

Practical Points in Cardiorenal Syndrome

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Acute Heart Failure:
60-Day Readmission: 50%

Patients with **Inadequate Decongestion** at Discharge:

Are Known to be a Higher Risk of Admission
and Mortality

Each Readmission:
Increased (**Doubling**) Mortality!

Number of Hospitalizations	Median Survival Time (95% CI), y
1	2.4 (2.3-2.5)
2	1.4 (1.2-1.5)
3	1.0 (0.9-1.1)
4	0.6 (0.5-0.9)

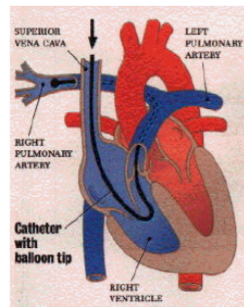
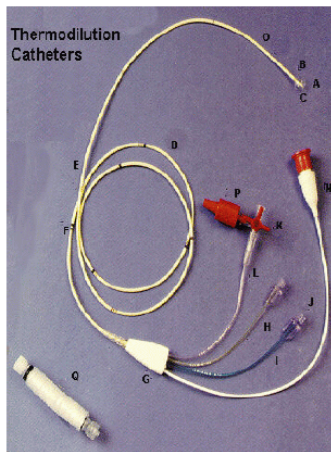
Relief of Congestion is an Appropriate Target in the Treatment of Acute HF

Diuretics

Goal
Adequate Decongestion (**Dry and Warm**)

Method to Assessment

The Swan-Ganz Catheter



“TAILORED THERAPY”

Hemodynamic goals

- PCWP <16 mmHg
- RA <8 mm Hg
- SVR <1200
- Cardiac index >2.0
- BP > 95 mmHg

Biomarker Guided Treatment

NT-proBNP, hsTnT,
Hemoconcentration, or
Transient Worsening Renal Function

Current Goals for Decongestion

Congestion Score: Based on Extent of
Orthopnea, JVP, Edema (each on scale 0-3)

Adequate Decongestion (Warm & Dry)

Resolution of Orthopnea

Trace to No Edema

JVP of < 8 cm H₂O

The Clinical Course and Prognosis Value of Congestion: Finding from EVEREST trial

	Congestion Score*			
	0	1	2	3-9
HF hospitalization	26%	35%	35%	35%
Death	19%	25%	25%	43%
HF hosp. or Death	36%	46%	46%	60%

*Discharge/Day 7 Congestion score: Based on extent of orthopnea, JVD, edema (each on scale 0-3)

Adequate Decongestion at Discharge is Associated with
a **Reduction in Readmission and Mortality**

Congestion at Rest?

NO

YES

Low Perfusion at Rest?

