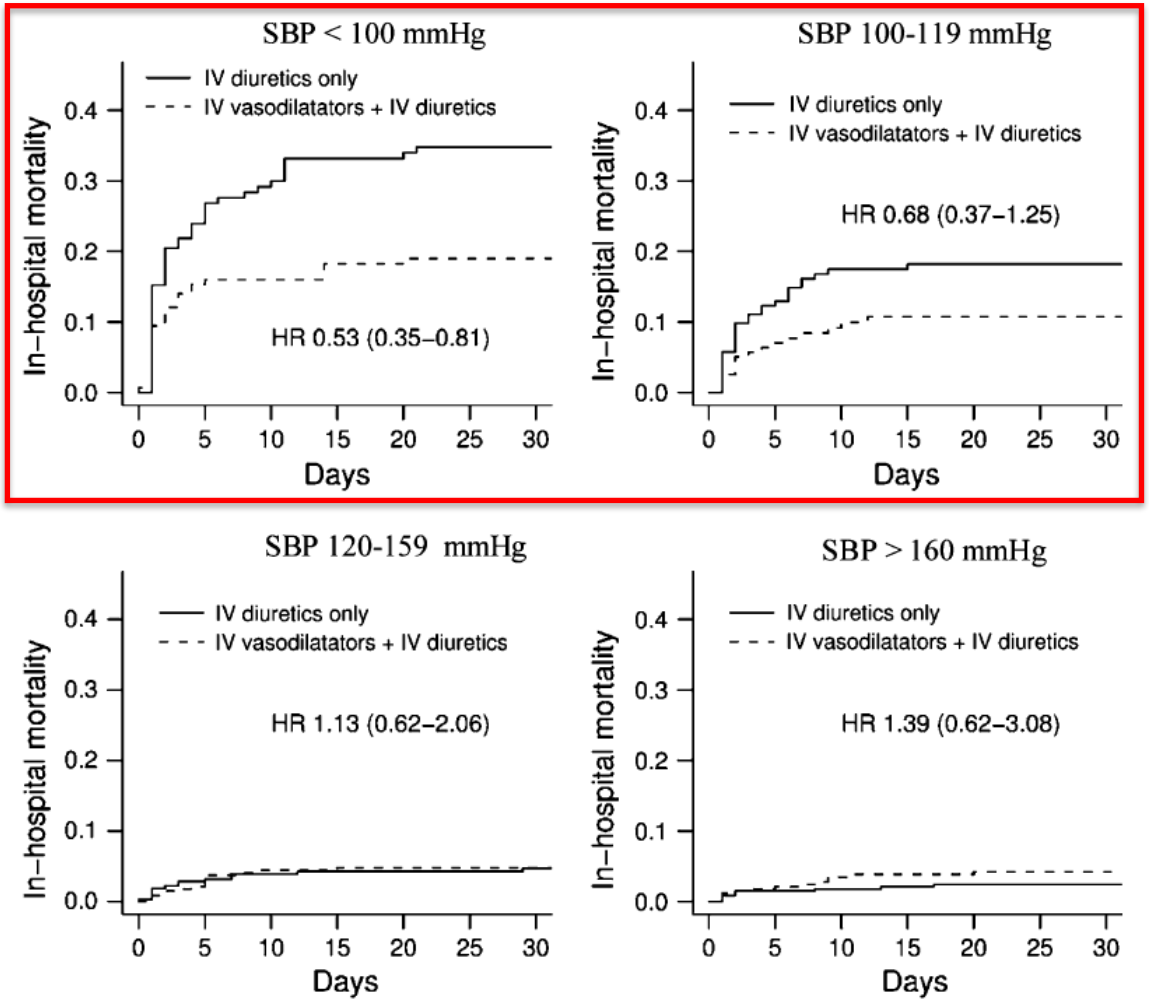
NO Difference

BE AGGRESSIVE

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



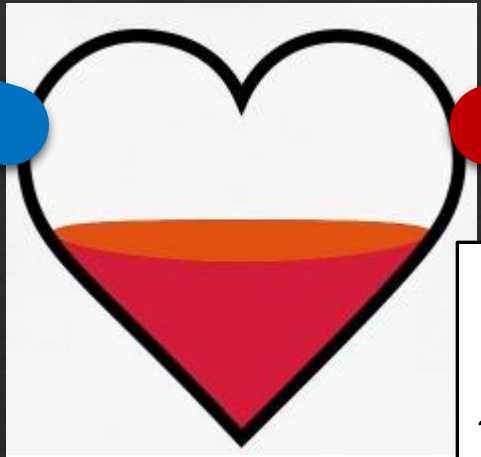
Mebazaa et al. Intensive Care Med 2011;37:290–301.

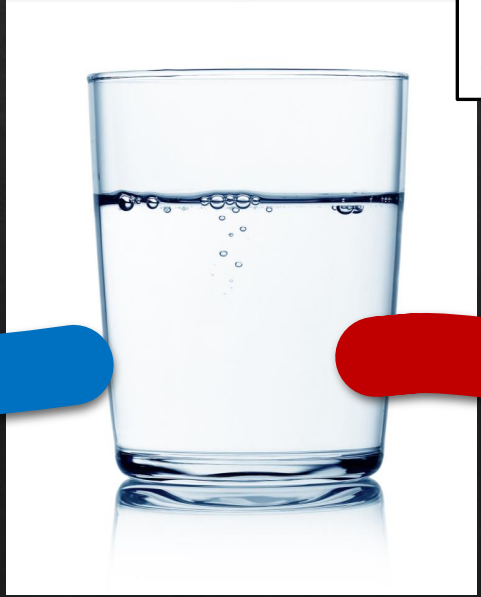


Mebazaa et al. Intensive Care Med 2011;37:290–301.

NIV, PPV, CPAP, BiPAP

Use it!





1. Pump
2. Volume
3. Tone

An approach …

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EMERGENCY MEDICINE

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