The 3rd Indonesia Symposium on Heart Failure and Cardiometabolic Disease 2023

Benefit of Aquaretic in Patients with Acute Decompensated Heart Failure and Chronic Kidney Disease

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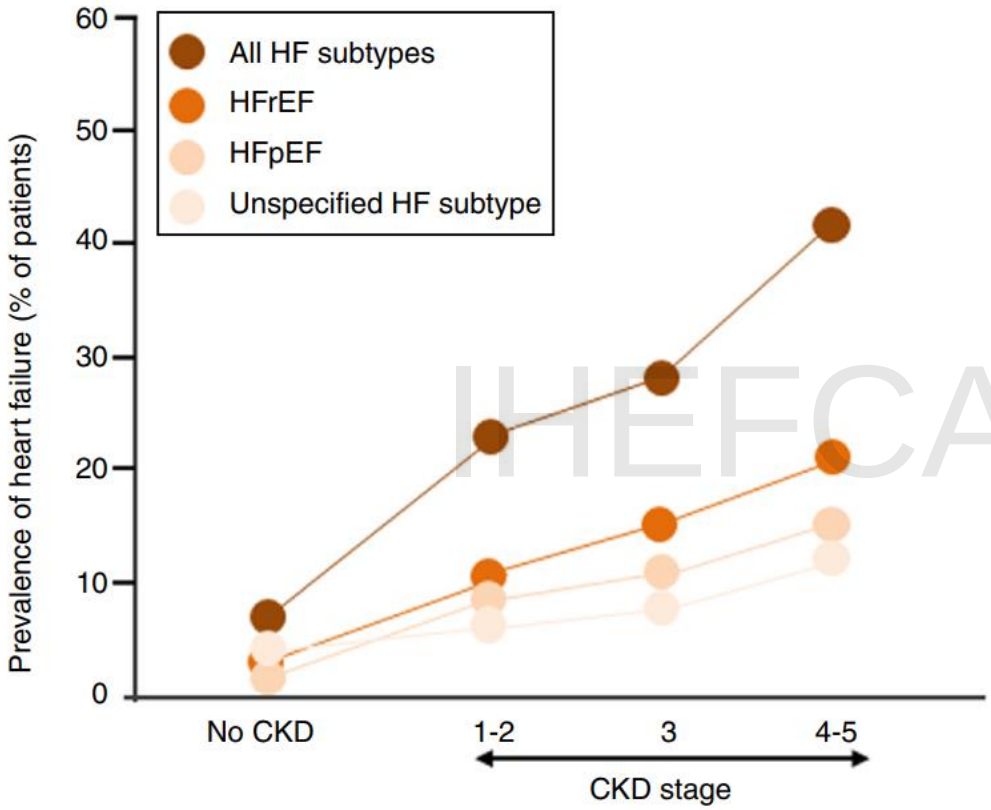
Disclosure

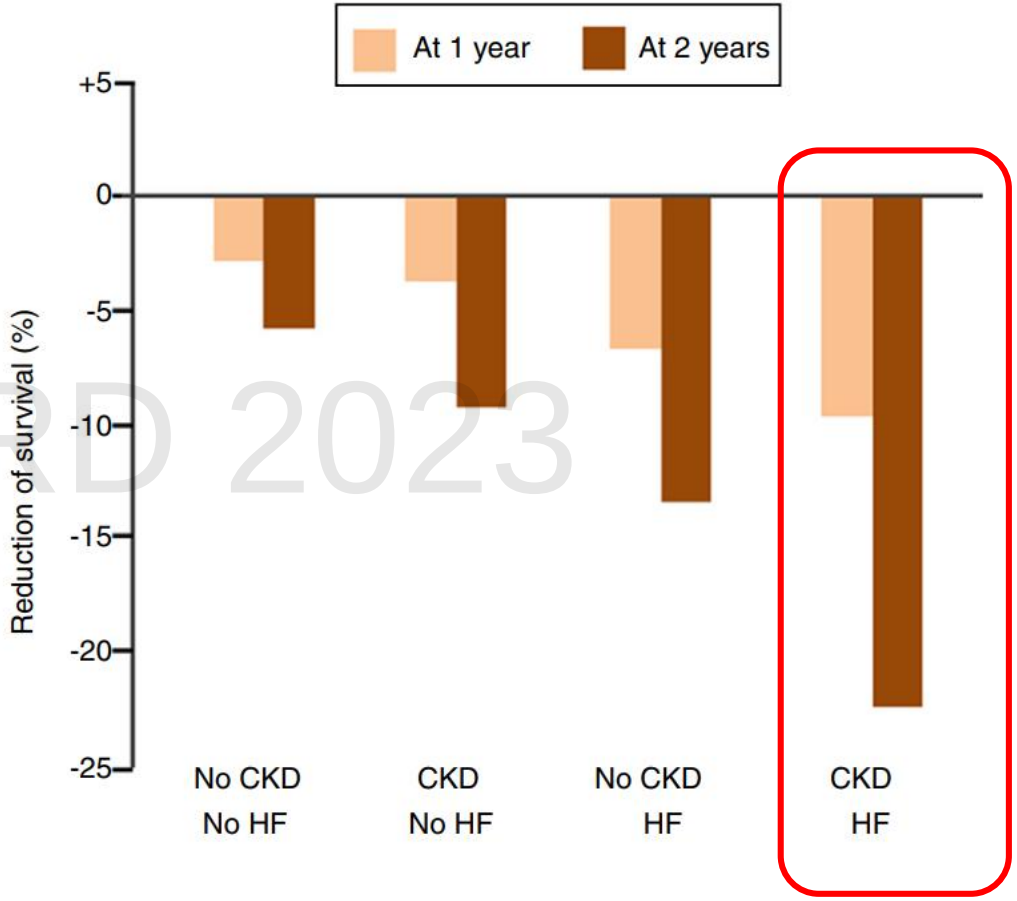
- This presentation supported by PT Otsuka Indonesia

Outline

- Burden of Heart Failure and Chronic Kidney Disease
- Heart and Renal Interaction
- Heart Failure and Chronic Kidney Disease Progression
- Decongestion Strategy and Aquaretic Benefit
- Aquaretic study in HF and CKD

