PLACE 2026
PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO
ROMA, 25 - 27 Giugno 2026

Insufficienza cardiaca acuta

AKI nello scompenso cardiaco acuto

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Disclosures

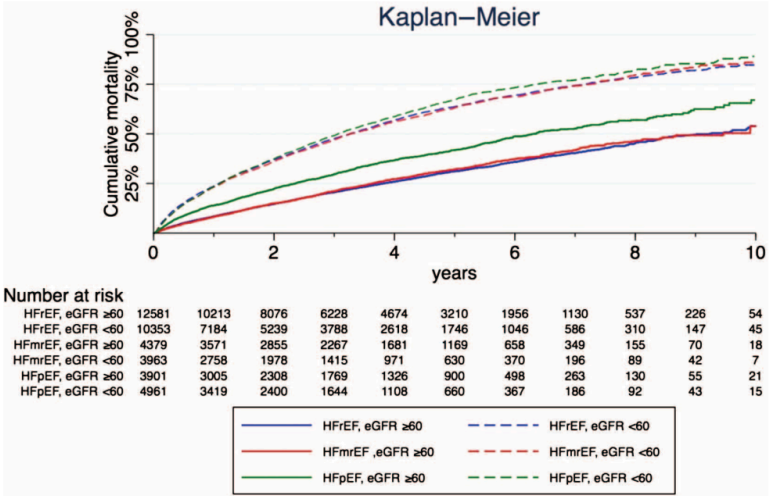
Astra Zeneca, Novo Nordisk, Pfizer, Boehringer, Alnylam, Bayer speaking fees.

Why do we care about renal function?

Associations with and prognostic impact of chronic kidney disease in heart failure with preserved, mid-range, and reduced ejection fraction

Ida Löfman[1]*, Karolina Szummer[1], Ulf Dahlström[2], Tomas Jernberg[3], and Lars H. Lund[4]

SwedeHF registry.



	HFpEF ($n = 8860$)		HFmrEF ($n = 8350$)		HFrEF ($n = 22\,953$)	
	eGFR ≥60	eGFR <60	eGFR ≥60	eGFR <60	eGFR ≥60	eGFR <60
1-year mortality	13.4%	22.6%*	7.8%	22.4%*	8.0%	23.0%*
5-year mortality	41.8%	67.1%	32.0%	63.1%	31.1%	63.7%
Deaths/100 patient-years, *n*	2.79	4.41	2.23	4.79	2.04	4.49

*P <0.001 comparing eGFR ≥60 vs. <60 within each EF group.

European Journal of Heart Failure (2017) **19**, 1606–1614

Why do we care about renal function?

Circulation
Volume 102, Issue 2, 11 July 2000; Pages 203-210
https://doi.org/10.1161/01.CIR.102.2.203

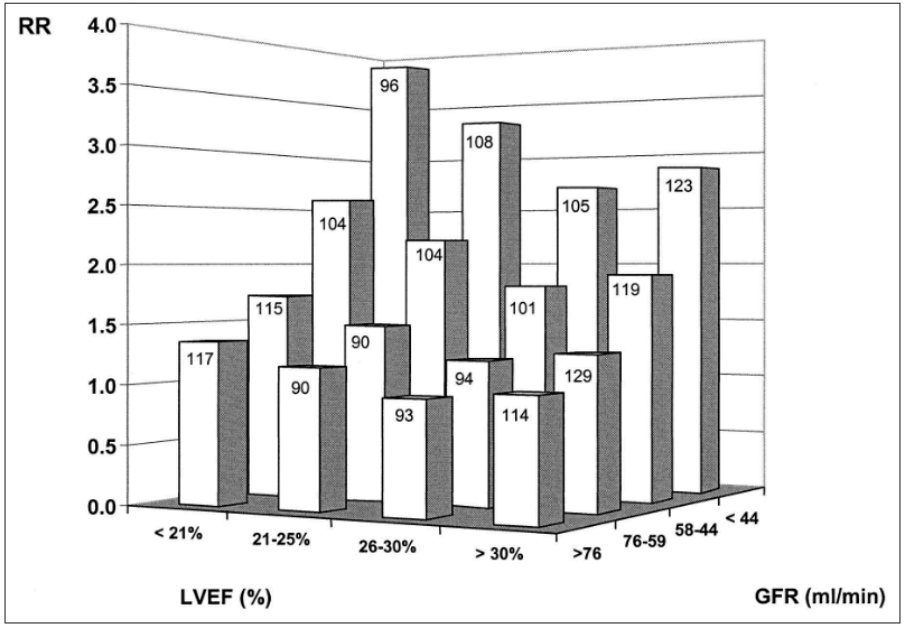
CLINICAL INVESTIGATION AND REPORTS

Renal Function, Neurohormonal Activation, and Survival in Patients With Chronic Heart Failure

Hans L. Hillege, Armand R. J. Girbes, Pieter J. de Kam, Frans Boomsma, Dick de Zeeuw, Andrew Charlesworth, John R. Hampton, and Dirk J. van Veldhuisen

- Patients in the lowest quartile of GFR values (<44 ml/min) had almost 3 times the risk of mortality (RR 2.85; $p<0.001$) of patients in the highest quartile (>76 ml/min).
- Impaired LVEF was only modestly predictive ($p=0.053$).

Mortality



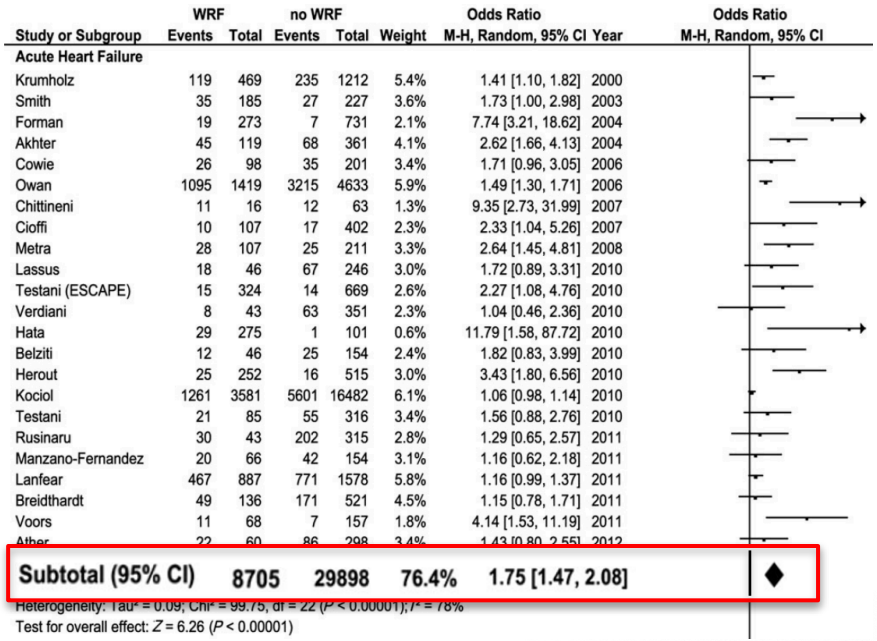
Why do we care about CHANGES renal function?

Renal impairment, worsening renal function, and outcome in patients with heart failure: an updated meta-analysis

Kevin Damman[1]*, Mattia A.E. Valente[1], Adriaan A. Voors[1], Christopher M. O'Connor[2], Dirk J. van Veldhuisen[1], and Hans L. Hillege[1,3]

Prevalence of WRF in acute HF 23%.

