Pathophysiology of Acute Heart Failure and Cardiorenal Interactions

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Acute Decompensated Heart Failure (ADHF)

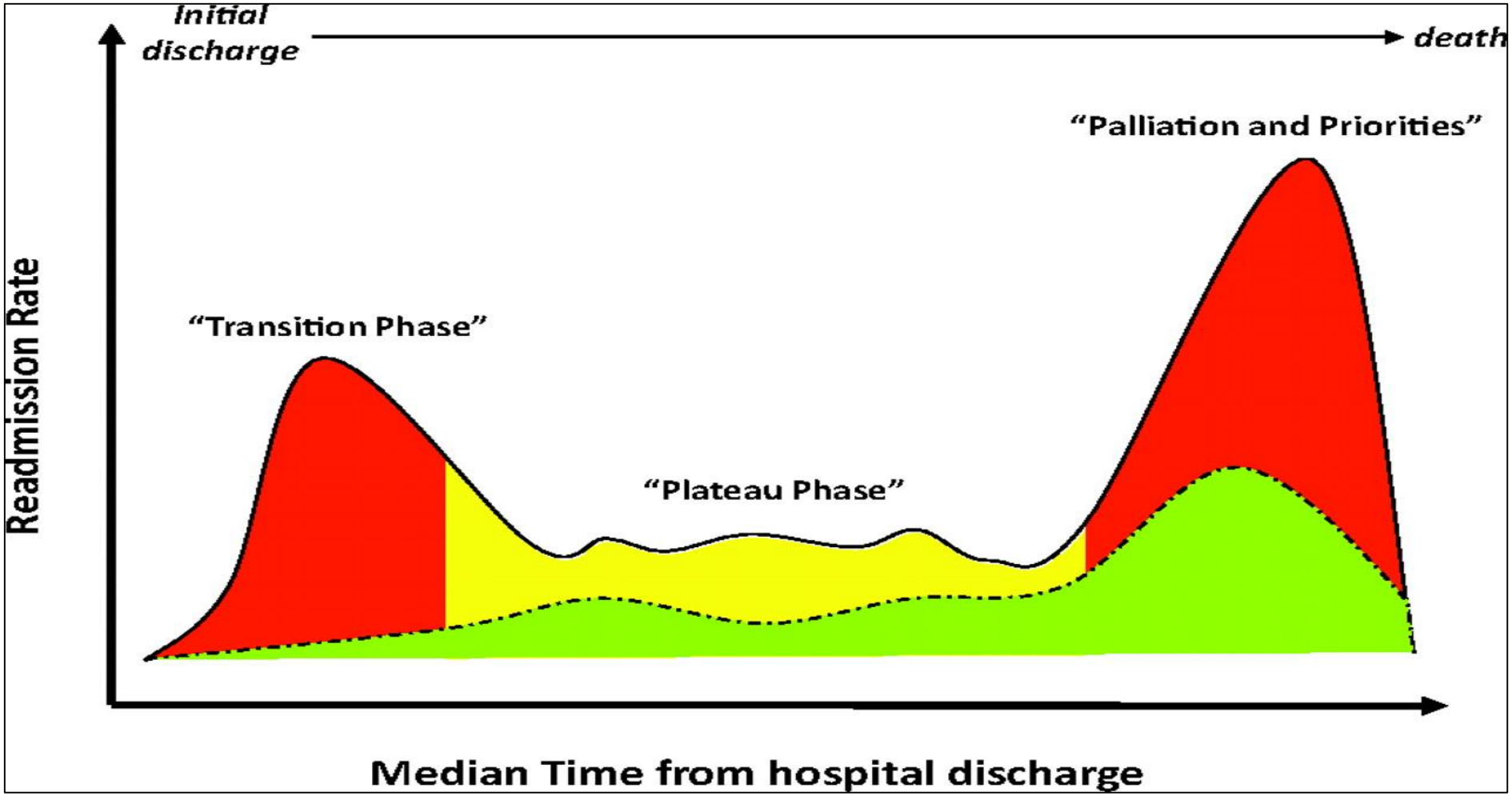
A syndrome (generally) characterized by the acute onset of volume overload and symptoms of congestion in the setting of cardiac dysfunction.

Epidemiology of Acute Heart Failure Syndromes

Hospitalizations Due to Heart Failure Continue to Rise

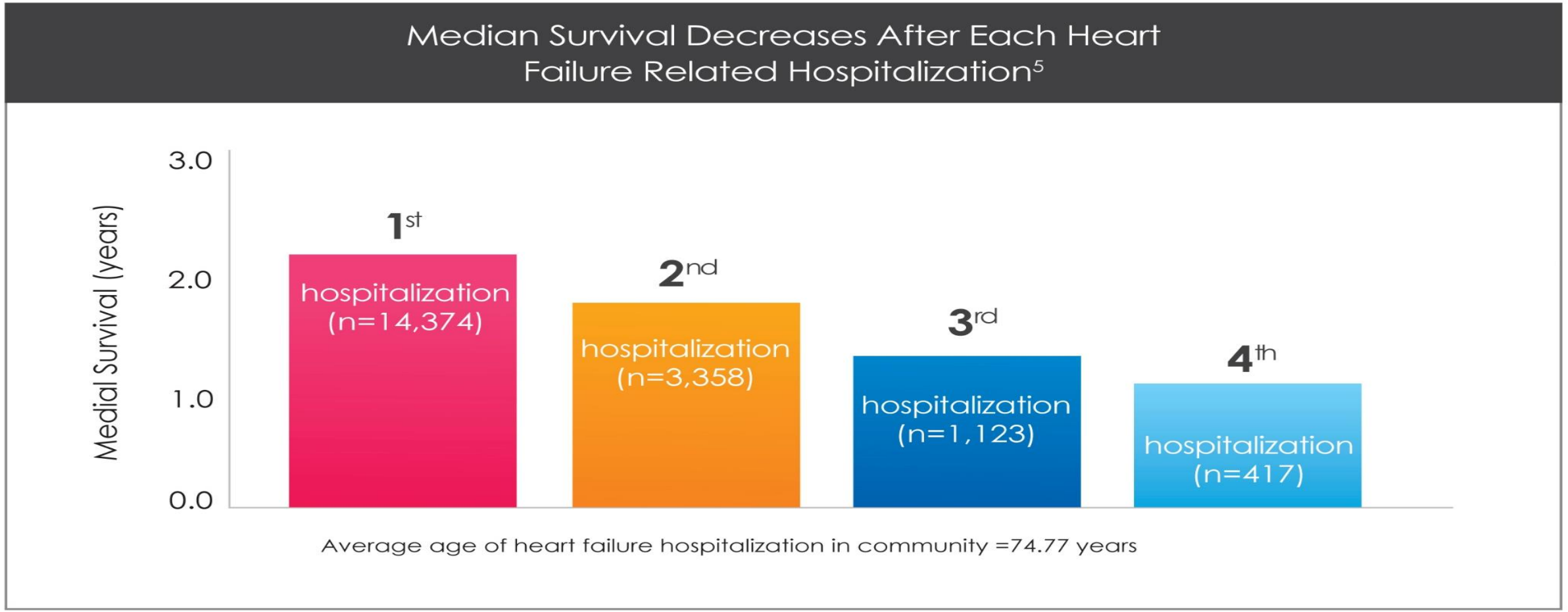
- Heart failure is a progressive disease.
- Incidence of heart failure is rising.
  - Population is aging.
  - Improved survival with acute myocardial infarction.
- Heart failure not managed appropriately during hospitalization and after discharge.
- Patients do not adhere to diet and drugs.

Three-phase terrain of lifetime readmission risk after heart failure hospitalization.