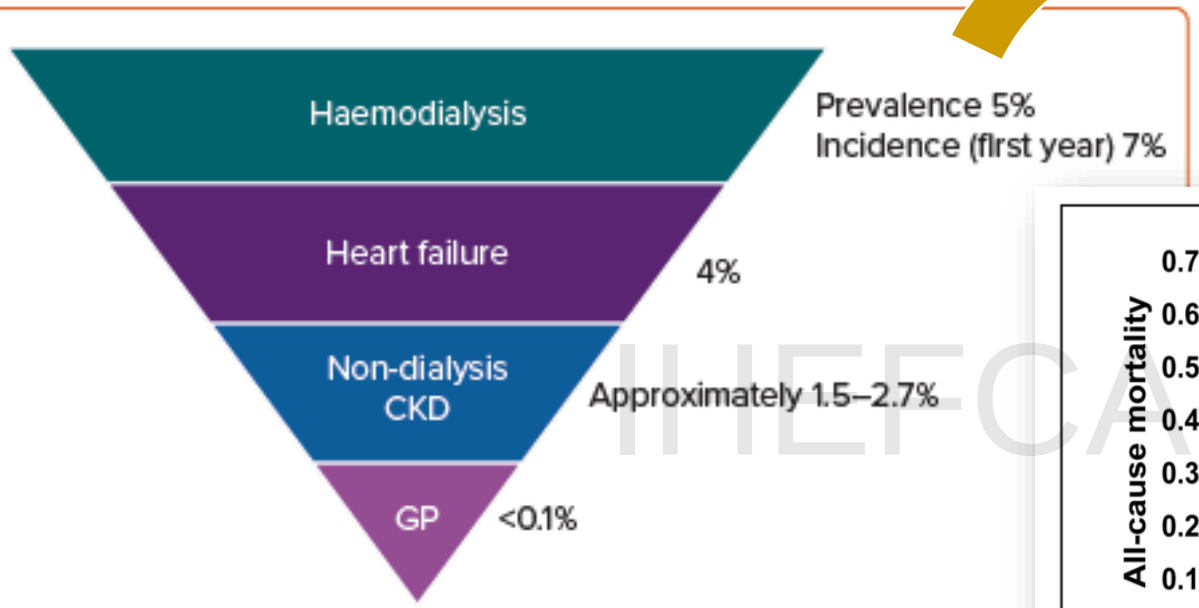
Heart failure (HF) in patients with and without chronic kidney disease (CKD)





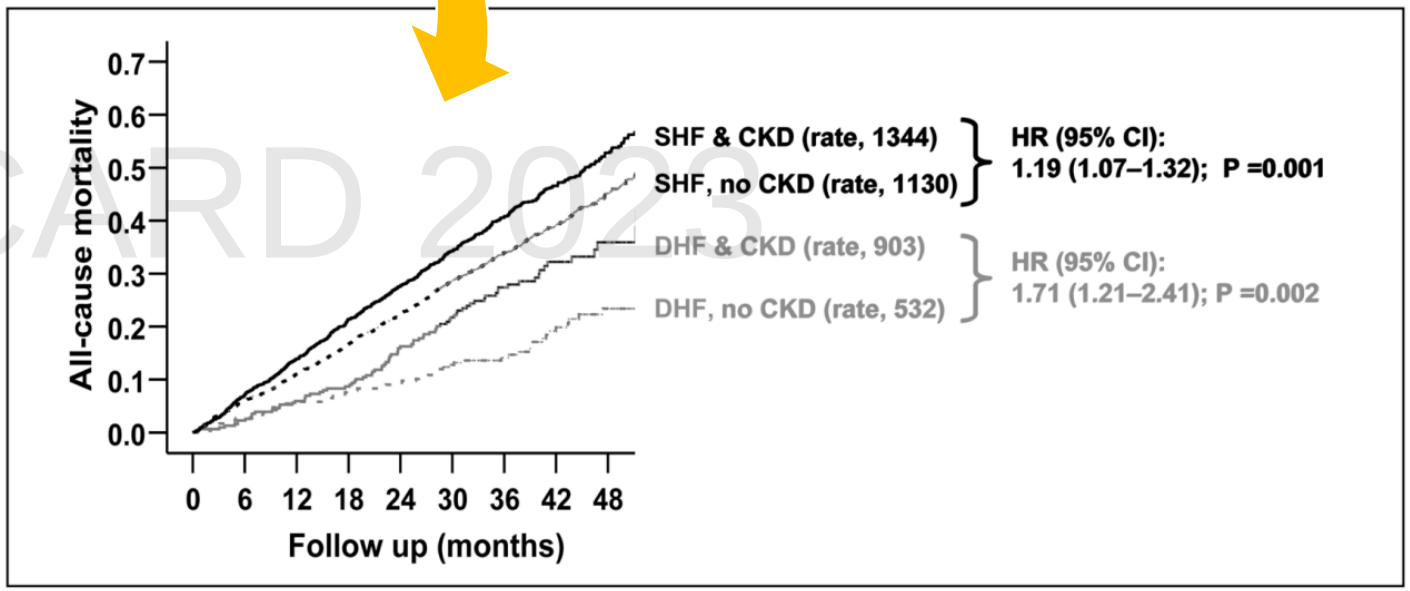
González GR et al. Nefrologia. 2020;4 0(3):223–236

Sudden Cardiac Death in HF and CKD



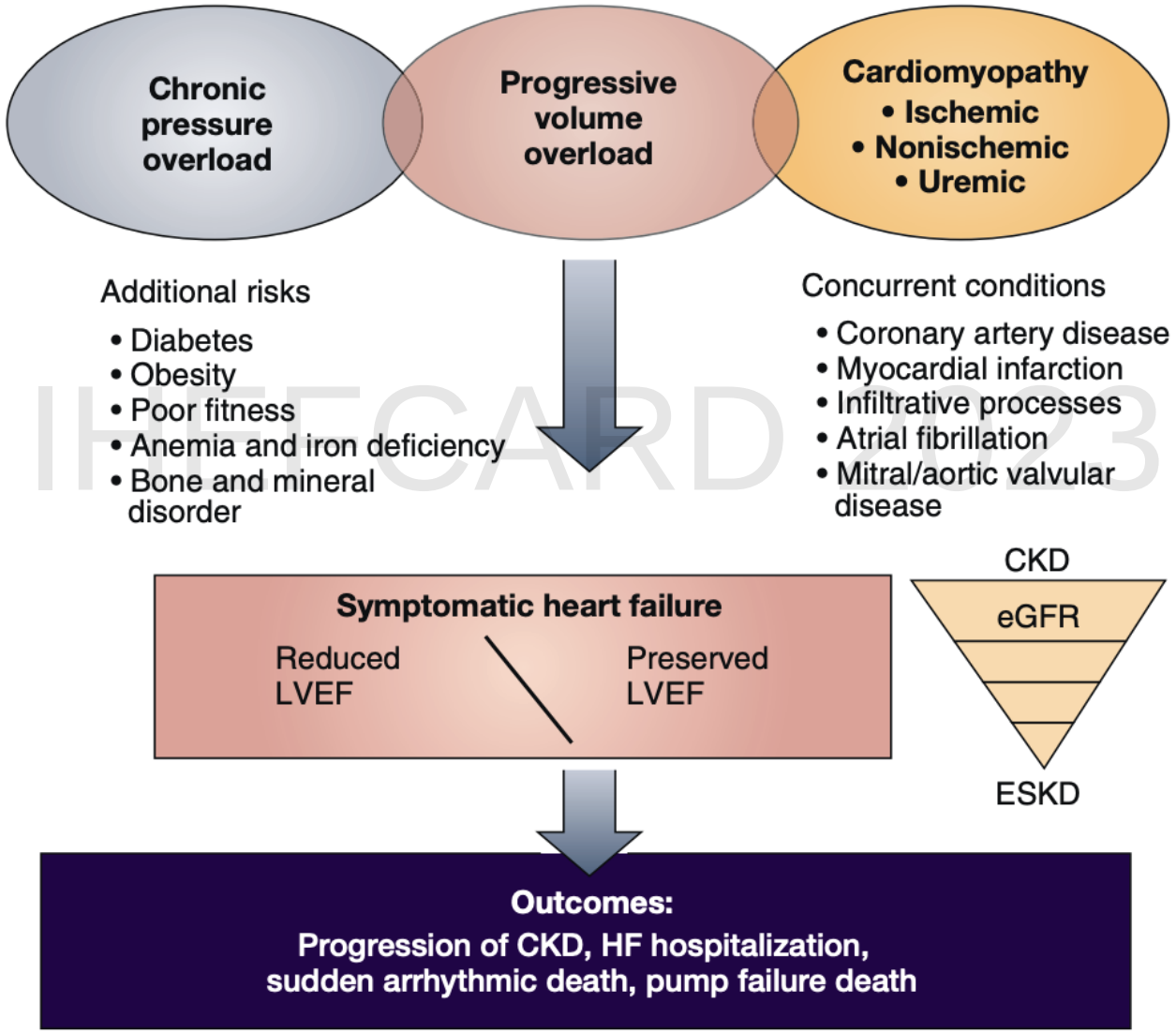
CKD = chronic kidney disease; GP = general population. Source: Turakhia et al. 2019.[41]
Reproduced with permission from Oxford University Press.