All-cause mortality



Study or Subgroup	WRF Events	WRF Total	no WRF Events	no WRF Total	Weight	Odds Ratio M-H, Random, 95% CI	Year	Odds Ratio M-H, Random, 95% CI
Acute Heart Failure								
Krumholz	119	469	235	1212	5.4%	1.41 [1.10, 1.82]	2000	
Smith	35	185	27	227	3.6%	1.73 [1.00, 2.98]	2003	
Forman	19	273	7	731	2.1%	7.74 [3.21, 18.62]	2004	
Akhter	45	119	68	361	4.1%	2.62 [1.66, 4.13]	2004	
Cowie	26	98	35	201	3.4%	1.71 [0.96, 3.05]	2006	
Owan	1095	1419	3215	4633	5.9%	1.49 [1.30, 1.71]	2006	
Chittineni	11	16	12	63	1.3%	9.35 [2.73, 31.99]	2007	
Cioffi	10	107	17	402	2.3%	2.33 [1.04, 5.26]	2007	
Metra	28	107	25	211	3.3%	2.64 [1.45, 4.81]	2008	
Lassus	18	46	67	246	3.0%	1.72 [0.89, 3.31]	2010	
Testani (ESCAPE)	15	324	14	669	2.6%	2.27 [1.08, 4.76]	2010	
Verdiani	8	43	63	351	2.3%	1.04 [0.46, 2.36]	2010	
Hata	29	275	1	101	0.6%	11.79 [1.58, 87.72]	2010	
Belziti	12	46	25	154	2.4%	1.82 [0.83, 3.99]	2010	
Herout	25	252	16	515	3.0%	3.43 [1.80, 6.56]	2010	
Kociol	1261	3581	5601	16482	6.1%	1.06 [0.98, 1.14]	2010	
Testani	21	85	55	316	3.4%	1.56 [0.88, 2.76]	2010	
Rusinaru	30	43	202	315	2.8%	1.29 [0.65, 2.57]	2011	
Manzano-Fernandez	20	66	42	154	3.1%	1.16 [0.62, 2.18]	2011	
Lanfear	467	887	771	1578	5.8%	1.16 [0.99, 1.37]	2011	
Breidthardt	49	136	171	521	4.5%	1.15 [0.78, 1.71]	2011	
Voors	11	68	7	157	1.8%	4.14 [1.53, 11.19]	2011	
Ather	22	60	86	298	3.4%	1.43 [0.80, 2.55]	2012	
Subtotal (95% CI)	**8705**		**29898**		**76.4%**	**1.75 [1.47, 2.08]**		

Heterogeneity: Tau² = 0.09; Chi² = 99.75, df = 22 ($P < 0.00001$); I^2 = 78%
Test for overall effect: $Z = 6.26$ ($P < 0.00001$)

European Heart Journal (2014) **35**, 455–469

definitions of changes in renal function

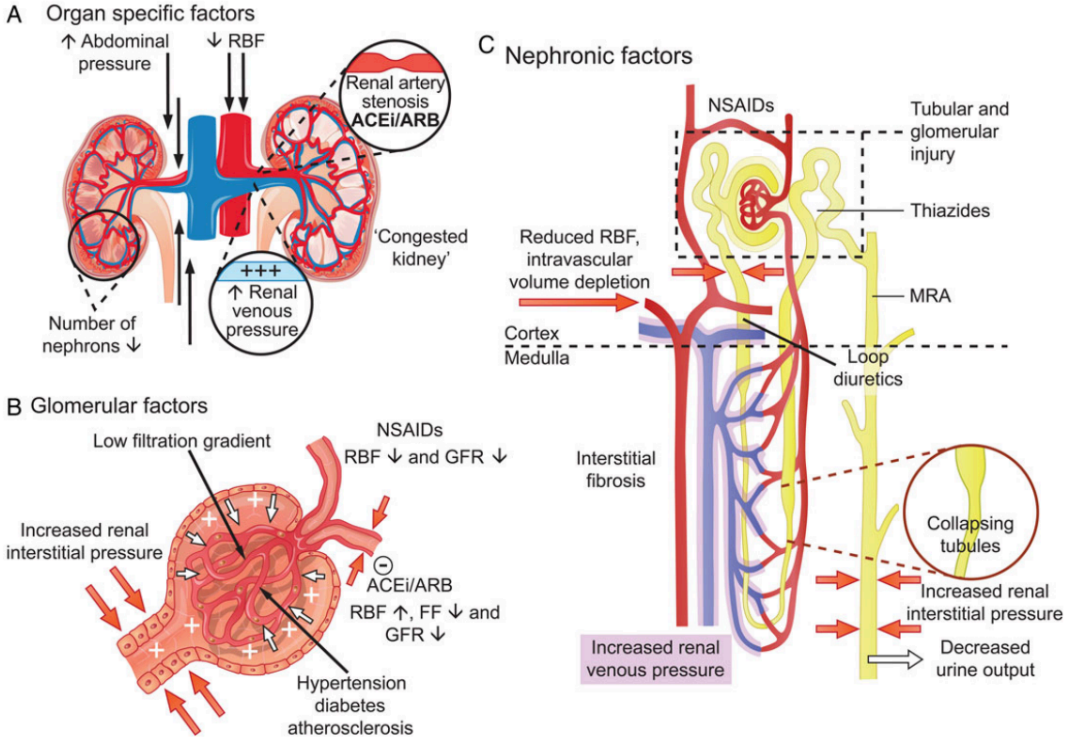
Table 1 Definition of changes in renal function in heart failure

WRF		
GFR-based definitions	**Cystatin C-based definitions**	**Creatinine-based definitions**
• ≥20% decrease • ≥25% decrease • >5 mL/min/1.73 m^2 per year decrease	• >0.3 mg/dL increase	• ≥0.3 mg/dL increase • ≥0.3 mg/dL increase and >25% increase • ≥0.5 mg/dL increase • 1.5× baseline • >25% increase + above 2.0 mg/dL

AKI			
UO component	**Scr component**		
	KDIGO	**AKIN**	**RIFLE**
Grade 1 <0.5 mL/kg/h for 6-12 h	Scr to 1.5–1.9× baseline over 7 days or absolute increase ≥0.3 mg/dL over 48 h	Scr to 1.5–2.0× baseline or absolute increase ≥0.3 mg/dL over 48 h	Scr to ≥1.5× within 7 days sustained for 24 h
Grade 2 <0.5 mL/kg/h for ≥12 h	Scr to 2.0–2.9× baseline	Scr >2.0–3.0× baseline	Scr ≥2.0×
Grade 3 <0.3 mL/kg/h for ≥24 h or anuria for ≥12 h	Scr to ≥3.0× baseline or increase above ≥4.0 mg/dL or RRT	Scr to ≥3.0× baseline or increase above ≥4.0 mg/dL (with absolute increase >0.5 mg/dL) or RRT	Scr to ≥3.0× baseline or increase above ≥4.0 mg/dL (with absolute increase >0.5 mg/dL) or RRT

European Journal of Heart Failure (2020) **22**, 584–603

Cardiorenal interactions in HF



- Kidneys receive 20% of cardiac output (despite accounting for 0.5% of body weight).
- Cardiac function is a primary determinant of renal function.
- The kidneys regulate intravascular volume, thereby determining cardiac preload.
- Both forward and backward HF induce changes in the eGFR as:

