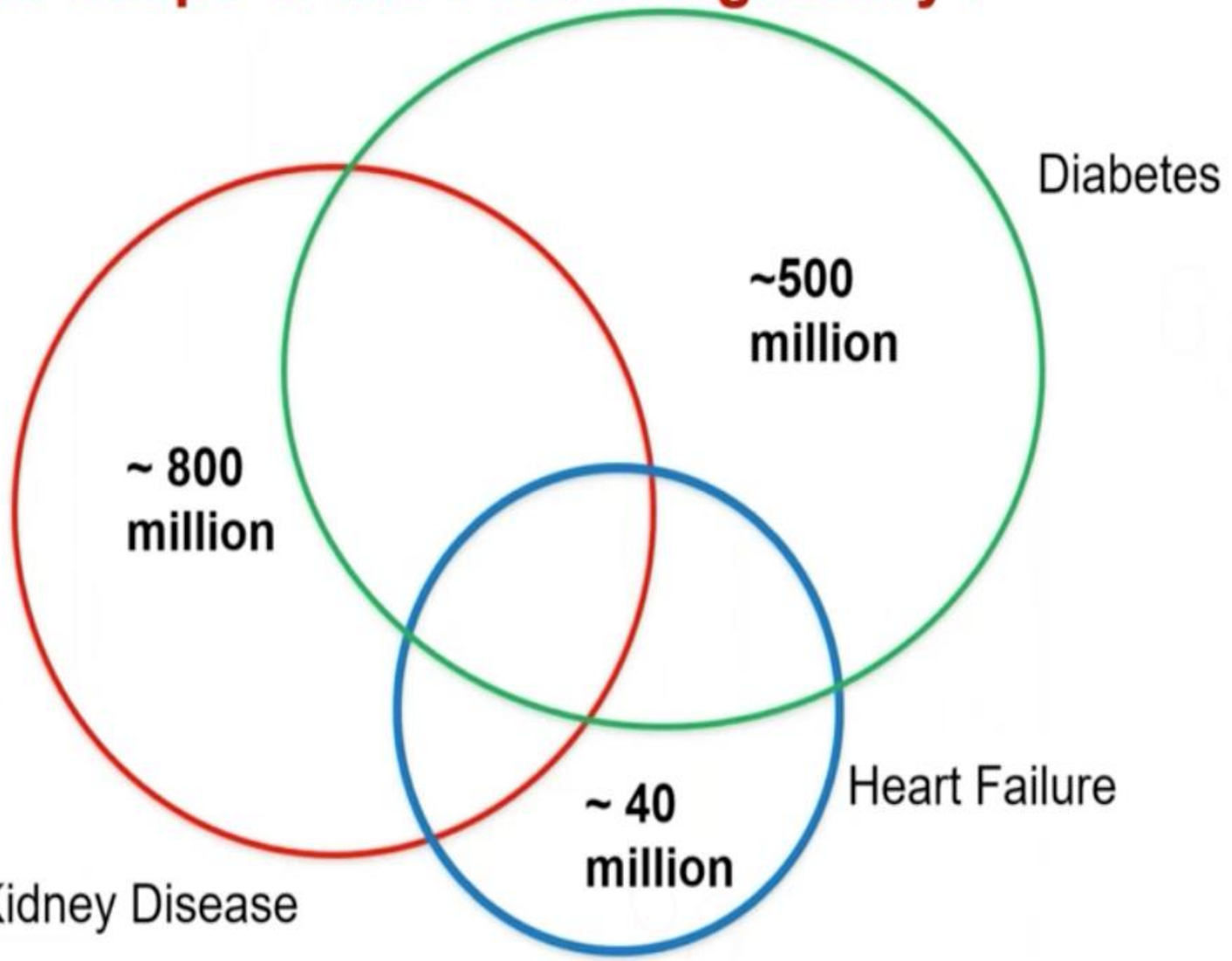
CKD & CHF

Sh.Atabak

2:46

What is the scope of the Problem globally?

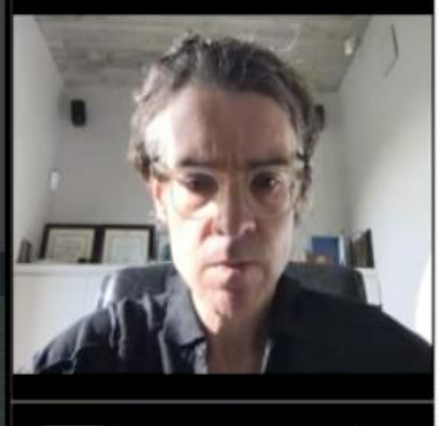


KDIGO 2019

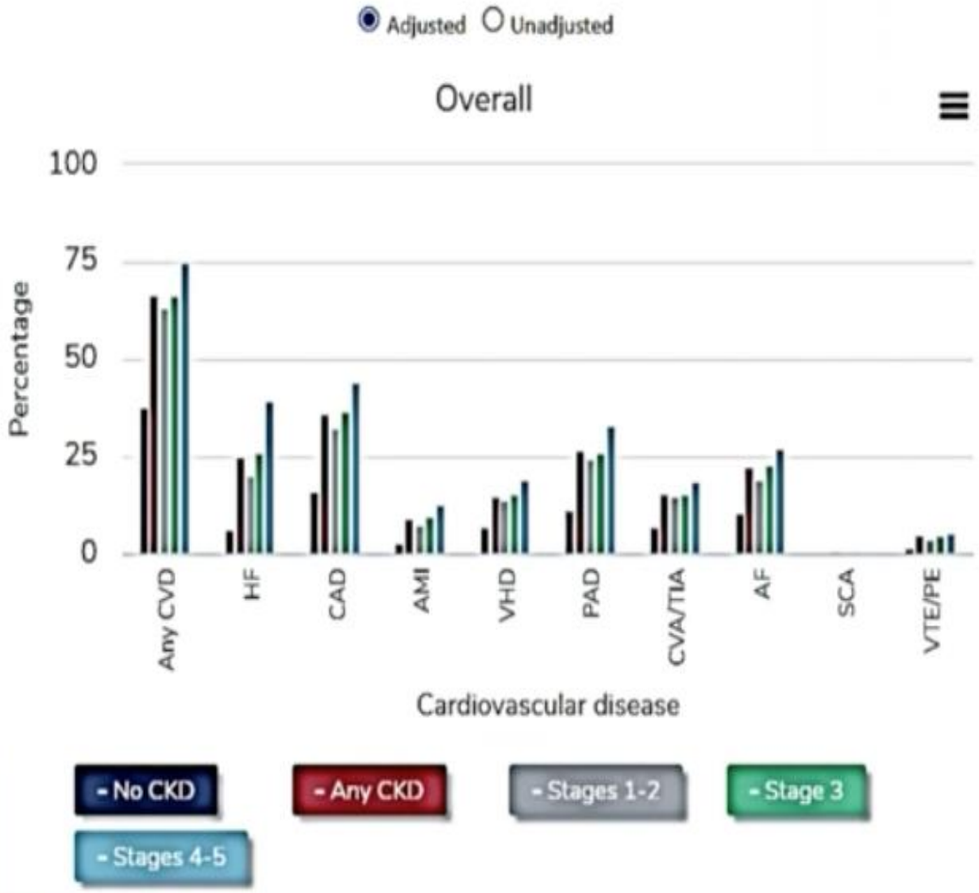
Between 45-65% of HF patients will have or will develop CKD