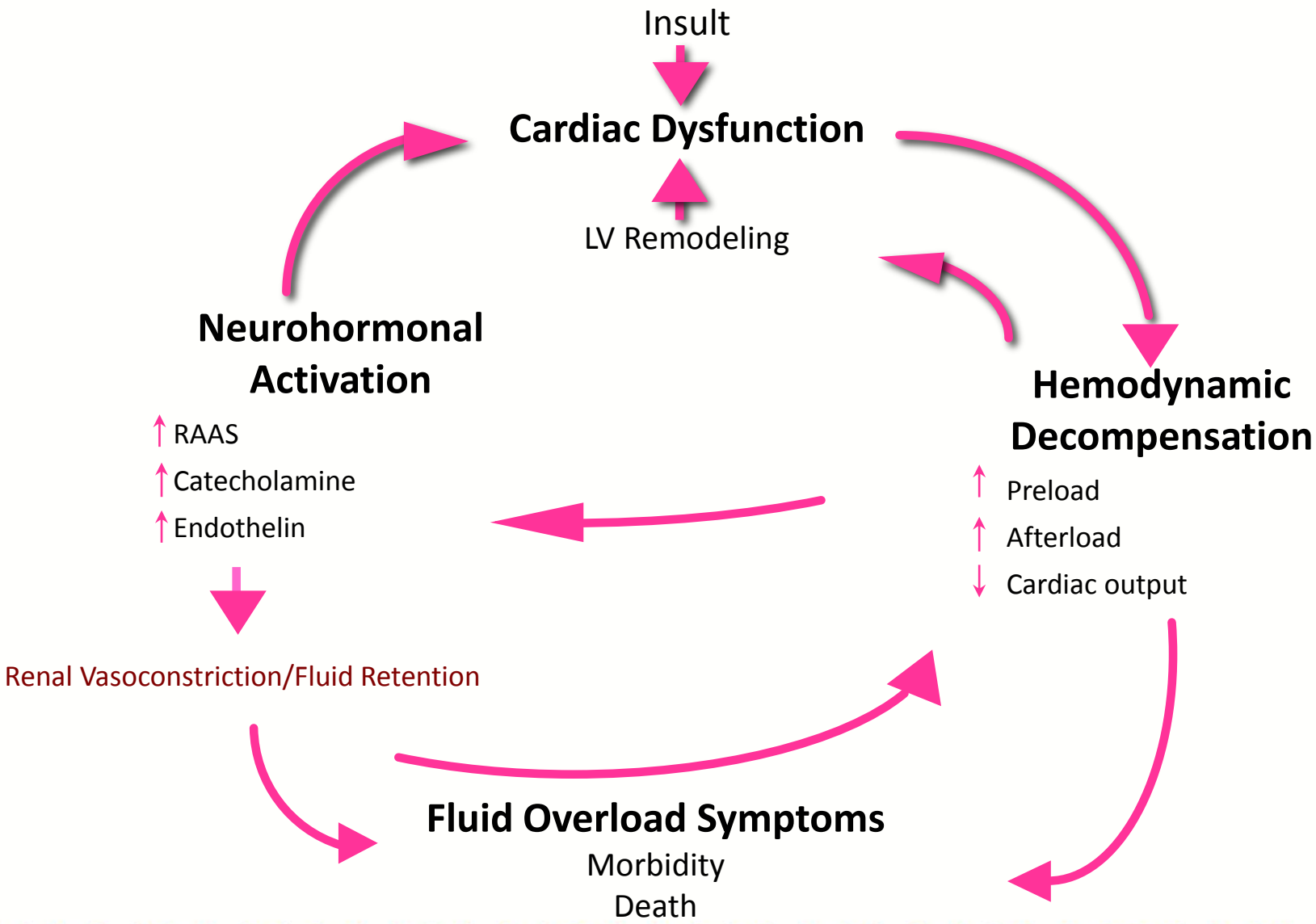
Akshay S. Desai, and Lynne W. Stevenson Circulation. 2012;126:501-506

Hospitalizations



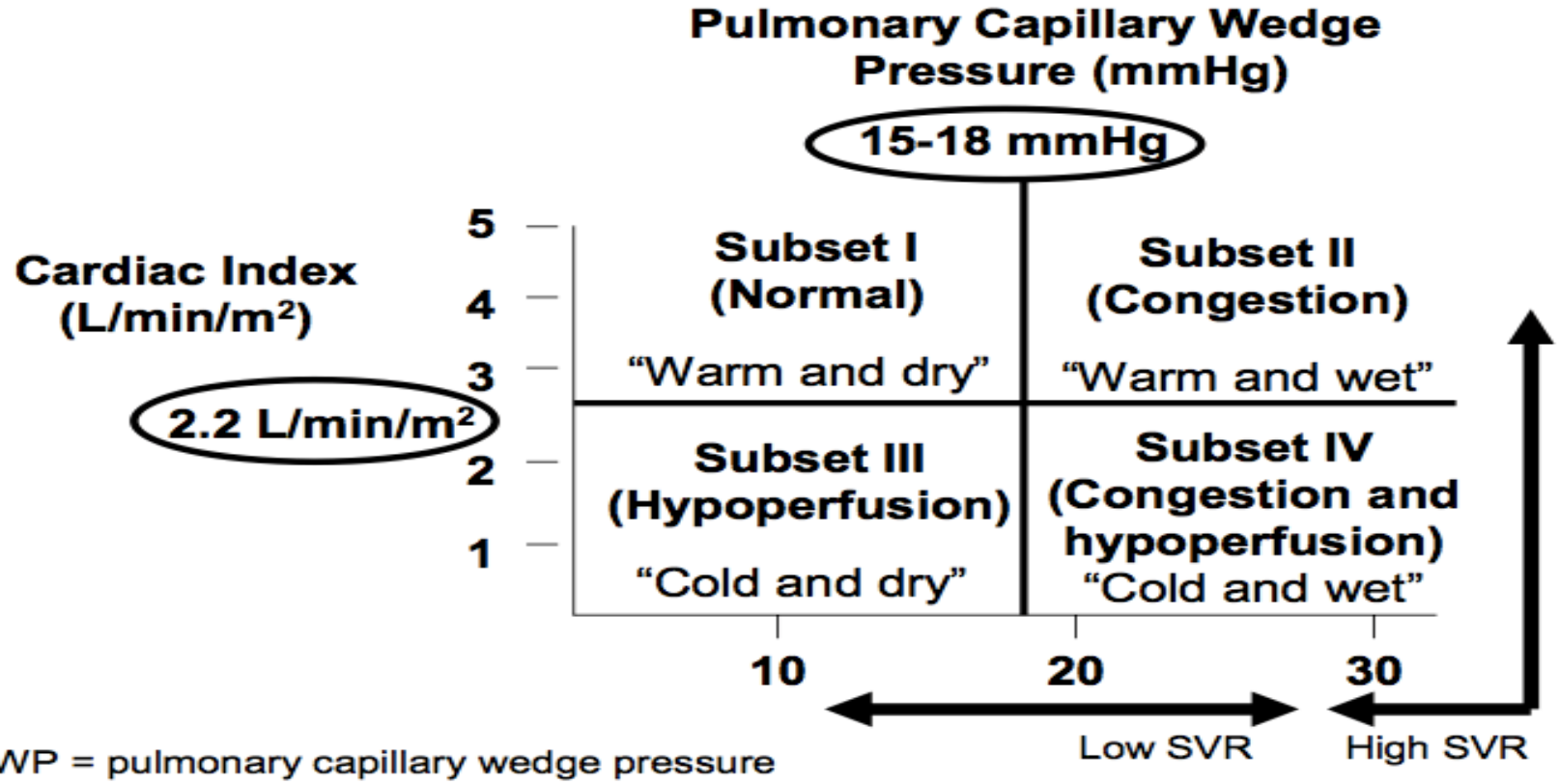
[5] Miller L, Guglin M. Patient selection for ventricular assist devices: A moving target. J Am Coll Cardiol. 2013;61:1209-21.