Renal Perfusion Pressure

=

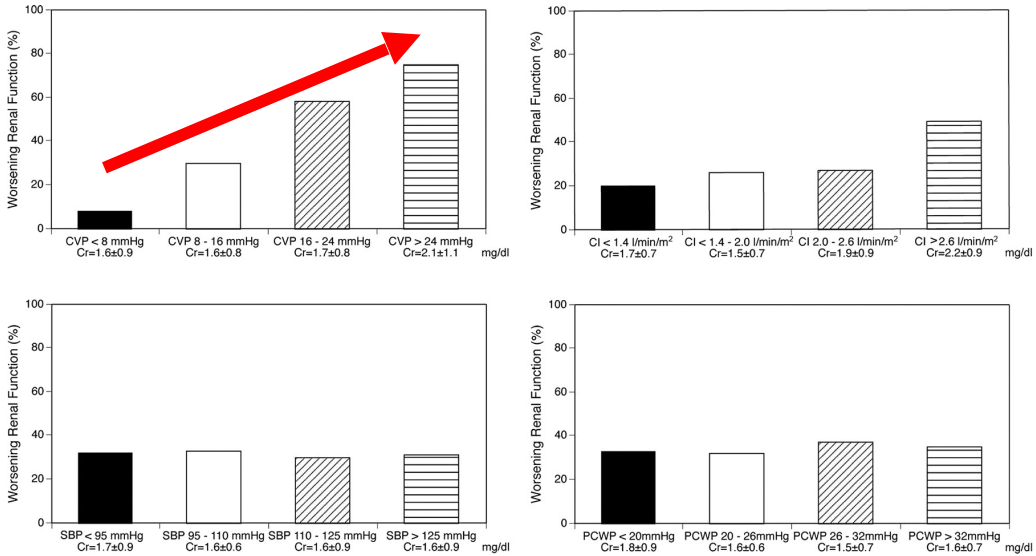
MAP – Renal Venous Pressure

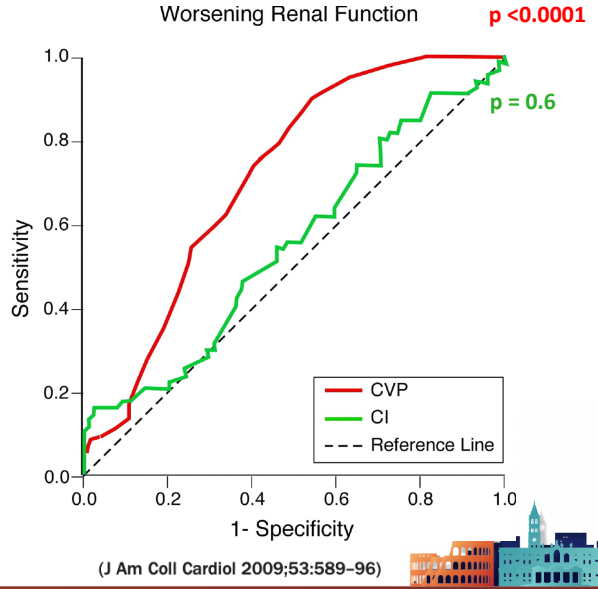
European Heart Journal (2014) **35**, 3413–3416

Hemodynamic drivers of worsening renal function in AHF

Importance of Venous Congestion for Worsening of Renal Function in Advanced Decompensated Heart Failure

Wilfried Mullens, MD, Zuheir Abrahams, MD, PHD, Gary S. Francis, MD, FACC, George Sokos, DO, David O. Taylor, MD, FACC, Randall C. Starling, MD, MPH, FACC, James B. Young, MD, FACC, W. H. Wilson Tang, MD, FACC
Cleveland, Ohio





(J Am Coll Cardiol 2009;53:589–96)

Renal function

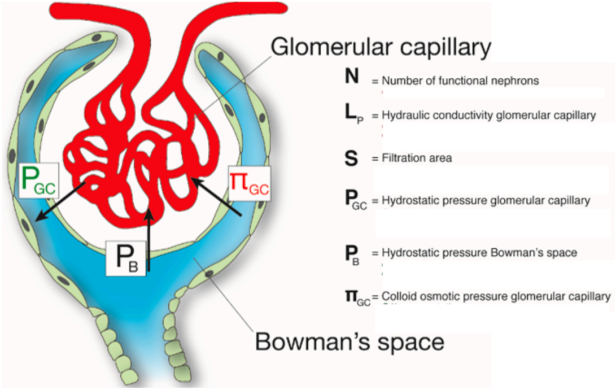
- Renal function ≠ eGFR.
- Not all eGFR changes are created equal.
- Context of change matters.

Renal function > eGFR

RENAL FUNCTION

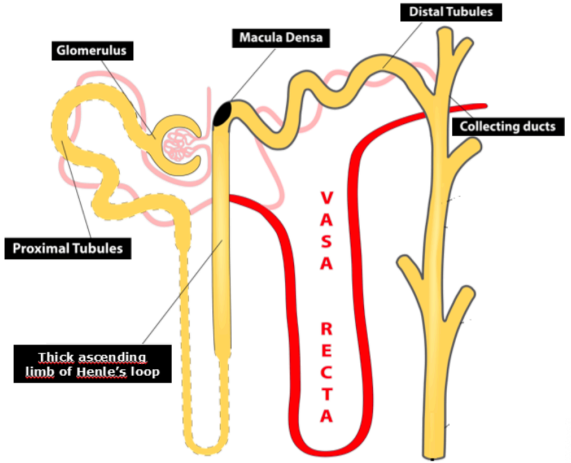
Glomerular filtration rate (GFR)

$$GFR = N \times L_P \times S \times (P_{GC} - P_B - \pi_{GC})$$



- N = Number of functional nephrons
- L_P = Hydraulic conductivity glomerular capillary
- S = Filtration area
- P_{GC} = Hydrostatic pressure glomerular capillary
- P_B = Hydrostatic pressure Bowman's space
- π_{GC} = Colloid osmotic pressure glomerular capillary

Tubular function



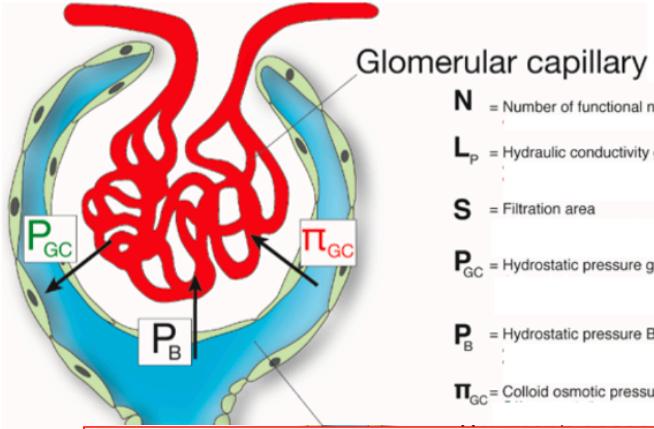
CLEARANCE

HOMEOSTASIS

Renal function & glomerular hemodynamics

Glomerular filtration rate (GFR)

$$GFR = N \times L_P \times S \times (P_{GC} - P_B - \pi_{GC})$$



- N = Number of functional nephrons
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- S = Filtration area
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- π_{GC} = Colloid osmotic pressure glomerular capillary

Single nephron kinetics

GFR= #nephrons * single nephron kinetics

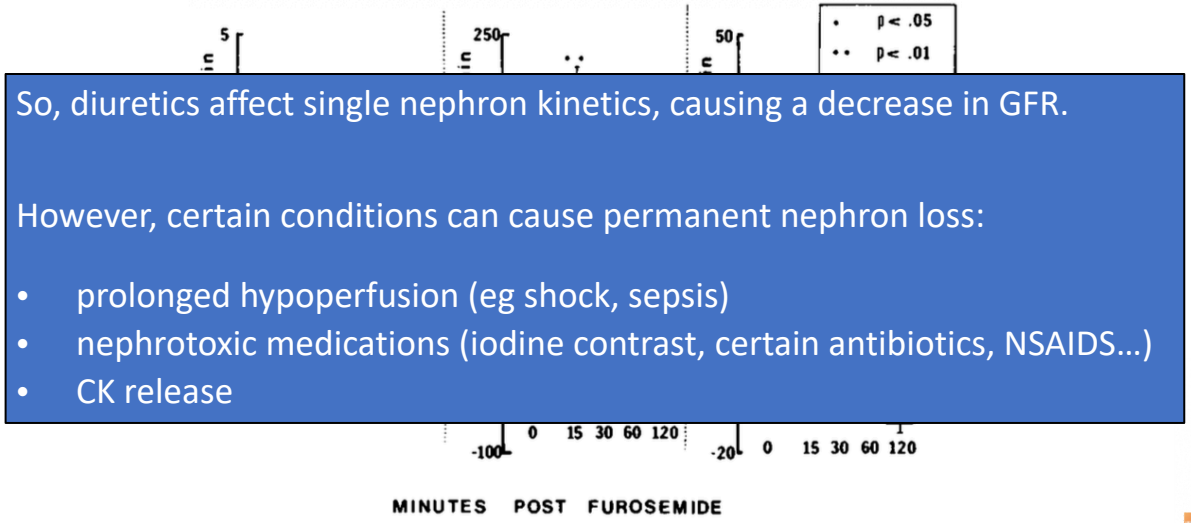
Do drops in eGFR reflect permanent nephron loss (BAD) or changes in single nephron kinetics (less relevant)?