Warrens H et al. European Cardiology Review 2022;17:e13.



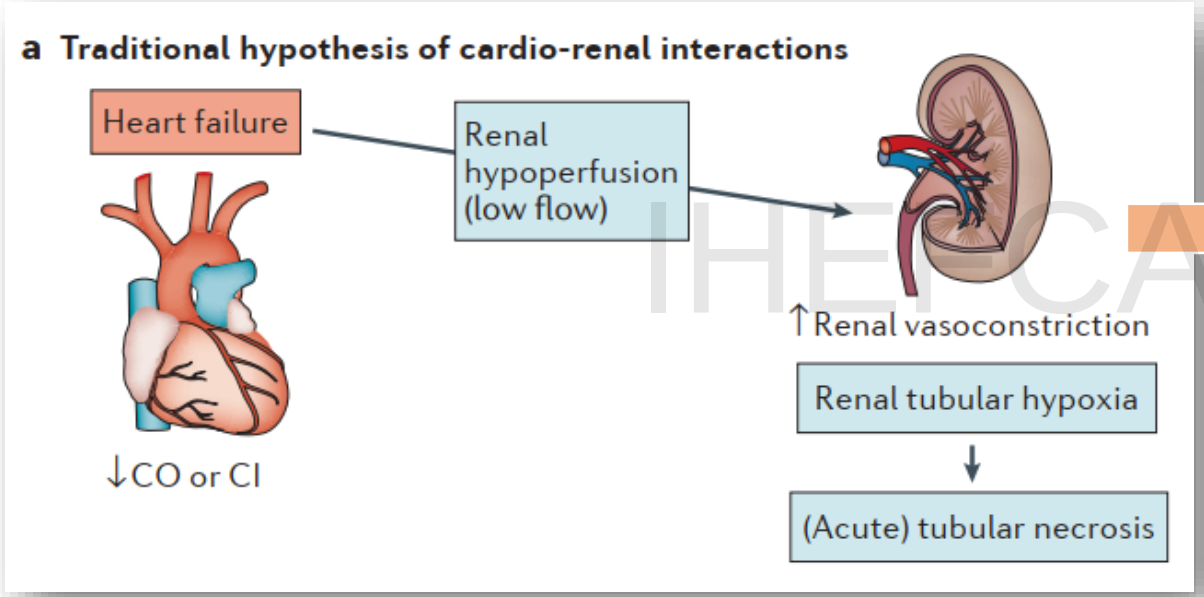
Ahmed and Campbel. Heart Fail Clin. 2008 October ; 4(4): 387–399

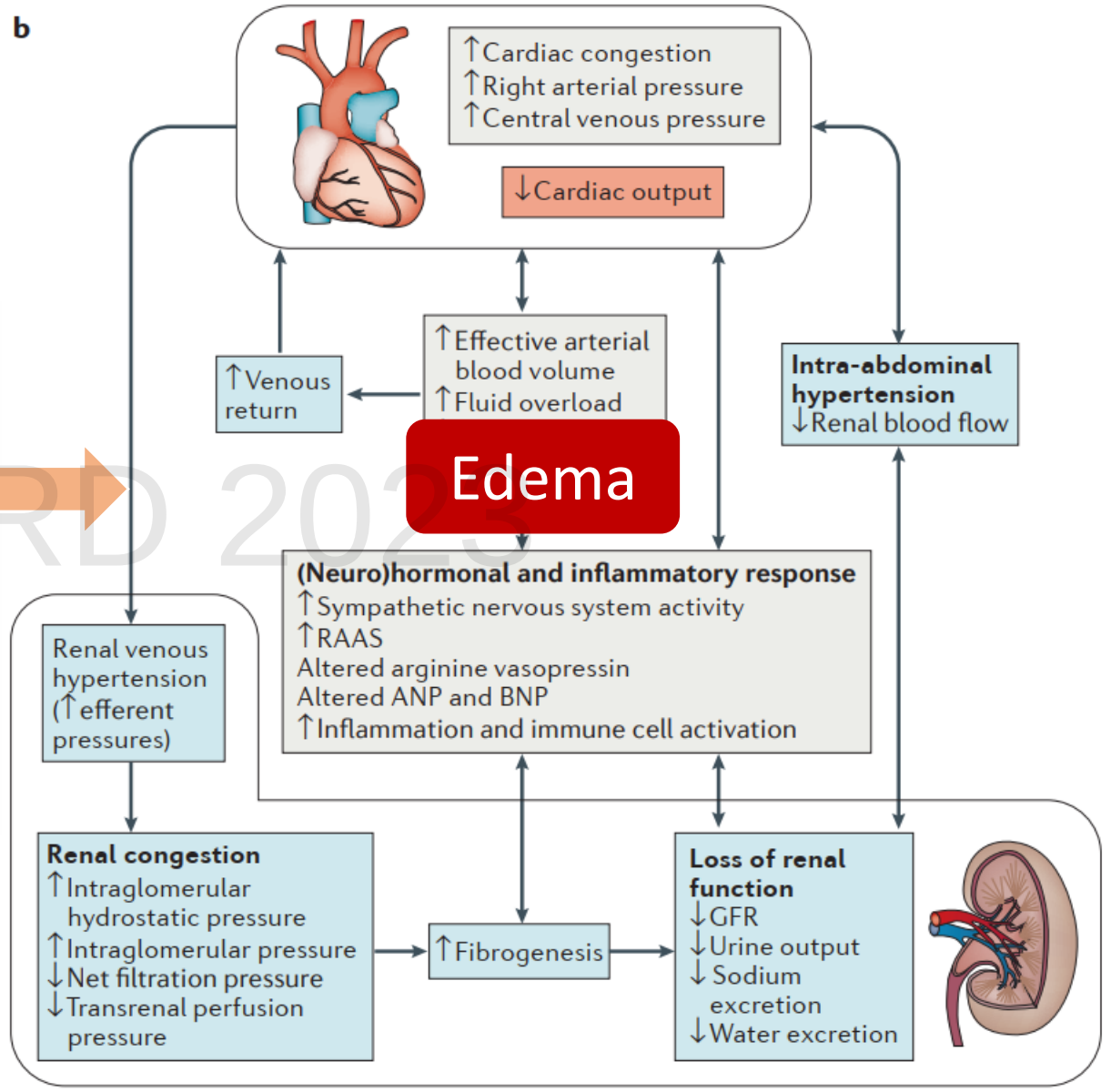
Pathophysiology of heart failure (HF) in chronic kidney disease (CKD) progressing to end-stage kidney disease (ESKD).