Important Concepts in ADHF Pathophysiology



Colucci WS, Braunwald E. In: Braunwald E, ed. *Heart Disease: A Textbook of Cardiovascular Medicine*. 5th ed. Philadelphia, PA: W.B. Saunders; 1997:394

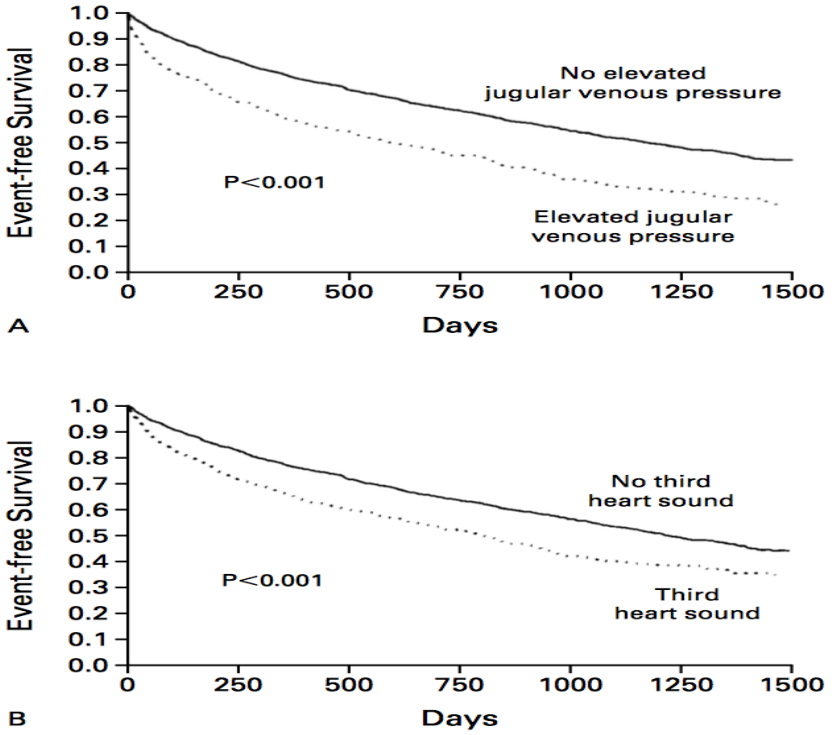
Clinical Presentation



PCWP = pulmonary capillary wedge pressure
CI = cardiac index
SVR = systemic vascular resistance

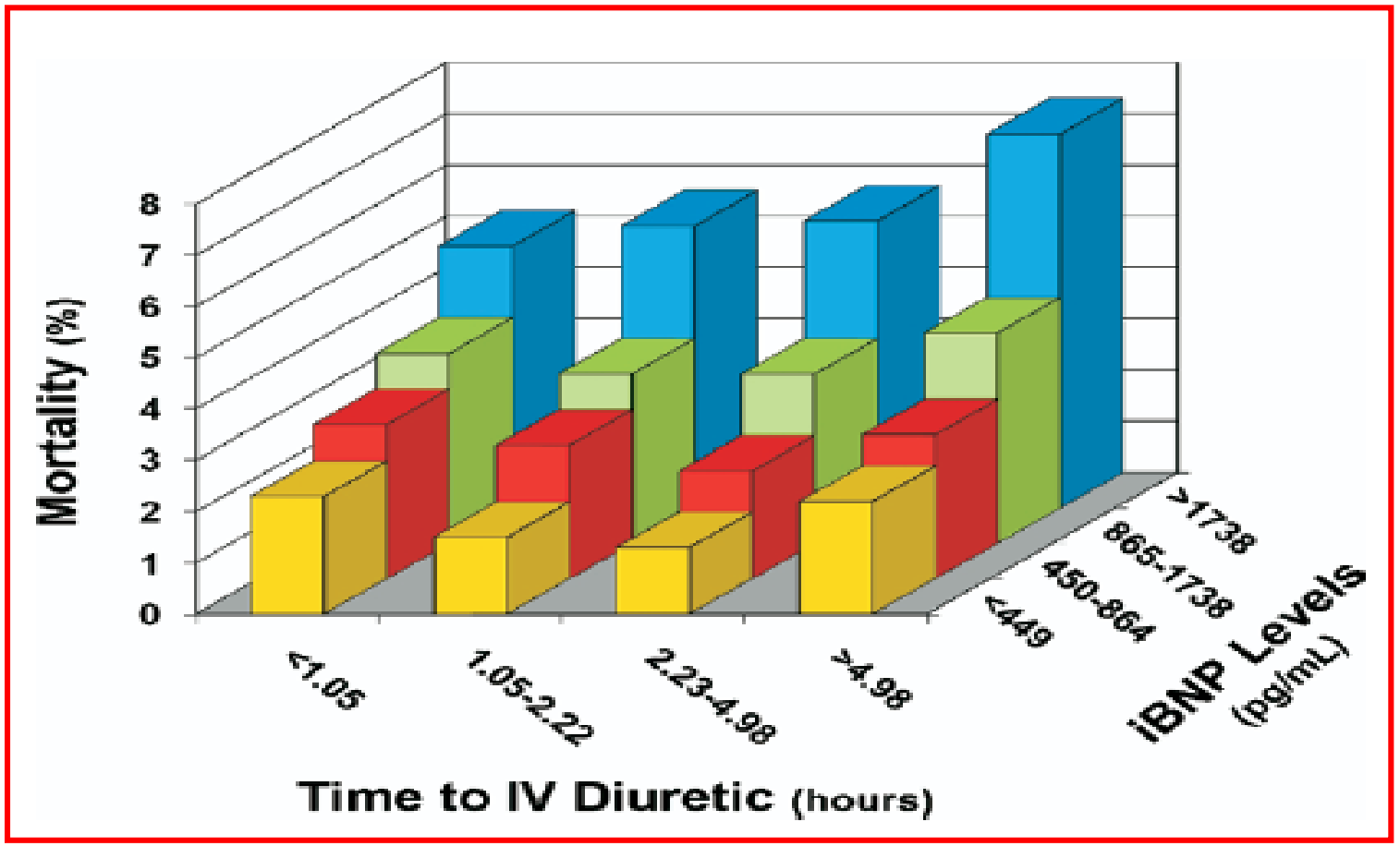
Adapted from Nohria A et al. *JAMA*. 2002; 287:628-40.