Diuretics cause changes in single nephron GFR

RENAL AND EXTRARENAL HEMODYNAMIC EFFECTS OF FUROSEMIDE IN CONGESTIVE HEART FAILURE AFTER ACUTE MYOCARDIAL INFARCTION

KRISHNA DIKSHIT, M.D., M.R.C.P., JOHN K. VYDEN, M.B., JAMES S. FORRESTER, M.D., KANU CHATTERJEE, M.B., M.R.C.P., RAVI PRAKASH, M.D., AND H.J.C. SWAN, M.B., PH.D., F.R.C.P.

(N Engl J Med 288:1087-1090,1973)

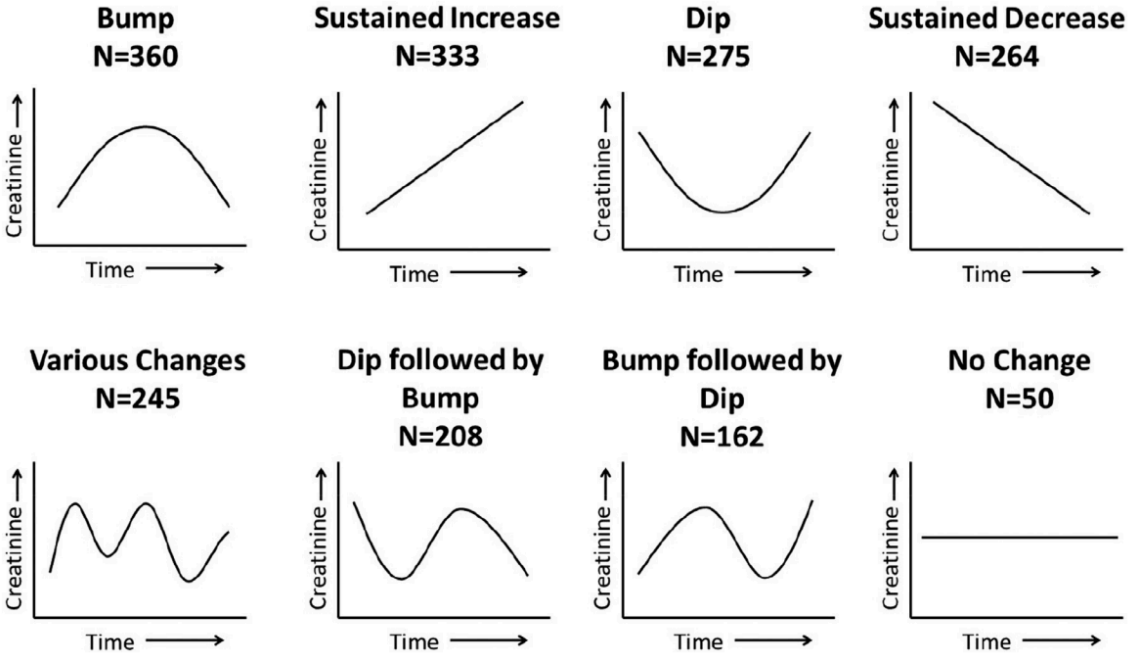


So, diuretics affect single nephron kinetics, causing a decrease in GFR.

However, certain conditions can cause permanent nephron loss:

- prolonged hypoperfusion (eg shock, sepsis)
- nephrotoxic medications (iodine contrast, certain antibiotics, NSAIDS…)
- CK release

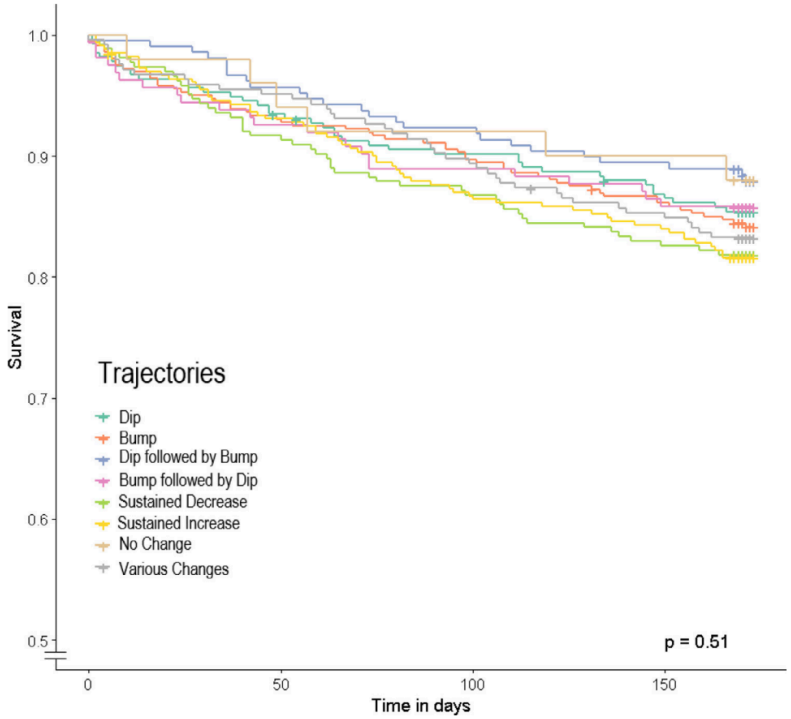
Many different patterns of GFR changes in AHF…



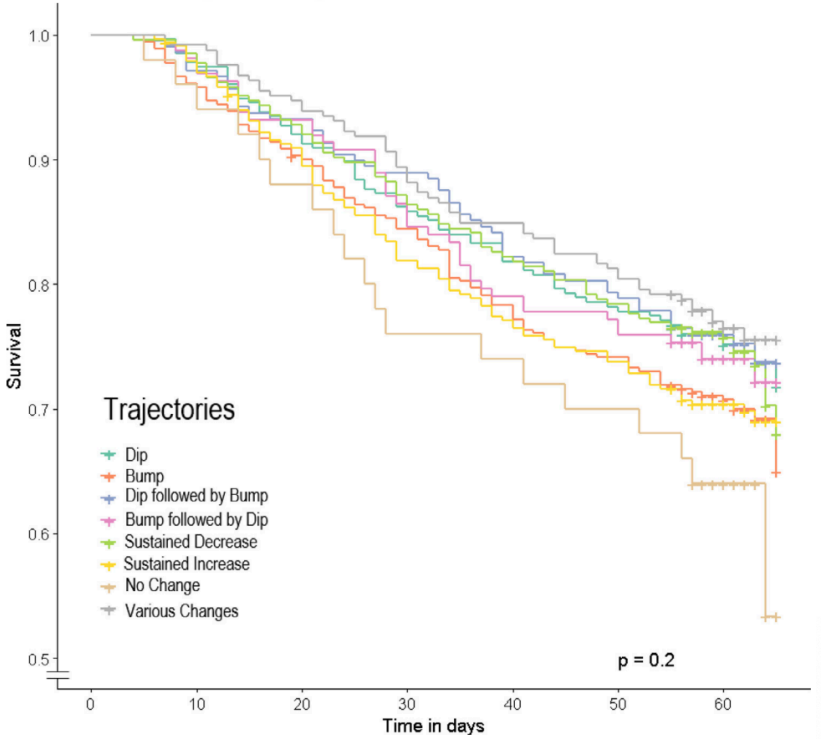
Journal of Cardiac Failure Vol. 25 No. 11 2019