House AA et al. Kidney International (2019) 95, 1304–1317

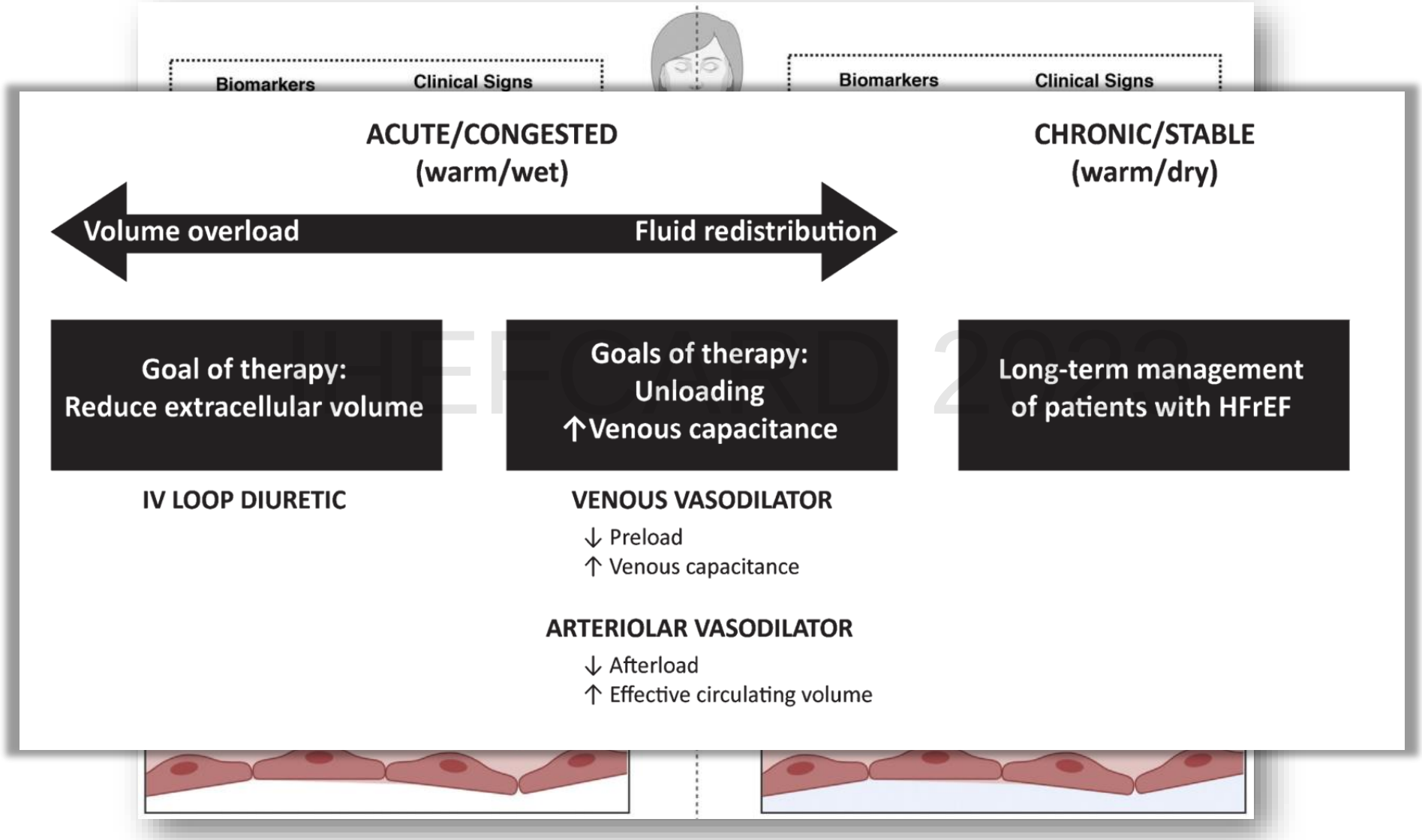
Haemodynamic Mechanisms in Cardio-Renal Interactions





Joerg C. Schefold at al. doi:10.1038/nrneph.2016.113

Intravascular Vs Tissue Congestion



Espriella et al. n e f r o l o g i a. 2022;42(2):145–162
Harjola PV et al. European Journal of Heart Failure (2017) 19, 821–836

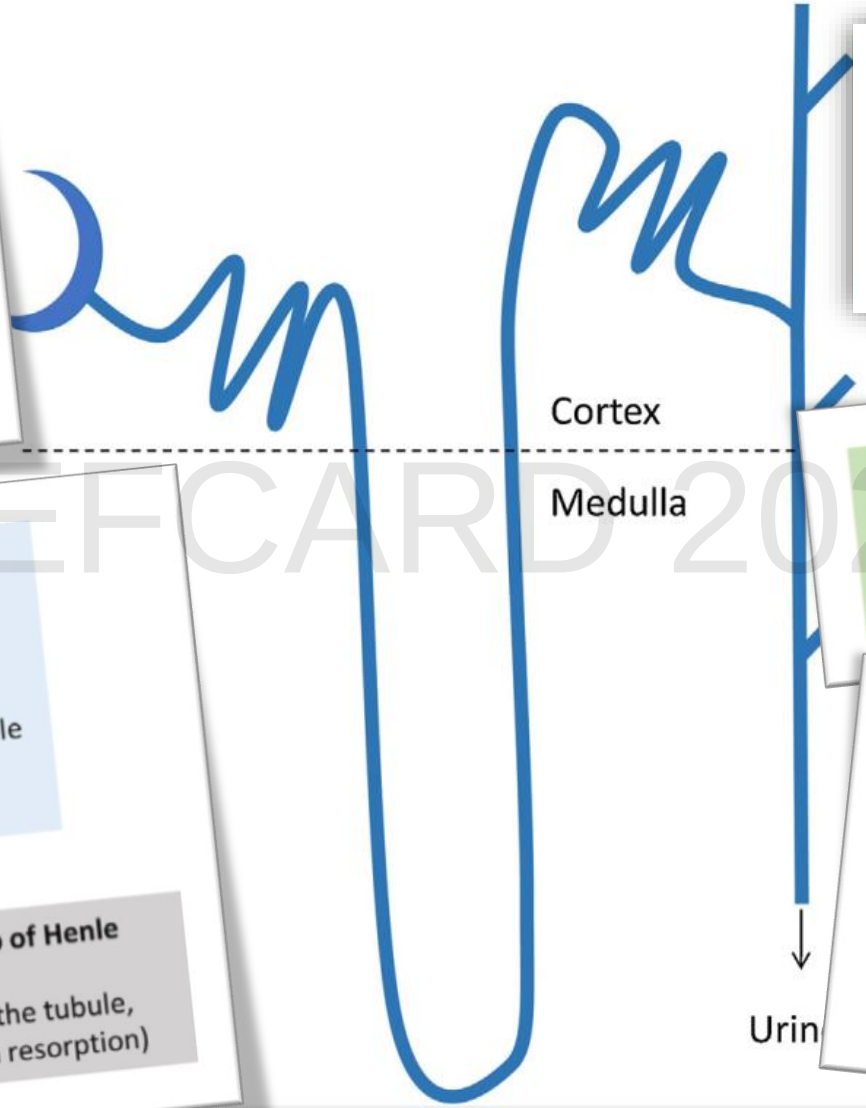
Mechanism of Impaired Diuretic Responsiveness

