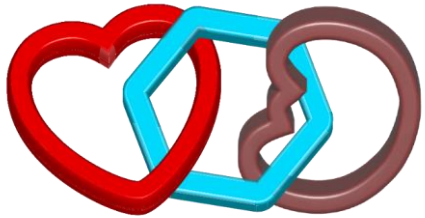


Hemodynamische en metabole complicaties van cardiorenale schade

Prof. dr. Carlo Gaillard

Internist-nefroloog, UMC Utrecht

Outline

Cardiorenale schade. Epidemiologie en classifcatie.

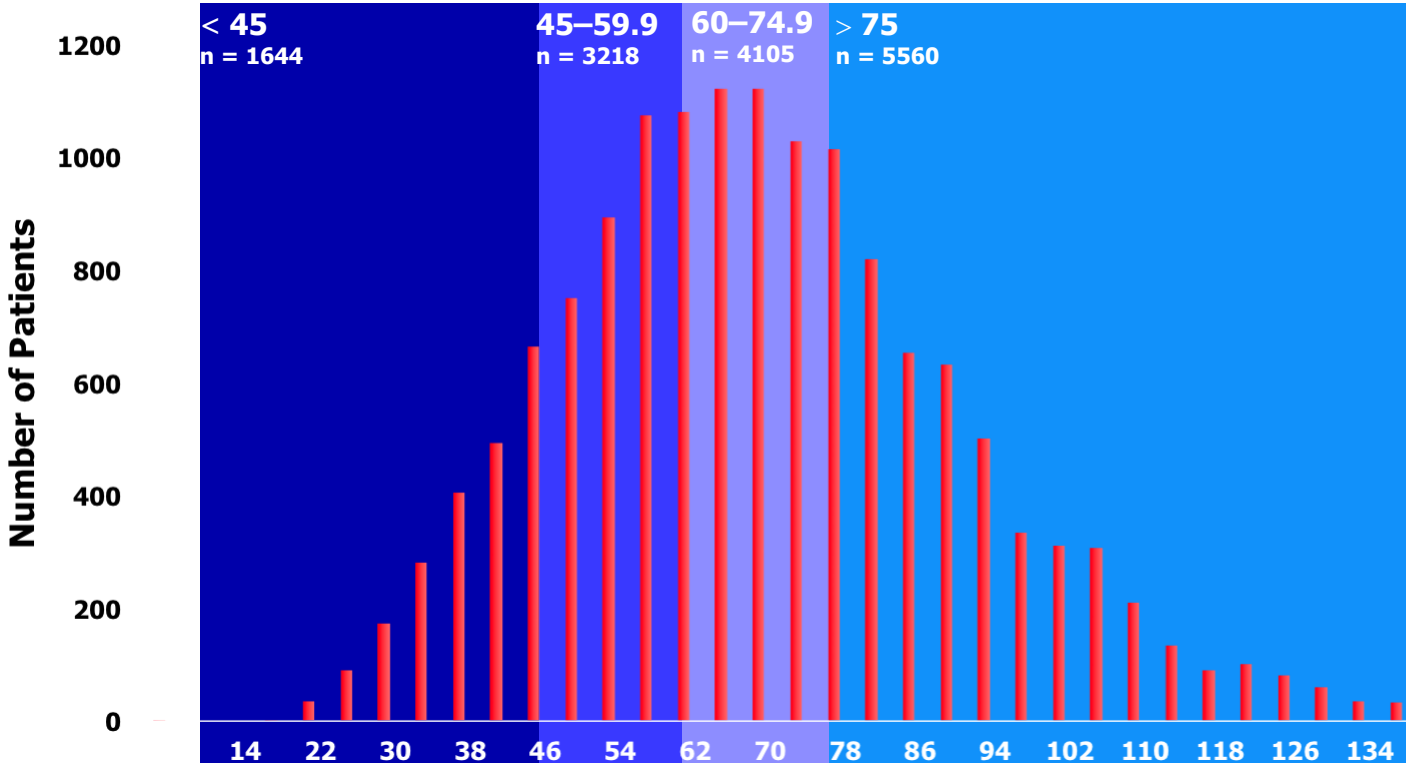
Co-occurrence of cardiorenal pathology, putative pathophysiological mechanisms

Conclusie

Evolving definitions of cardiorenal syndrome

- The frequent presentation of combined cardiac and renal dysfunction *2004*
- The presence or development of renal dysfunction in patients with heart failure *2004*
- Severe cardiorenal syndrome is a pathophysiological condition in which combined cardiac and renal dysfunction amplifies progression of failure of the individual organs *2006*
- Cardiorenal syndrome is a pathophysiological disorder in which acute or chronic dysfunction of one organ may induce acute or chronic dysfunction in the other *2008*
- Each dysfunctional organ has the ability to initiate and perpetuate disease in the other organ through common hemodynamic, neurohormonal, and immunological and/or biochemical feedback pathways *2010*