NO

Warm & Dry

Warm & Wet



YES

Cold & Dry

Cold & Wet

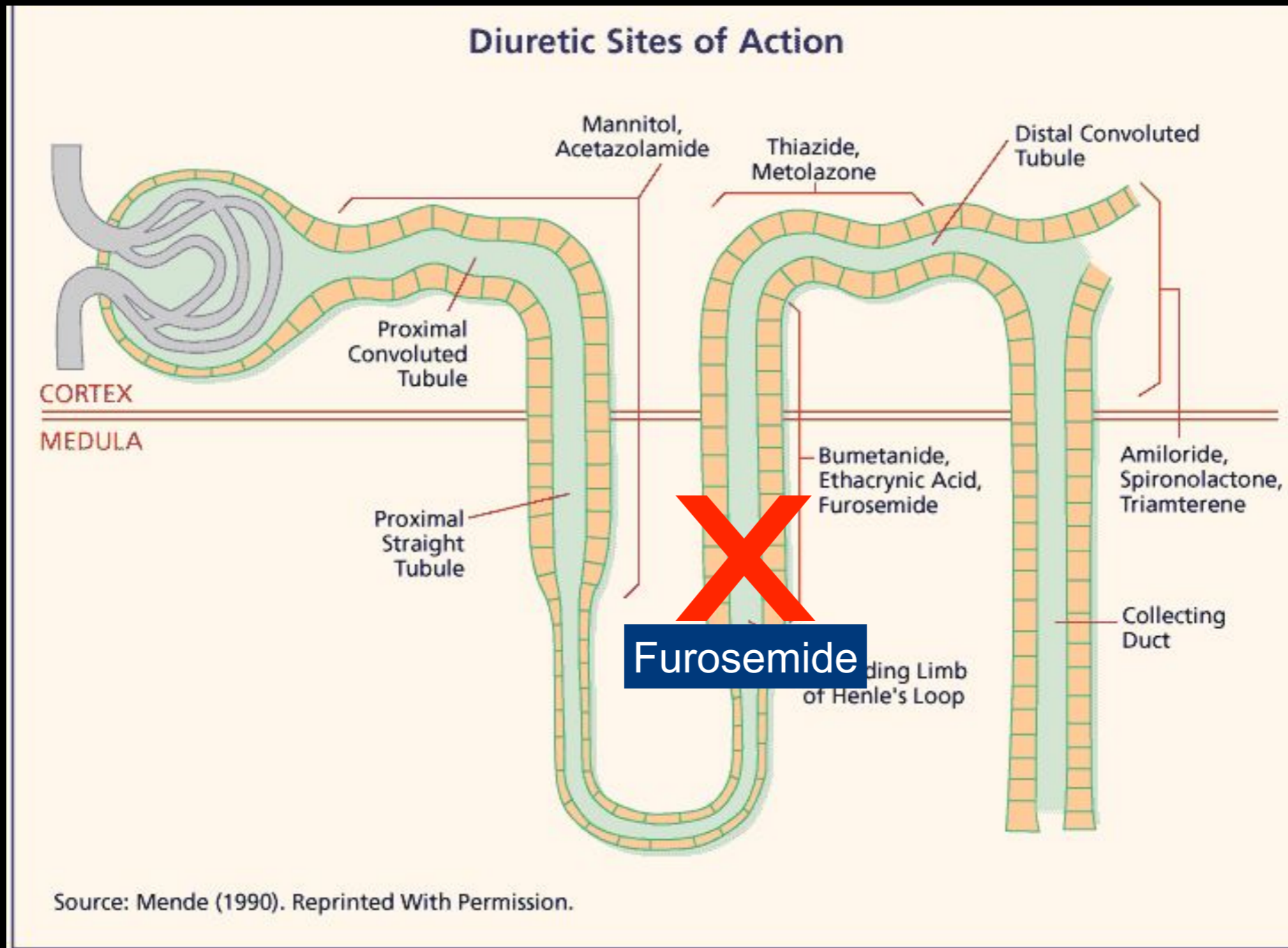
Signs/Symptoms Of Congestion

- Orthopnea/PND
- Elevated JVP
- Gut Congestion/Ascites
- Edema
- Rales

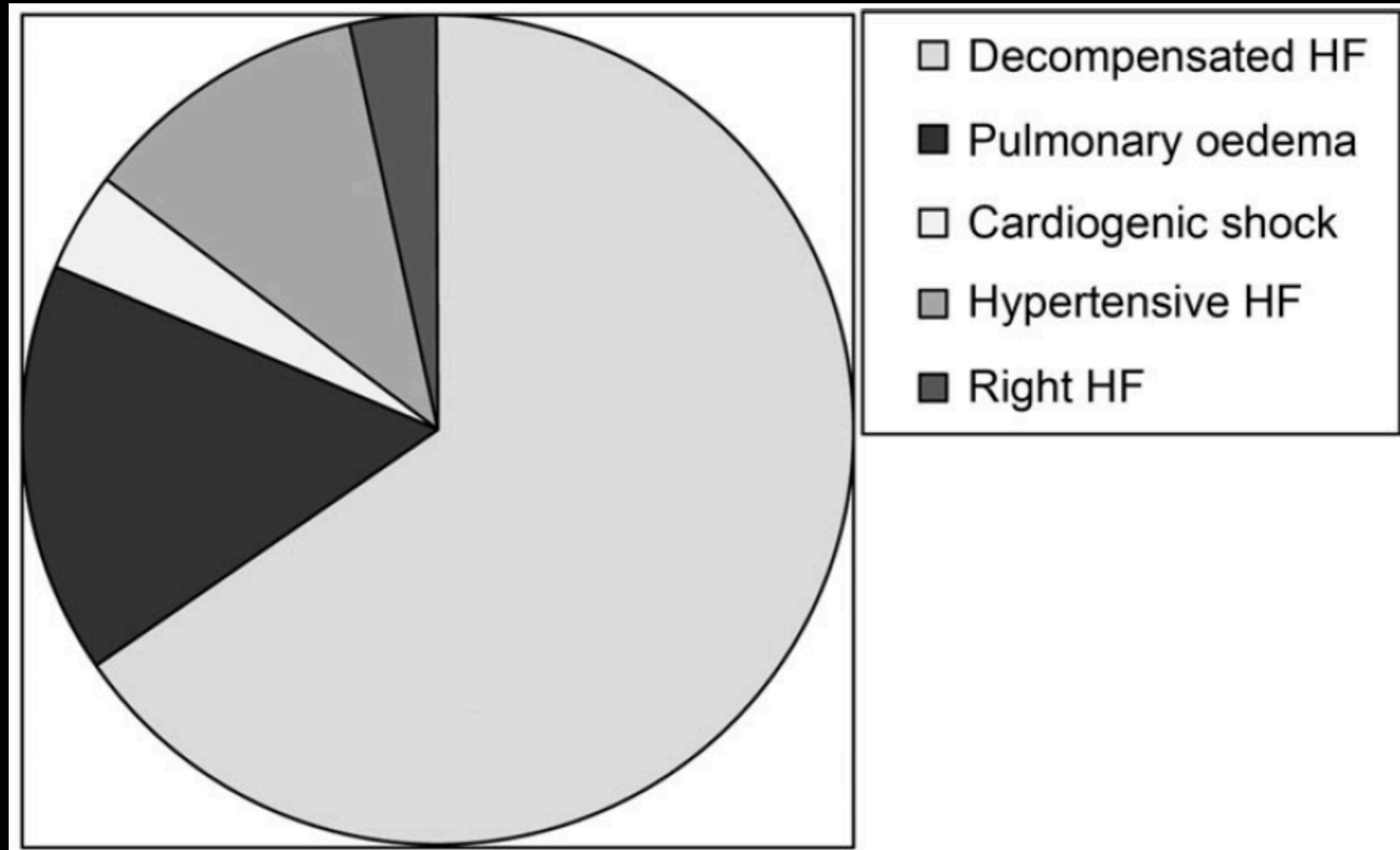
Evidence of Low Perfusion

- Cold Sweated Extremities
- Mental Confusion
- Postural Hypotension
- Oliguria

Sequential nephron blockade Increasing diuretic dosage



Congestion is the Main Cause of HF Hospitalization



Traditional Approach to Congestion in Heart Failure

Diuretics (Furosemide)

Relieve Symptom of Congestion and Edema

Diuretics in ADHF

Limitations

The Efficacy of diuretics to decrease mortality in HF
has never been established

Diuretic Resistance
Increased Mortality!