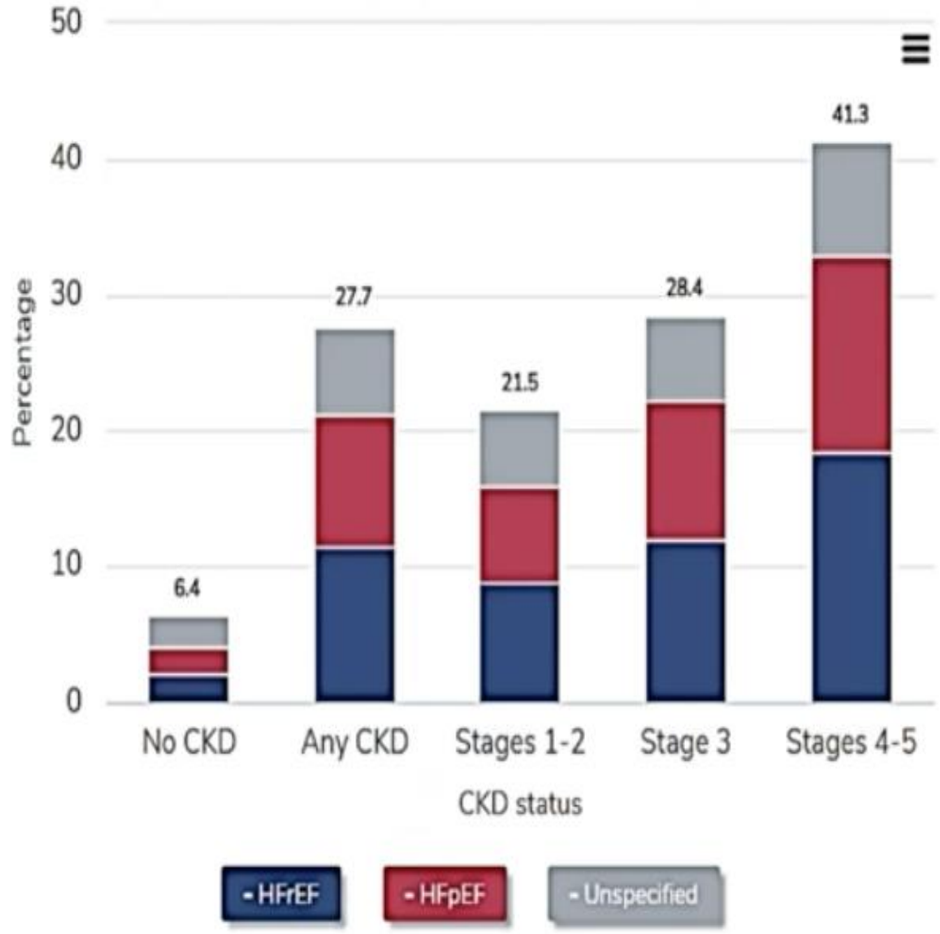
HD 3:03 / 1:28:05

1 / 1

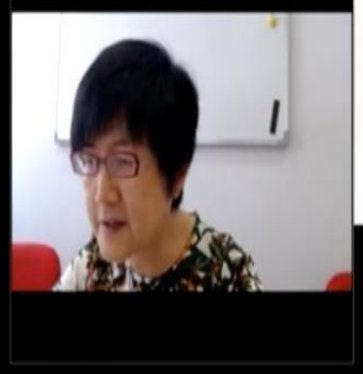


Adjusted Prevalence of Heart Failure in Medicare beneficiaries aged ≥66 years, by CKD stage



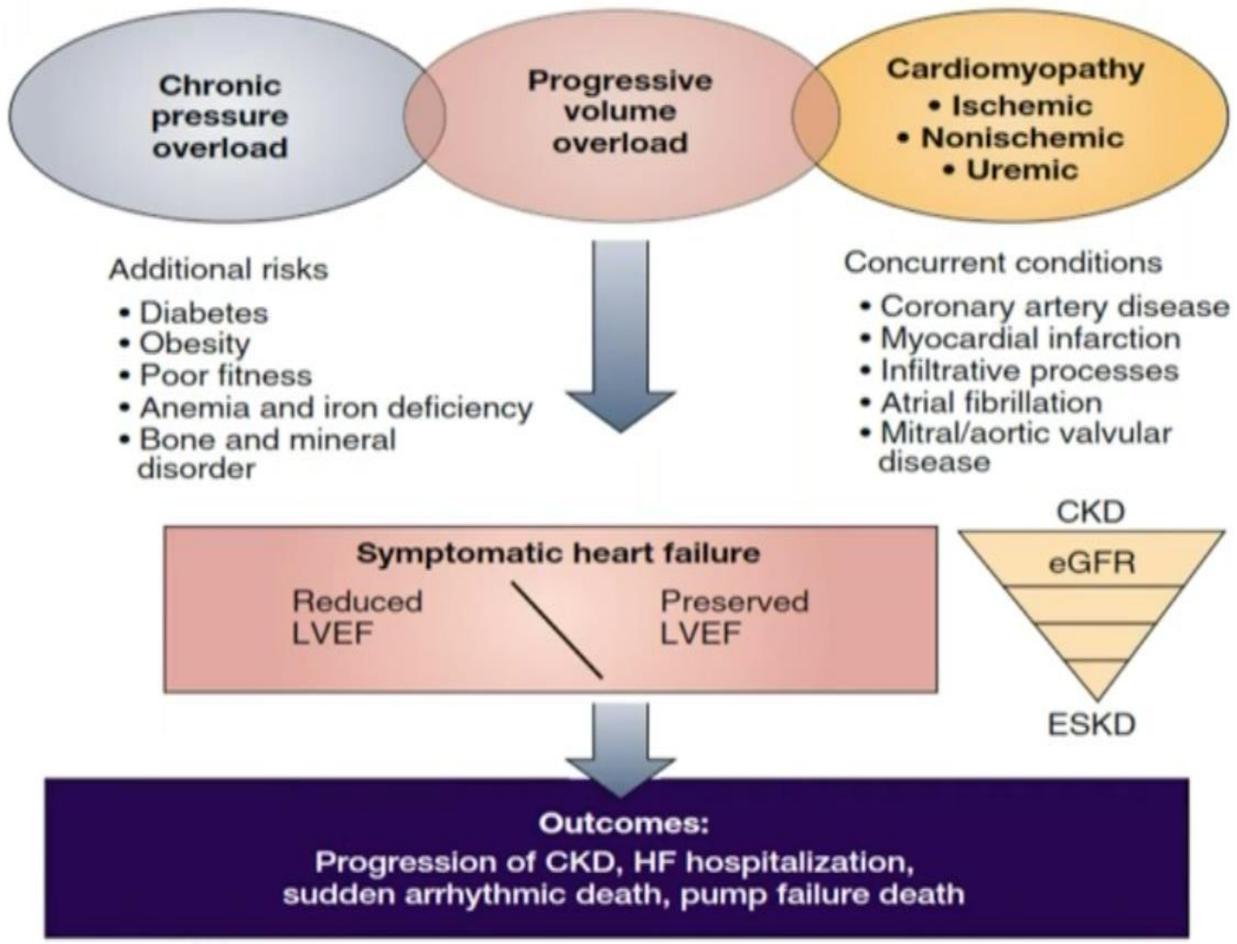


Data from USRDS 2019.



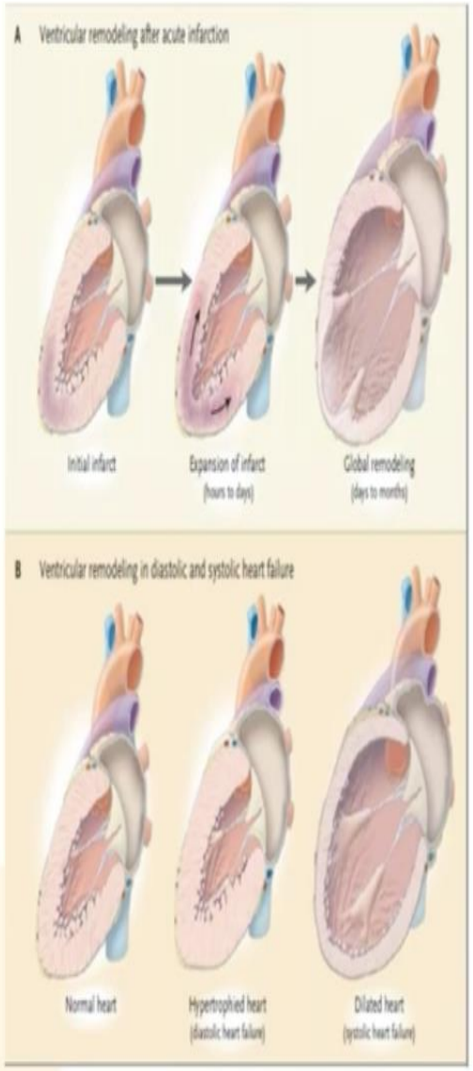
PATHOPHYSIOLOGY OF HEART FAILURE IN CKD PROGRESSING TO KIDNEY FAILURE

Pathophysiology of heart failure in CKD progressing to ESKD



House AA, et al. KDIGO Controversies Conference. Kidney Int 2019

Structural, Functional Left Ventricular Differences in HFpEF and HFrEF



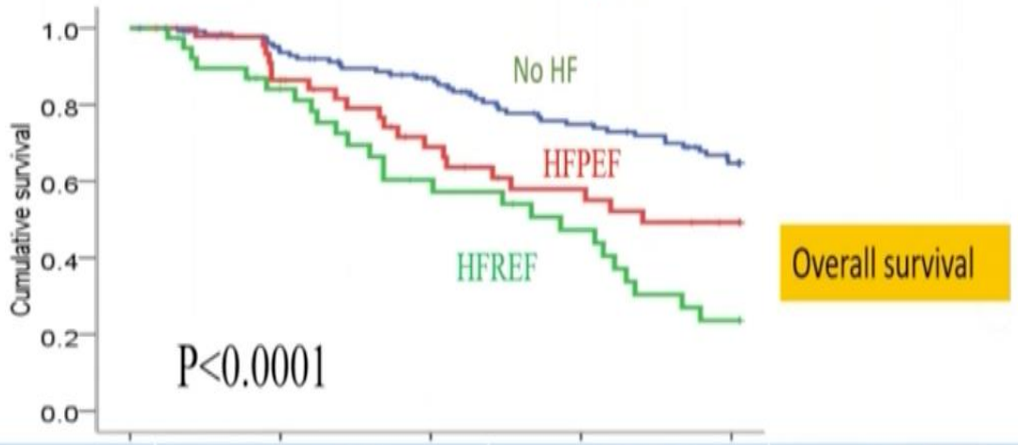
Jessup M, NEJM 2003

Table. Unequal Structural, Functional, and Ultrastructural LV Characteristics in HFpEF and HFrEF