Event-free Survival According to the Presence or Absence of Elevated JVP and S3



Drazner M et al. N Engl J Med 2001;345:574-581

Hospital Mortality, Time toTreatment, and BNP Level

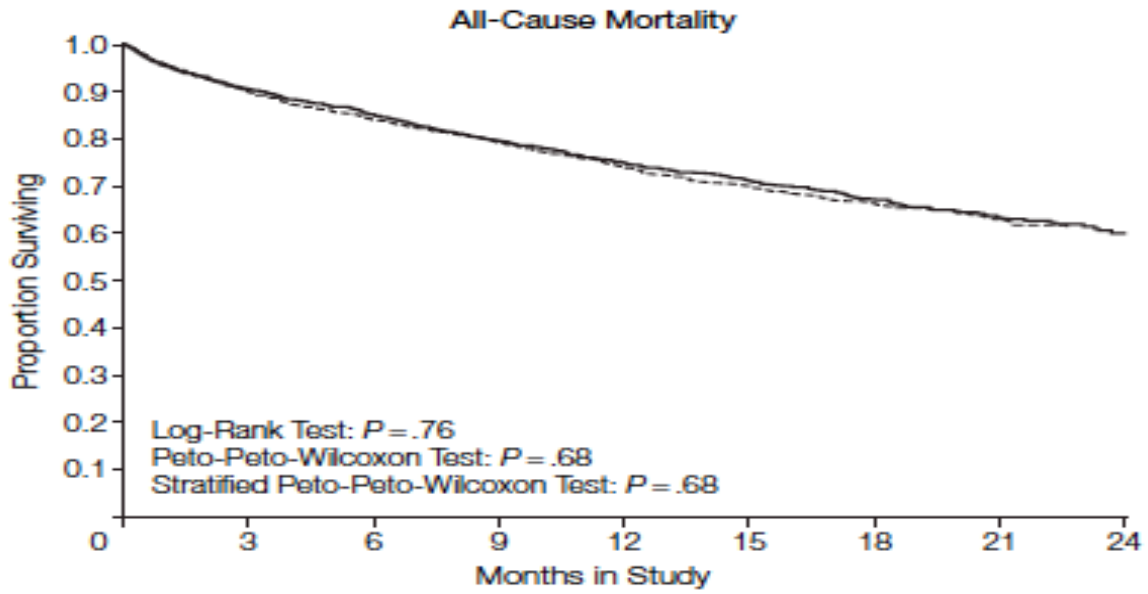


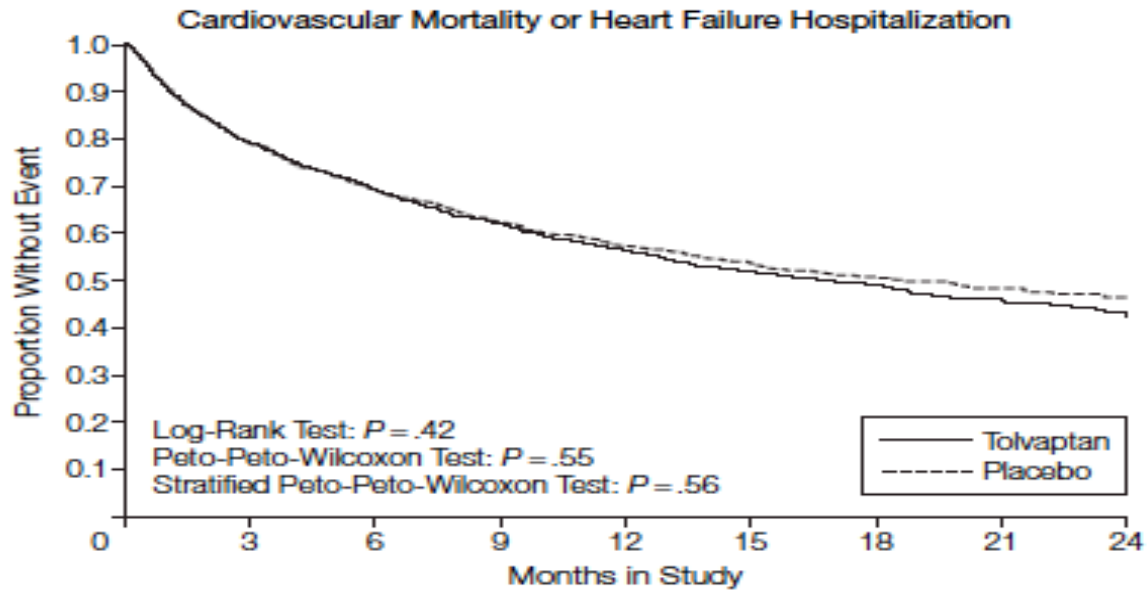
(J Am Coll Cardiol 2008;52:534–40)

Efficacy of Vasopressin Antagonism in Heart Failure: Outcome Study with Tolvaptan (EVEREST) trial.

Konstam, M. A. et al. JAMA 2007;297:1319-1331.

- More than 4,000 patients with ADHF, NYHA class III – IV, randomized to tolvaptan 30 mg once daily or placebo for at least 60 days.

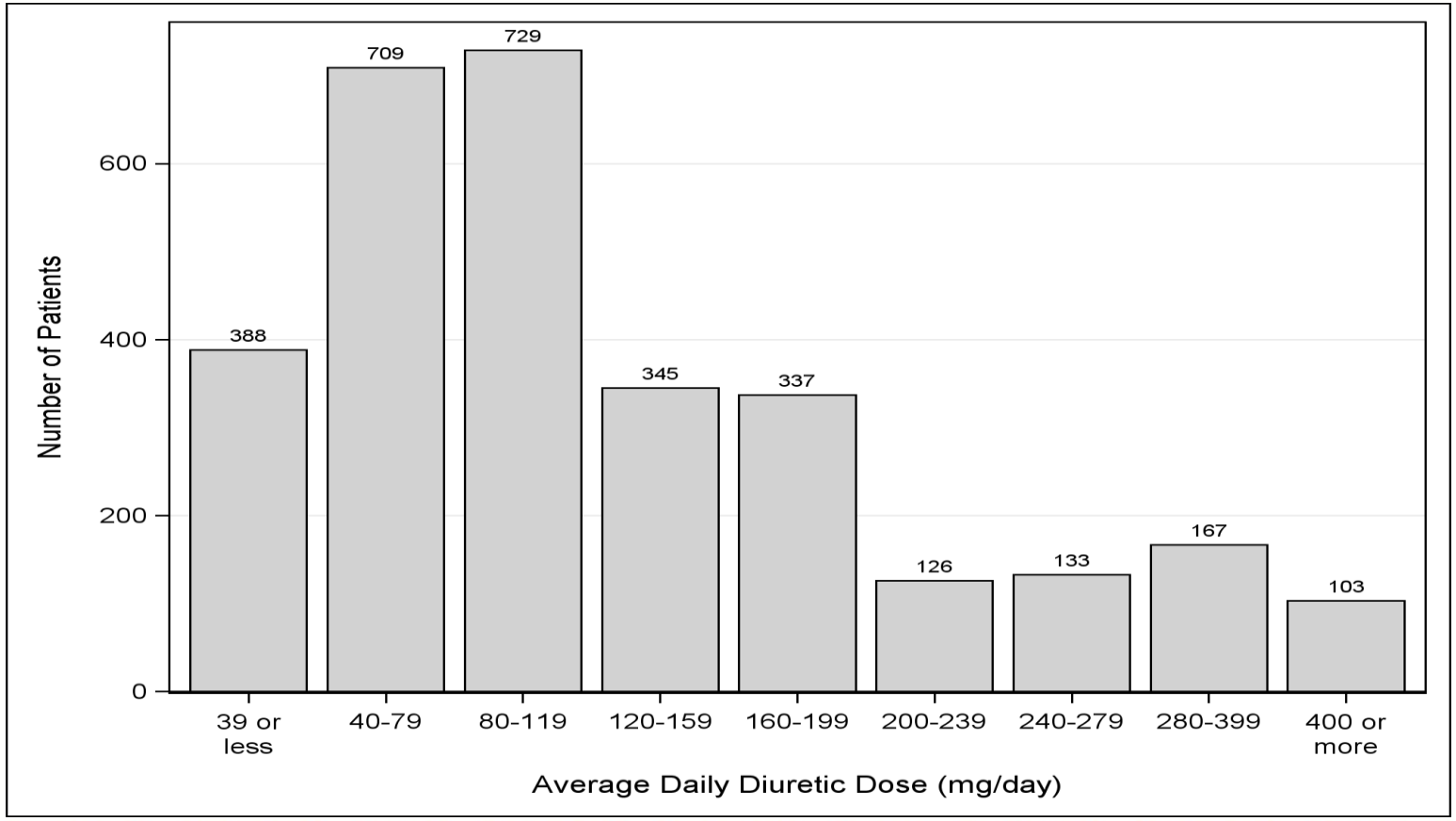




No. at Risk									
Tolvaptan	2072	1812	1446	1112	859	589	404	239	97
Placebo	2061	1781	1440	1109	840	580	400	233	95