Diuretic Resistance in HF

Definition

Persistent Congestion despite adequate diuretic dose
At least 80 mg of furosemide

Cardiorenal Syndrome (CRS) Type 1: Acute CRS

Acute Heart Failure leading to
Worsening Renal Function (WRF)

Cardiorenal Syndrome (CRS) Type 2: Chronic CRS

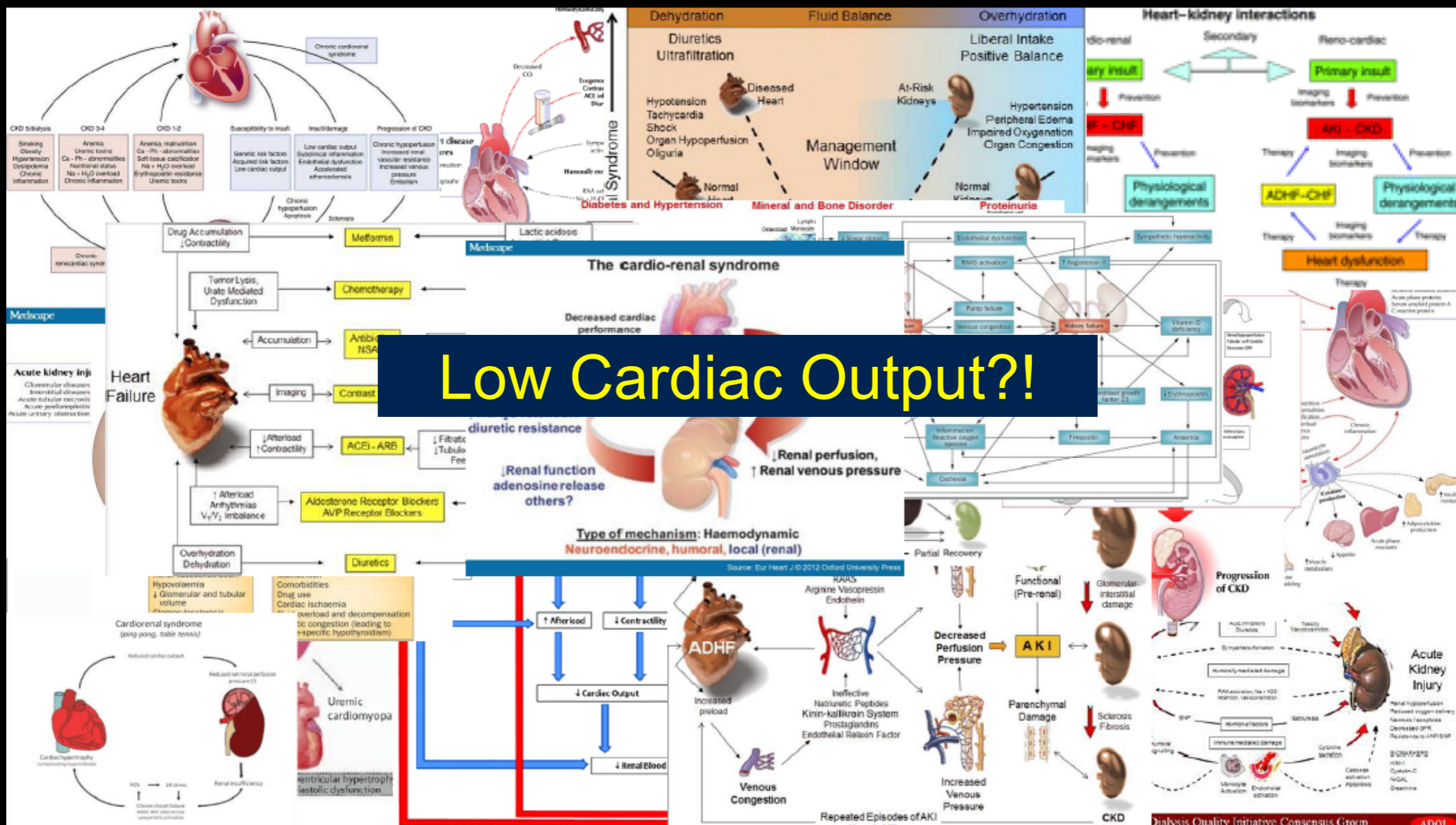
Chronic Heart Failure leading to WRF

Cardiorenal Syndrome (CRS) Type 3: Acute WRF leading to HF

Cardiorenal Syndrome (CRS) Type 4: CKD leading to HF

Cardiorenal Syndrome (CRS) Type 5: Systemic condition leading to simultaneous WRF and HF