	HFpEF	HFrEF
LV structure/function		
End-diastolic volume	↔	↑
End-systolic volume	↔	↑
Wall thickness	↑	↔
Mass	↑	↑
Mass/volume ratio	↑	↓
Remodeling	Concentric	Eccentric
Ejection fraction	↔	↓
Stroke work	↔	↓
End-systolic elastance	↔	↓
End-diastolic stiffness	↑	↓
LV ultrastructure		
Myocyte diameter	↑	↔
Myocyte length	↔	↑
Myocyte remodeling	Concentric	Eccentric
Fibrosis	Interstitial/reactive	Focal/ replacement

HFpEF indicates heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; and LV, left ventricular.

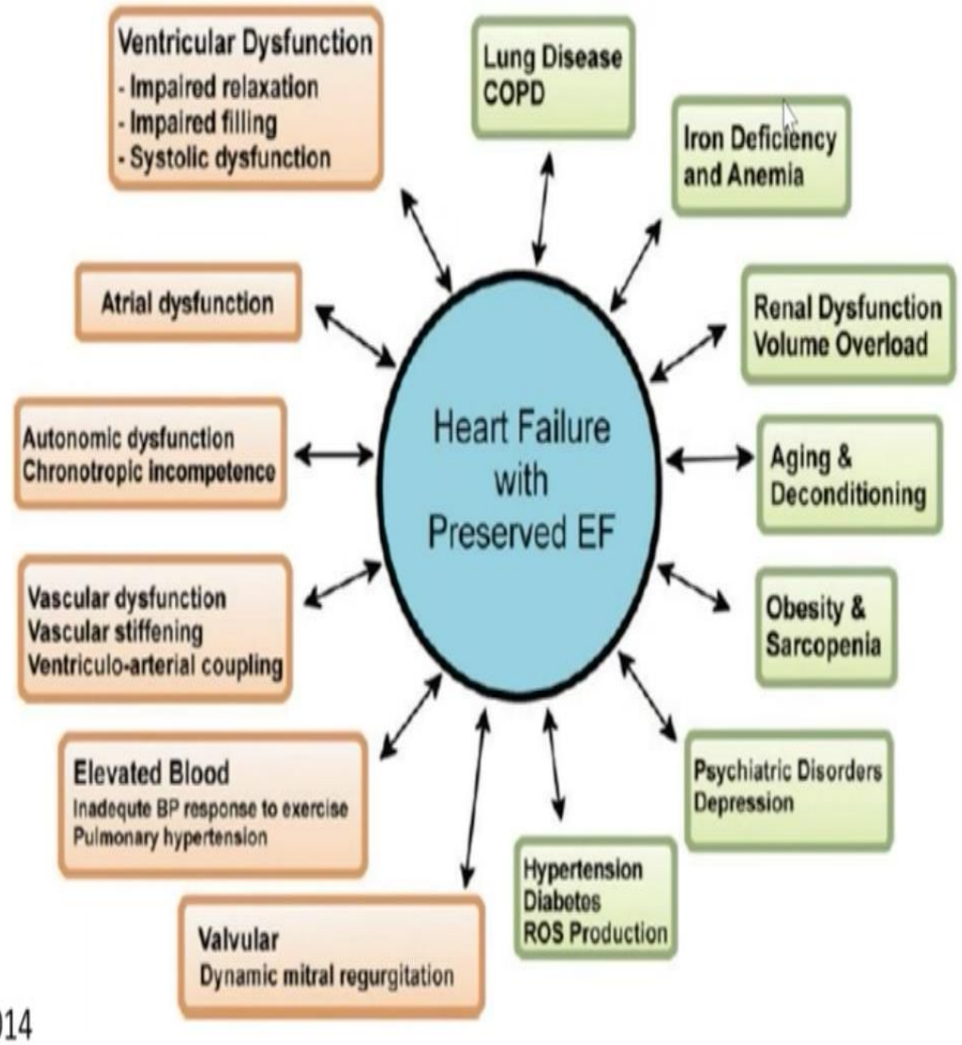
Clinical Outcomes of Dialysis Patients Having Heart Failure with Preserved or Reduced Ejection Fraction



	No HF	HFPEF	HFREF	P
Troponin T (ug/L)	0.02 (0.01, 0.08)	0.10 (0.02, 0.26)	0.14 (0.08, 0.25)	<0.001
NT-proBNP (pg/ml)	3206 (1408, 9433)	8946 (2679, 26055)	20883 (9366, 35000)	<0.001

Wang AY, et al. Am J Kidney Dis 2013

Heterogeneity of Heart Failure with Preserved Ejection Fraction Syndrome



Senni M, et al. EHJ 2014

9:29

HD 10:01 / 1:28:05

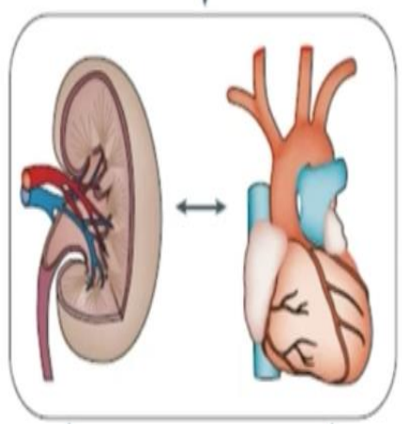
1 / 1






Complex Cardio-Kidney Interactions in Heart Failure

Haemodynamic mechanisms
- Fluid overload and retention of salt and water
- Renal and cardiac congestion (renal venous hypertension)
- Limited organ perfusion (forward failure)
- Vasoconstriction in end organs



(Neuro)hormonal mechanisms
- Activation of the RAAS
- Activation of the sympathetic nervous system

Cardiovascular disease-associated mechanisms
- Chronic inflammation and activation of cellular immunity
- Malnutrition, cachexia and wasting
- Bone–mineral disorder
- Acid–base metabolism disorder
- Anaemia and cardio-renal anaemia

Uremia metabolites

Insulin resistance and diabetes

Nature Reviews Nephrol 2016

Proinflammatory coexisting conditions

Systemic microvascular endothelial inflammation

Increases in oxidative stress
Decreases in NO–cyclic GMP signaling

Muscle inflammation

Microvascular dysfunction and rarefaction

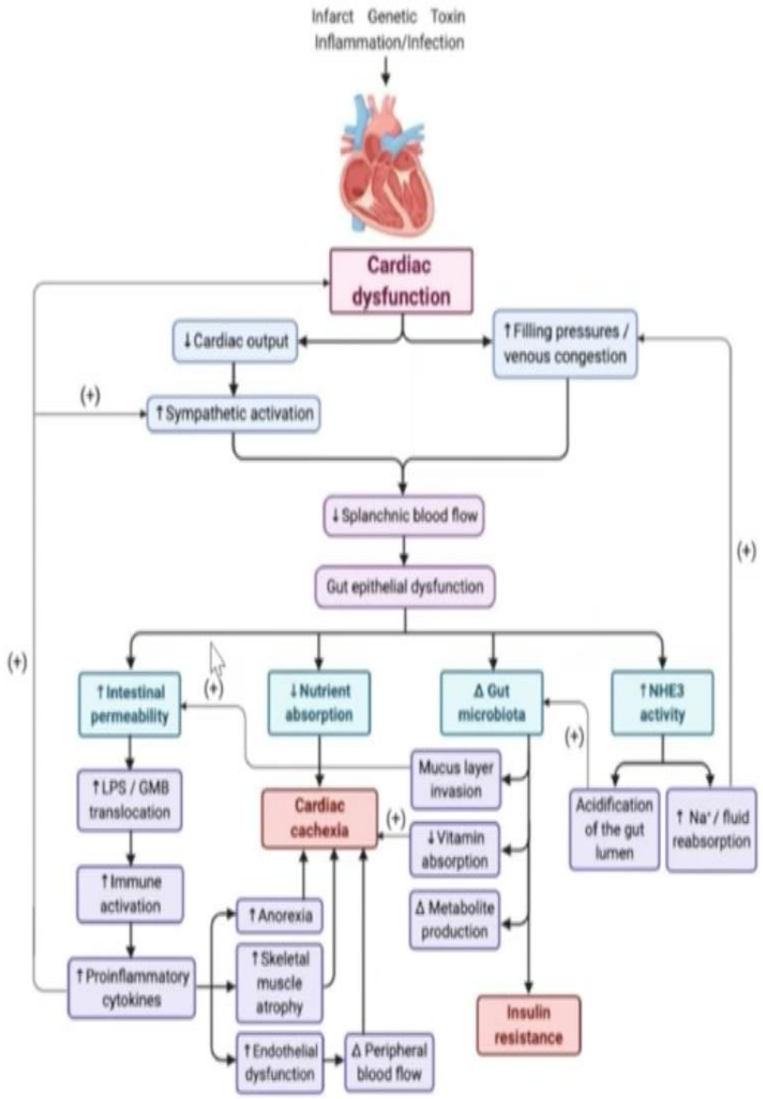
Myofiber stiffness
Cardiomyocyte hypertrophy