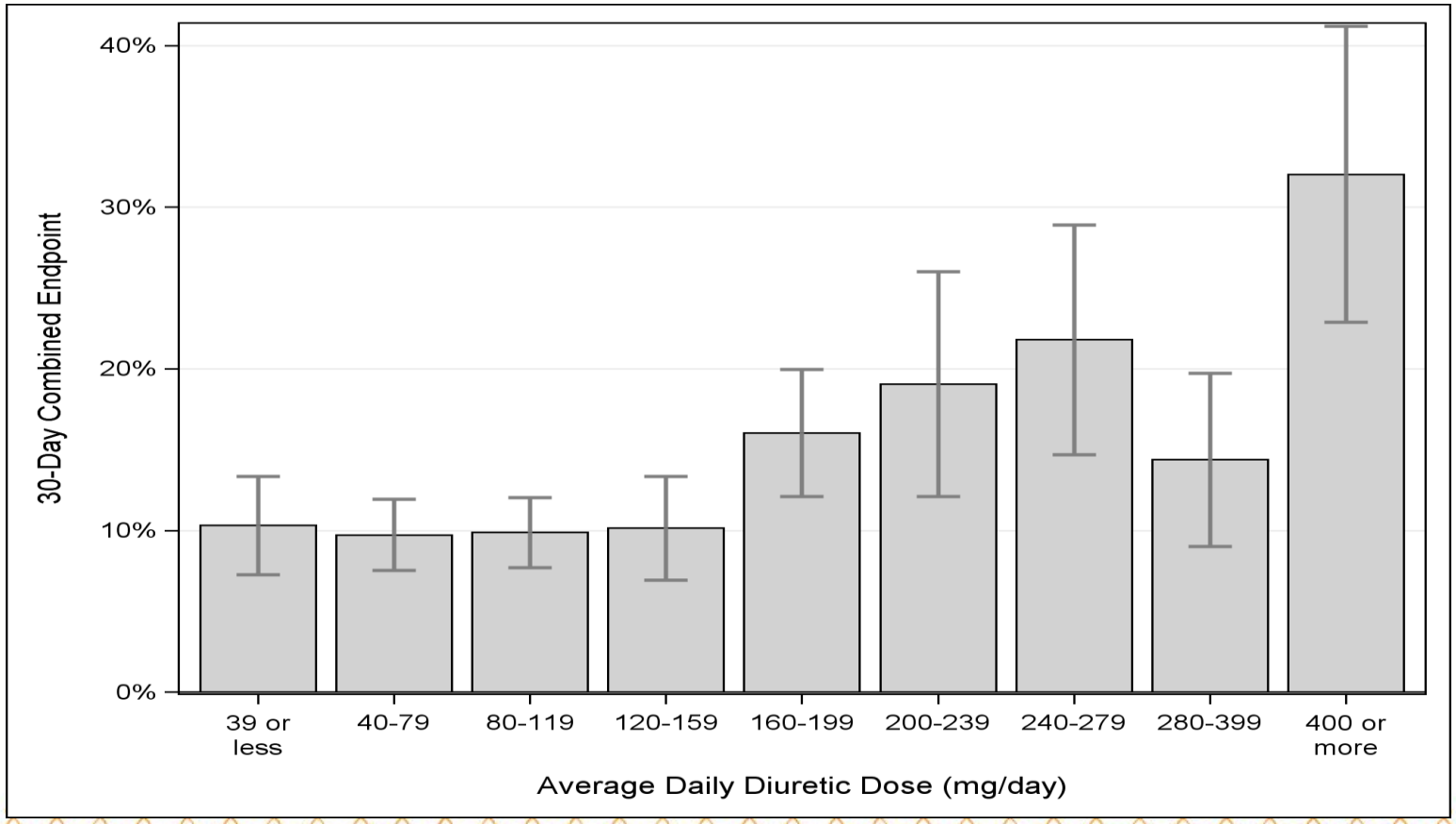
2072	1562	1446	834	607	396	271	149	58
2061	1532	1137	819	597	385	255	143	55

Average Loop Diuretic Dose in the EVEREST Study



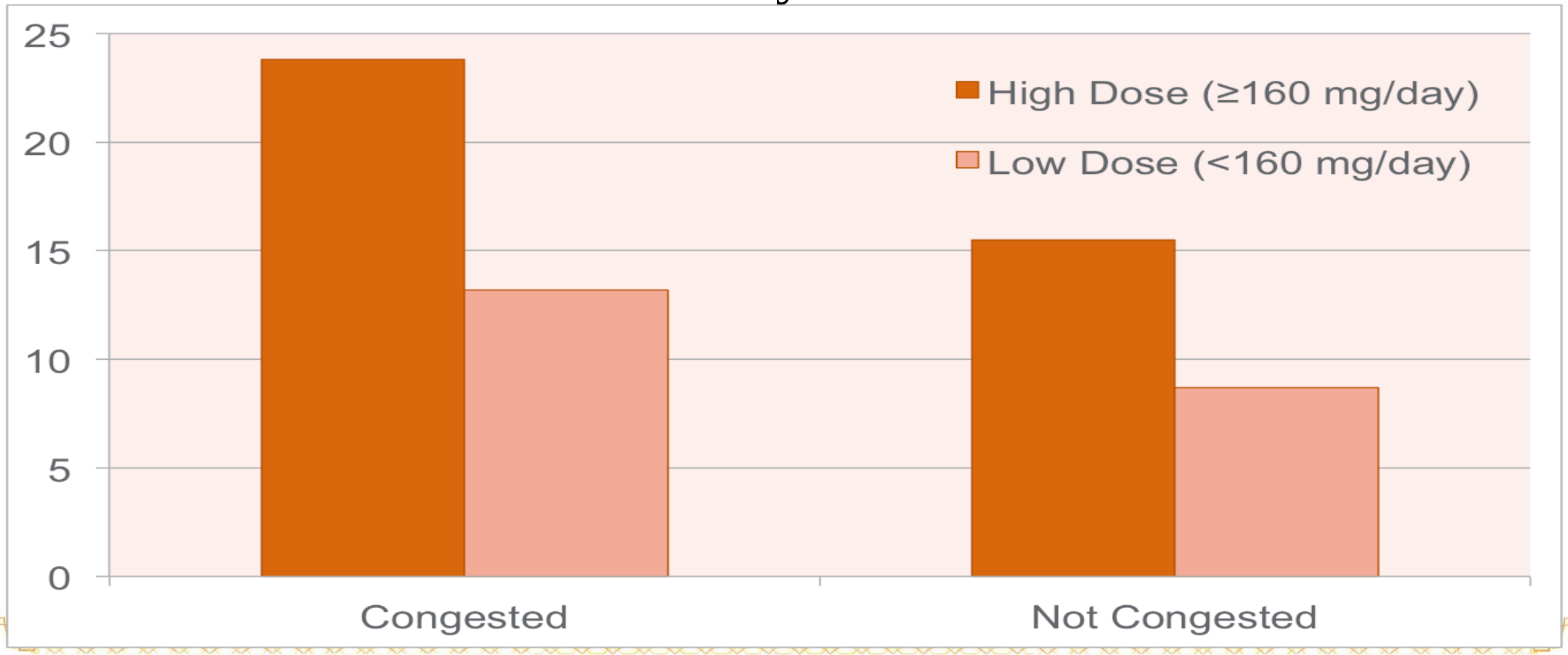
Mecklai et al, JACC Heart Fail. 2016 Jul;4(7):580-8.

Loop Diuretic Dose and Adverse Outcomes in ADHF: EVEREST Study



Mecklai et al, JACC Heart Fail. 2016 Jul;4(7):580-8.