Same outcomes

All-cause death



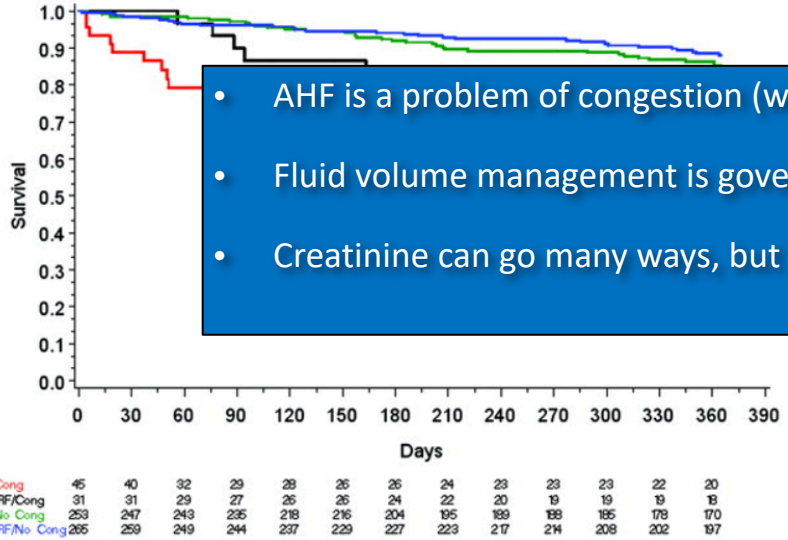
Death or CV/renal hospotalization

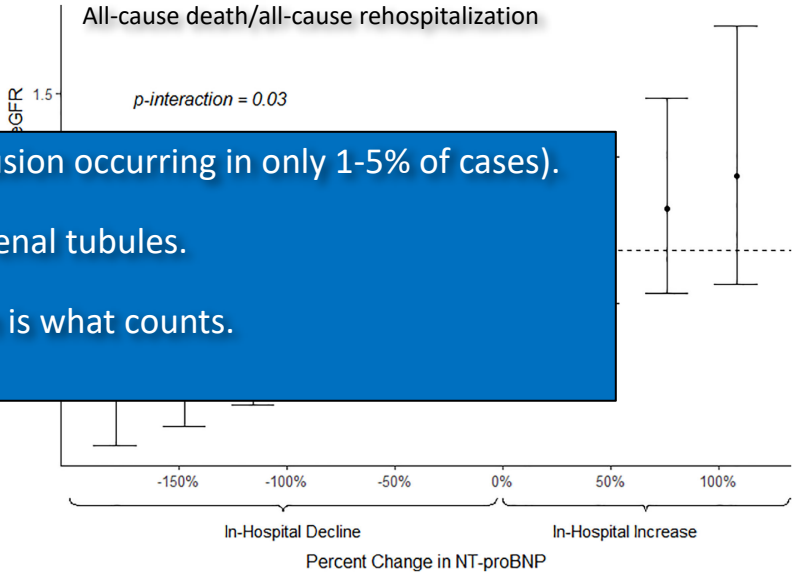


Journal of Cardiac Failure Vol. 25 No. 11 2019

While persistent congestion is bad

- AHF is a problem of congestion (with hypoperfusion occurring in only 1-5% of cases).
- Fluid volume management is governed by the renal tubules.
- Creatinine can go many ways, but decongestion is what counts.





Circulation: Heart Failure
Volume 5, Issue 1, January 2012; Pages 54-62
https://doi.org/10.1161/CIRCHEARTFAILURE.111.963413

Am J Med. 2020 January ; 133(1): 115–122.e2.

How to find your bearings when things get complicated?

ESC European Society of Cardiology

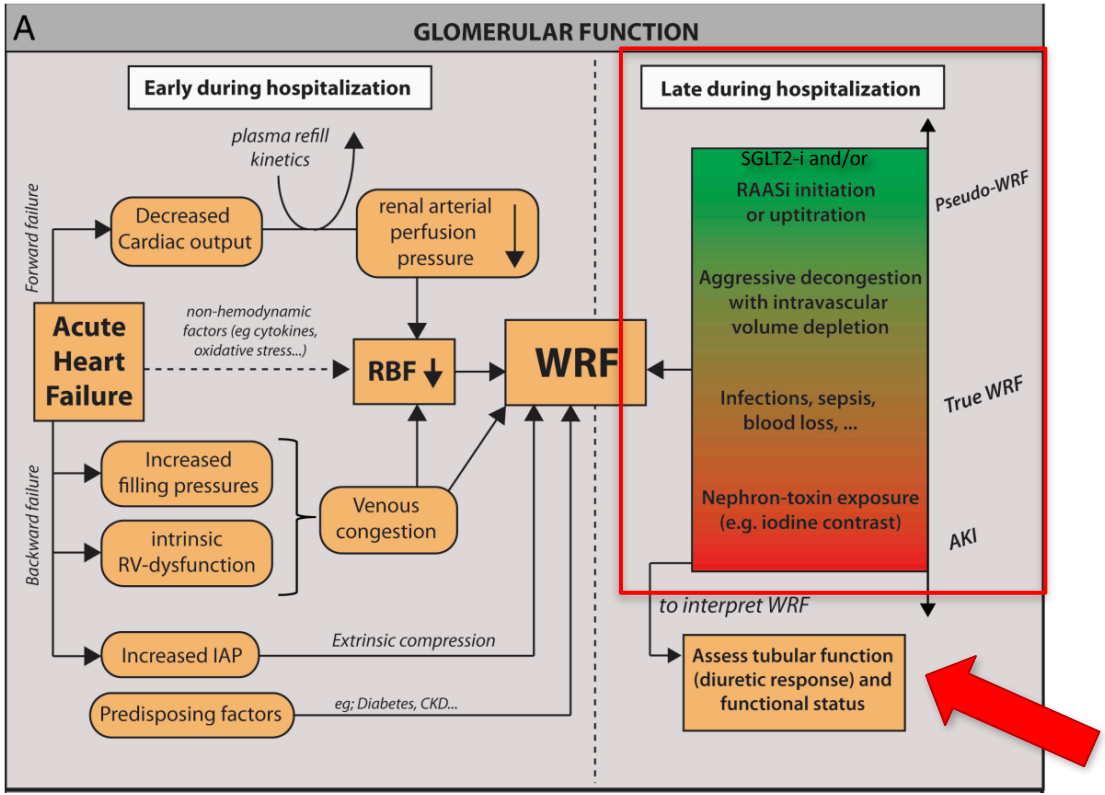
European Journal of Heart Failure (2020) 22, 584–603
doi:10.1002/ejhf.1697

POSITION PAPER

Evaluation of kidney function throughout the heart failure trajectory – a position statement from the Heart Failure Association of the European Society of Cardiology

Wilfried Mullens[1]*, Kevin Damman[2], Jeffrey M. Testani[3], Pieter Martens[1], Christian Mueller[4], Johan Lassus[5], W.H. Wilson Tang[6], Hadi Skouri[7], Frederik H. Verbrugge[8], Francesco Orso[9], Loreena Hill[10], Dilek Ural[11], Mitcha Lainscak[12], Patrick Rossignol[13], Marco Metra[14], Alexandre Mebazaa[15], Petar Seferovic[16], Frank Ruschitzka[17], and Andrew Coats[18]

