1

Novel Strategies for Managing Acute Decompensated Heart Failure

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2

Disclosures

- Site-PI for VENUS HF and FASTR II Trial
- No financial disclosures

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3

Objectives

1. Foundational Understanding
   - Removers, Dilators, Pushers, Pullers
2. Diuretic Resistance and Evaluate response to therapy
   - MHI UNa algorithm
3. Technological Advancements
   - MHI Involvement

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Background

- The primary therapeutic goal in patients hospitalized for acute heart failure (AHF) is decongestion
  - ~20% of patients fail to lose weight
  - ~50% of patients have residual congestion at discharge
- Multifactorial causes, including
  - Poor decongestive data fidelity to guide therapy
  - Insufficient diuretic dosing and slow uptitration
  - Diuretic resistance and lack of identification
  - Fear of worsening renal function (WRF)

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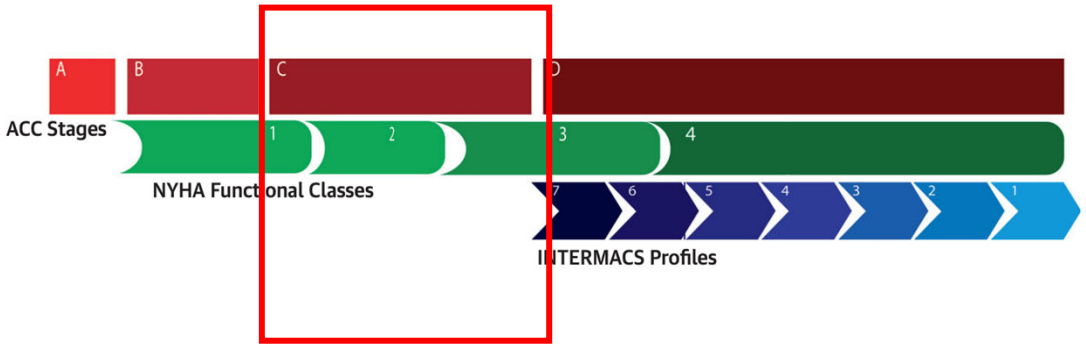
5

Heart Failure Spectrum



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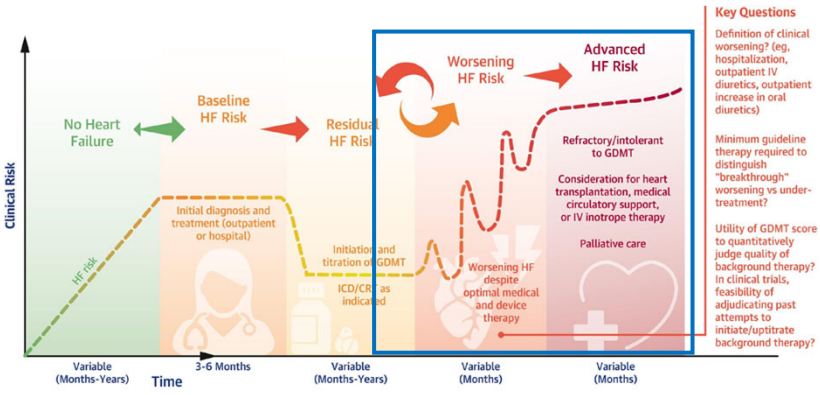
Truby, L.K. et al. J Am Coll Cardiol HF. 2020;8(7):523–36.

6

ADHF Grim Facts

- 33% will be re-hospitalized within 60-90 days
- 66% will die or re-hospitalized within 1 year



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7

Therapeutic Strategies

Removers:
Direct Removal of Sodium and Water

Dilators:
Increasing Venous Capacitance and Decreasing Afterload

Pullers:
Decreasing Renal Venous Pressure

Pushers:
Increasing Renal Arterial Pressure

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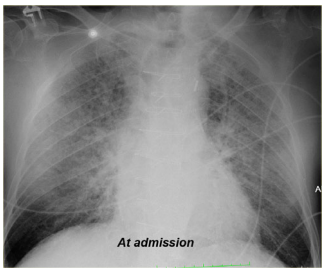
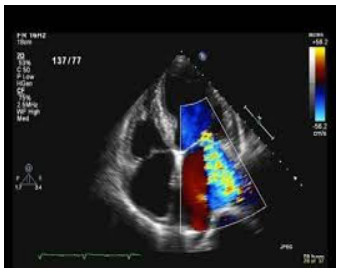
65-year-old Woman with ADHF







- BP: 103/76/85 mmHg
- HR: 94 bpm
- SpO2 89% at room air

- eGFR 35 mL/min/1.73m2 (down from 62 mL/min/1.73 m2
- Na+/Cl-/K+ = 132/94/4.2

R/ Furosemide 40 mg IV

After 2.5 hours:
- 160 mL UOP
- UNa+ = 62 mmol/L

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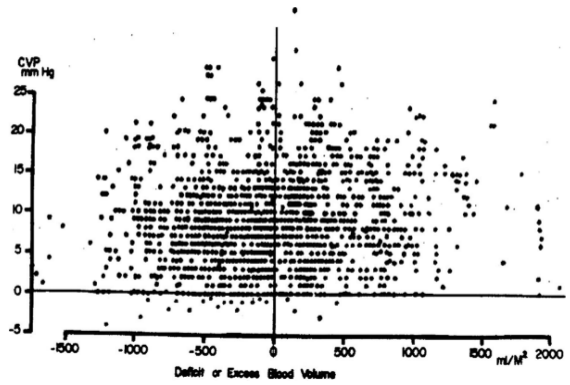
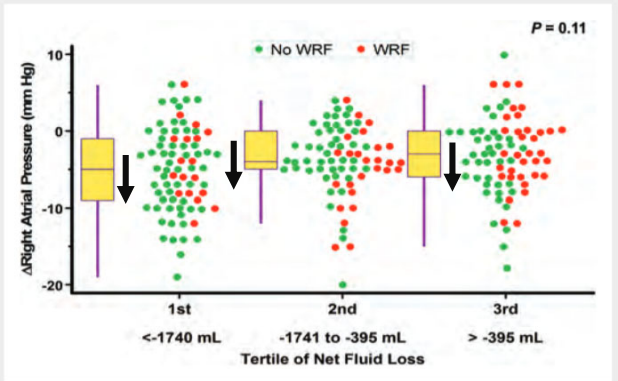
1. Assess Volume Status & Cardiac Filling Pressures



Marik PE et al. Chest, 2008



Aronson D et al. Eur J Heart Fail, 2013

Volume ≠ Cardiac filling pressures

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Acute Heart Failure: Toolkit for Management

	Cardiac filling pressures Normal	Cardiac filling pressures Elevated
No signs of fluid overload	TARGET	Vasodilators Consider: Revascularization Fix valve lesions
Signs of fluid overload (oedema, ascites, pleural effusion, 3th space)	SLOW DIURESIS	RAPID DIURESIS

Loop diuretic therapy:

- Intravenous therapy
- The dose of diuretic should be decided based on renal function
- The frequency of the diuretic should be determined based on signs of fluid overload.

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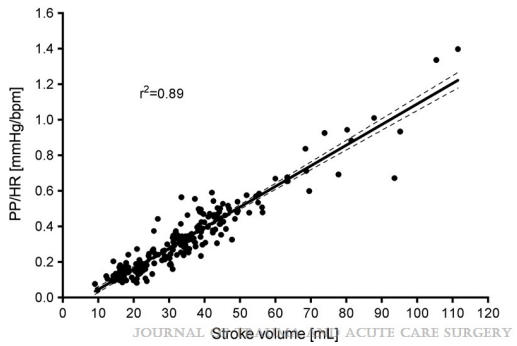
11

2. Optimize kidney perfusion first

	Low pulse pressure (<25-30 mmHg)	Normal pulse pressure (>30 mmHg)
Low DBP (<65 mmHg)	• Hypovolemia • Advanced HF (Cold & dry) • Advanced Shock	• Vasoplegia • Aortic regurgitation
Preserved DBP (>65 mmHg)	Exaggerated vasoconstriction	Normal