Pathophysiology of Cardiorenal Syndrome



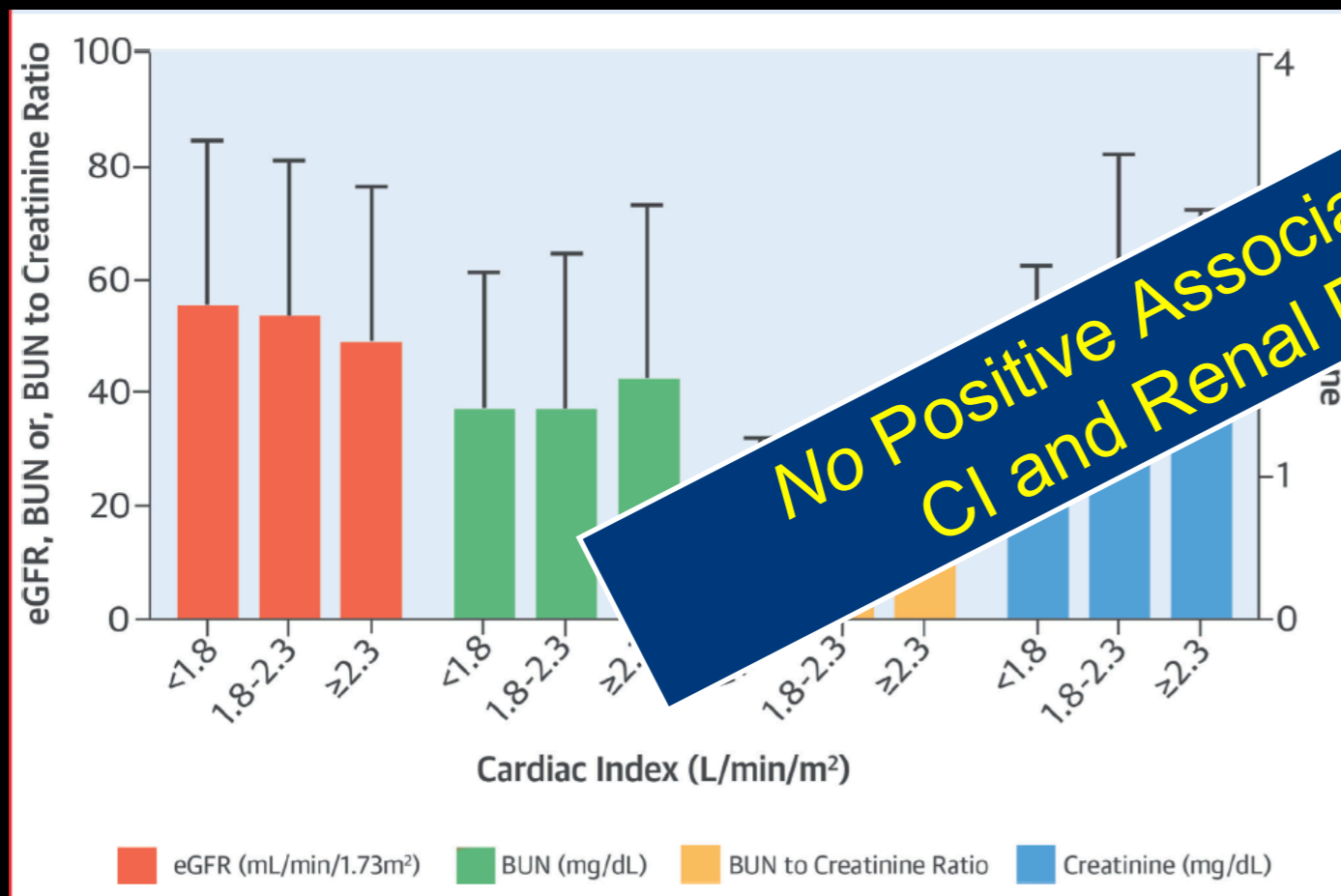
Low Cardiac Output?!

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



Comprehensive analysis of the association between CI and renal function:
575 patients from ESCAPE trial, ESCAPE registry (PAC guided Tx)

Advanced HF with LVEF 23 (+/-12) %, CI 2.3 (+/- 2.1) L/min/m²
Systolic BP <=125 mmHg, Creatinine <= 3.5 mg/dL
Without Inotropic Drugs (Mirinone, Dopamine, or Dobutamine)



No Positive Association Between CI and Renal Dysfunction

Overall and Specific Subgroup

- Low LVEF <35%
- High RAP
- Low Systolic BP (<100 mmHg, 41%)
- More Impaired Renal (GFR <30)

Does Increasing CO improve renal function?