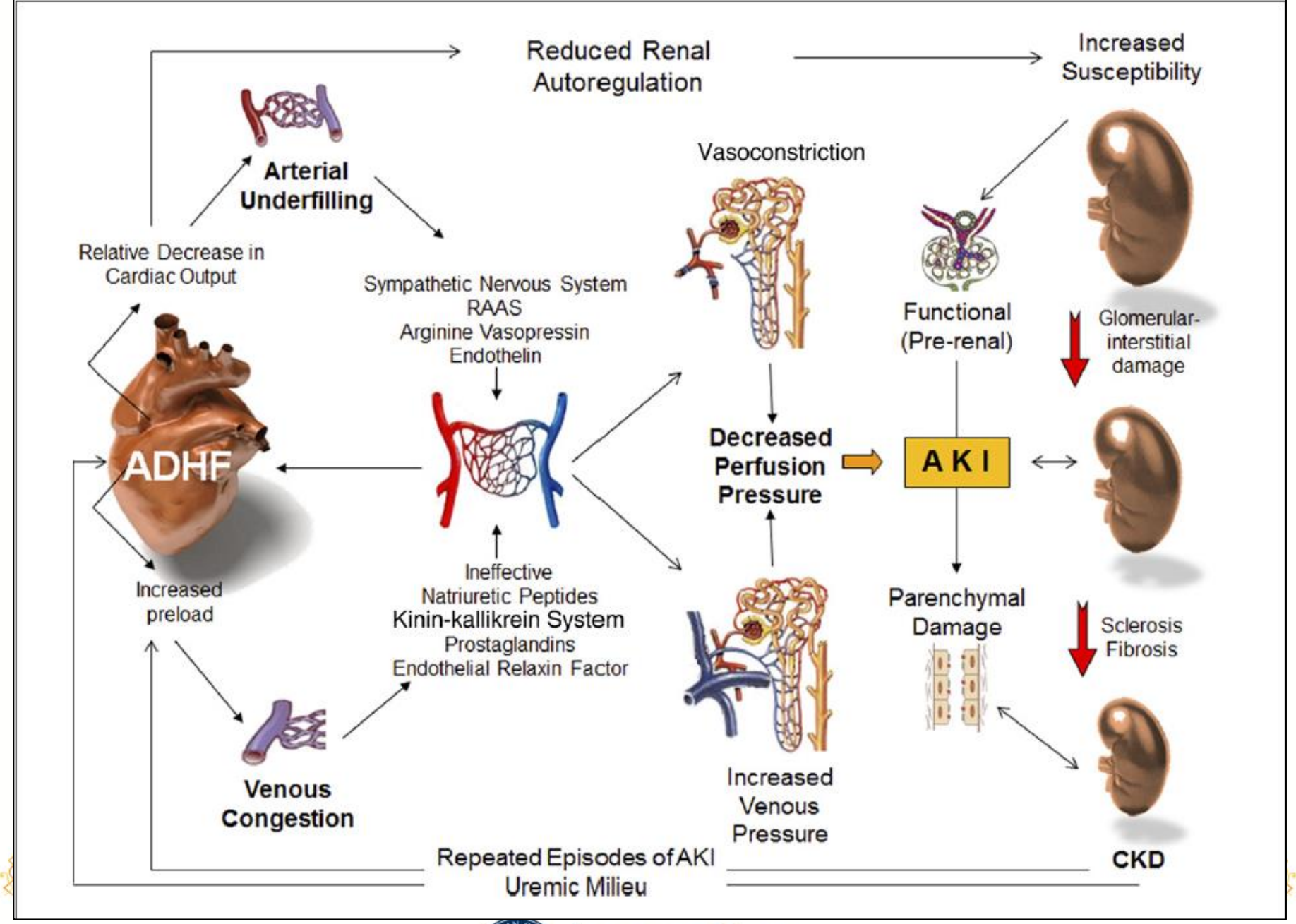
30-Day Outcomes by Discharge Congestion Status and Diuretic Dose: EVEREST Study



Mecklai et al, JACC Heart Fail. 2016 Jul;4(7):580-8.

The concept of Cardiorenal syndrome (CRS)- Type 1

- Worsening of renal function in the setting of ADHF management. True CRS (associated with poor prognosis and worse survival) is manifested by:
- Serum Cr worse by ≥ 25% or 0.3 mg/dL.
- Persistent clinical congestion.
- Persistent worsening of renal function through 30 days.
- When accompanied by hemoconcentration, it is an indication of aggressive diuresis and is associated with better survival.
- "Cardiorenal rescue" is improving renal function in the setting of decongestion.



J Am Coll Cardiol 2012;60:1031–42

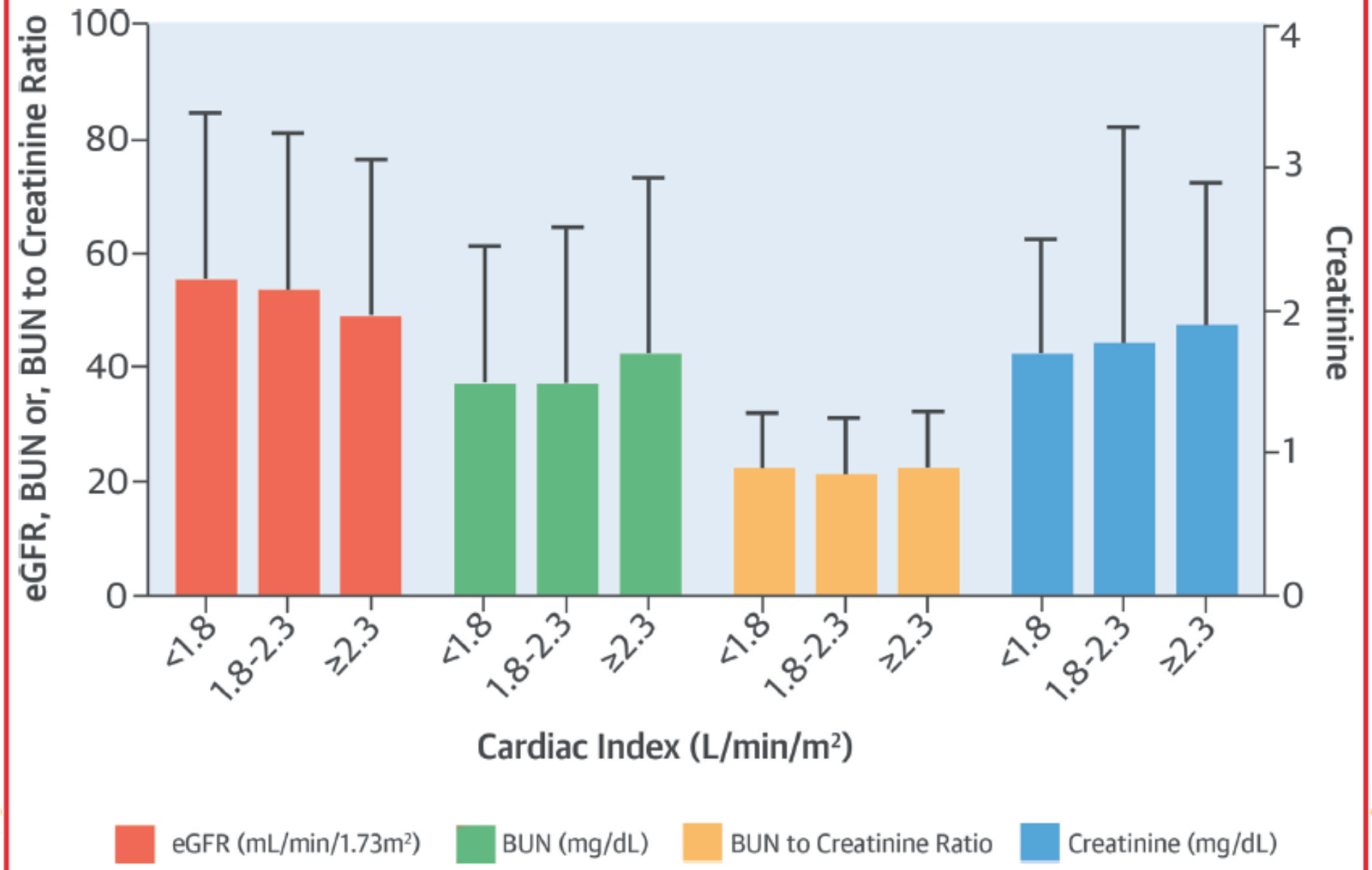
Cardiac Index?