VALIANT: Renal disease in heart failure



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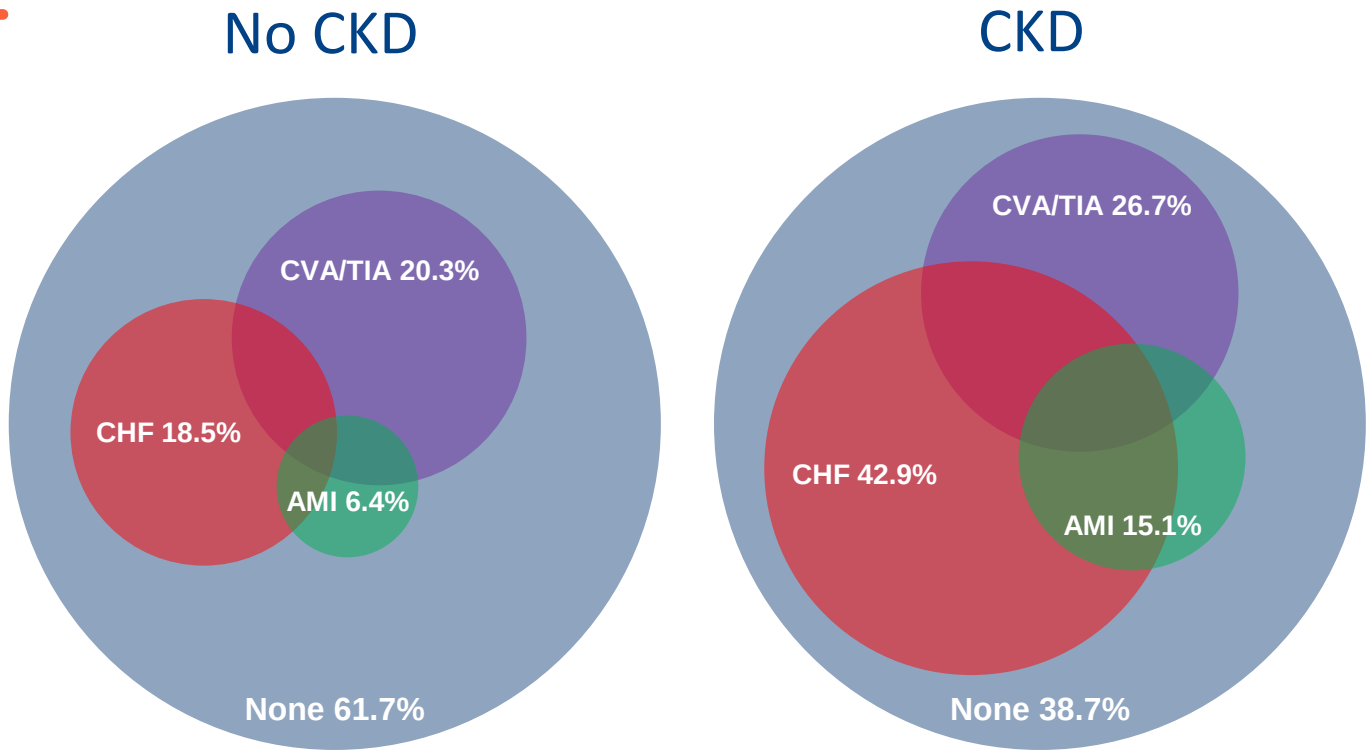
Anavekar N Engl J Med 2004

Cardiovascular disease and heart failure in CKD



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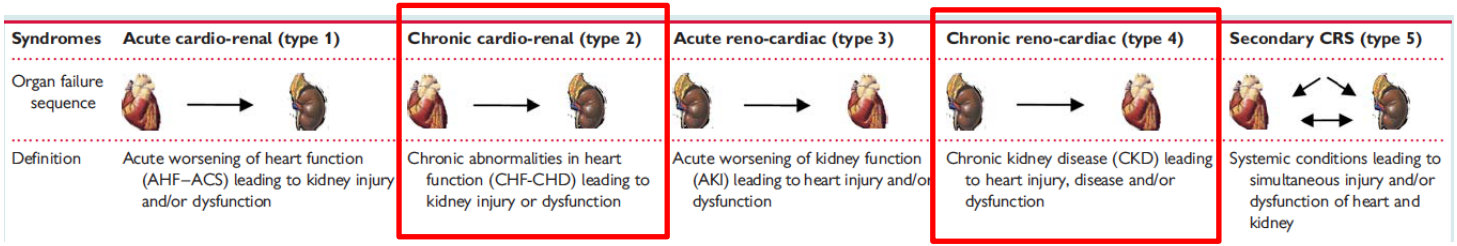
U.S. Renal Data System 2013 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2013

Classification of cardiorenal interaction



Syndromes	Acute cardio-renal (type 1)	Chronic cardio-renal (type 2)	Acute reno-cardiac (type 3)	Chronic reno-cardiac (type 4)	Secondary CRS (type 5)
Organ failure sequence					
Definition	Acute worsening of heart function (AHF–ACS) leading to kidney injury and/or dysfunction	Chronic abnormalities in heart function (CHF-CHD) leading to kidney injury or dysfunction	Acute worsening of kidney function (AKI) leading to heart injury and/or dysfunction	Chronic kidney disease (CKD) leading to heart injury, disease and/or dysfunction	Systemic conditions leading to simultaneous injury and/or dysfunction of heart and kidney