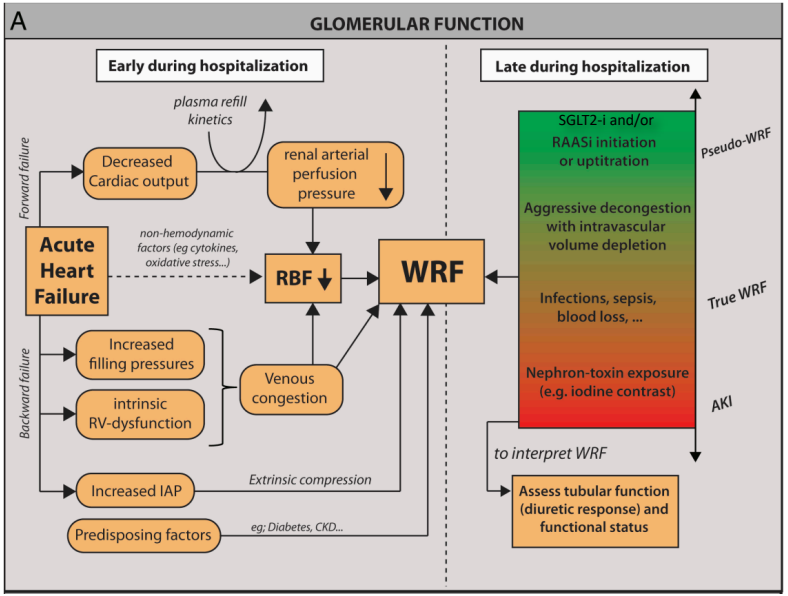
How to find your bearings when things get complicated?

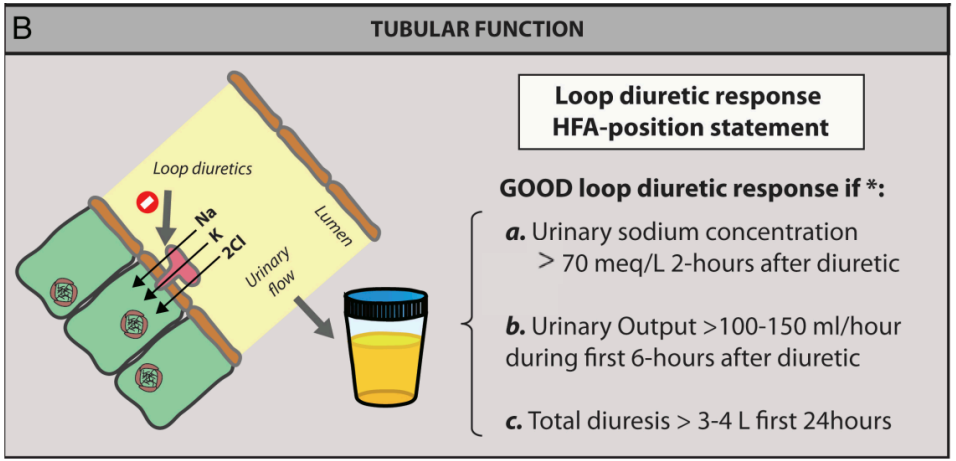


Context really matters.

Modified from European Journal of Heart Failure (2020) **22**, 584–603

How to find your bearings when things get complicated?





Modified from European Journal of Heart Failure (2020) **22**, 584–603

How to find your bearings when things get complicated?

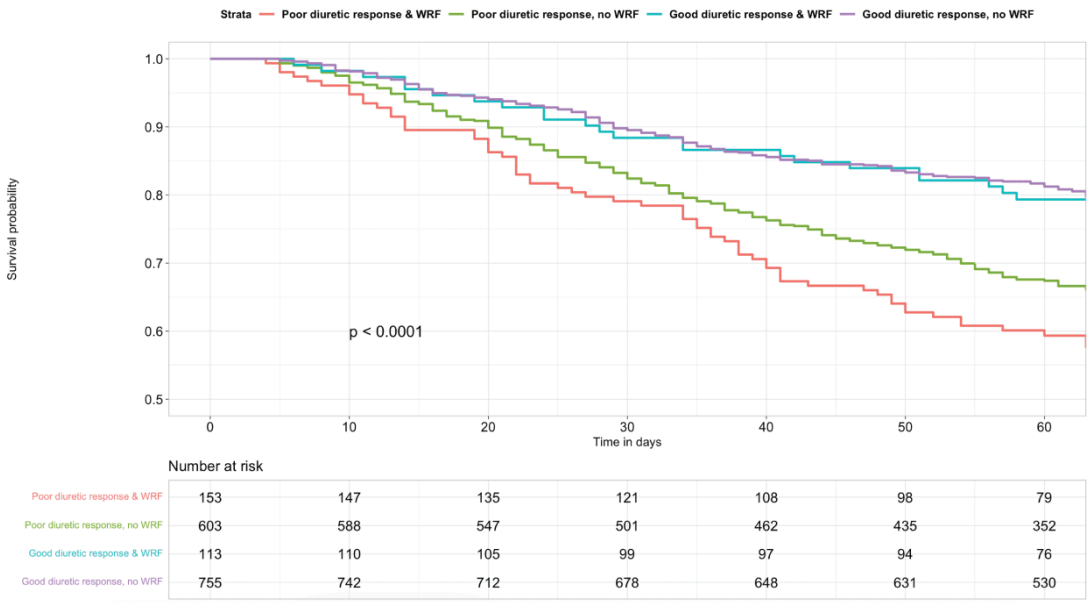
Worsening renal function in acute heart failure in the context of diuretic response

Johanna E. Emmens[1†], Jozine M. ter Maaten[1†], Yuya Matsue[2,3], Sylwia M. Figarska[1], Iziah E. Sama[1], Gad Cotter[4], John G.F. Cleland[5,6], Beth A. Davison[4], G. Michael Felker[7,8], Michael M. Givertz[9], Barry Greenberg[10], Peter S. Pang[11], Thomas Severin[12], Claudio Gimpelewicz[12], Marco Metra[13], Adriaan A. Voors[1*], and John R. Teerlink[14]

WRF was not associated with worse outcomes when patients had a good diuretic response.

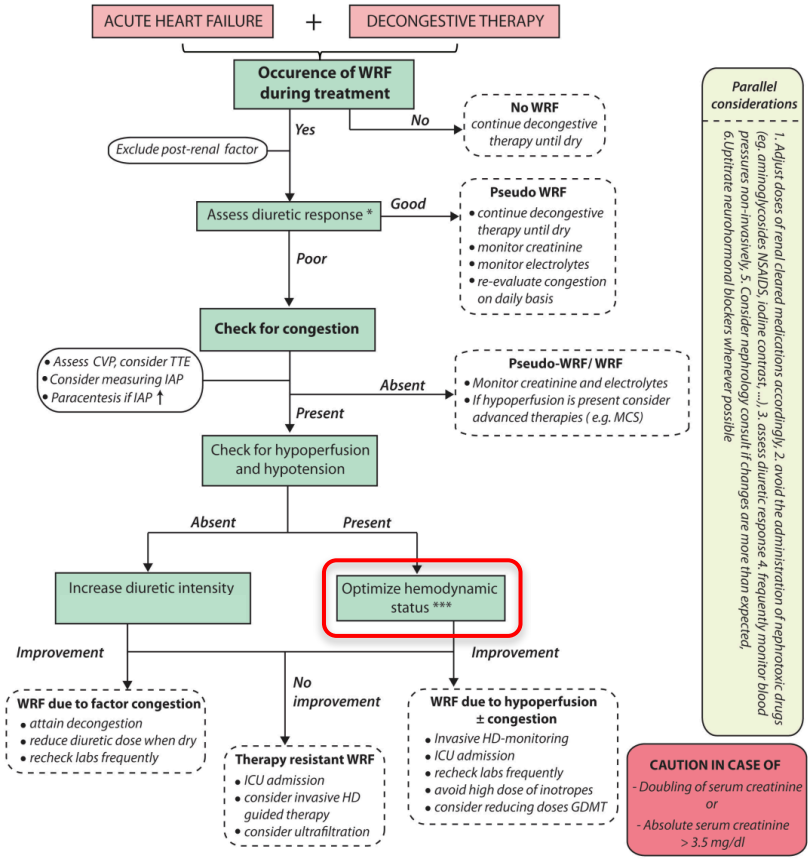
Understanding context -> better subsequent choices (thorough decongestion, continuation/ implementation of GDMT).