Fibrosis

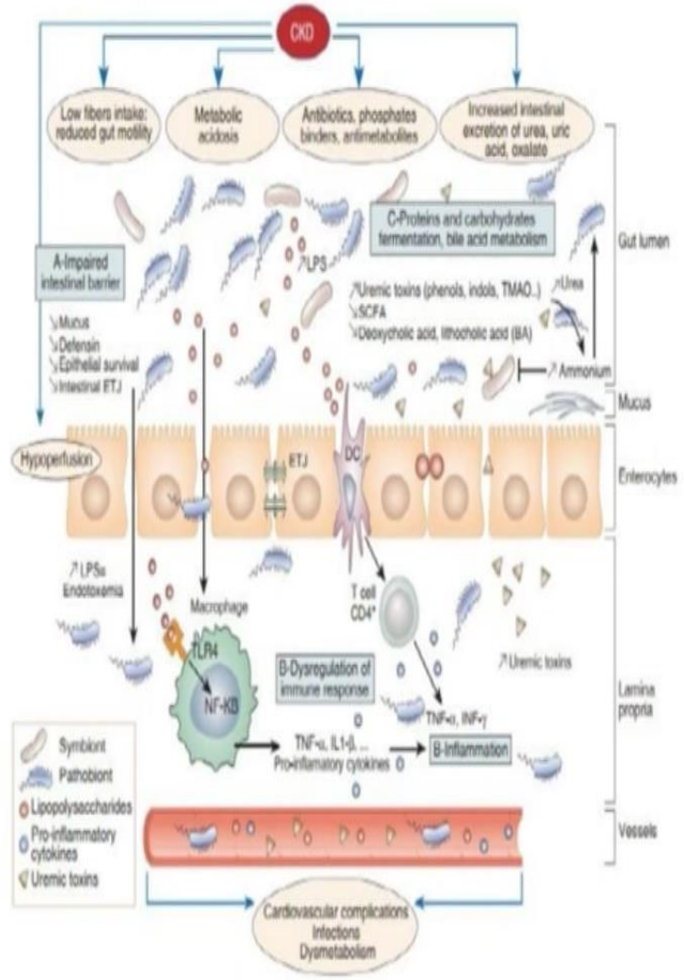
Global cardiac remodeling and dysfunction
Impaired coronary flow reserve
Impaired oxygen delivery, uptake, and utilization in skeletal muscle

Redfield M. N Engl J Med 2016

Gut Hypothesis of Heart failure in CKD



Tang WH, et al. 2021



Koppe L, et al. Kidney Int 2015

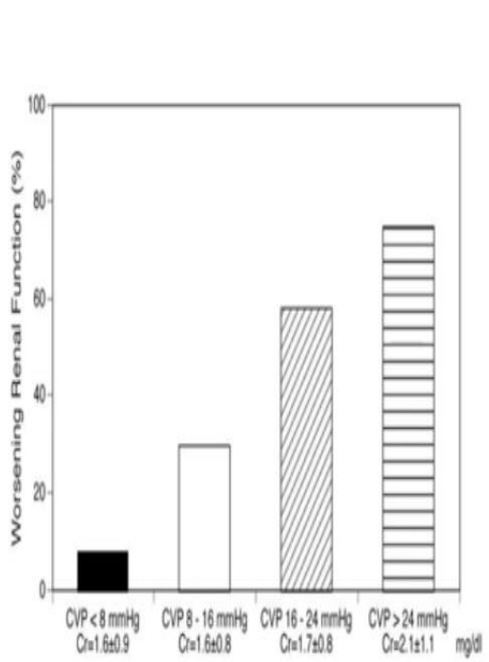


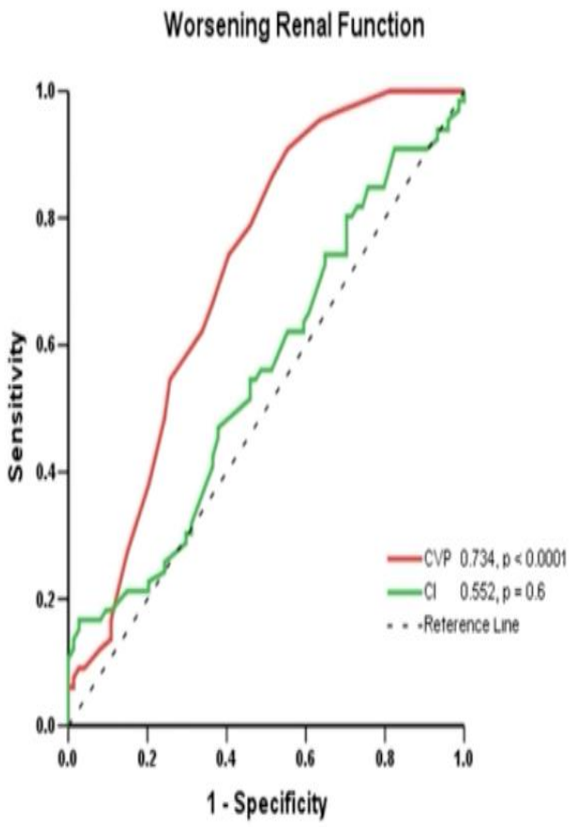


Conclusions

- CKD and heart failure pose huge global health challenges and have significant healthcare costs implications
- The presence of both complications are associated with adverse clinical outcomes.
- CKD patients with HFREF and HFPEF represent different phenotypes with different clinical outcomes and have implications on treatment strategies.
- Microvascular disease and rarefaction represent a hallmark feature in the uremic myocardium.

Cardiac Output or Central Venous Pressure





Increased CVP contributes to WRF in patients admitted with low-ouput HF

Mullens W et al. J Am Coll Card 2009;53:589-96.

Case: 75 year male

- 2018: HFrEF – NICMP

  Lab: creat 1.2 mg/dl (eGFR 51)

  Medically treated: candesartan 32, bisoprolol 5, spiro 25

  LVEF improved from 30 to 45%

- 2018-2020: doing fine

- Jan 7, 2021: @GP with progressive dyspnea after upper airway infection

  GP: nt-proBNP 5500, creat 1.5 (eGFR 43), volume overload

  R/ bumetanide 1 mg orally – rest medication similar

Case: 75 year male

- Jan 9, 2021 – Saturday 5 pm: @ER more dyspnea

Clinical exam:

BP 125 / 64 – SR 110 bpm

CVP + 12 , HJR +

Systolic murmer apex

Diminished breath sounds bilateral

Edema up to knee

Lab: nt-proBNP 8540, s creat 1.8 (eGFR 35), K 4.6, Na 132

TTE: LVEF 25%, RV dysf, MR 3+, TR 2+, DDF grade III, PAP 60

Chest X ray: cardiomegaly + bilateral pleural effusion

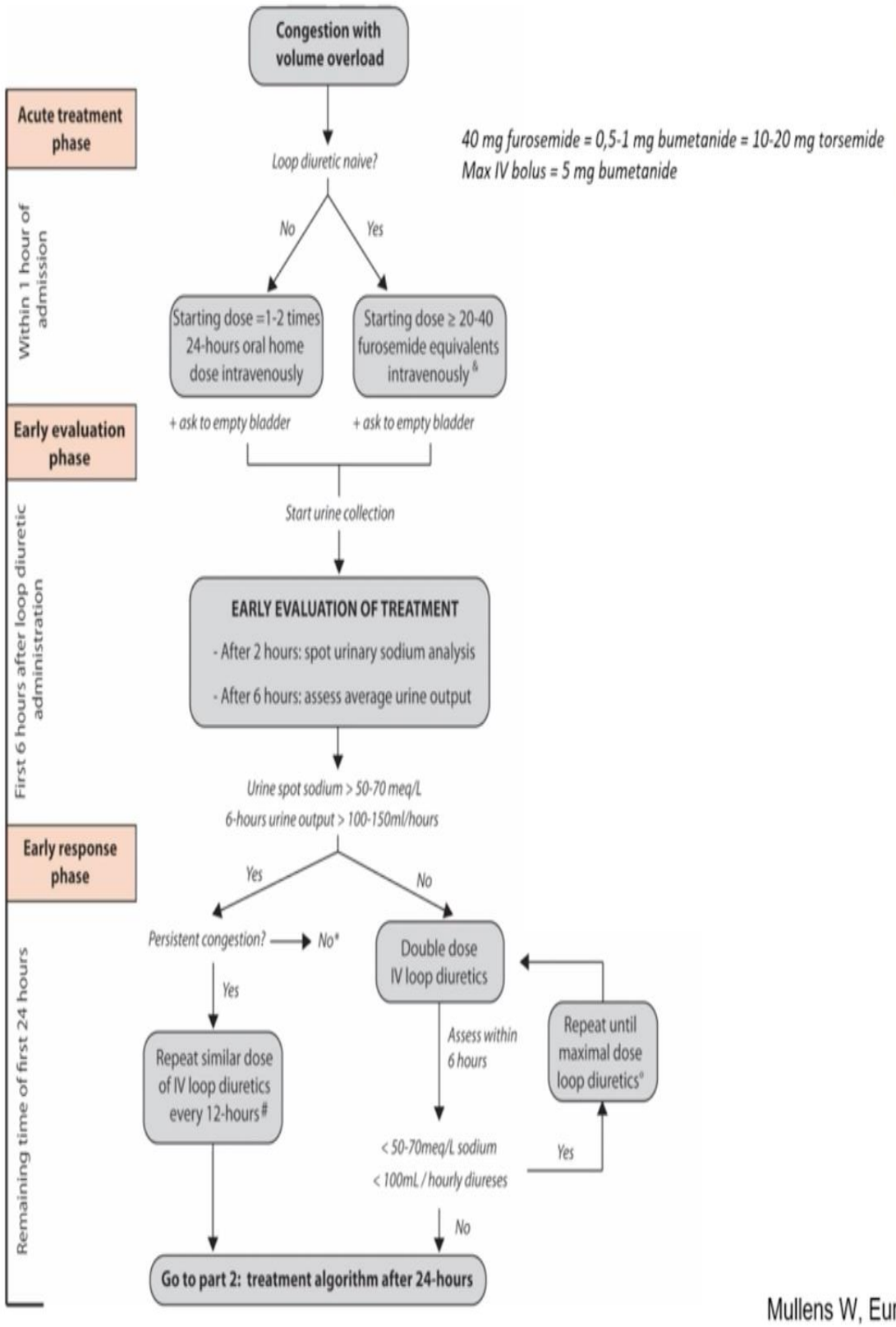
Question; What is your preferred diuretic strategy ?

A. Discharge on more oral loop diuretics

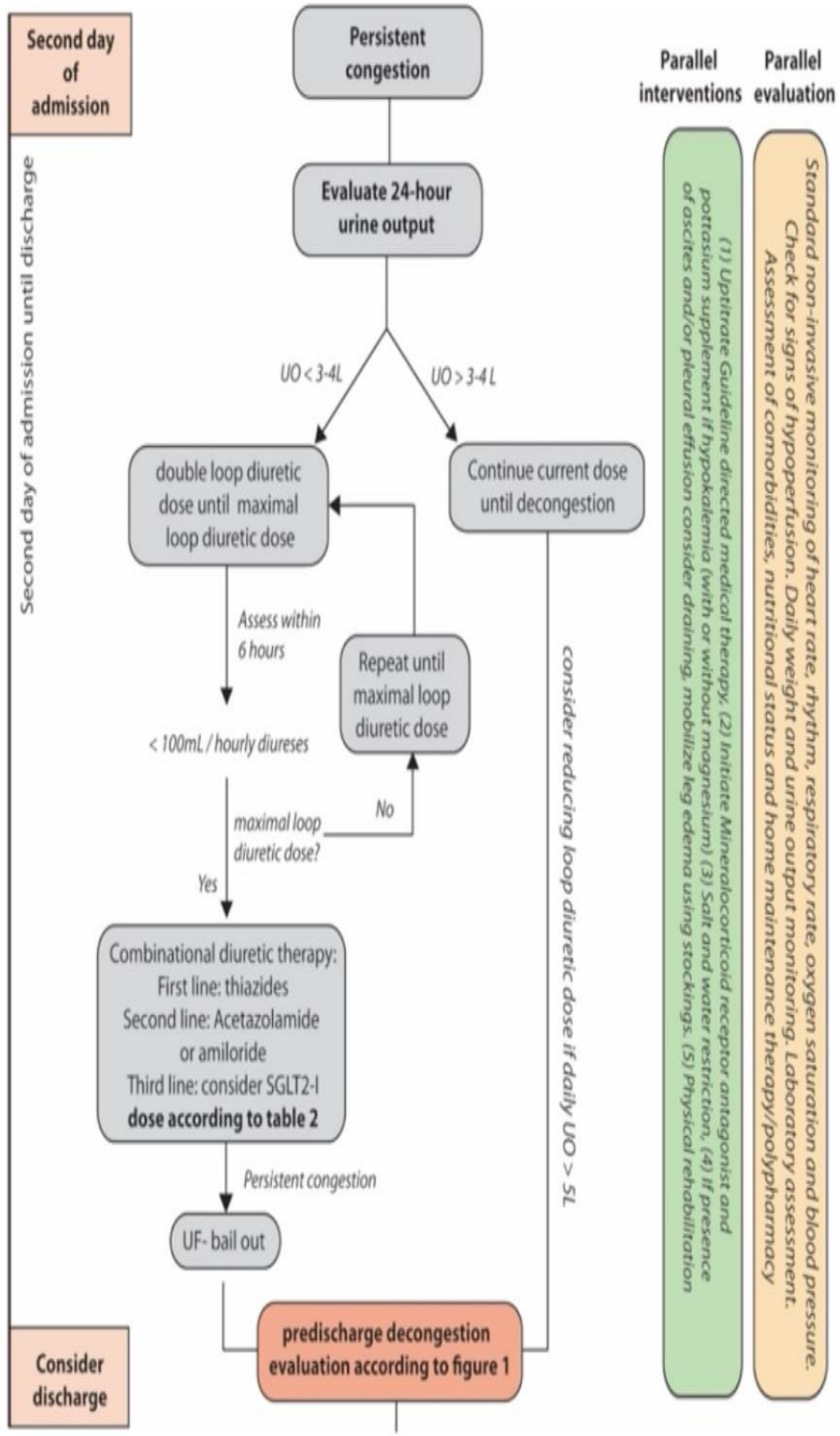
B. Bolus IV loop diuretic

C. Continuous IV loop diuretic

D. IV loop diuretic + low dose inotrope / inodilator



Mullens W, Eur J Heart Fail 2019; 21:137-155.



Mullens W, Eur J Heart Fail 2019; 21:137-155.

Case: 75 year male – trajectory 1

- Jan 9, 2021 – 5 pm: *bumetanide 2 mg IV bolus*

- Jan 9, 2021 – 7 pm: Na 90 mmeq/l urinary spot analysis

  11 pm diuresis 2600 cc (= 435 cc/h)

  Moderate congestion

  What to do next ?

  Bumetanide 2 mg IV bolus

- Jan 10, 2021 – 8 am: additional 2200 cc (= 360 cc/h)

  S creat 2.2 (eGFR 30), K 3,4 mmol/l, Na 134 mmol/l

  BP 110/67, SR, HR 76 bpm, less than moderate congestion

Case: 75 year male – trajectory 2

- Jan 9, 2021 – 5 pm: *bumetanide 2 mg IV bolus*

- Jan 9, 2021 – 7 pm: Na 40 mmeq/l urinary spot analysis

  11 pm diuresis 400 cc (= 65 cc/h)

  Moderate congestion

  What to do next ?

  bumetanide 4 mg IV bolus

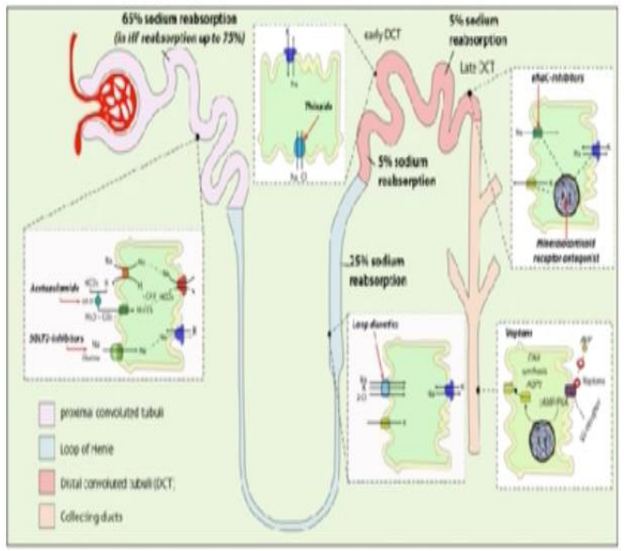
- Jan 10, 2021 – 8 am: additional 400 cc (60 cc/h)

  S creat 2.2 (eGFR 30), , K 3,4 mmol/l, Na 134 mmol/l

  BP 110/67, SR, HR 76 bpm, moderate congestion

How to treat a patient with AHF + WRF and a poor diuretic response ?