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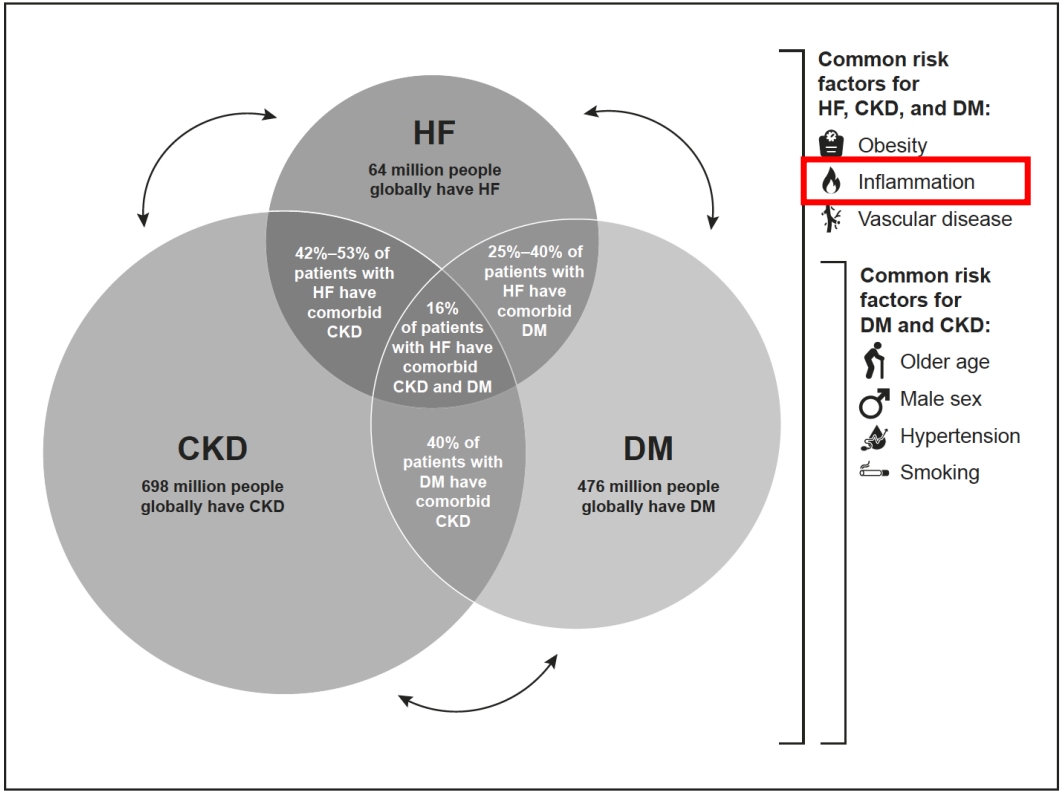
Ronco Eur Heat J 2010

DM, HF en CKD



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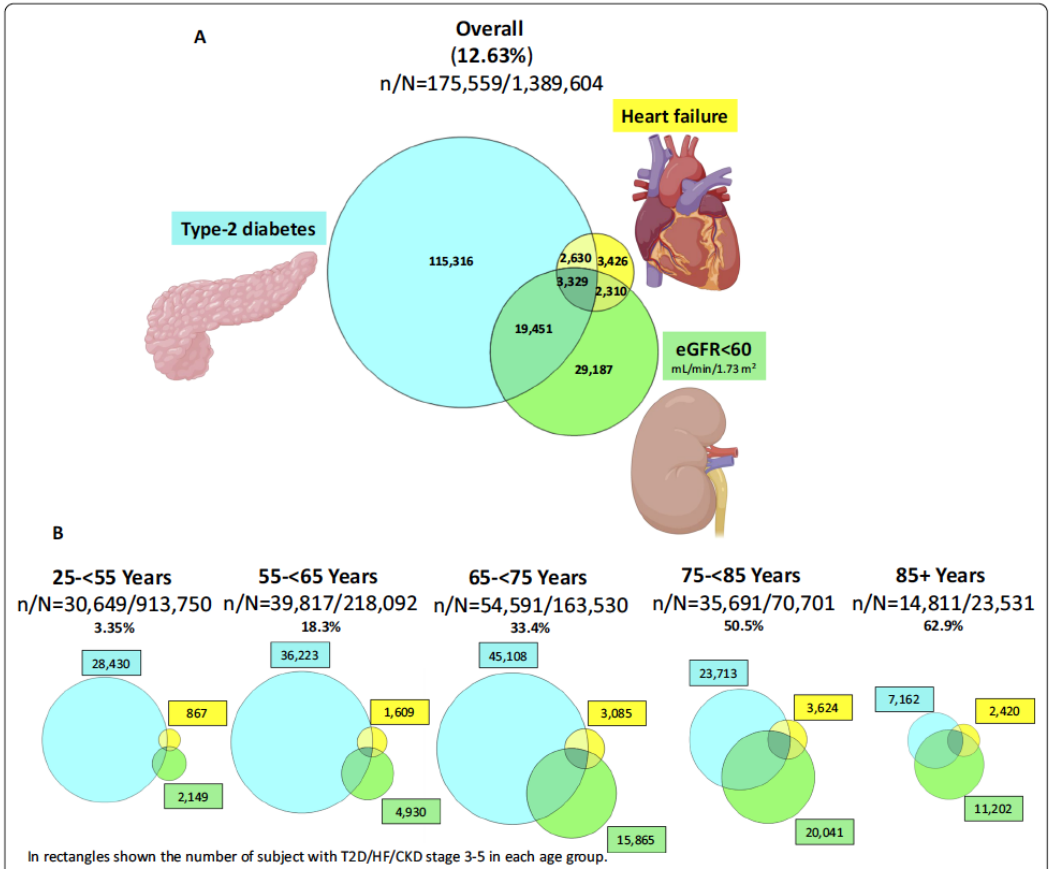
Vijay Cardiorenal Medicine 2022