Reduced Cardiac Index Is Not the Dominant Driver of Renal Dysfunction in Heart Failure

Jennifer S. Hanberg, BA,[a] Krishna Sury, MD,[b] F. Perry Wilson, MD, MSCE,[a,b,c] Meredith A. Brisco, MD, MSCE,
Tariq Ahmad, MD, MPH,[b] Jozine M. ter Maaten, MD,[e] J. Samuel Broughton, BS,[a] Mahlet Assefa, BS,[a]
W.H. Wilson Tang, MD,[f] Chirag R. Parikh, MD, PhD,[a,b,c] Jeffrey M. Testani, MD, MTR[a,b]

JACC 2016; 67 (19): 2199-208

CENTRAL ILLUSTRATION CI and Renal Dysfunction in HF



Hanberg, J.S. et al. J Am Coll Cardiol. 2016;67(19):2199-208.

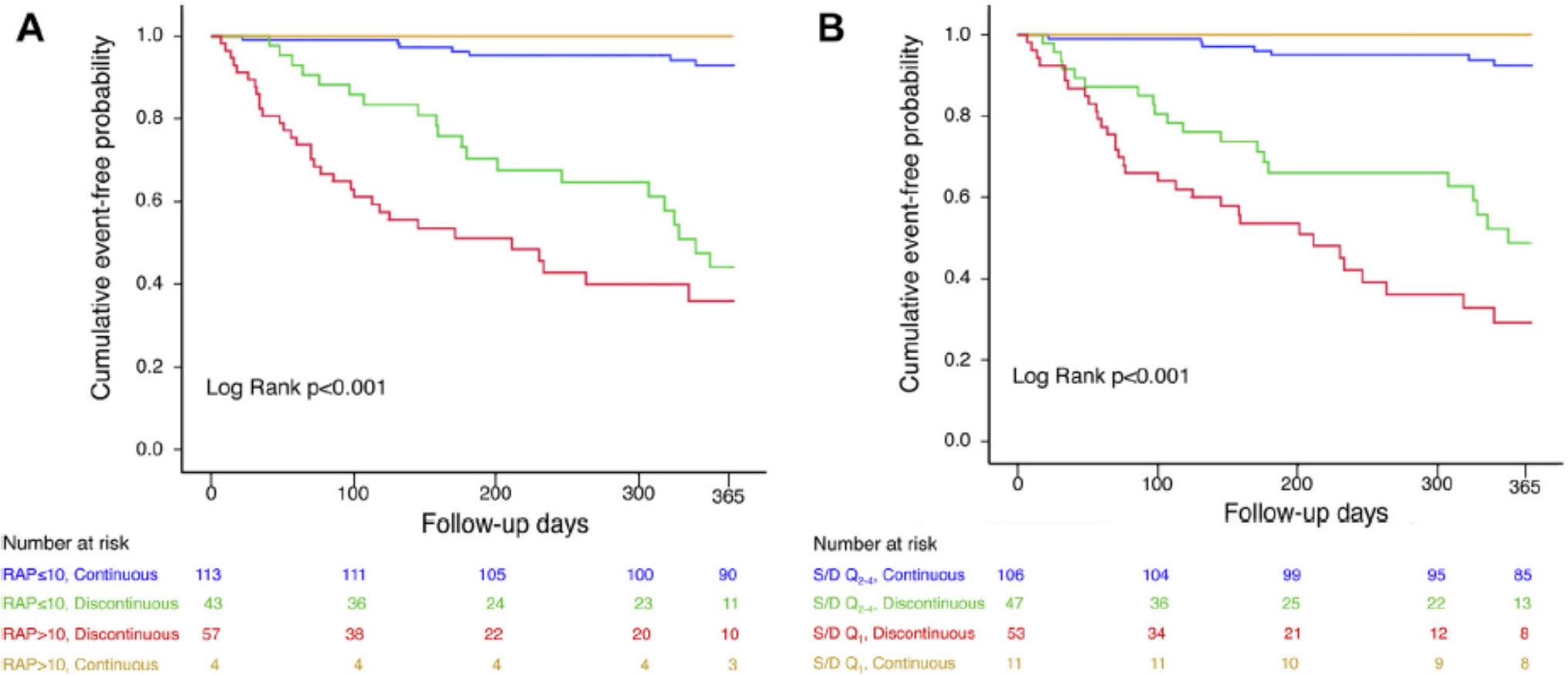
Clinical Implications of Intrarenal Hemodynamic Evaluation by Doppler Ultrasonography in Heart Failure

Noriko Iida, BA,[a] Yoshihiro Seo, MD,[b] Seika Sai, MD,[b] Tomoko Machino-Ohtsuka, MD,[b] Masayoshi Yamamoto, MD,[b]

TABLE 1 Clinical Characteristics and Echocardiographic and Intrarenal Doppler Ultrasound Data

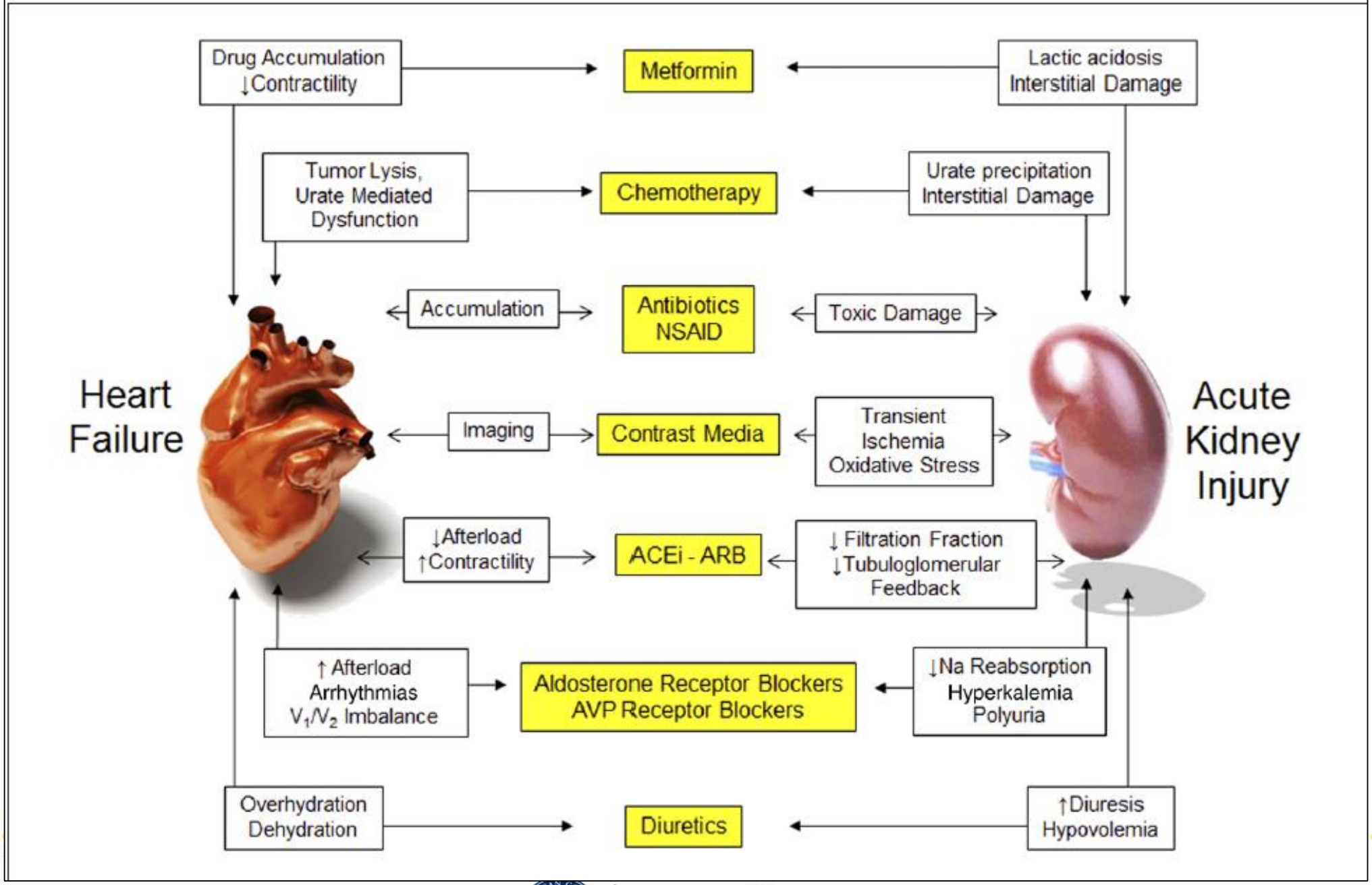
	Total (N = 217)	RI <0.70 (n = 113)	RI ≥0.70 (n = 104)	p Value	IRVF Continuous (n = 117)	Biphasic (n = 51)	Monophasic (n = 49)	p Value ANOVA
Catheterization data	n = 103	n = 57	n = 46		n = 65	n = 21	n = 17	
PCWP, mm Hg	13 ± 7.4	**11 ± 6.6**	**16 ± 7.6**	**0.003**	**11 ± 6.4**	**13 ± 6.7**	**19 ± 6.4***	**<0.001**
Mean PAP, mm Hg	26 ± 13	25 ± 13	26 ± 13	0.65	**23 ± 9.3***	**32 ± 14**	**31 ± 7.8**	**0.03**
Mean RAP, mm Hg	7.5 ± 4.7	**6.6 ± 3.9**	**8.7 ± 5.3**	**0.02**	**5.4 ± 2.5**	**9.5 ± 3.5†**	**15 ± 4.3***	**<0.001**
Cardiac index, l/min/m^2	2.8 ± 0.8	2.8 ± 0.8	2.7 ± 0.7	0.38	2.8 ± 0.8	2.9 ± 0.8	2.7 ± 0.8	0.72