CV death or CV/renal hospitalization



European Journal of Heart Failure (2022) **24**, 365–374

How to find your bearings when things get complicated?



Measuring diuretic response

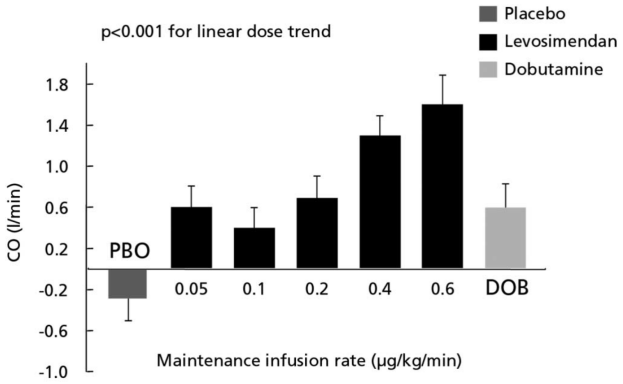
=

Assessing tubular function

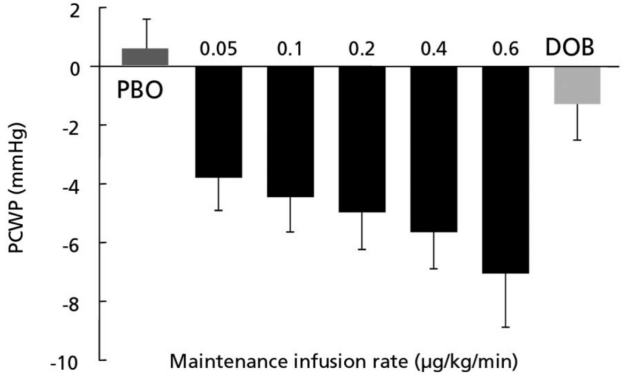
- Na output
- Urine output
- Weight change

Modified from European Journal of Heart Failure (2020) **22**, 584–603

Are all inotropes the same?



(J Am Coll Cardiol 2000;36:1903–12)



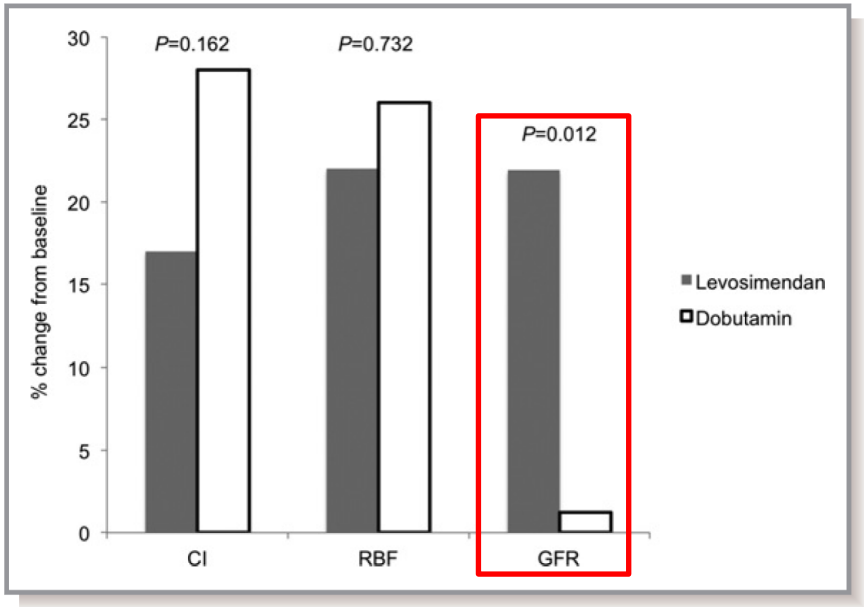
	Levosimendan baseline	Levosimendan 1 h	*P*-value	Control baseline	Control 1 h	*P*-value	*P* for interaction
PCWP (mmHg)	22.0 ± 2.35	16.43 ± 3.85	<0.001	21.28 ± 1.6	21.86 ± 1.34	0.1	<0.001
Mean PAP (mmHg)	34.1 ± 10.8	23.6 ± 8.5	0.008	39.6 ± 15.1	37.2 ± 18	0.7	0.02
Mean right atrial pressure (mmHg)	8.2 ± 4.5	4.5 ± 4.3	0.03	10.9 ± 5.5	9.5 ± 6.5	0.6	0.04

European Journal of Heart Failure (2014) **16**, 281–288

Are all inotropes the same?

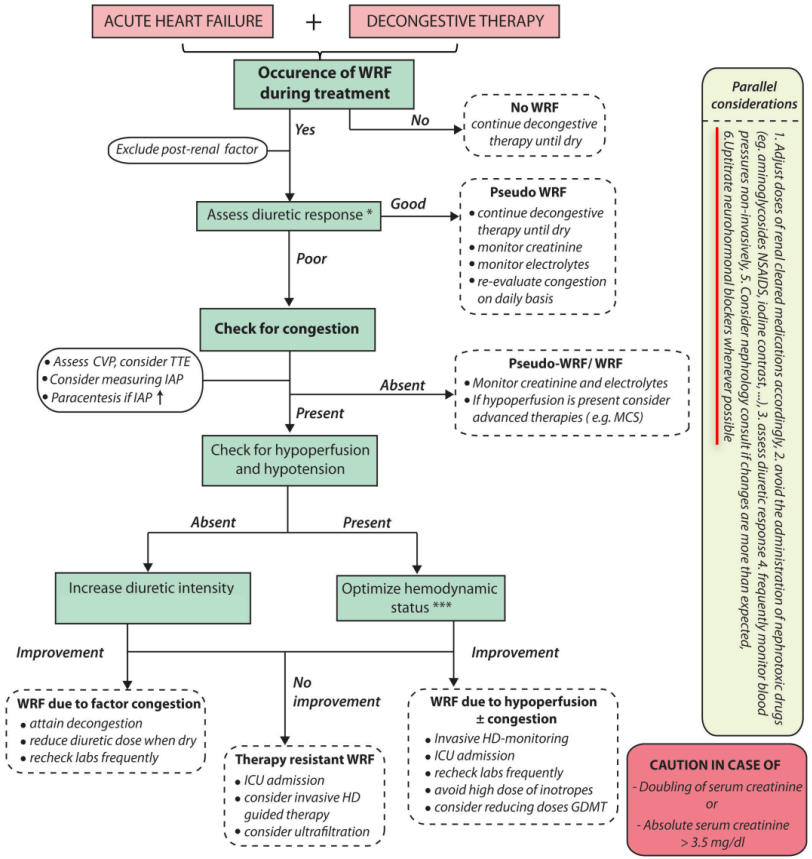
Differential Effects of Levosimendan and Dobutamine on Glomerular Filtration Rate in Patients With Heart Failure and Renal Impairment: A Randomized Double-Blind Controlled Trial

Lukas Lannemyr, MD; Sven-Erik Ricksten, MD, PhD; Bengt Rundqvist, MD, PhD; Bert Andersson, MD, PhD; Sven-Erik Bartfay, MD; Charlotta Ljungman, MD, PhD; Pia Dahlberg, MD; Niklas Bergh, MD, PhD; Clara Hjalmarsson, MD, PhD; Thomas Gilljam, MD, PhD; Entela Bollano, MD; Kristjan Karason, MD, PhD