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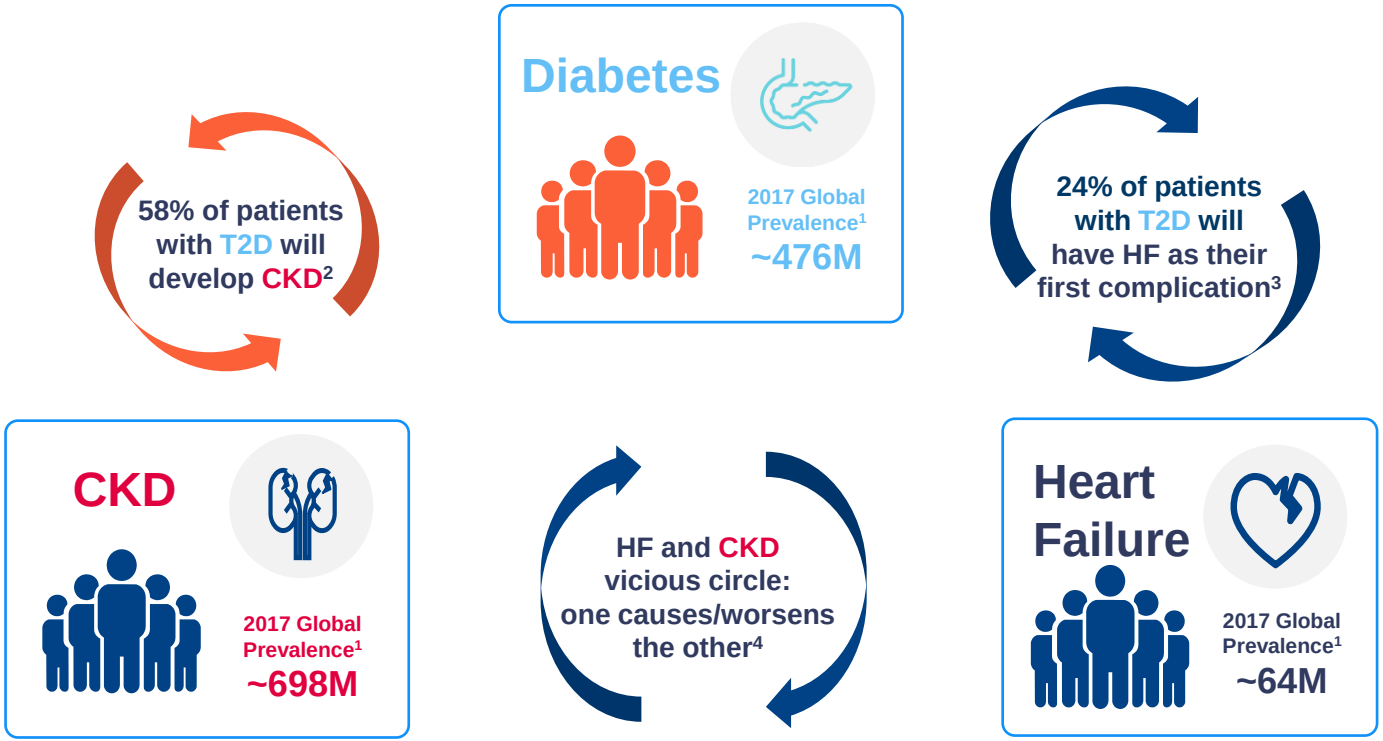
Schechter et al. Cardiovascular Diabetology 2022

CKD, heart failure, and type 2 diabetes are interrelated, leading to a vicious circle of cardiac, renal and metabolic risk



CKD, chronic kidney disease; HF, heart failure; T2D, type 2 diabetes.

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet.* 2018;392:1789-1858; 2. Parving HH et al. *Kidney Int.* 2006;69:2057-2063; 3. Birkeland KI et al. *Diabetes Obes Metab.* 2020:22:1607-1618; 4. Ronco C et al. *J Am Coll Cardiol.* 2008;52:1527-1539.