OPTIME-CHF Trial and ROSE-AHF Study that addresses this question

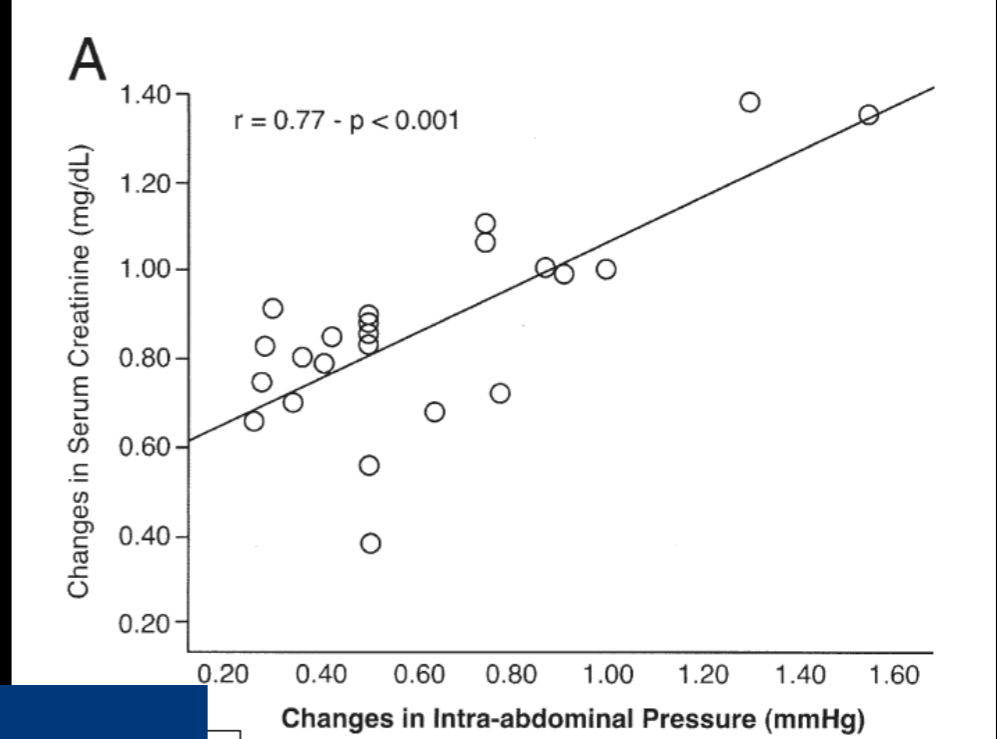
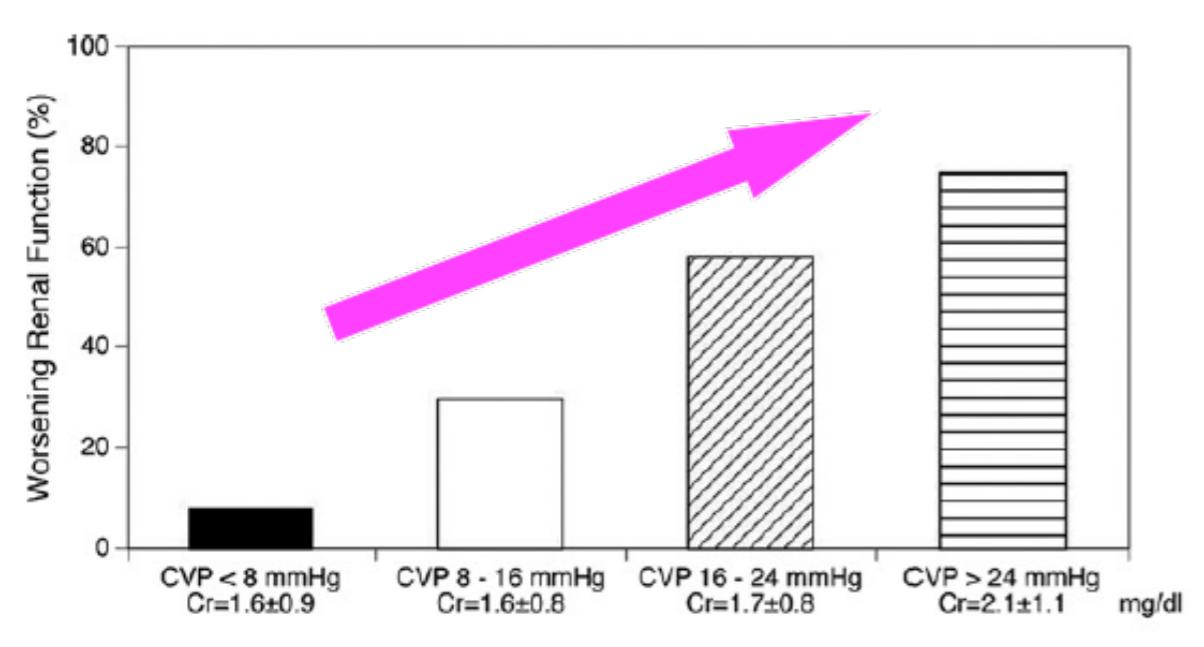
Milrinone 0.5 mcg/kg/min vs Placebo
Low-dose dopamine vs Placebo

No difference in the rate of WRF between groups

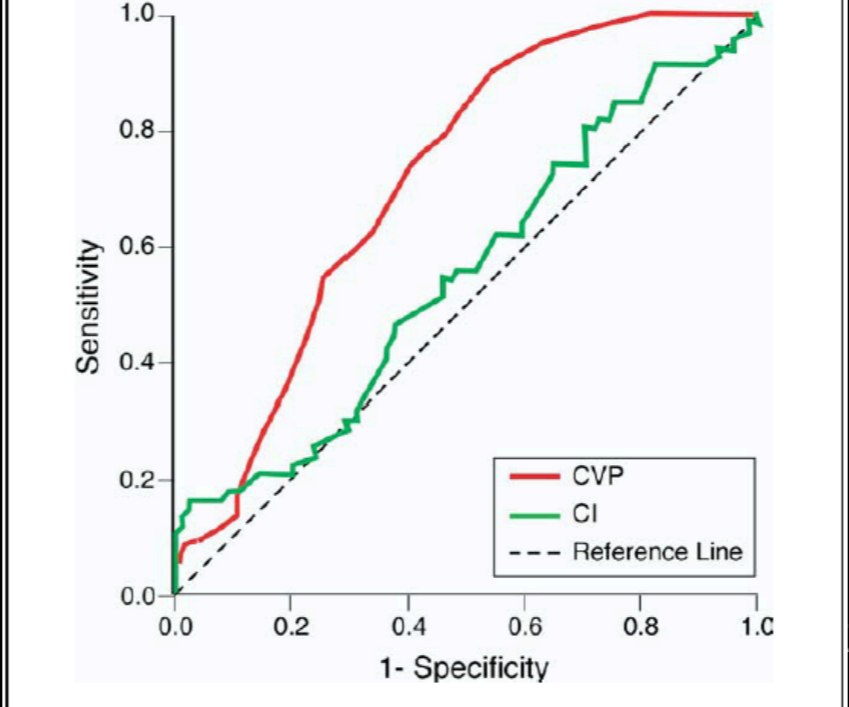
patients admitted with ADHF Treated with Pulmonary Artery Catheter Guided Therapy

Increased CVP is Associated with WRF

Elevated IAP is associated with WRF



CVP but not CI predicted WRF



Decongestion Strategy

Wet&Warm

Post hoc analysis

DOSE-AHF trial

ROSE-AHF trial

CARRESS-HF trial

“Stepwise Pharmacological Care Algorithm” (SPCA)

Urine-output-guided diuretic adjustment

VS

Standard Decongestion Therapy

SPCA: Greater in Decongestion,
Without WRF

Target = Adequate Decongestion (Warm&Dry)