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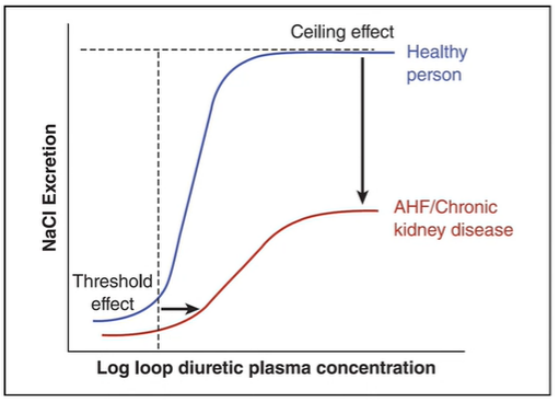
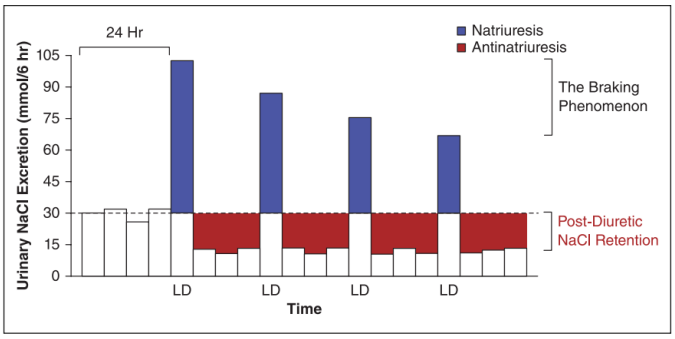
Journal of Trauma and Acute Care Surgery74(6):1438-1445, June 2013.

12

3. Administer Diuretics





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Verbrugge FH et al. Eur Heart J Acute Cardiovasc Care, 2018

13

Importance of specific cause/mechanism on diuretic resistance	Diuretic Resistance Categorization			
	Pre-Renal	Intra-Renal		
		Pre-Loop of Henle	Loop of Henle	Post-Loop of Henle
Significant	Venous congestion	Increased proximal tubule sodium reabsorption	Loop diuretic dose	Compensatory distal tubular sodium reabsorption
Unknown but hypothesized to be significant	Increased intra-abdominal pressure	*Reduced GFR*	Response at the level of the Loop of Henle	Proteolytic activation of ENaC by filtered proteases
Not significant with the mild to moderate derangement found in the average HF patient	*Reduced cardiac output*	*Increased organic anions*	Hypochloremic alkalosis	Upregulation of NCC, Pendrin, NDCBE, ENaC
	Hypoalbuminemia	*Albuminuria*		
	High sodium intake			

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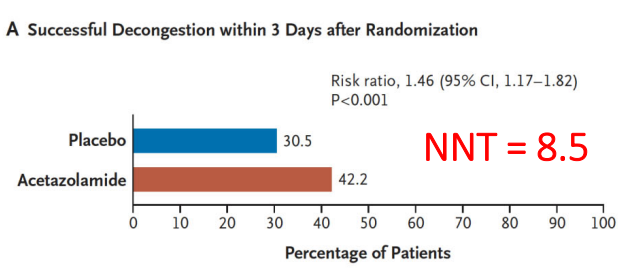
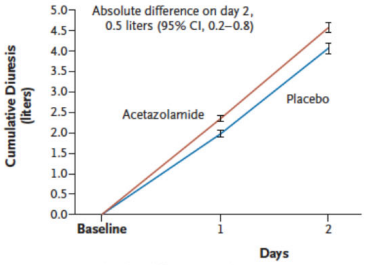
Felker GM; JACC 2020 Mar, 75 (10) 1178–1195

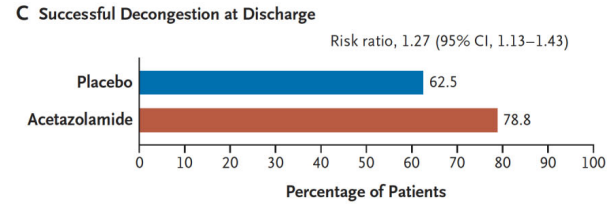
14

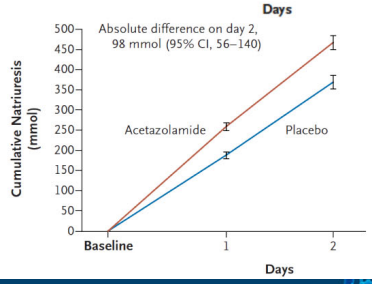
Prevention of Diuretic Resistance with Acetazolamide
The ADVOR Results



NNT = 8.5







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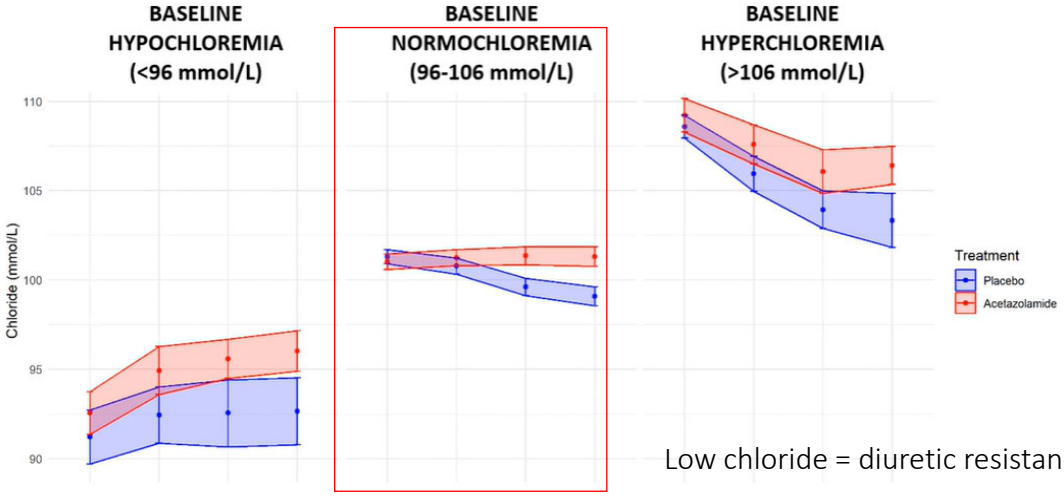
Mullens et al. N Engl J Med 2022; 387:1185-1195

15

It's All About the Chloride…



Low chloride = diuretic resistance

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Van den Eynde J et al. Circ Heart Fail, 2024.

16

4. Assess Diuretic Response

UNa+ <55 mmol/L:
Severe diuretic resistance with poor prognosis

UNa+ <80 mmol/L:
Diuretic resistance: change therapy

UNa+ >100 mmol/L:
Excellent diuretic efficiency

Diuretic administration in a heart failure patient* with volume overload

*Voided empty before diuretic administration

URINE SODIUM CONCENTRATION

Spot sample 1-2 h after diuretic administration

TOTAL NATRIURESIS

QUALITATIVE DECONGESTION (Diuretic response)

QUANTITATIVE DECONGESTION (Extracellular volume removed)

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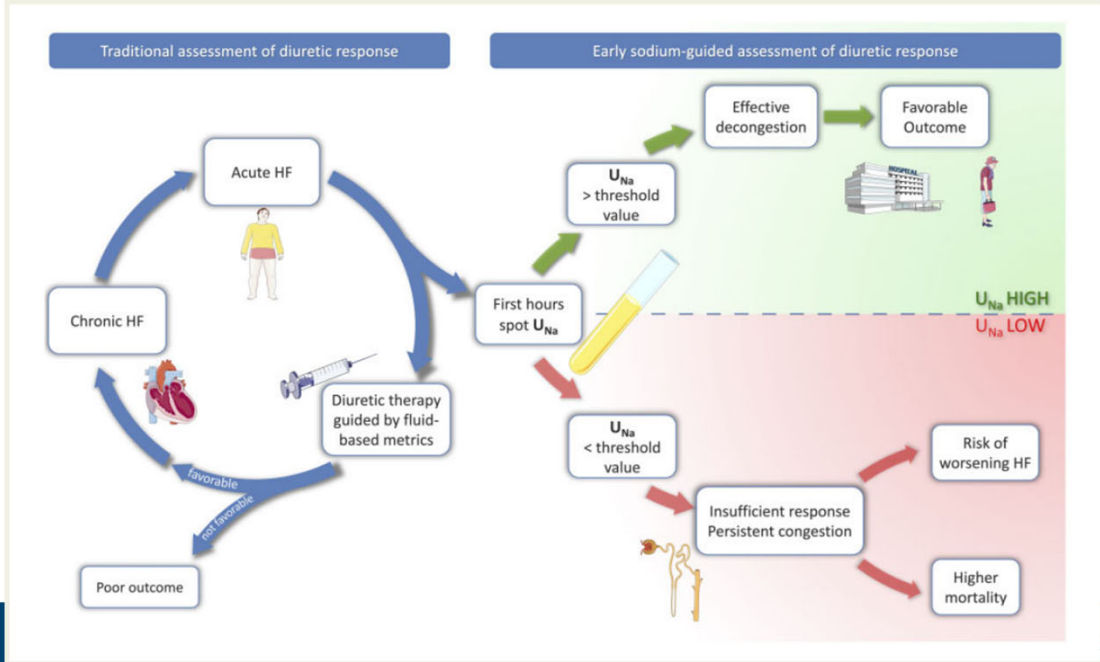

Figure 2 Role of urinary sodium assessment in acute heart failure. HF, heart failure; U_{Na}, urinary sodium, if needed: Figure modified from Servier Medical Art, licensed under a Creative Common Attribution 3.0 Generic License. http://smart.servier.com/).