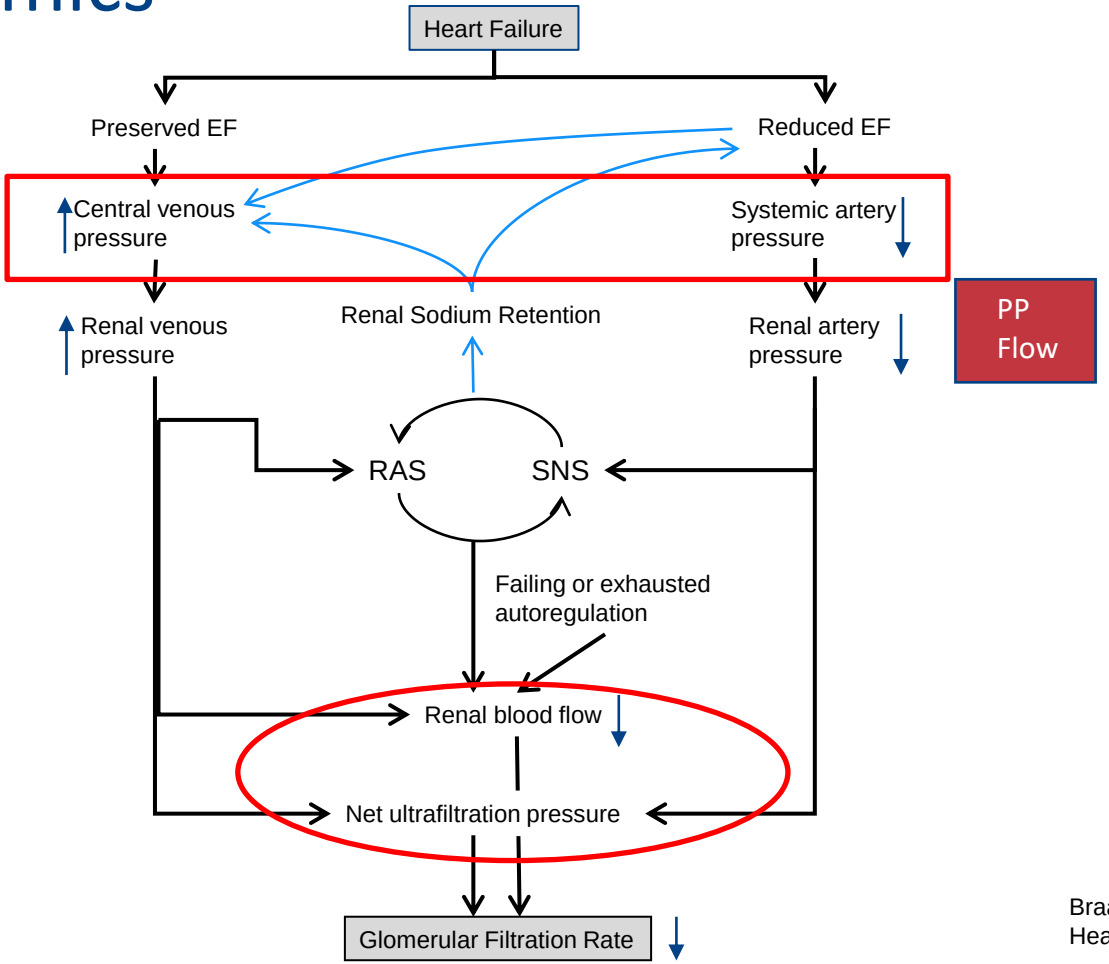
Co-occurrence of cardiorenal pathology: putative pathophysiological interaction

Hemodynamics

Non hemodynamic “connectors”

Others

Hemodynamics



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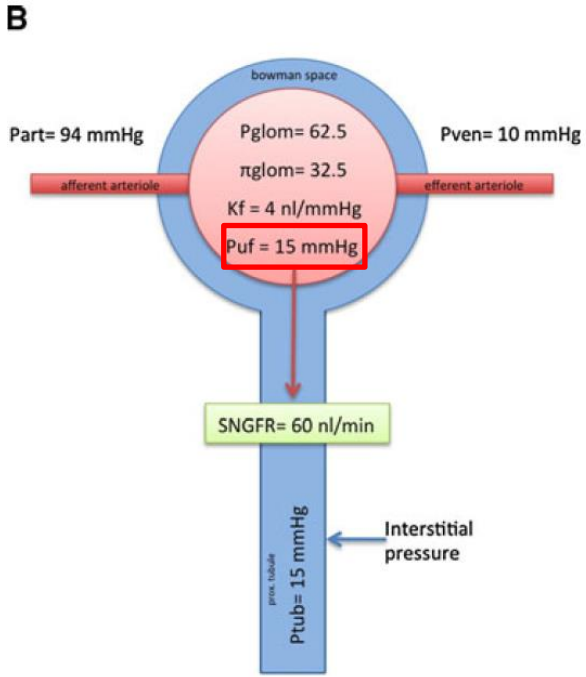
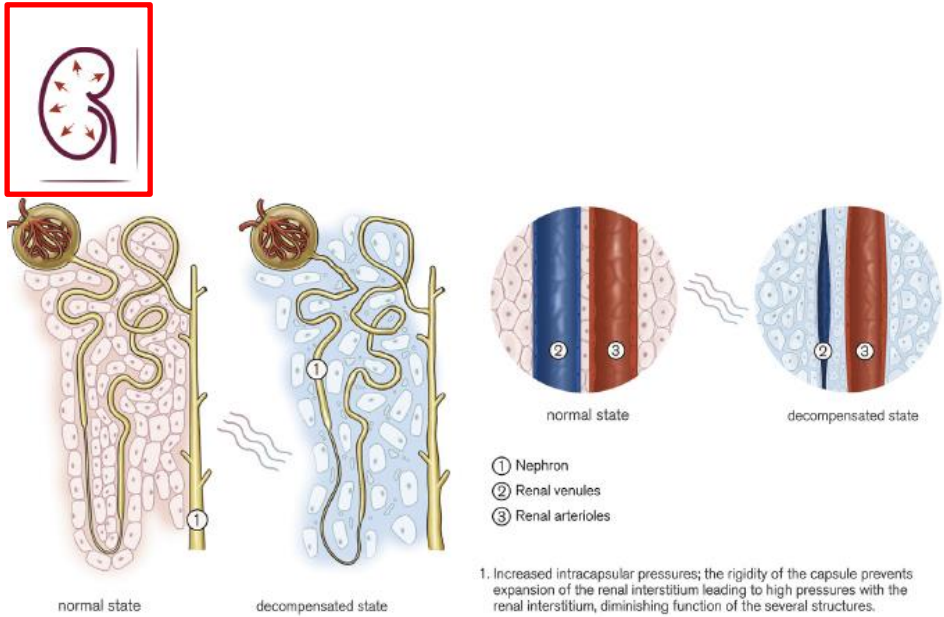
Braam, Cupples, Joles, Gaillard,
Heart Failure Reviews 2011