Reduced GFR
This may occur secondary to:
- Abnormal glomerular haemodynamics (e.g. NSAIDs)
- Reduced renal perfusion from low cardiac output states or venous congestion
- Worsening renal function and chronic kidney disease

These states can reduce delivery of diuretics, reduce active secretion of loop diuretic into tubule

Excessive sodium uptake in the proximal tubule
This may occur secondary to:
- Excessive neuro-hormonal activation;
- *Braking phenomenon* (No diuretic in the tubule, leading to rebound excessive sodium resorption)
- Reduce active secretion of loop diuretic into tubule therefore less diuresis
- Excessive sodium intake

Excessive sodium resorption in the Loop of Henle because of:
- *Braking phenomenon* (No diuretic in the tubule, leading to rebound excessive sodium resorption)



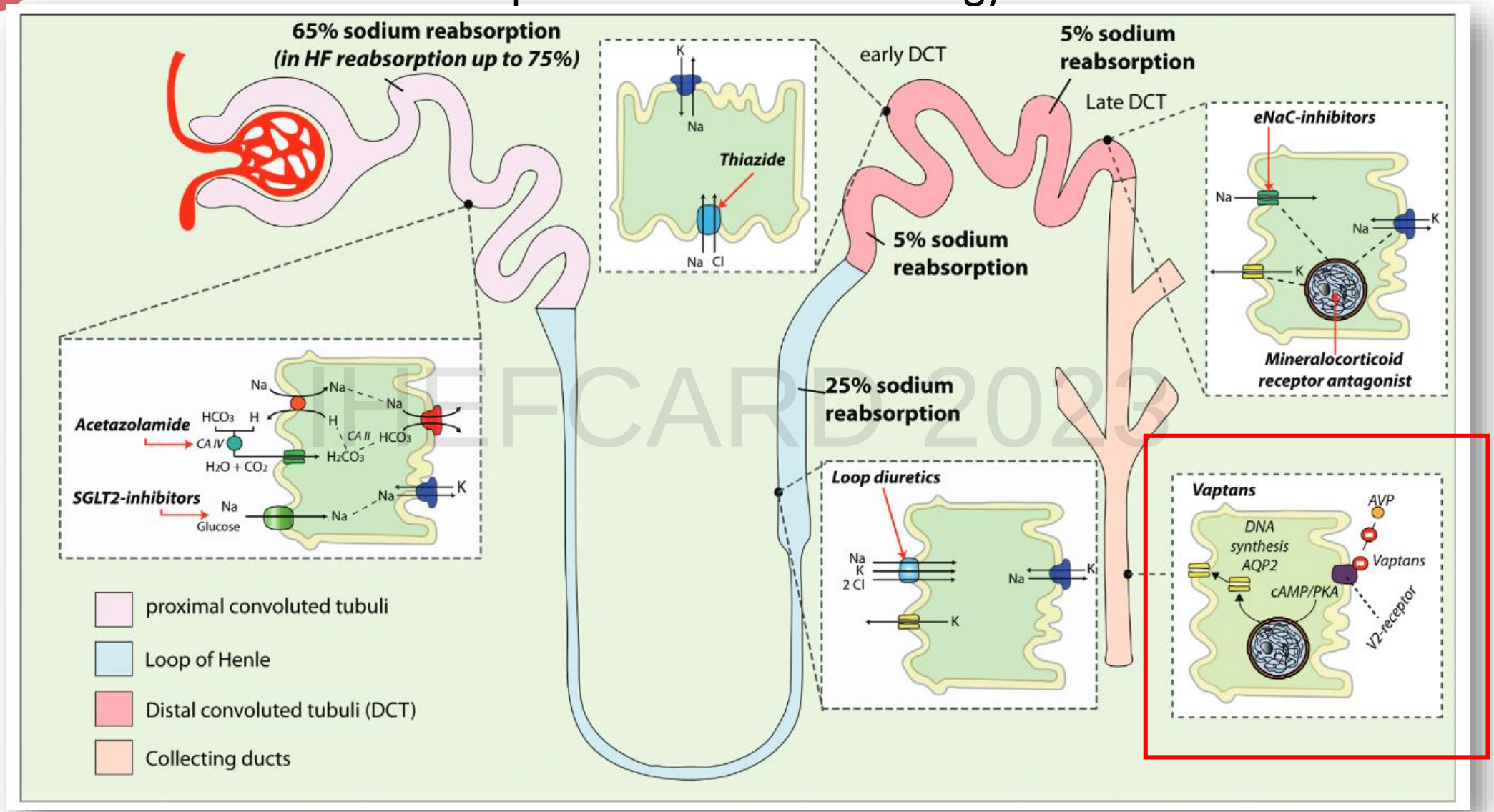
Renal Adaptation:
- Chronic diuretic use can lead to excessive amounts of sodium arriving in the distal tubule leading to distal tubule hypertrophy leading to rebound sodium retention

Excessive Sodium and water retention in the distal Nephron and collecting ducts may occur secondary to:
- Excessive Aldosterone and vasopressin

Non-nephron related cause of diuretic resistance
- Reduced drug bioavailability (especially with oral furosemide) due to reduced absorption from the oedematous bowel

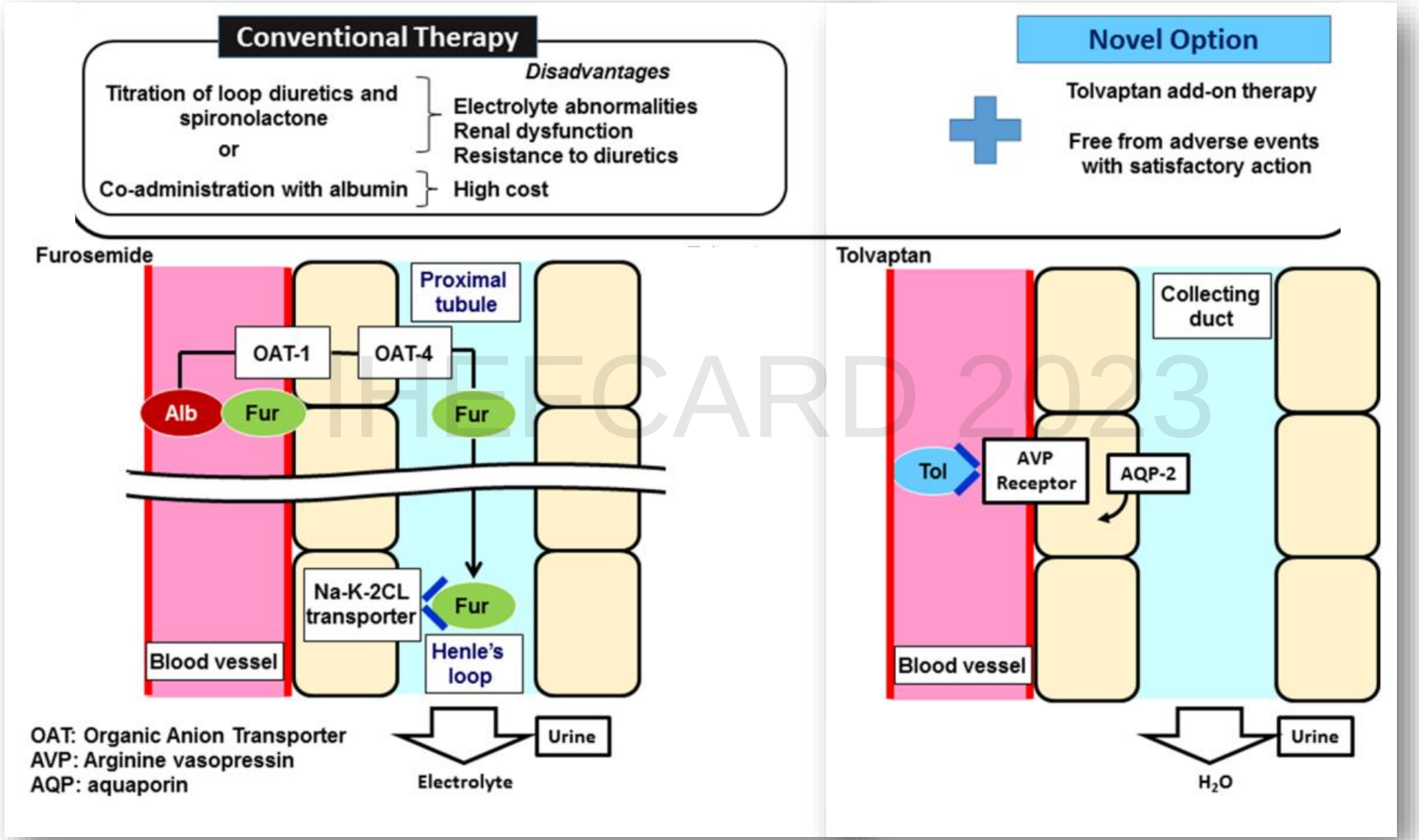
Vaizr and Cowie. Indian heart journal 68 (2016) s61–s68