18

Why Natriuresis and Not Diuresis?

- **Pragmatic:** easier to measure than urine collection (i.e personalized dosing)
- **Physiological:** physiological response to diuretic (i.e best indicator of quality of urine)
- **Prognostic:** natriuresis correlates much better than diuresis (weight loss) with hard endpoints

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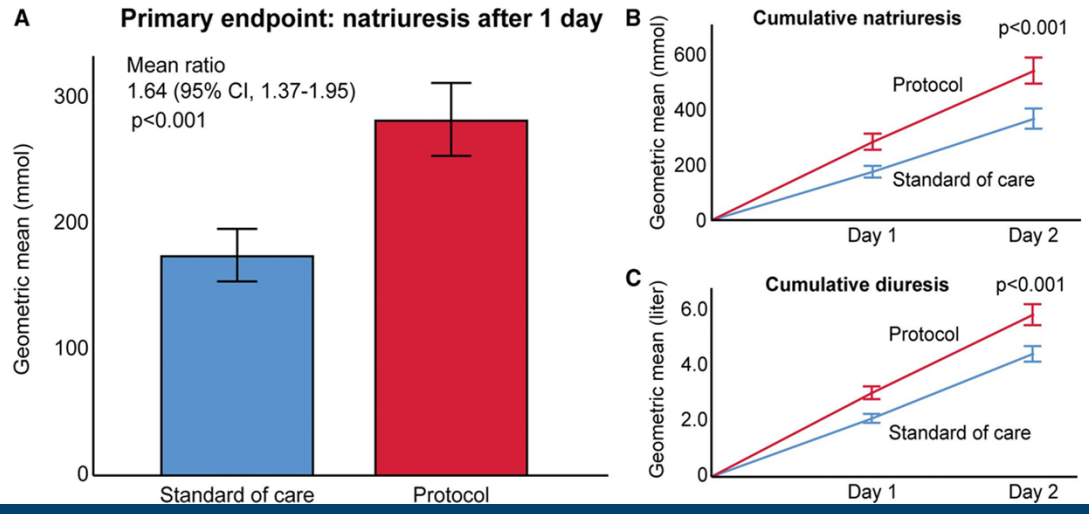
19

ENACT - HF



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Dauw J et al. Circ Heart Fail. 2024;17:e011105

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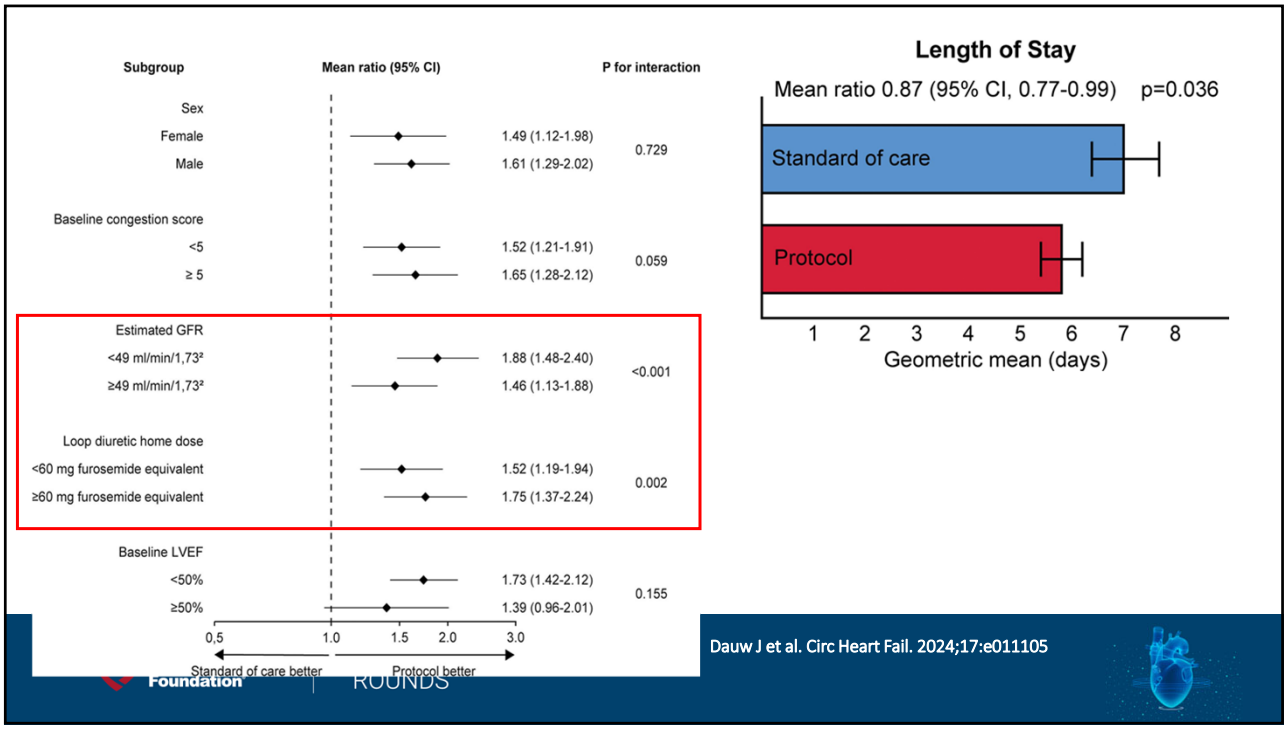
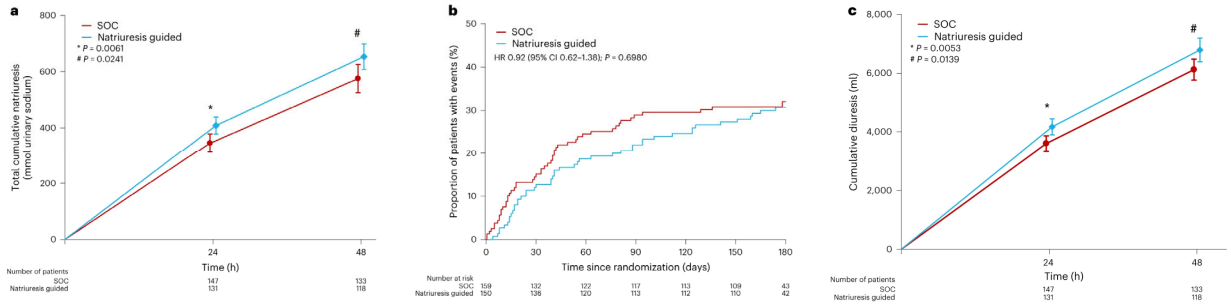


21

PUSH-HF

- 150 patients with furosemide titration according to natriuresis
- 160 patients with standard of care



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Ter Maaten JM; Nature Medicine 29, 2625-2632. 2023

22

PUSH-HF

- Pragmatic trial. Reflective of daily clinical practice
- Natriuresis guided irrespective of GFR and/or WRF
  - Natriuresis (not WRF) associated with better outcomes
- GFR decrease in the natriuresis guided → no increase adverse events
- No overall effect on HFH/mortality.
- Low GFR did better with Na-guided diuresis

23

EASY-HF

Readily available Urinary Sodium analysis in Patients with Acute Decompensate Heart Failure