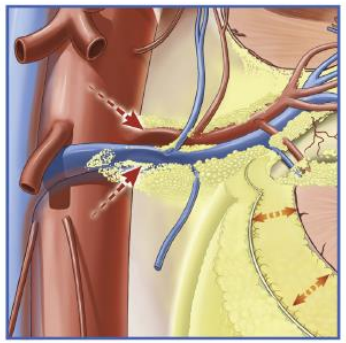


Braam, Cupples, Joles and Gaillard. Heart failure reviews 2011

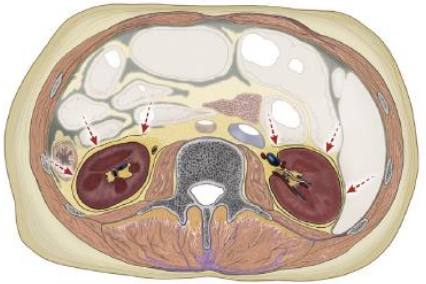
The renal tamponade hypothesis



1. Increased intracapsular pressures; the rigidity of the capsule prevents expansion of the renal interstitium leading to high pressures with the renal interstitium, diminishing function of the several structures.



2. Increased perirenal pressure; increases in perirenal adipose tissue compress renal vasculature, exacerbating intrarenal congestion.



3. Increased peritoneal pressure; the weight of the peritoneal space, from either fat or fluid, compresses the renal vasculature, exacerbating renal congestion.

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Boorsma, E.M. et al. J Am Coll Cardiol HF. 2022;10(3):175–183.