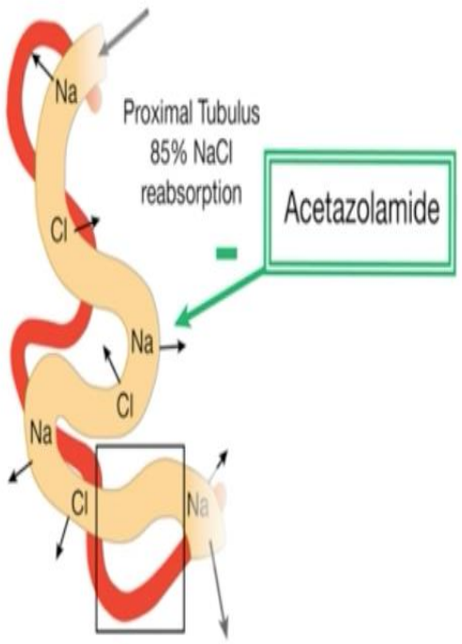
Thiazides, know how to use them

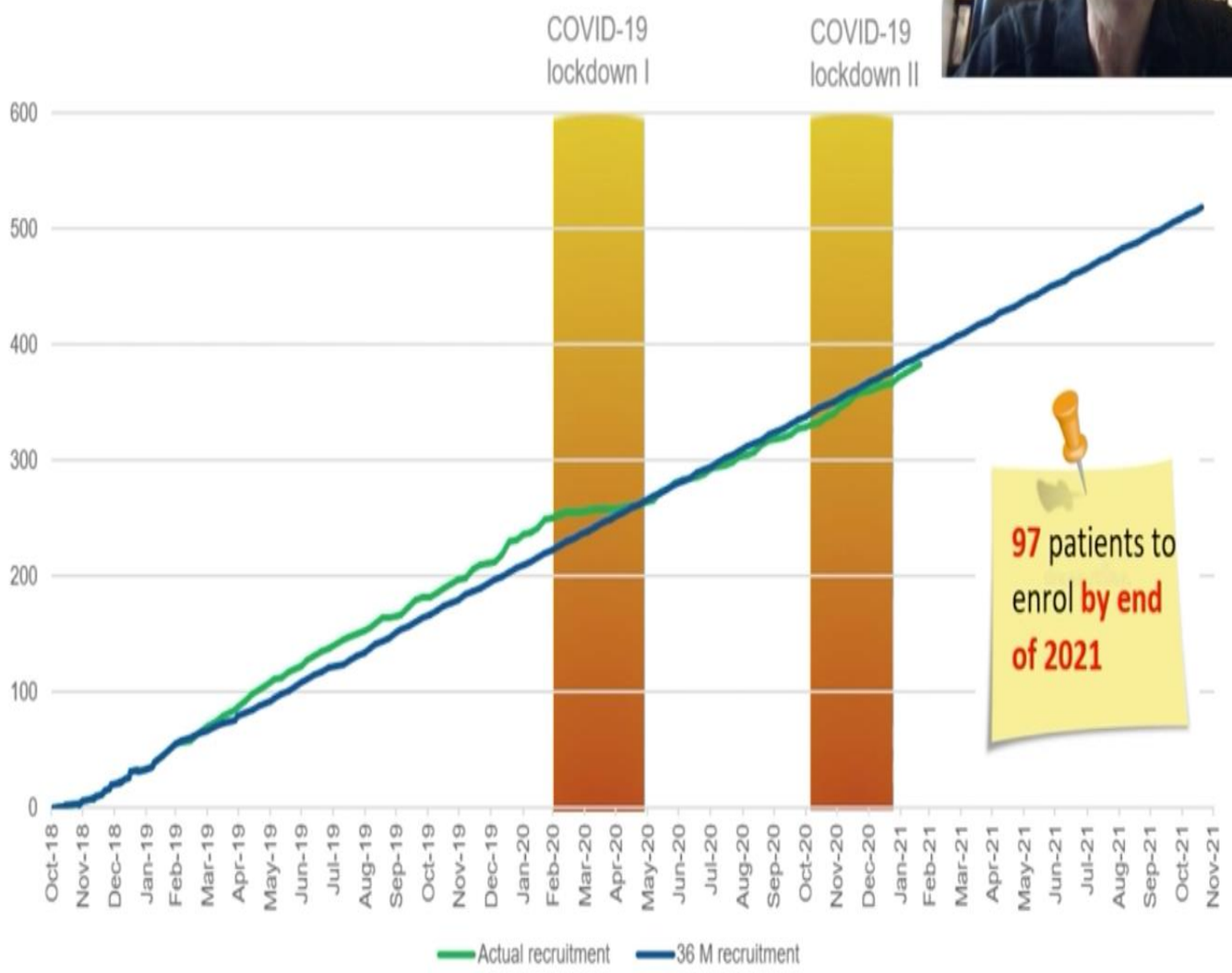


- Work distal in nephron (poor diuretic effect)
- Might counterbalance distal hypertrophy with chronic use of high dose LD
- Also work in low eGFR states
- Slow GI absorption (need to be given hours before LD)
- Protein bound like loop diuretics
- Long half life

Mullens W, Eur J Heart Fail 2019; 21:137-155.

Renal Preservation: Acetazolamide (ADVOR trial)
(500 mg IV bolus once daily on top of loop diuretics)