Aquaretic as Diuretic Strategy



Mullens W et al. European Journal of Heart Failure (2019)21,137–155
Finley et al. *Circulation*. 2008;118:410-421.

New theurapetic strategy



Isao Sakaida et al. J Gastroenterol (2015) 50:1047–1053

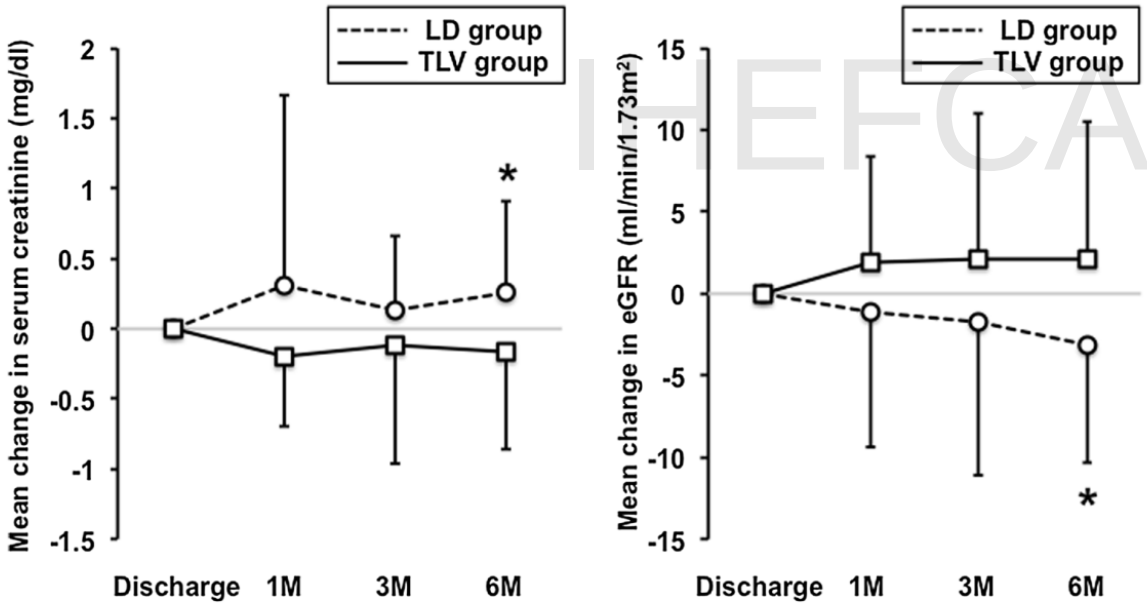
K-STAR Study

-Clinical Benefit of Aquaretic in Patients with ADHF and CKD-

Retrospective study:
(ADHF+ advanced CKD- eGFR <45 mL/min/1.73 m2)

33 pts (Tolvaptan+Furosemide) vs **36 pts** High dose Furosemide

Changes in serum creatinine and eGFR during a 6-month follow-up



Clinical outcome during a 6-month follow-up

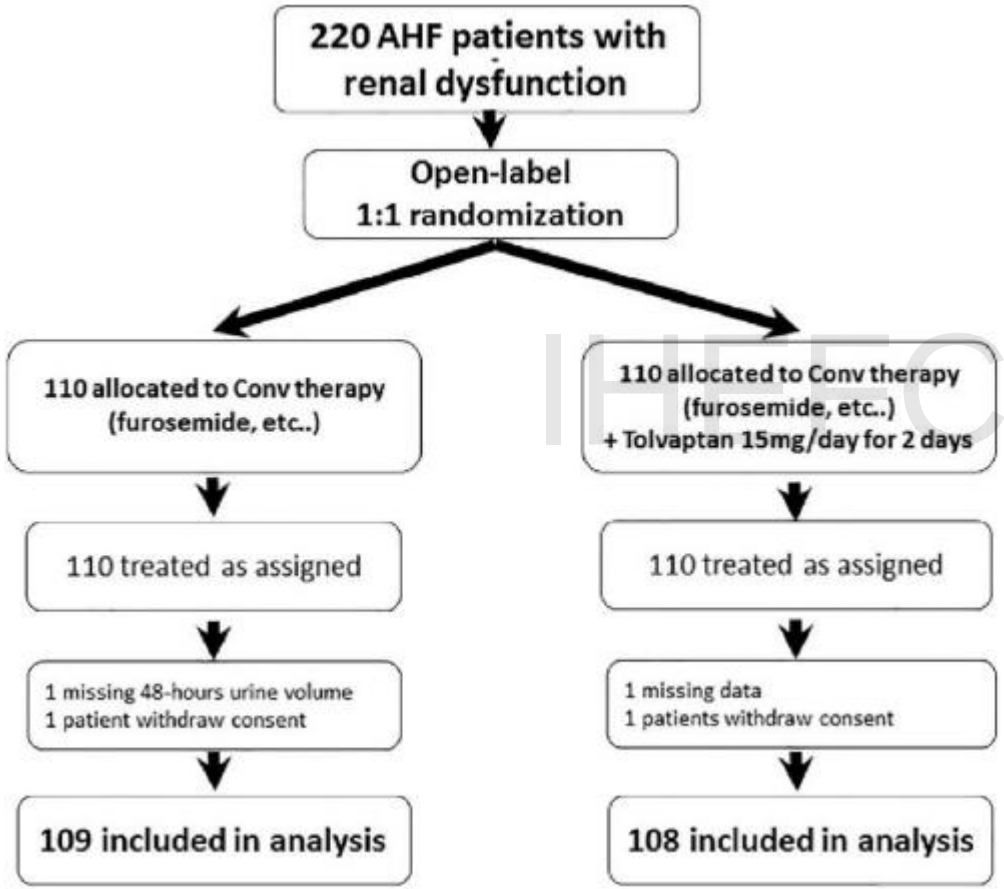
	LD group ($n = 36$)	TLV group ($n = 33$)	p value
All-cause death (%)	4 (11.1 %)	3 (9.1 %)	n.s.
Cardiac death (%)	4 (11.1 %)	1 (3.0 %)	n.s.
Heart failure hospitalization	22 (61.1 %)	12 (36.4 %)	0.04

n.s. not significant

Inomata T. et al. : Circ K., 2017, DOI : 10.1253/circj.CJ-17-0179

AQUAMARINE - Study

(Patients With Acute Heart Failure and Kidney Dysfunction)