Background

UNa-guided protocol

Efficacy

Time-consuming
Multiple steps
Prone to error

Methods

N=60
R
1:1

SOC: Diuretic titration at discretion physician

Protocolised: Nurse-led urinary sodium-based diuretic protocol
Diuretic intensification:
UNa < 70mmol/L or Diuresis <3L/24h

Study design

Prospective
Single-centre
Open-label
RCT

ADHF
NTproBNP ↑
GFR ≥20ml/min/1.73m²

From March 2022 to August 2023

Findings

	SOC	Protocolised	
48h natriuresis (mmol)	657 ± 273	820 ± 279	P=0.027
48h diuresis (L)	6.0 ± 1.9	7.3 ± 2.4	P=0.019

General agreement nurses:
Sensor and protocol easy and usable in daily practice

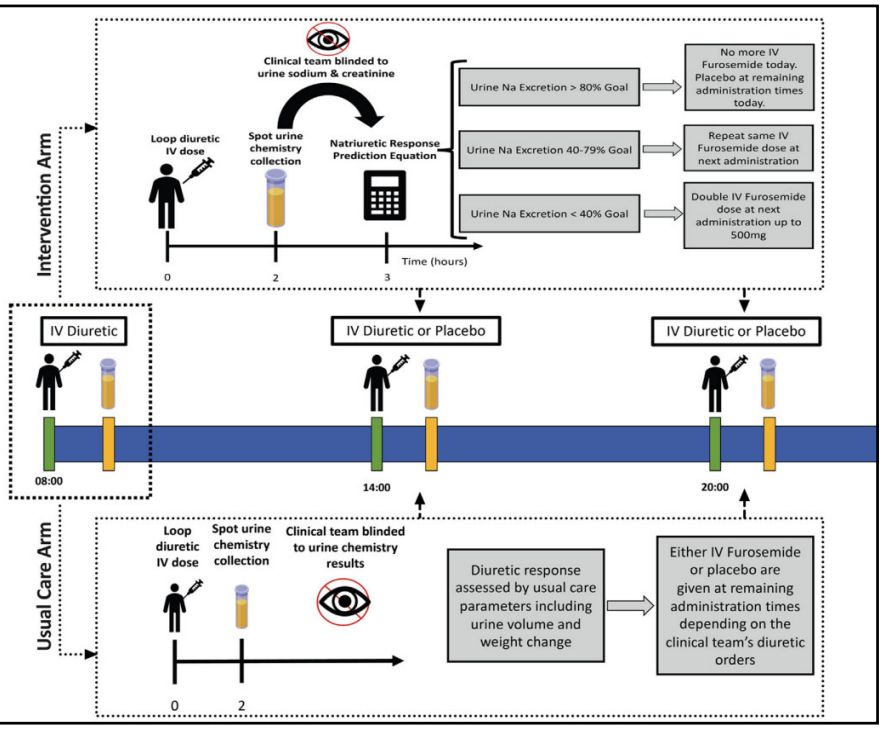
CONCLUSION

A nurse-led urinary sodium-based diuretic protocol via bedside POC sodium sensor allows individualised diuretic titration in ADHF patients, while it improves 48h natriuresis and diuresis.

Meekers E et al. Eur J Heart Failure. 2024;26:2129-2139

24

ESCALATE Trial:



Cox ZL, Stevenson LW; Am Heart J. 2023 Nov: 265:121-131

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25

Back to our case…

- Low pulse pressure with preserved DBP indicates low CO/exaggerated vasoconstriction -> worse with MR
  - Pause BB
  - R/ IV Nipride
- High filling pressure & clear fluid overload: rapid diuresis
  - Loop diuretics q6-8h
  - Loop diuretic dose IV
  - Upfront acetazolamide 500 mg IV
- Assess post diuretic spot urine sodium
  - Add thiazide-like diuretic if <80 mmol/L

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26

Therapeutic Strategies: Technological Advancements

Removers:
Direct Removal of Sodium and Water

Dilators:
Increasing Venous Capacitance and Decreasing Afterload

Pullers:
Decreasing Renal Venous Pressure

Pushers:
Increasing Renal Arterial Pressure

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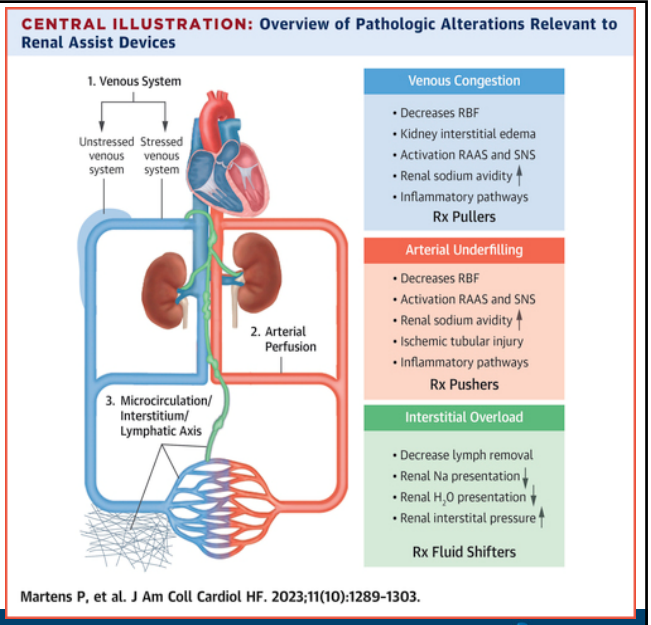
27

Device-Based Therapies

- The unmet need for treatment of patients with ADHF has increased interest in developing device therapy to:
  - Renal assist devices are being developed targeting patients with acute cardiorenal syndrome and worsening renal function
  - These devices can target venous, arterial and interstitial/lymphatic axis alterations
  - Ongoing trials are necessary to determine the overall risk/benefit rate of these devices



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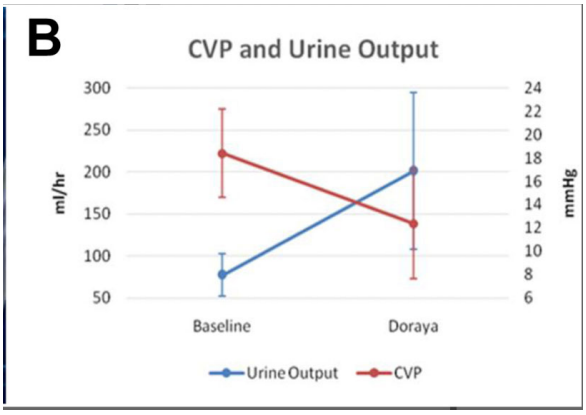
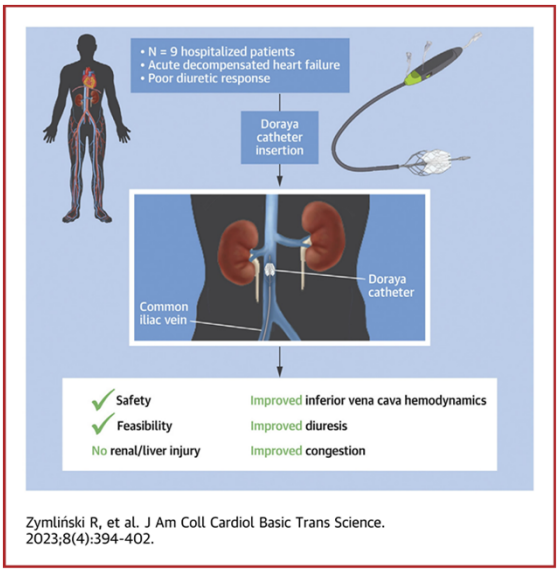
Pieter Martens et al. *J Am Coll Cardiol HF* 2023; 11:1289-1303.

28

Doraya Catheter





Zymliński R, et al. J Am Coll Cardiol Basic Trans Science. 2023;8(4):394-402.