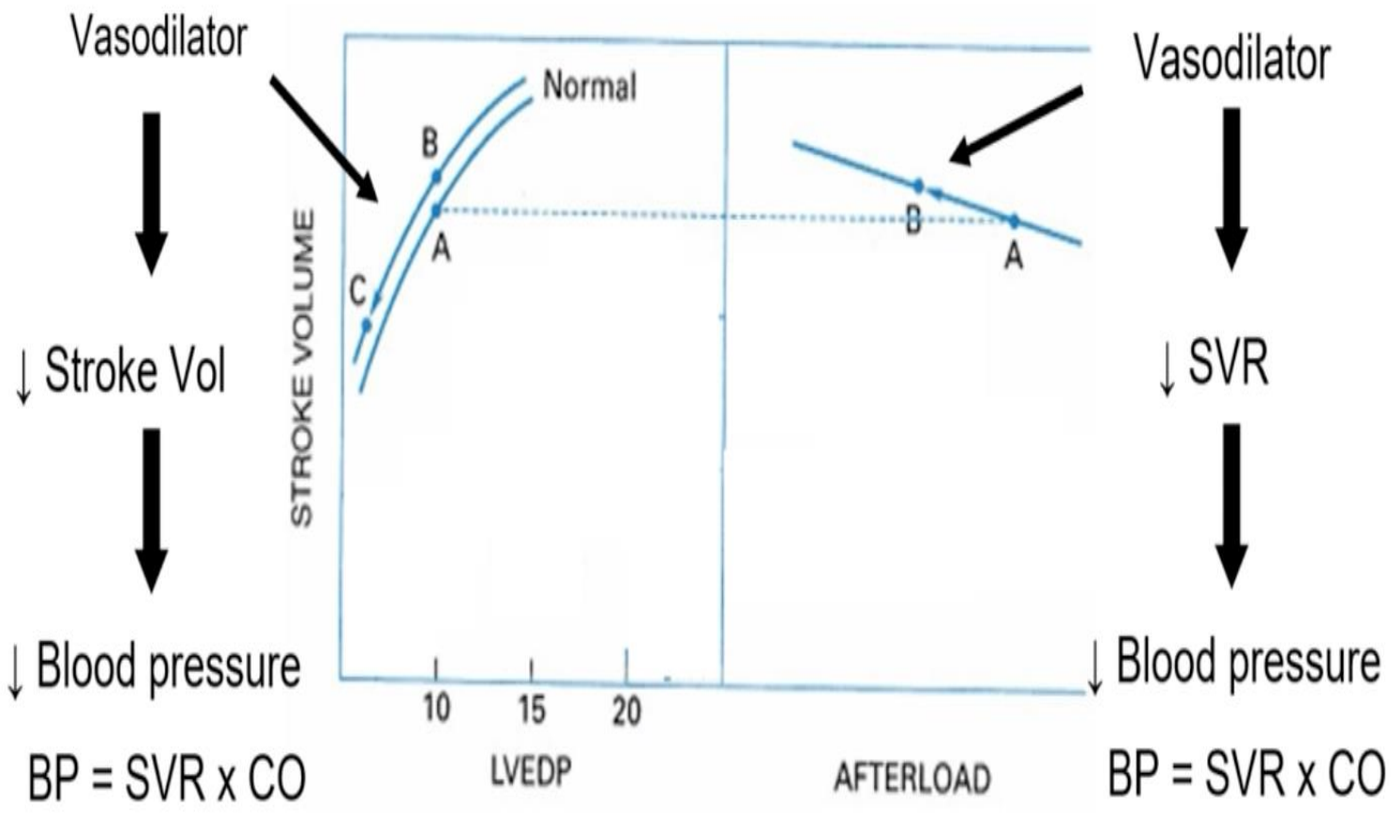




Inhibition Na reabsorption Proximal Tubule (Acetazolamide)

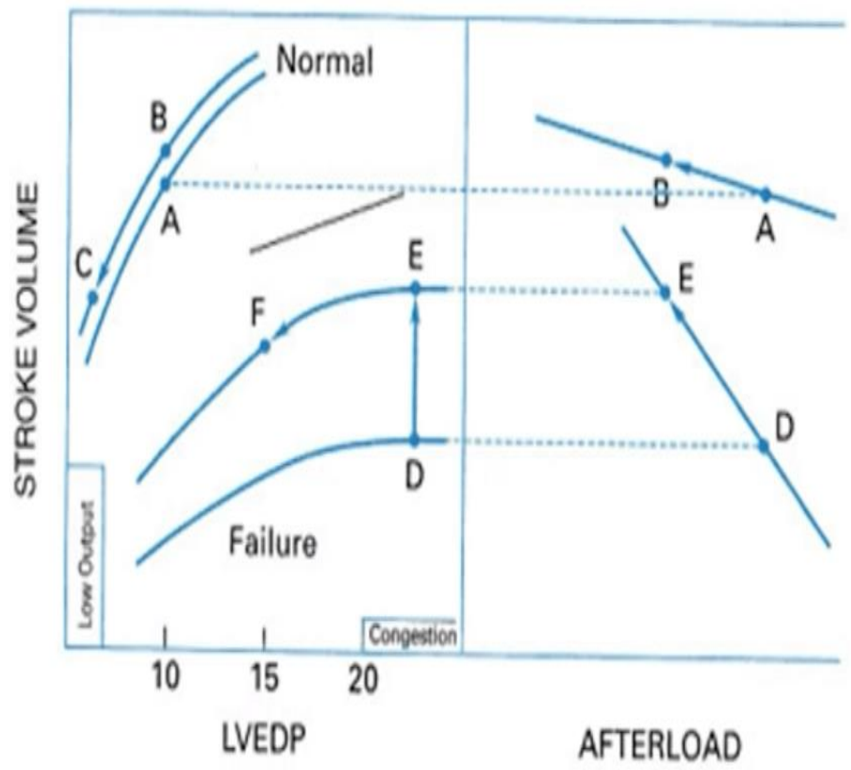
Mullens W et al. Eur J Heart Fail. 2018;20:1591-1600 .

Pathophysiology: pre- and afterload normal heart



Normal heart = “preload” dependent

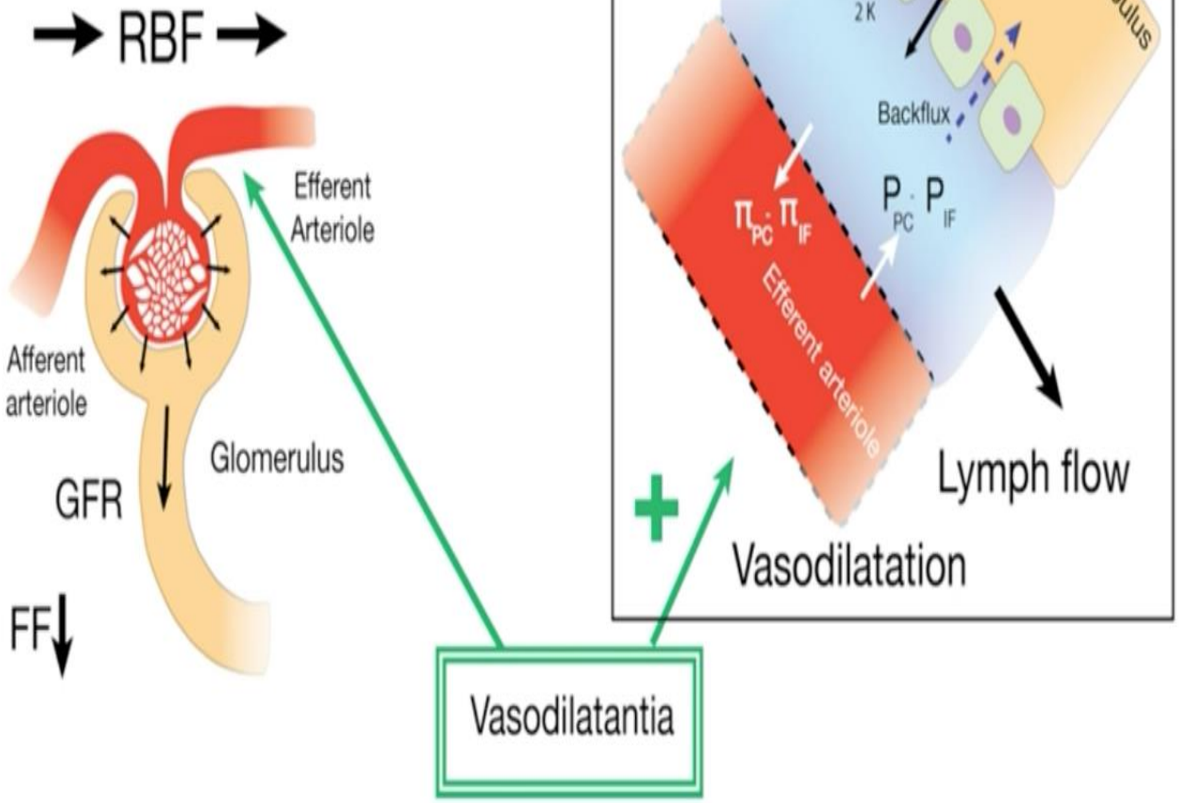
Pathophysiology: pre- and afterload failing HFrEF



Normal heart = “preload” dependent

Heart failure = “afterload” dependent

‘Renal Preservation’