FIGURE 3 Kaplan-Meier Estimate Curves of Four Groups According to IRVF and Parameters of CVP



Kaplan-Meier curves of four classifications based on the IRVF continuous and discontinuous patterns and parameters of CVP: RAP **(A)** and the Q of S/D ratio **(B)**.
CVP = central venous pressure; Q = quartile; RAP = right atrial pressure; S/D = systolic and diastolic hepatic vein flow velocities ratio.

J Am Coll Cardiol HF 2016;4:674–82



J Am Coll Cardiol 2012;60:1031–42

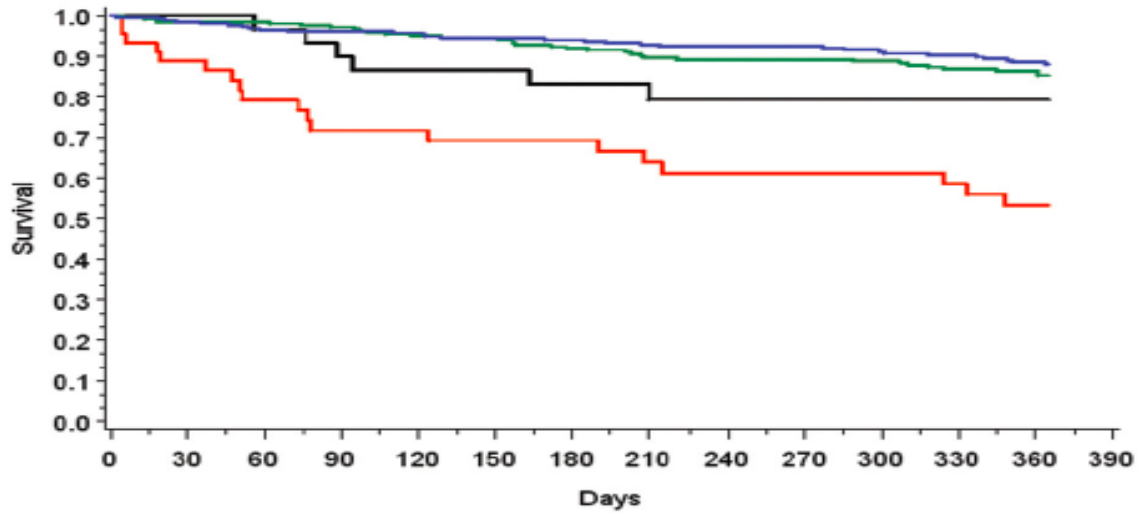
Is Worsening Renal Function an Ominous Prognostic Sign in Patients With Acute Heart Failure?

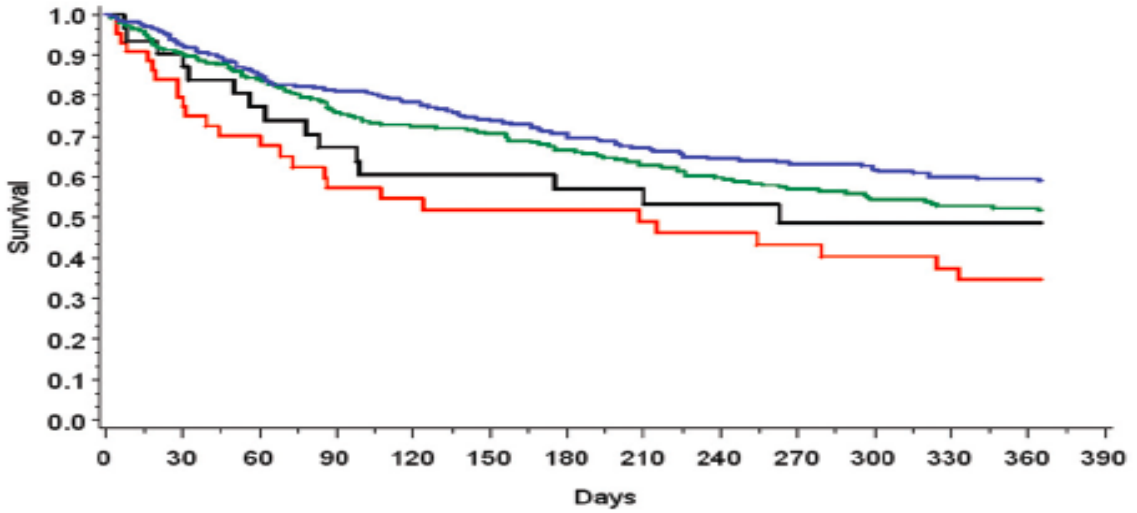
The Role of Congestion and Its Interaction With Renal Function

Marco Metra, MD; Beth Davison, PhD; Luca Bettari, MD; Hengrui Sun, MD; Christopher Edwards, BS; Valentina Lazzarini, MD; Barbara Piovanelli, MD; Valentina Carubelli, MD; Silvia Bugatti, MD; Carlo Lombardi, MD; Gad Cotter, MD; Livio Dei Cas, MD

Background—Worsening renal function (WRF), traditionally defined as an increase in serum creatinine levels ≥0.3 mg/dL, is a frequent finding in patients with acute heart failure (AHF) and has been associated with poorer outcomes in some but not all studies. We hypothesized that these discrepancies may be caused by the interaction between WRF and congestion in AHF patients.

Methods and Results—We measured serum creatinine levels on a daily basis during the hospitalization and assessed the persistence of signs of congestion at discharge in 599 consecutive patients admitted at our institute for AHF. They had a postdischarge mortality and mortality or AHF readmission rates of 13% and 43%, respectively, after 1 year. Patients





Summary

- ADHF is a difficult clinical condition with high morbidity and mortality. Long-term outcomes are worse with each admission.
- ADHF has a complex pathophysiology, primarily related to neurohormonal activation.
- Congestion is likely the main contributor in the development of CRS. It is also a critical prognostic element.
- The key approach is relieving congestion, sometimes even at the expense of mild renal dysfunction; and initiating therapies known to improve long- term outcomes.

Thank You

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