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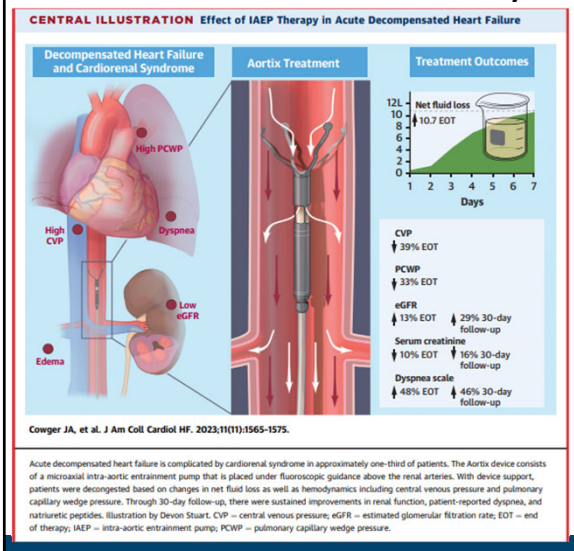
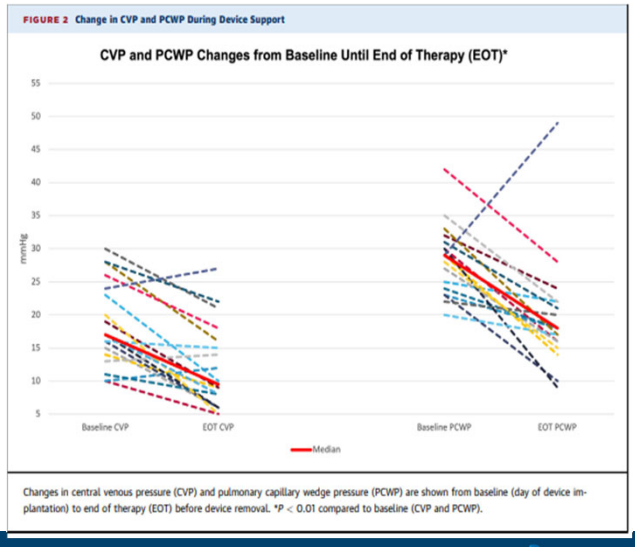
29

Procyrion Aortix Device





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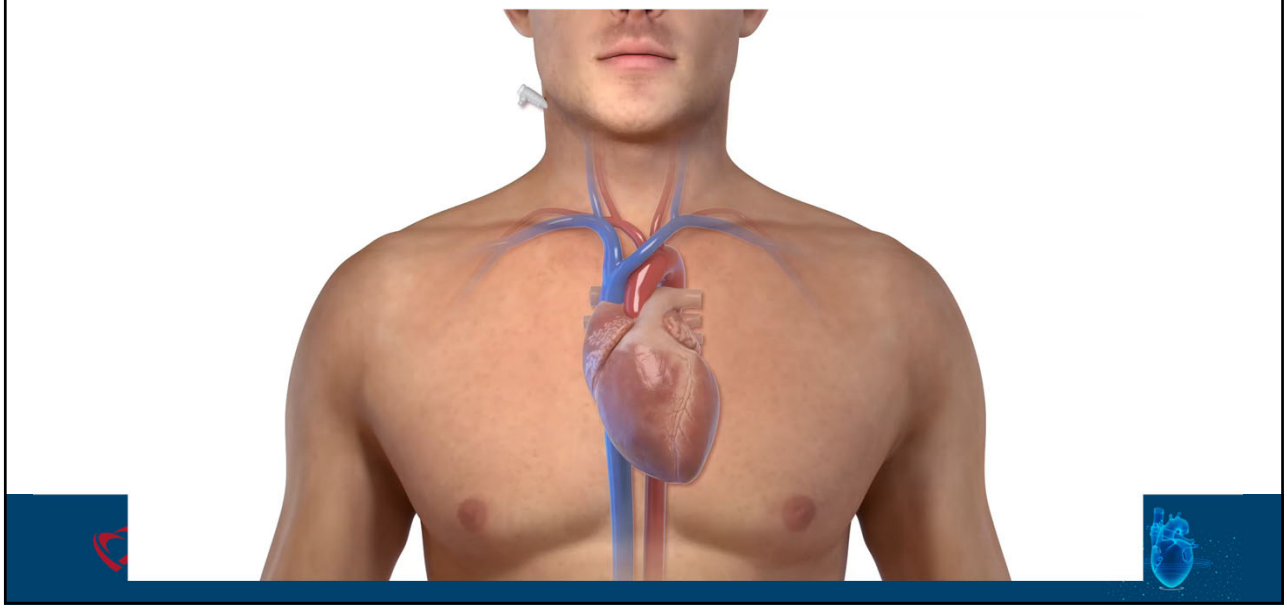
30

PreCardia Device – SVC Occlusive Device



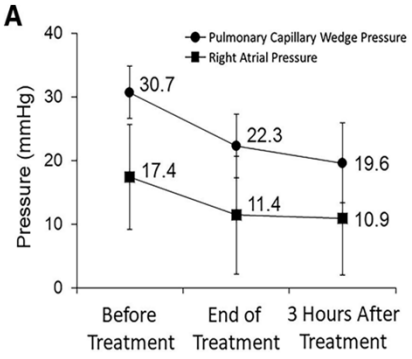
31

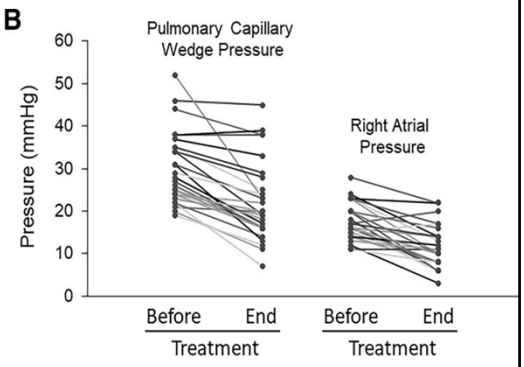
VENUS-HF Early Feasibility Study

Primary end point:
Freedom from device or procedure related MAE

Secondary end points (Hemodynamic and UOP)

- RAP decrease by 34%
- PCWP decreased by 27%
- Unchanged MAP or CI
- UOP increased by 130% with no WRF
- UOP increased with no diuretic change.





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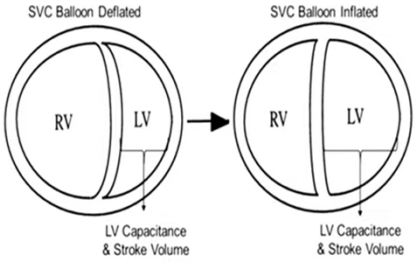
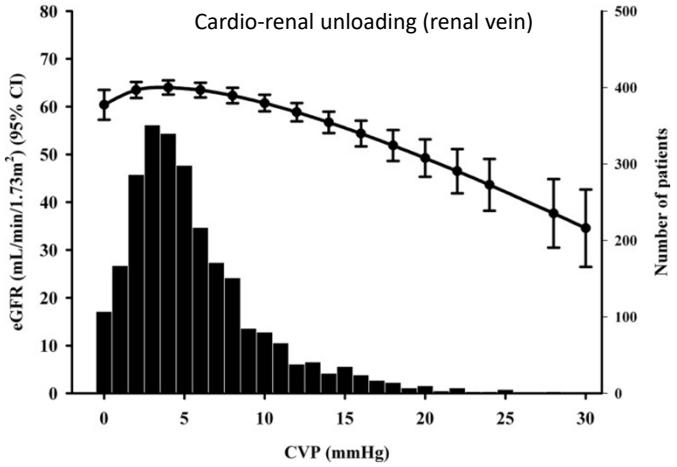
Kapur N et al Circ Heart Fail. 2022;15

32

Mechanism of Action of Venus Occlusive Devices



BiVentricular Inter-Dependence



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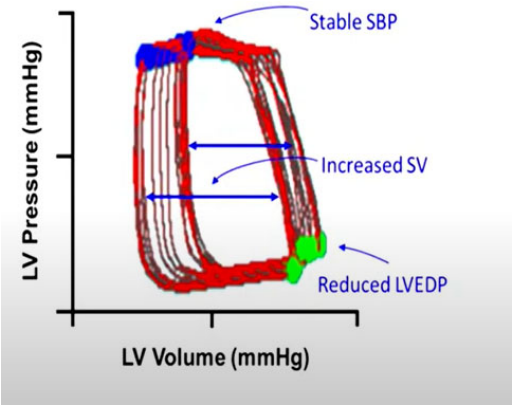
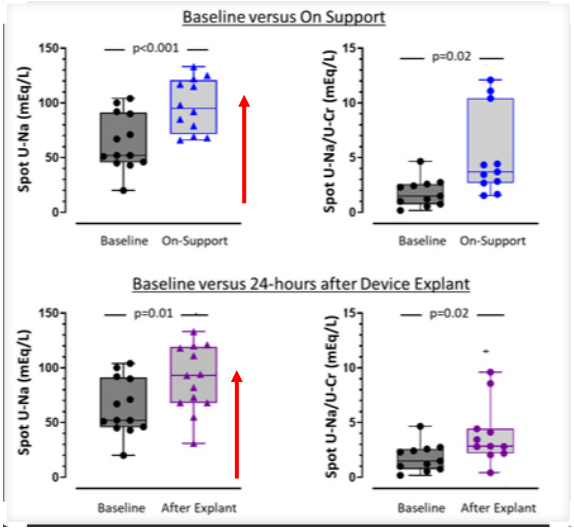
Kostam et al Circulation 2018