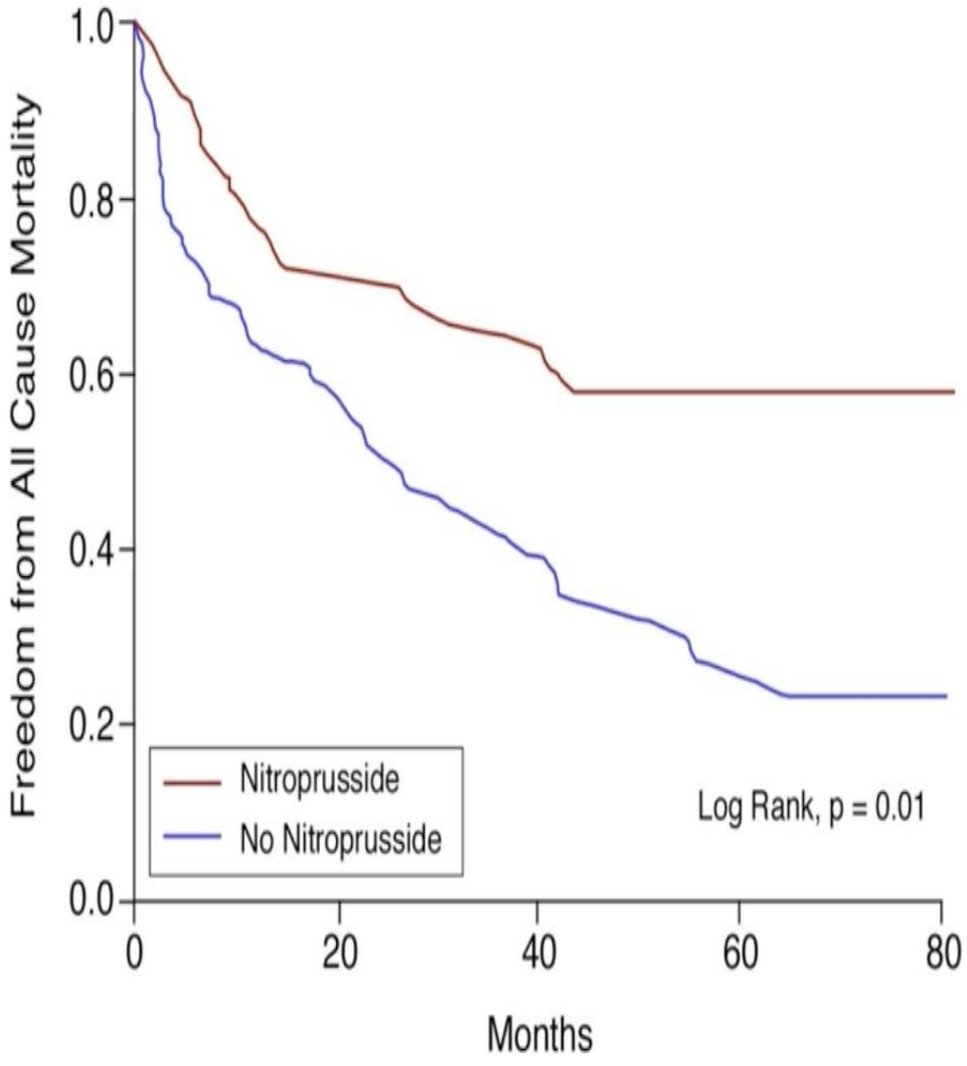


Increase RBF / reduce FF / reduce lymph flow (Vasodilators)

Mullens W et al. Eur Heart J, 2017;38:1872-1882

Verbrugge F, Mullens W et al. J Am Col Card 2015;65:480-92.

Nitroprusside for advanced decompensated HFrEF



Mullens W et al. J Am Coll Card 2008;52:200-7.

Case: 75 year male

- Jan 14, 2021: discharge with no residual congestion, BP 118/70, 66

  S creat 1.9 (eGFR 33)

  + *Bisoprolol 5*

  + *Sacubitril/Valsartan 24/26 BID*

  + *Spiro 25*

  + *Bumetanide 1*

  Include in multi-disciplinary cardiac rehabilitation

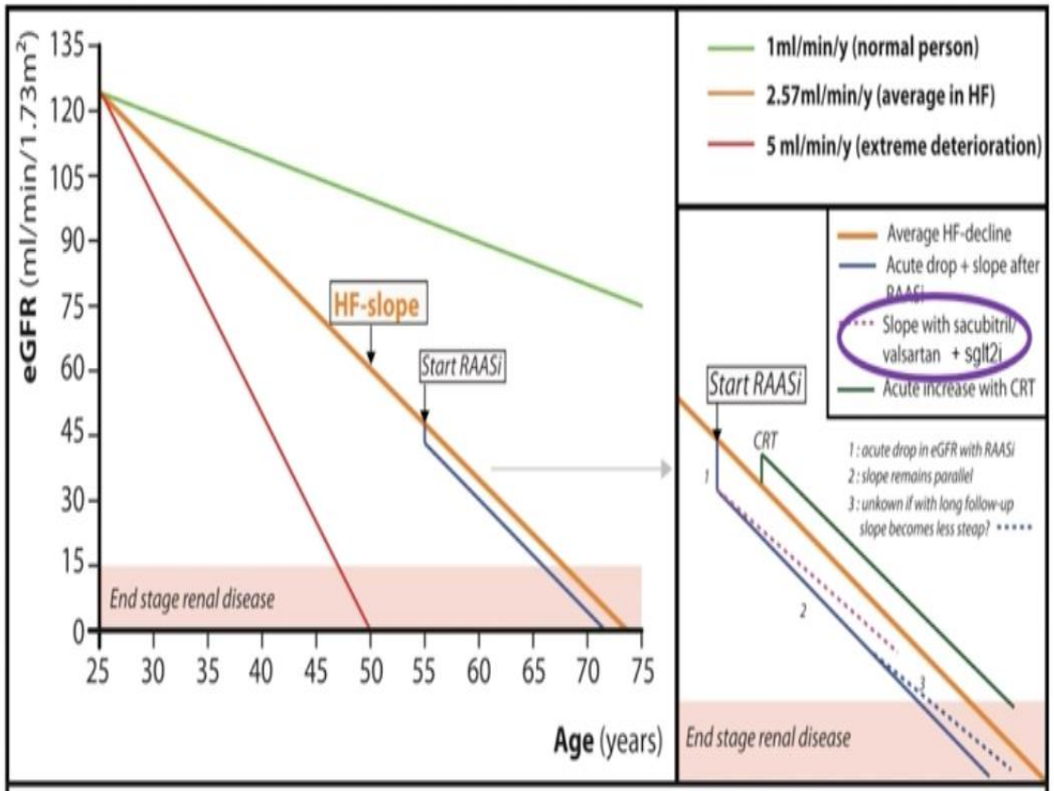
  Lab test within 10 days

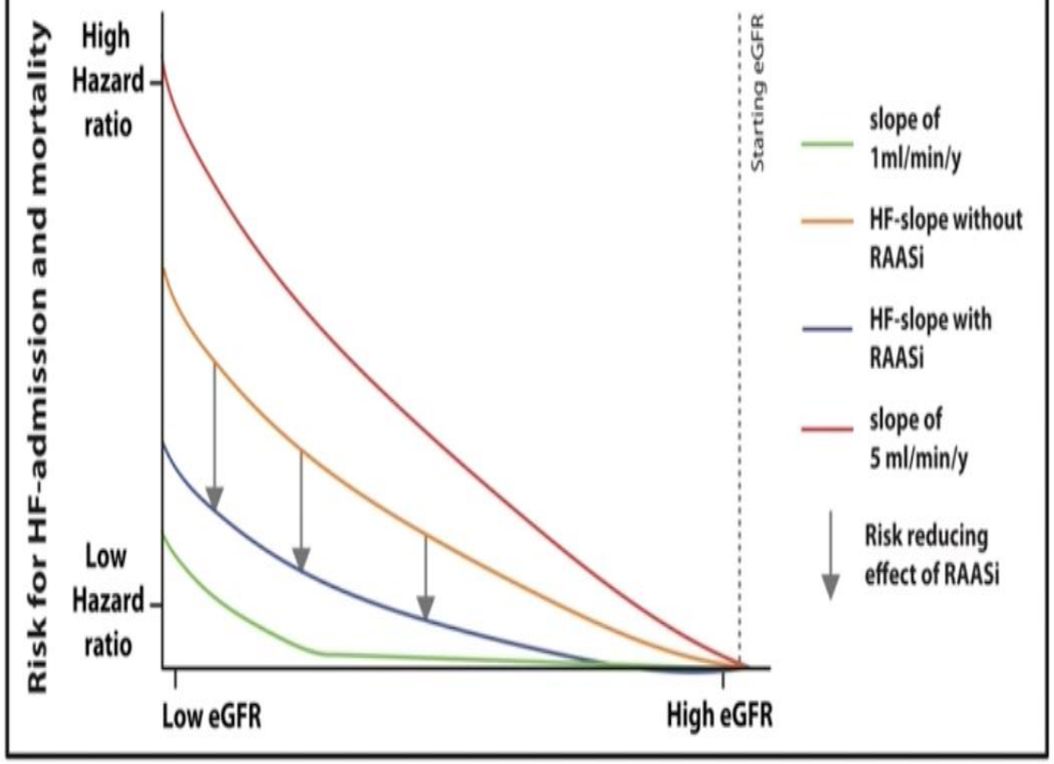
  Heart Failure education

  Letter for GP with instructions

- Jan 24: S creat 2.0 (eGFR 31), mg/dl, BP 112/68

How to treat a patient with chronic HF + WRF ?





Mullens W, Eur J Heart Fail 2020; 22:584-603.

Conclusions

- Judicious use of early diuretic therapy in optimal doses, with early and recurrent evaluation of diuretic effect and the need for diuretics is absolutely needed

- CKD = doubling of risk for all-cause mortality (far more stronger predictor than LVEF)

- Misinterpretation of eGFR changes often results in inappropriate discontinuation of HF therapy

  AHF + WRF + good diuretic response + ongoing congestion = continue diuretic efforts

  AHF + WRF + poor diuretic response + ongoing congestion = intensify diuretics + consider IV vasodilator

  CHF + WRF = balance eGFR changes to long-term risk reduction with disease modifying agents

- Chronic prevention of congestion through uptitration of neurohumoral blockade + treatment co-morbidities + multi-disciplinary disease management + individualization of loop diuretic