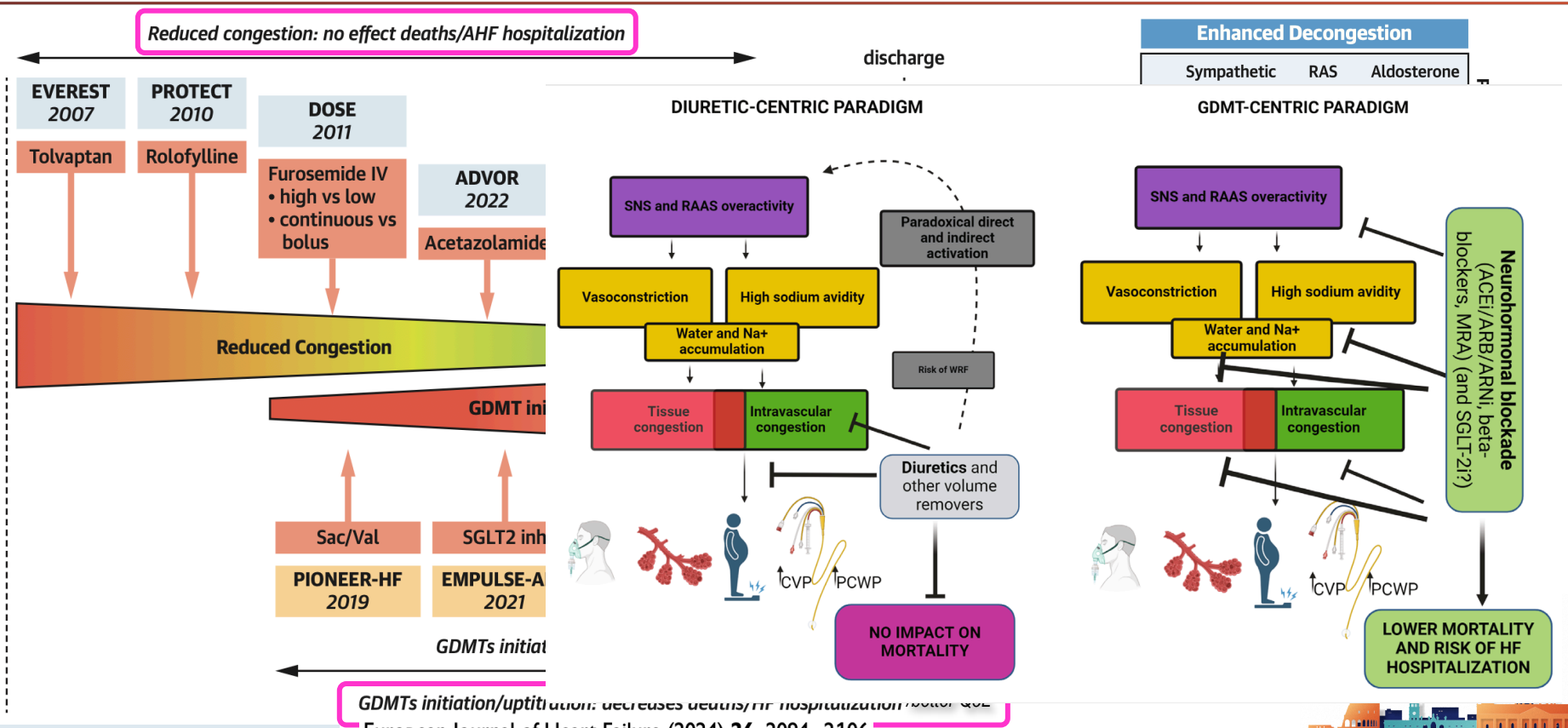
J Am Heart Assoc. 2018;7:e008455.

How to find your bearings when things get complicated?



Modified from European Journal of Heart Failure (2020) **22**, 584–603

Decongestion & early GDMT initiation

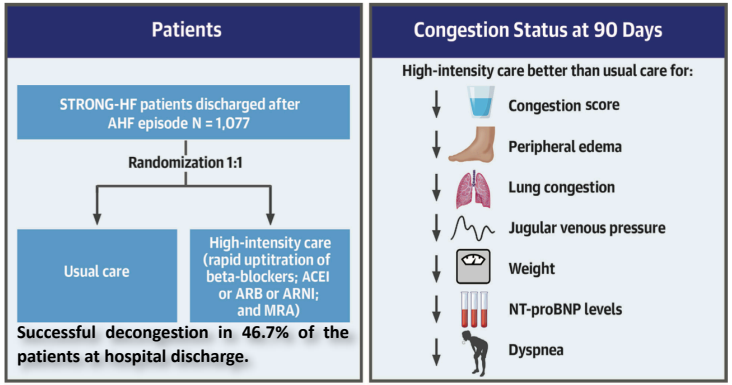


(J Am Coll Cardiol 2024;83:1243-1252)

European Journal of Heart Failure (2024) **26**, 2094–2106

Effects of Rapid Uptitration of Neurohormonal Blockade on Effective, Sustainable Decongestion and Outcomes in STRONG-HF

CENTRAL ILLUSTRATION Uptitration of Guideline-Directed Medical Therapy Leads to Effective, Sustainable Decongestion in Acute Heart Failure



Biegus J, et al. J Am Coll Cardiol. 2024;84(4):323-336.

TABLE 3 Mean Daily Doses of Loop Diuretics (Furosemide or Equivalents) According to Treatment

	All Patients (N = 1078)	High-Intensity Care Group (n = 542)	Usual Care Group (n = 536)	P Value[a]
Prerandomization	62.7 ± 46.34	63.9 ± 48.78	61.4 ± 43.76	0.3217
Postrandomization	59.9 ± 45.60	61.0 ± 47.50	58.9 ± 43.61	0.4576
Visit 3: Week 1	58.9 ± 46.50	58.9 ± 46.50		
Visit 4: Week 2	57.7 ± 47.27	57.7 ± 47.27		
Visit 5: Week 3	59.6 ± 62.31	59.6 ± 62.31		
Visit 6: Week 6	57.1 ± 52.19	57.1 ± 52.19		
Visit 7: Day 90	56.1 ± 51.27	52.8 ± 45.89	59.4 ± 56.07	0.0376
Visit 8: Day 180	48.7 ± 43.89	48.0 ± 42.46	49.5 ± 45.35	0.6332

Values are mean ± SD. Visit 8 (Day 180) analyses are restricted to patients at sites where patients were followed up to day 180. [a]P value from an analysis of covariance model with fixed terms for treatment, left ventricular ejection fraction ≤40%/>40%, and region.

FIGURE 3 Relationship Between GDMT Dose and Body Weight Change

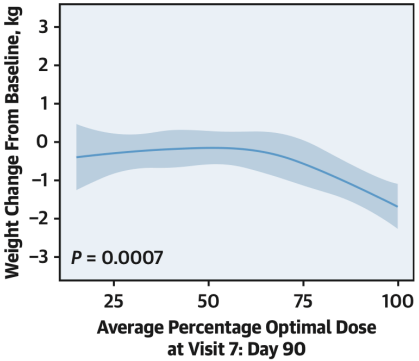
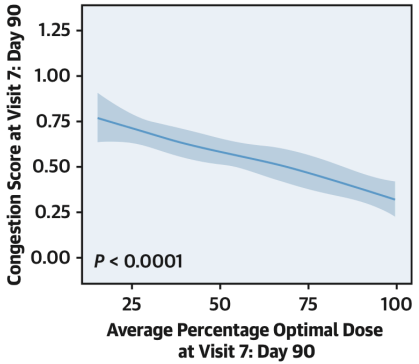


FIGURE 4 Relationship Between GDMT Dose and Congestion Score



Take home messages

- Renal function ≠ eGFR.
- Not all eGFR changes are created equal.
- Context of change matters.