33

Mechanism of Action of SVC-Occlusive Device

At the time of balloon inflation





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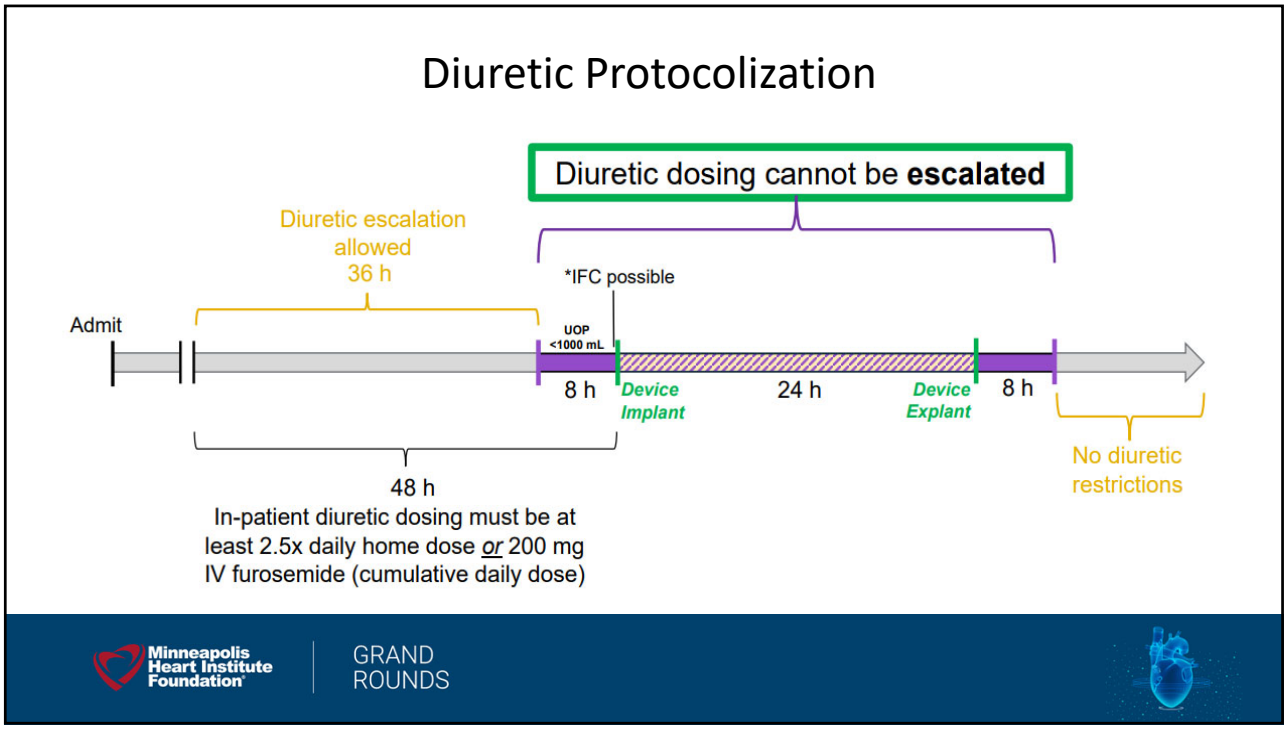
Abraham J, Kapur N AHA 2022

34


Diuretic Protocolization
Diuretic dosing cannot be escalated
Diuretic escalation allowed 36 h
*IFC possible
Admit
UOP <1000 mL
8 h
Device Implant
24 h
Device Explant
8 h
No diuretic restrictions
48 h
In-patient diuretic dosing must be at least 2.5x daily home dose or 200 mg IV furosemide (cumulative daily dose)
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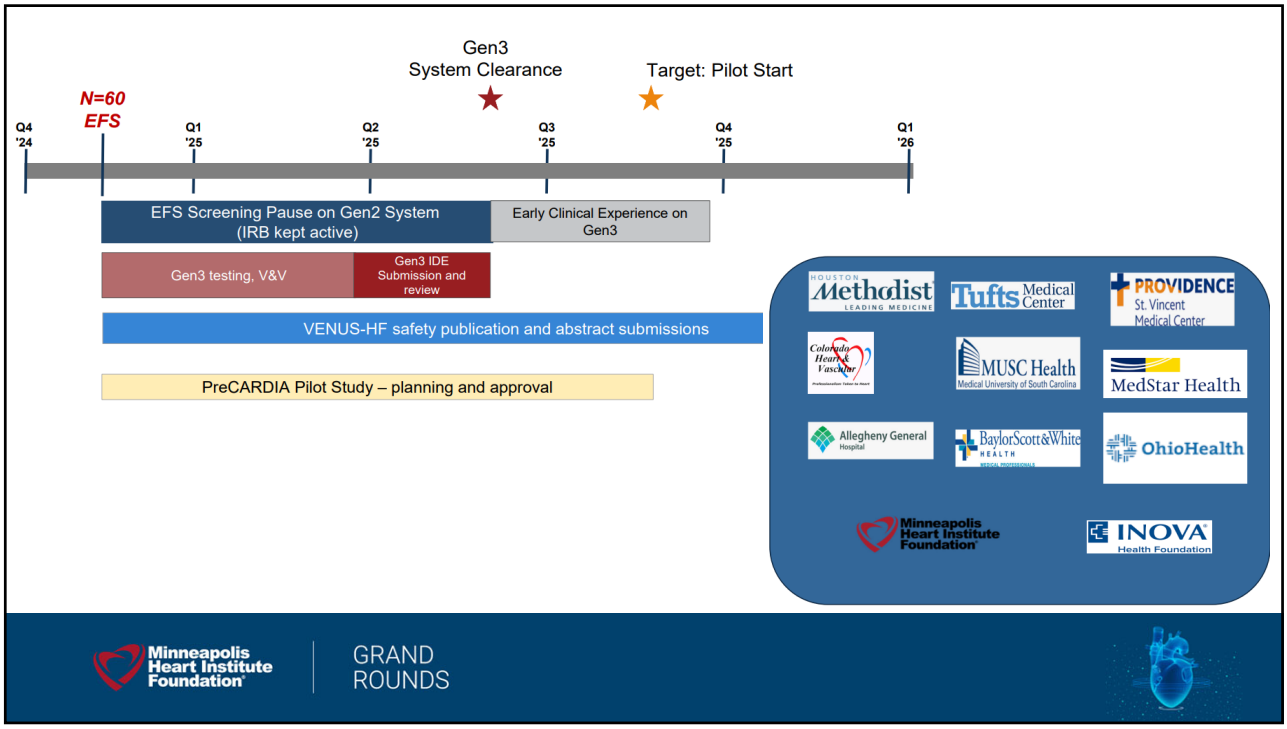
Gen3 System Clearance
Target: Pilot Start
N=60 EFS
Q4 '24
Q1 '25
Q2 '25
Q3 '25
Q4 '25
Q1 '26
EFS Screening Pause on Gen2 System (IRB kept active)
Early Clinical Experience on Gen3
Gen3 testing, V&V
Gen3 IDE Submission and review
VENUS-HF safety publication and abstract submissions
PreCARDIA Pilot Study – planning and approval
Houston Methodist
Tufts Medical Center
PROVIDENCE St. Vincent Medical Center
Colorado Heart & Vascular
MUSC Health
MedStar Health
Allegheny General Hospital
Baylor Scott & White Health
OhioHealth
Minneapolis Heart Institute Foundation
INOVA Health Foundation
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36