Dyspnea, Orthopnea: None

Edema: Absent/trace

JVP \leq 8 cm H₂O

“Stepwise Pharmacological Care Algorithm” (SPCA)

Diuretic Dosing Table

Step	Current Dose		Suggested Dose	
	Loop (/day)	Thiazide	Loop (/day)	Thiazide
A	≤ 80	±	40 mg iv bolus + 5 mg/hr	0
B	81 - 160	±	80 mg iv bolus + 10 mg/hr	5 mg metolazone qd
C	161 - 240	±	80 mg iv bolus + 20 mg/hr	5 mg metolazone bid
D	> 240	±	80 mg iv bolus + 30 mg/hr	5 mg metolazone bid

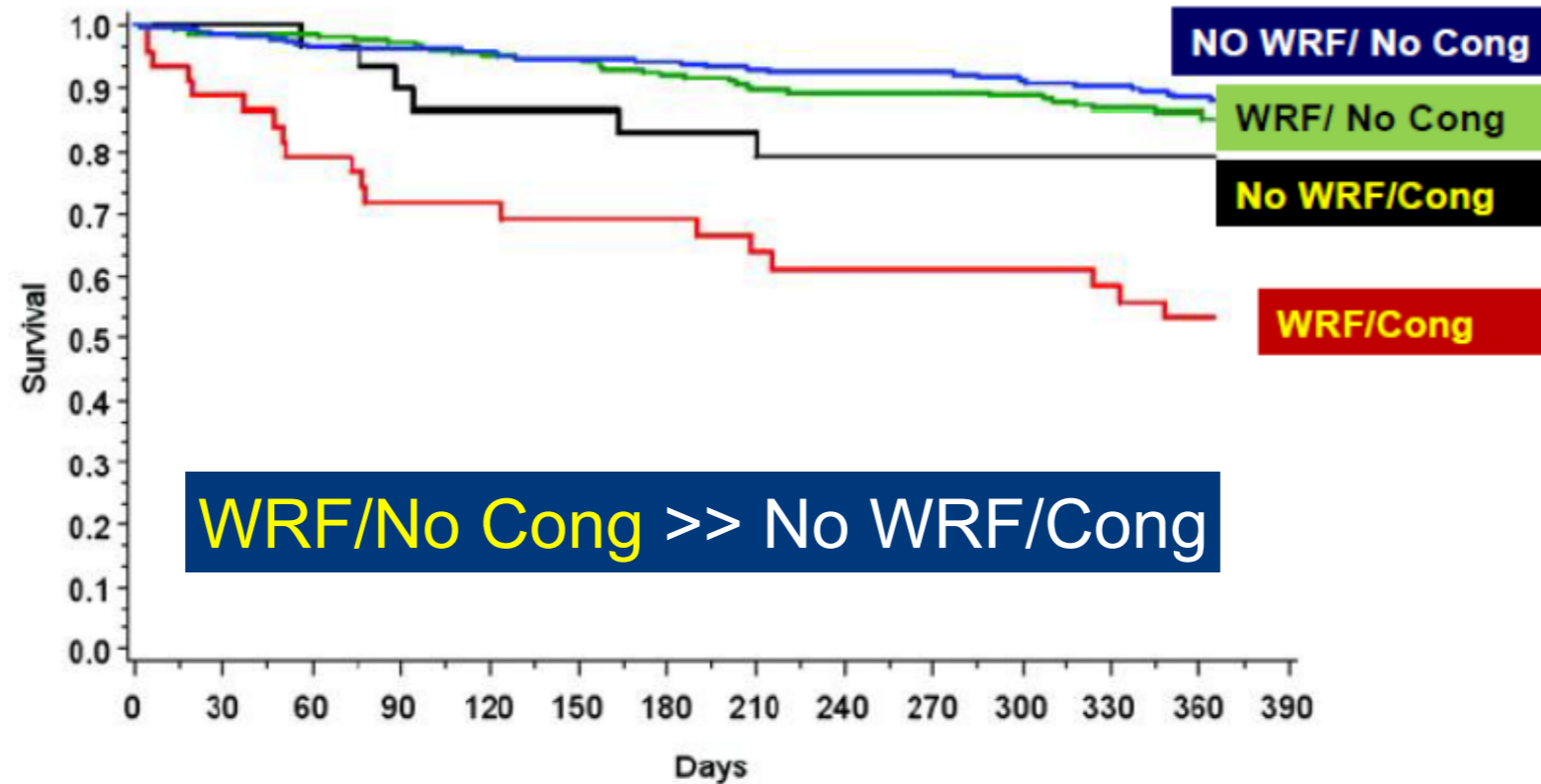
Adjust it to the next step in Table
upward if UO is < 3L/day

At 48-72 hours, Persistent Congestion (Wet&Warm)
Low dose Dopamine/Dobutamine (2 ug/kg/min)

NTG/Nesiritide

Advanced Cardiorenal Therapy

Decongestion Related WRF Does Not Alter Acute-HF Prognosis



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	195	189	188	185	178	170
No WRF/No Cong	265	259	249	244	237	229	227	223	217	214	208	202	197

Adequate Decongestion = Improved Renal Function

Heart Failure Phenotype:

Predominantly related to **Congestive Renal Failure Phenotype**

How to identify **Congestive Renal Failure** Phenotype of HF?