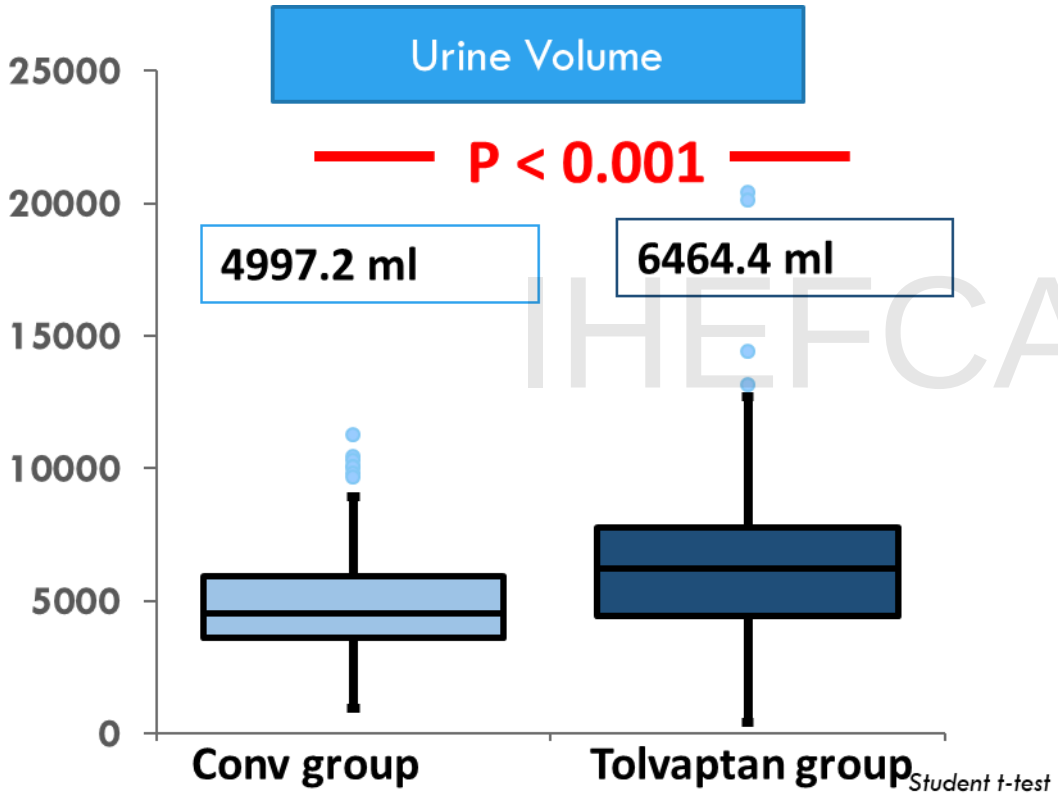
The **primary end point**: amount of urine output within 48 hours

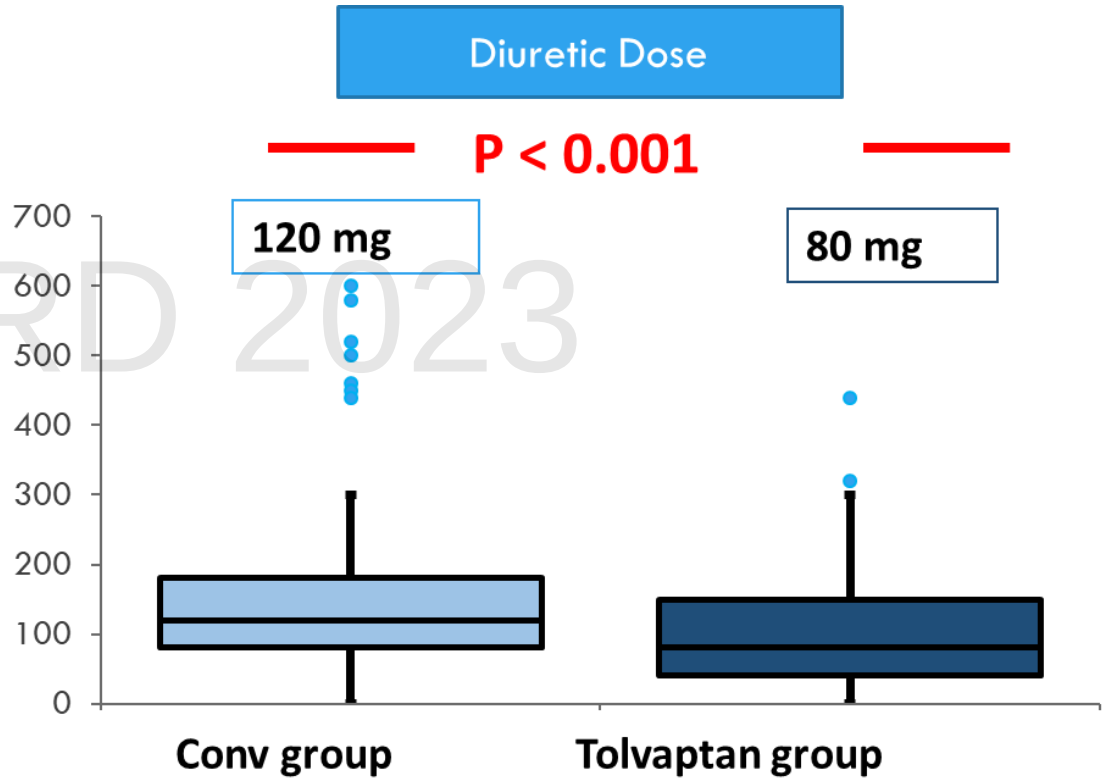
The **secondary end points**:

1. Incidence of WRF at 6, 12, 24, and 48 hours
2. Moderate or marked improvement of dyspnea (patient-reported 7-point Likert scale) at 6, 12, 24, and 48 hours
3. Amount of furosemide-equivalent loop diuretics used within 48 hours
4. Changes in BP, HR, serum sodium, serum potassium, serum creatinine, eGFR, and BUN at 6, 12, 24, and 48 hours
5. Changes in BNP and body weight at 48 hours
6. Incidence of any adverse events
7. Combined end point of all-cause death and heart failure rehospitalization within 90 days

Matsue et al. Journal of Cardiac Failure Vol. 22 No. 6 June 2016

Aquaretic promotes more diuresis than diuretic despite significantly lower dose of loop diuretic used