Reprieve Decongestion Management

- Diuretic Infusion – Dose finding phase
  - Target UOP 525 mL/hr or 200 mg of furosemide
  - 50% of IV furosemide = 10 mg/hr
- Normal Saline Infusion
  - UNa entered manually
  - NS at a rate of 50% of Na lost in urine – “diuretic resistance”
- Therapy Escalation and Stopping
  - Estimated Fluid Remaining – updated every 24 hours
  - How to handle “low UOP”
    - Sequential Nephron Blockage vs stopping

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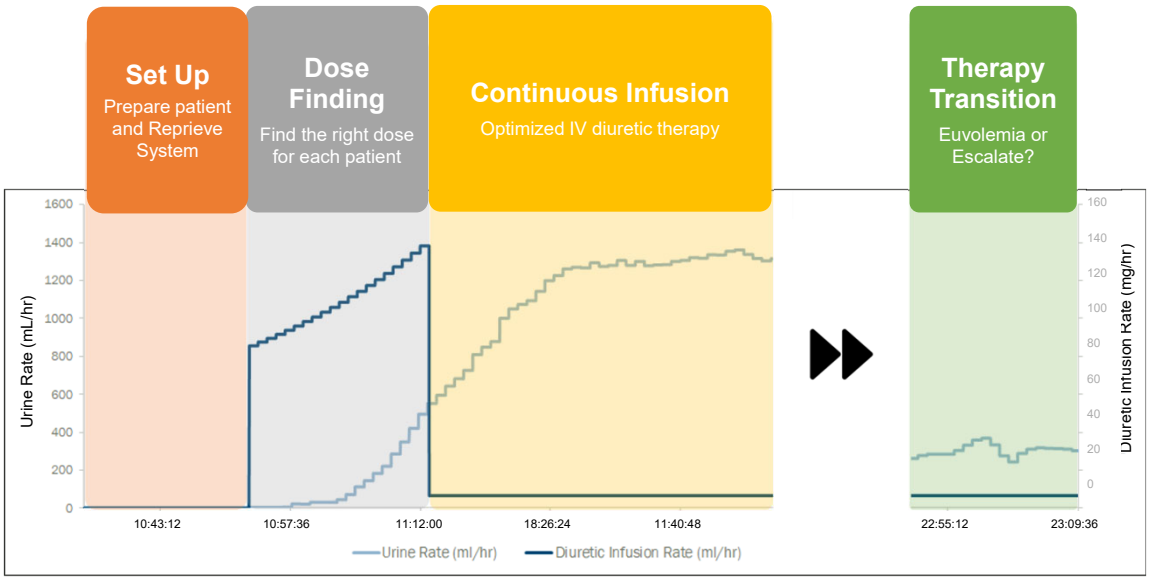
37



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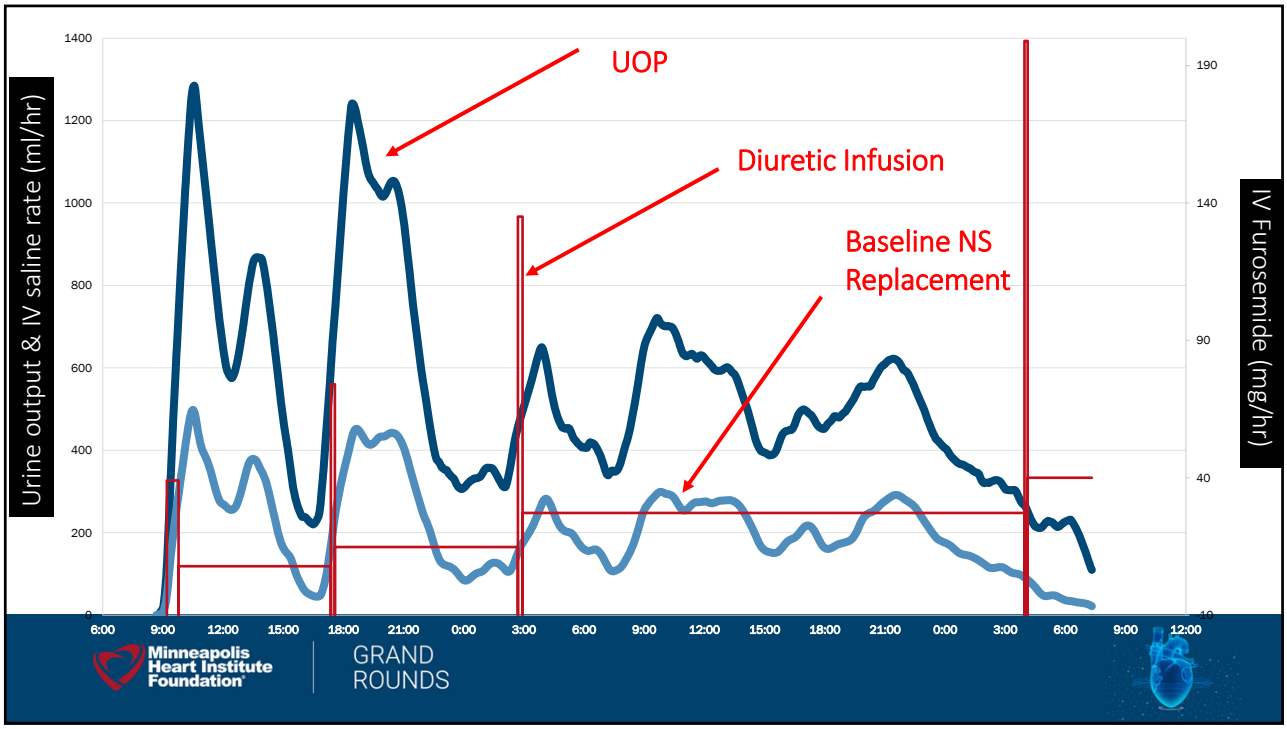
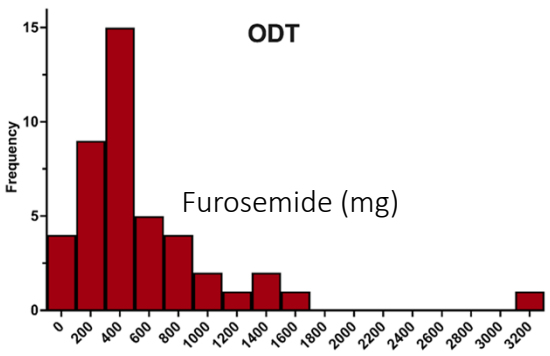
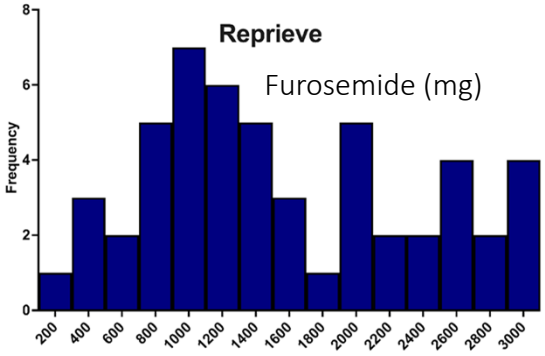
38



39

The FASTR Trial: Treatments Received up to 72H





Therapy Duration (hr)		
Reprieve	ODT	P value
41.7 ± 19.2	55.8 ± 21.5	P<0.001

IV diuresis complete by 72H (%)		
Reprieve	ODT	P value
71%	41%	P=0.003

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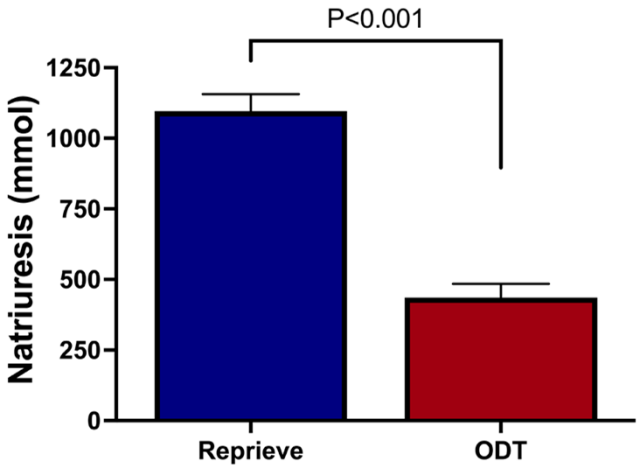
40