Clinical Findings:

Venous Congestion (Elevated JVP), Acute CRS, Warm Response to Treatment

Multimarker Biomarker Strategies

Identify phenotypic variables

History/Clinical findings

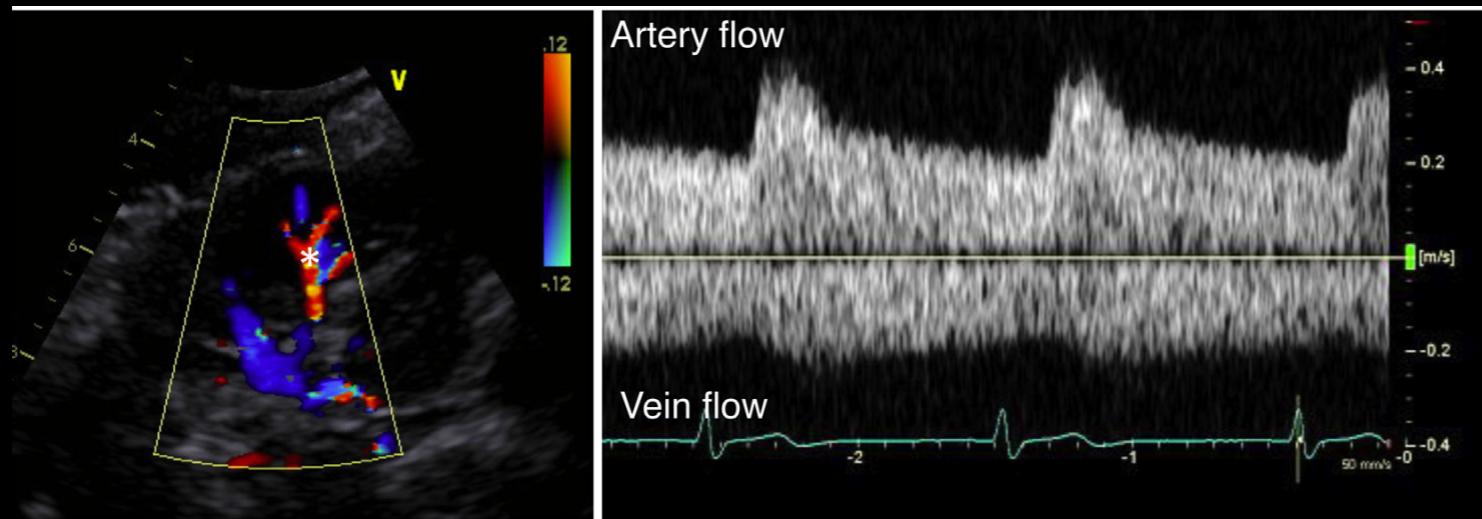
Labs

Biomarkers (clinical labs and omics)

ECG

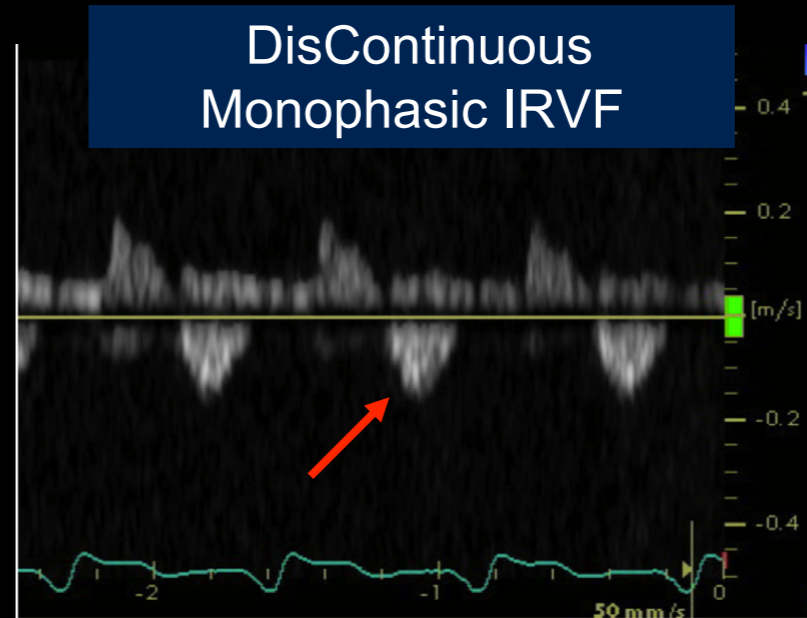
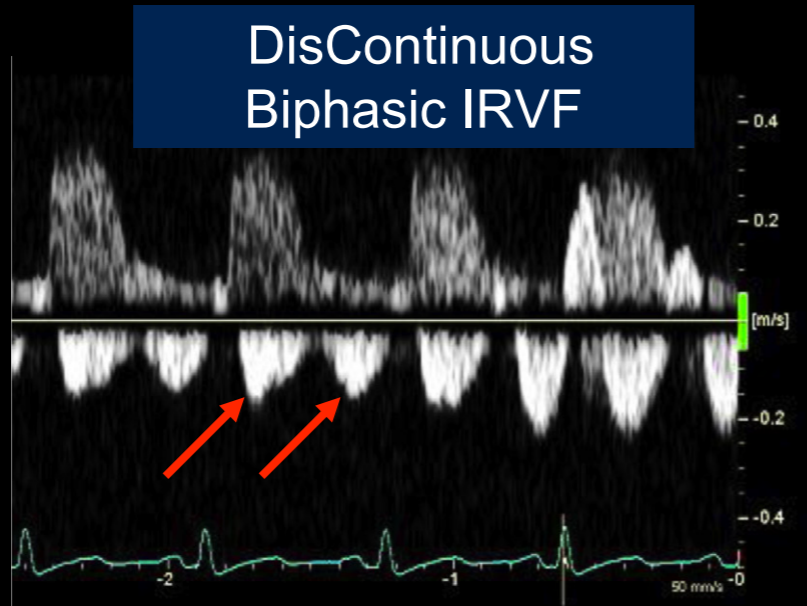
Comprehensive Imaging