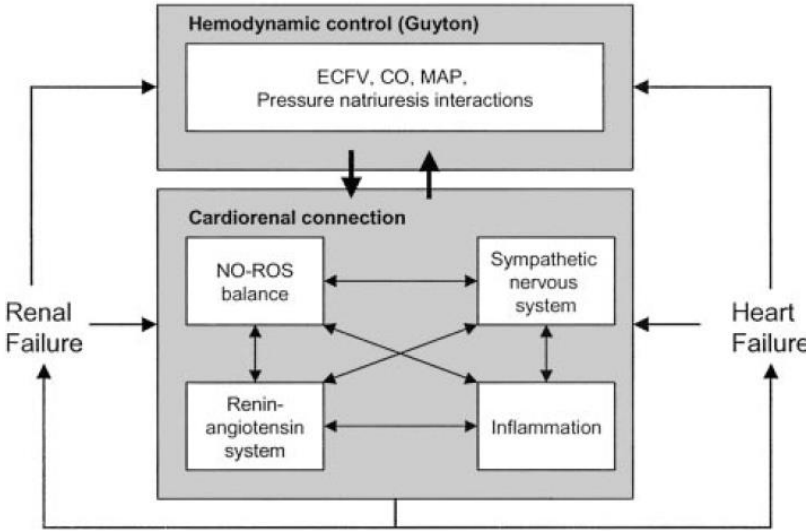
Non-hemodynamic connectors

Renin Angiotensin Aldosteron System

Sympathetic Nervous System

Inflammation

Reactive Oxygen Species



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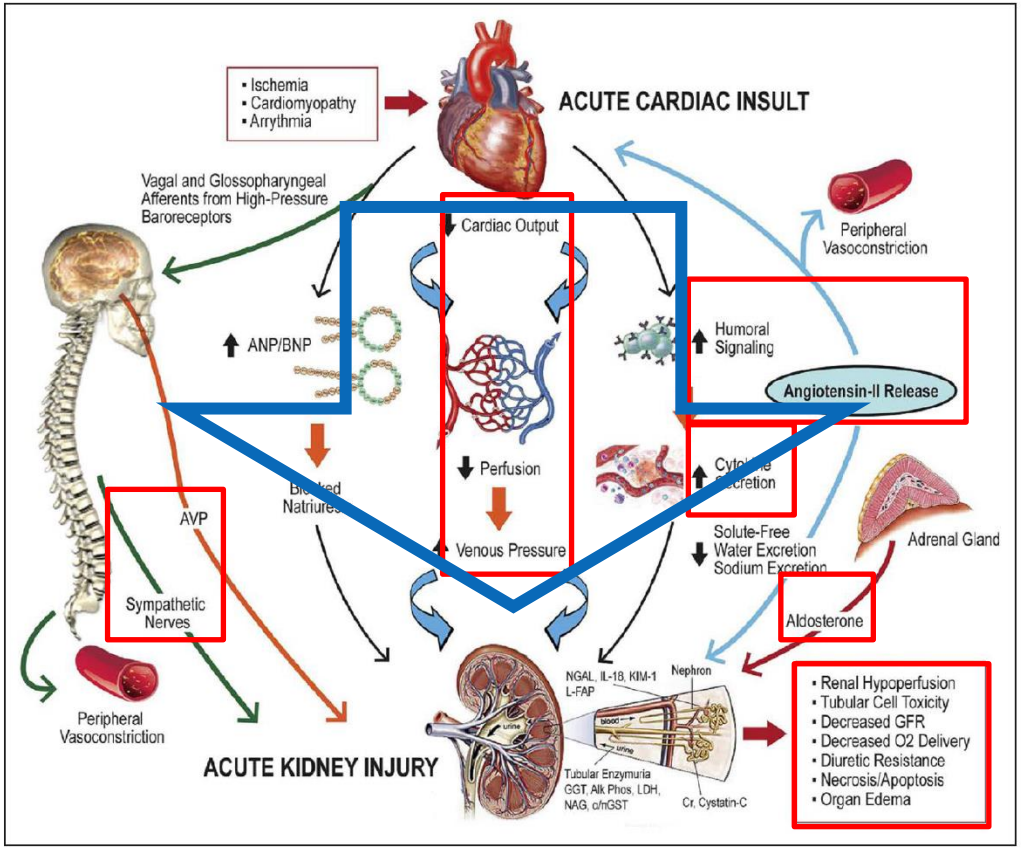
Bongartz Eur Heart J 2004

Pathophysiology of neurohumoral and inflammatory pathways involved in cardiorenal syndrome



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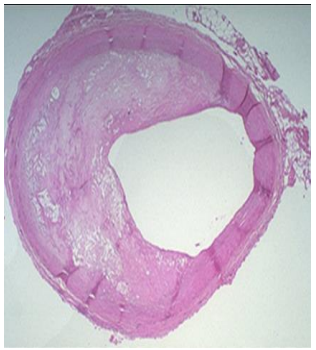
Rangaswami Circulation 2019

What identifies renal-disease-induced cardiovascular disease?

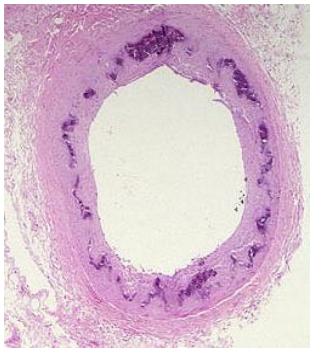
Accelerated atherosclerosis: a different, more rapid and extensive atherosclerotic process

Uremic cardiomyopathy/HFpEF

Underlying metabolic disorder



Atherosclerosis



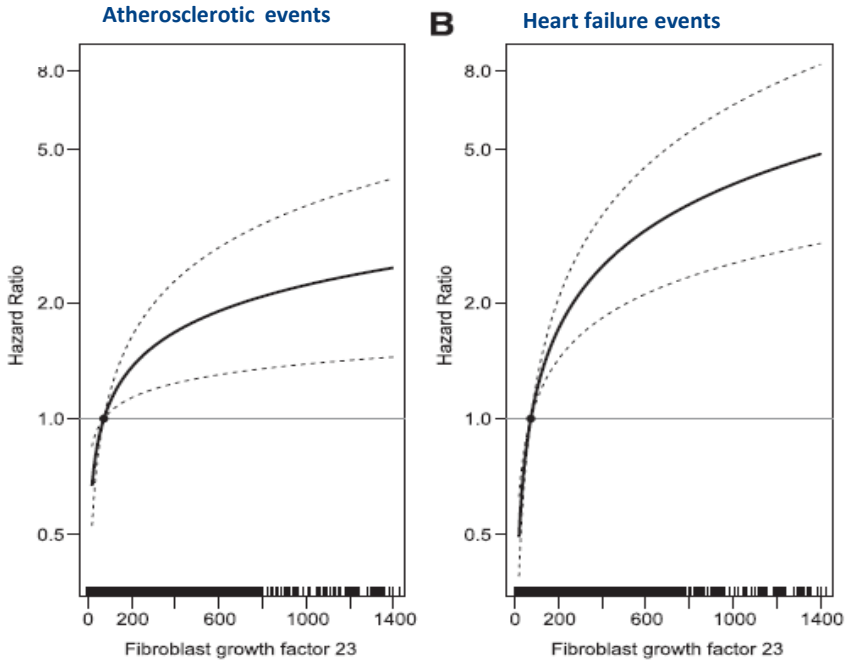
Mönckeberg's arteriosclerosis

Fibroblast growth factor 23: course in CKD

Fibroblast growth factor 23 (FGF23) is osteocyte-derived hormone which is an essential regulator of phosphate metabolism

FGF23 has been shown to be associated with an increased risk of mortality in RTR, and in many other patient populations

Calcium phosphate metabolism, LVH, Sodium regulation, Infection, Red cell production