Matsue et al. Journal of Cardiac Failure Vol. 22 No. 6 June 2016

AQUAMARINE - Study

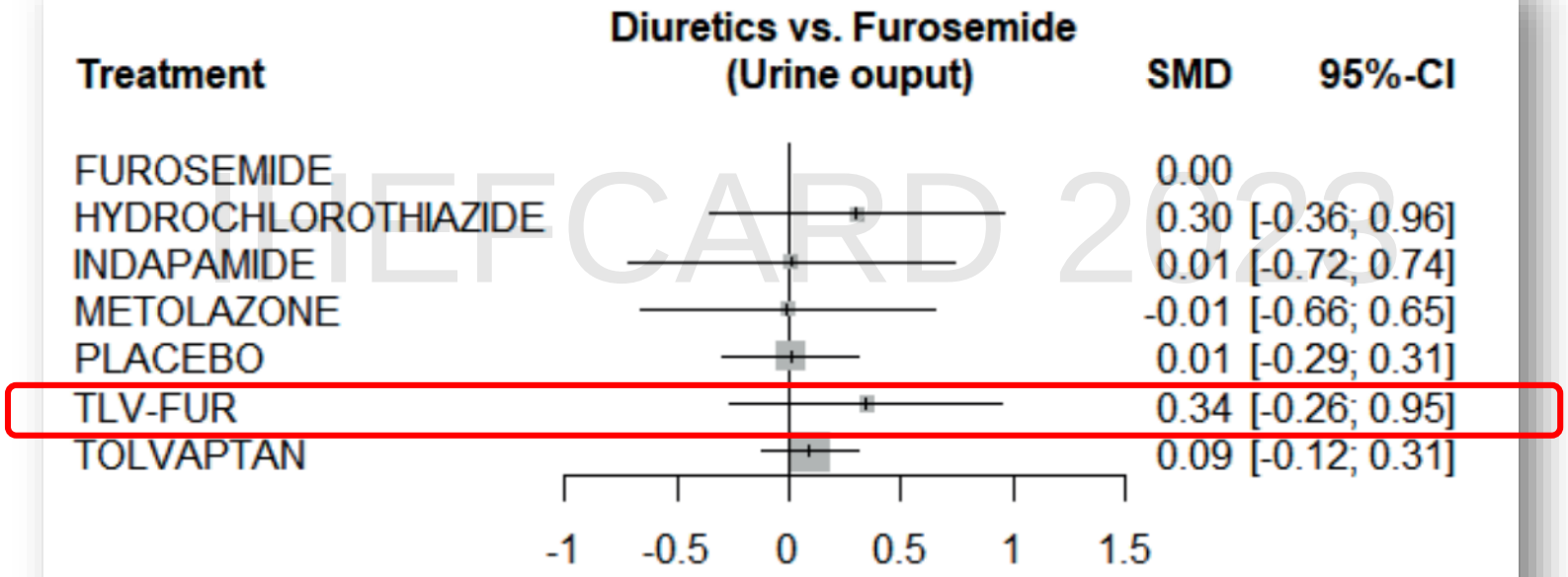
(Patients With Acute Heart Failure and Kidney Dysfunction)

Outcome	Conventional Group (n = 109)	Tolvaptan Group (n = 108)	*P* Value
Primary outcome			
48-hour urine volume (mL)	4997.2 ± 2101.4	6464.4 ± 3173.0	<.001
Secondary outcomes			
Worsening of renal function (%)	30 (27.8)	26 (24.1)	.642
Dose of diuretics use within 48 h (mg)	120 (80–180)	80 (40–150)	<.001 ★
Net fluid loss within 48 h (mL)	3697.9 ± 2112.0	4700.1 ± 2443.3	.004
Change in BNP from baseline to 48 h (pg/mL)	−306.1 (−153.7 to −662.1)	−285.3 (−110.7 to −650.9)	.602
Change in body weight from baseline to 48 h (kg)	−1.99 ± 2.17	−3.16 ± 2.66	<.001 ★
Length of hospital stay (d)	14.6 (10.3–27.2)	14.2 (8.9–20.3)	.36
Adverse events	6 (5.5)	10 (9.3)	.313
In-hospital death	5 (4.6)	4 (3.7)	>.99

Results are presented as mean ± SD, n (%), or median (interquartile range). BNP, B-type natriuretic peptide.

Matsue et al. Journal of Cardiac Failure Vol. 22 No. 6 June 2016

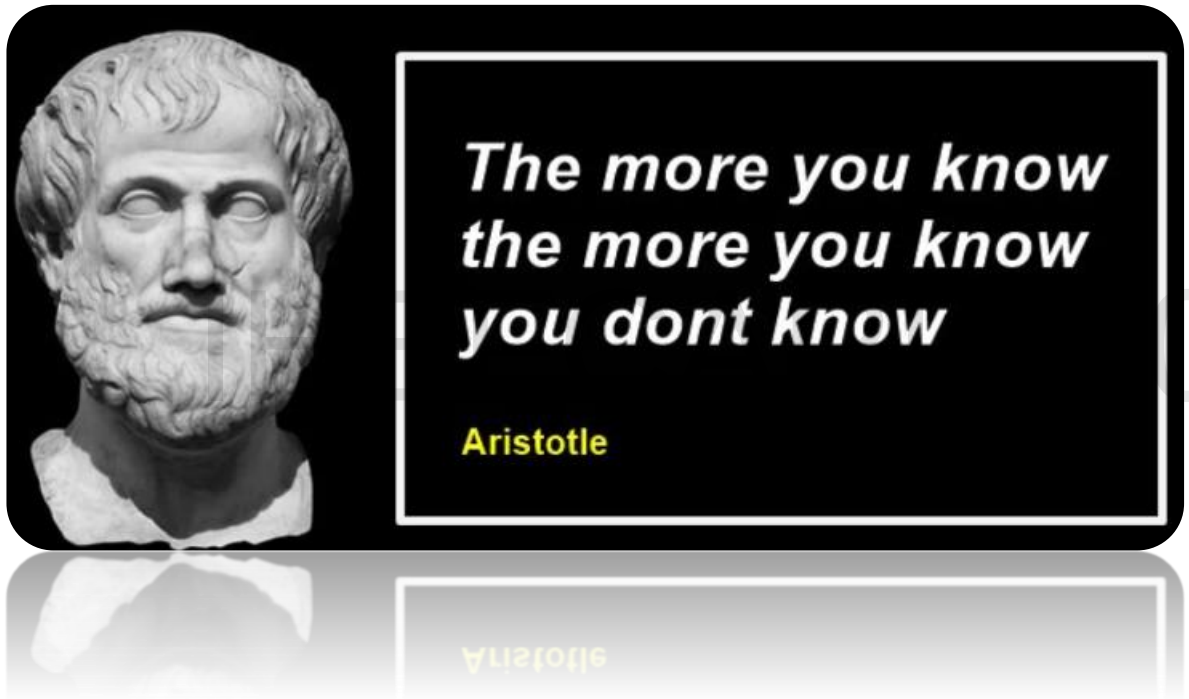
Comparison of Diuretic Strategies in Diuretic-Resistant Acute Heart Failure: A Systematic Review and Network Meta-Analysis



Orso et al. European Review for Medical and Pharmacological Sciences 2021; 25: 2971-2980

Take Home Messages

- Heart failure and CKD is a global burden disease due to high morbidity, high mortality and high cost treatment.
- Heart failure and CKD as double risk for congestion with high risk for impaired diuretic responsiveness.
- Aquaretic (tolvaptan) has better diuretic response (even single or combine with furosemide), no interfere electrolyte level and prevent decrease kidney function.
- Good decongestion strategy will reduce rehospitalization.



Thank you…