Intrarenal Venous Flow Pattern: A Window into Congestive Renal Failure

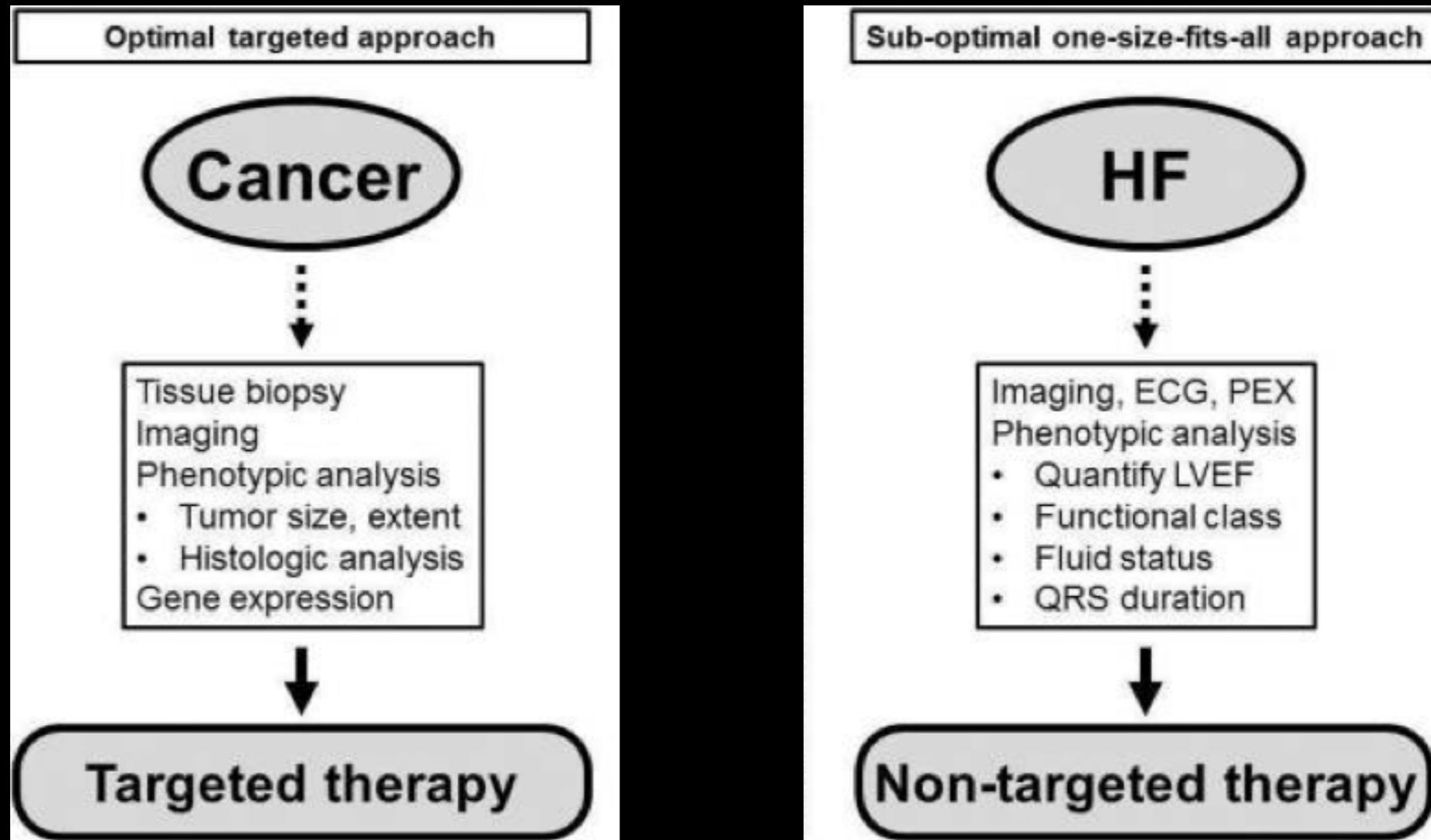


Normal Continuous Intrarenal venous flow (IRVF)

HF with Congestive Renal Failure



HF Treatment one-size-fits-all approach



HF Phenotype

Personalized Approach >> one-size-fits-all
Heart Failure with Congestive Renal Failure

Intravenous Diuretic Therapy for the Management of Heart Failure and Volume Overload in a Multidisciplinary Outpatient Unit



Leo F. Buckley, PHARM D,* Danielle M. Carter, PHARM D,* Lina Matta, PHARM D, MPH,* Judy W. Cheng, PHARM D, MPH,†
Craig Stevens, PHARM D,* Roman M. Belenkiy, PHARM D,* Laura J. Burpee, NP,† Michelle A. Young, NP,†

Hemodynamic Stable HF
60% with Diuretic Resistance
80% NYHA III-IV

Category	Maintenance diuretic dose (mg)*	IV furosemide dose		Optional†
		Bolus (mg)	Infusion (mg/hr)	
Low dose	≤ 40	20	20	--
Standard dose	41-160	Numeric equivalent of maintenance diuretic dose		--
High dose	161-300	200	20	200 mg
Mega dose	≥ 301	200	20	200 mg Thiazide diuretic‡

Conclusion

Congestion is the Main Causes of ADHF

Venous Congestion (JVP, Gut Congestion) rather than reduced CO, may be the primary hemodynamic factor driving **WRF in ADHF**

Congestive Renal Failure

HypoTENSION ≠ HypoPERFUSION

Diuretic Resistance:

Increasing Diuretic Dosage
Sequential Nephron Blockade with Different Diuretics

Urine-output-guided diuretic adjustment
“Stepwise Pharmacological Care Algorithm” (SPCA)



Thank You

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