FASTR Efficacy Normalized to 24-hours



Net Sodium Excretion (mmol)		
Reprieve	ODT	P value
587 ± 303	436 ± 317	P<0.001

Total Urine Output (L)		
Reprieve	ODT	P value
9.4 ± 3.6	4.5 ± 2.8	P<0.001

Weight loss (kg)		
Reprieve	ODT	P value
3.8 ± 1.8	2.7 ± 2.8	P=0.002

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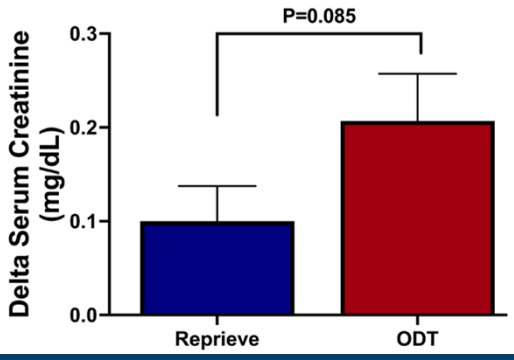
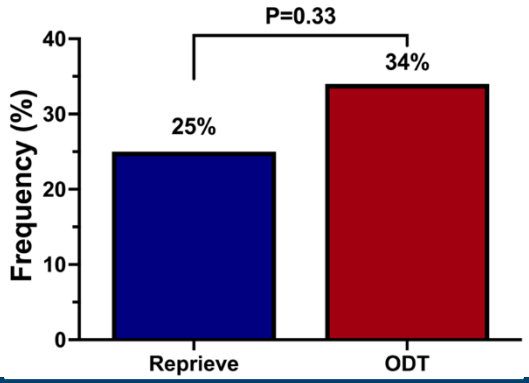
41

FASTR Kidney Parameters

Change in creatinine baseline to end-of-therapy



Creatinine Increase > 0.3mg/dL



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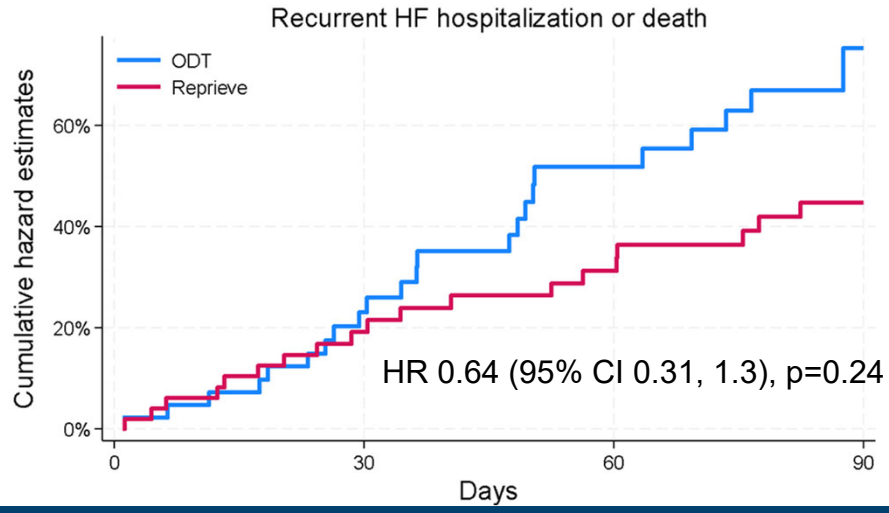
42

Death and Total Rehospitalization



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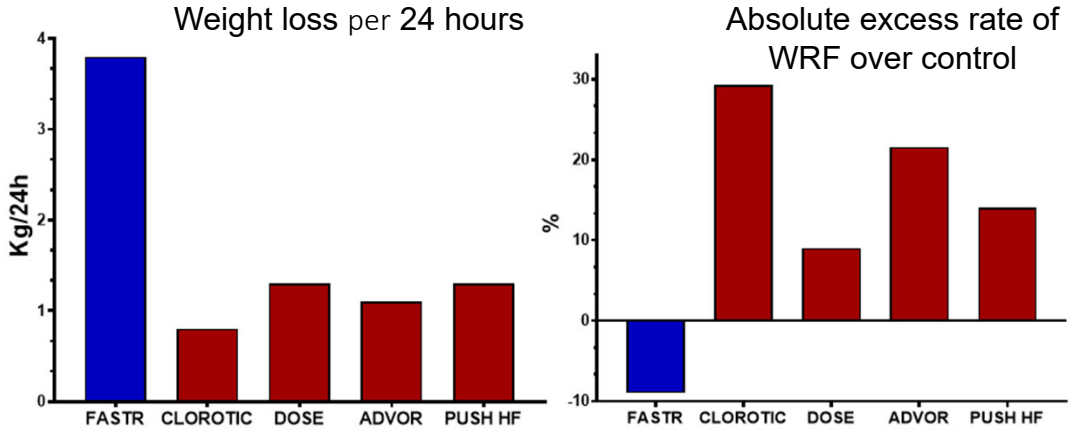
43

Putting These Results in Context of Contemporary Diuretic Trials:



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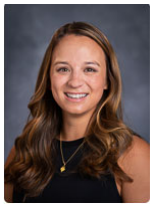
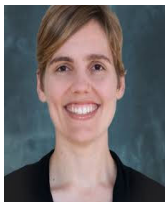
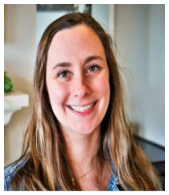
44

Allina Health MHI – Urinary Na-guided Diuresis

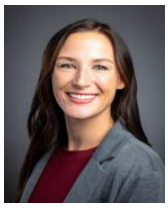

Kristina Techar, MD
Hospitalist


Amy Brendal, MD
Hospitalist


Emily Gorzycki, RN
CNS Telemetry


Steven Bradley, MD
Cardiologist


David Miranda, MD
Cardiologist


Christina Heyboer, MD
Hospitalist


Lisa Smith, APRN, MS
AHF NP MHI

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45

Urine Sodium Testing for Advanced Heart Failure Patients

Tip Sheet

About the Project
Starting on November 4th, Advanced Heart Failure patients on H4000 will be getting Urine Sodium orders when placed on an IV loop diuretic.

What do we do with results?
Urine sodium testing can help providers understand if a patient is responding to a diuretic or if adjustments are needed. This can help patients get on the right medications for them more quickly than trending weights or I&O alone.

What orders should we expect?
Nurses should expect to see a Urine Sodium order that is to be collected 1-2 hours **after** administering IV push diuretics. For patients on an infusion, patients may have UNa orders every 4-6 hours.

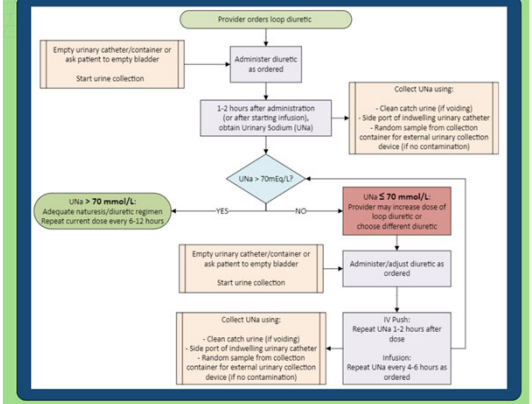
What do lab values mean?
A Urine Sodium **above 70** indicates that the kidneys are responding well to the diuretic. If it's less than 70, adjustments may be needed. The next page has an algorithm that nurses can follow to determine next actions.

What are we looking for?
MHI is looking to see if there are any changes in outcomes for patients with Urine Sodium orders. If successful, this could be expanded to other telemetry units.

Questions?
Emily.Gorzycki@allina.com
David.Miranda@allina.com

Urine Sodium Testing for Advanced Heart Failure Patients

Tip Sheet



Who to notify/when
Notify if level **less than 70** (secure chat, if no response in 1 hour, then send page)
- 7a-5p: AHF APP signed in to treatment team
- 5p-7p: AHF/CCU MD
- 7p-7a: CCU MD (not C5 APP)

Questions?
Emily.Gorzycki@allina.com
David.Miranda@allina.com

46

Take-Aways

1. Foundational Understanding
   - Removers, Dilators, Pushers, Pullers
2. Diuretic Resistance and Evaluate response to therapy
   - MHI UNa algorithm
3. Technological Advancements
   - MHI Involvement

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47

Thank You!

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48