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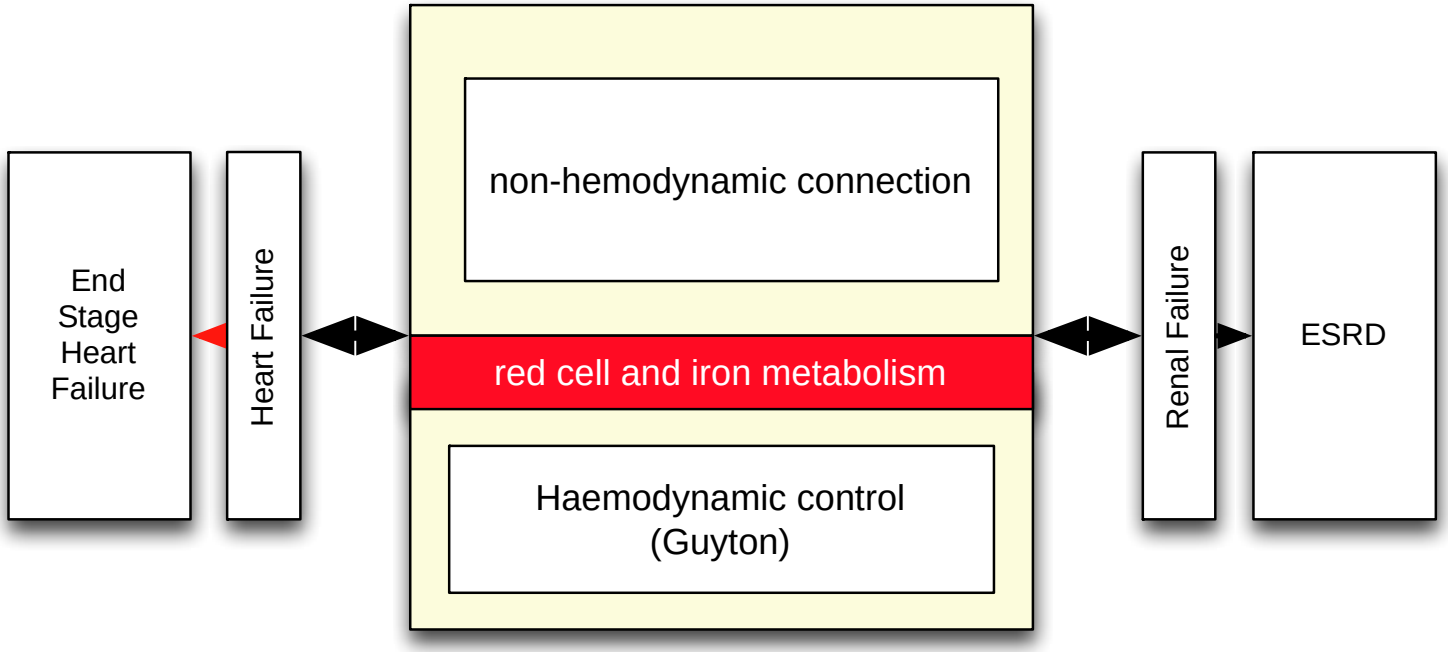
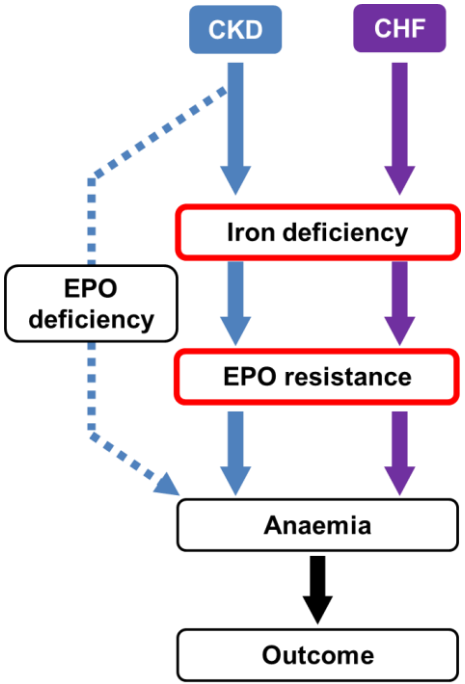
Scialla JS et al. J Am Soc Nephol 2014

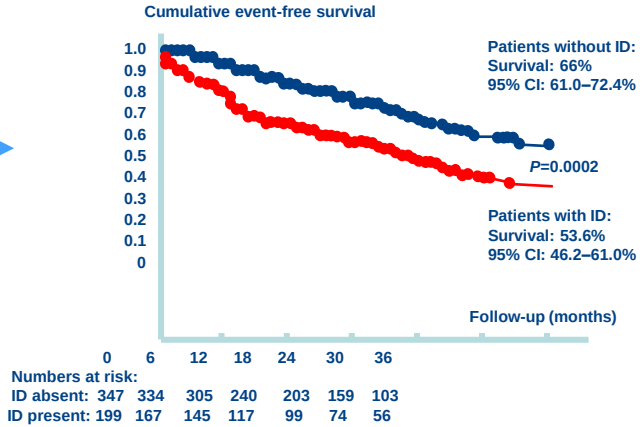
Isakova T et al Kidney Int 2011

Red cell and iron



Bongratz Eur Heart J 2005





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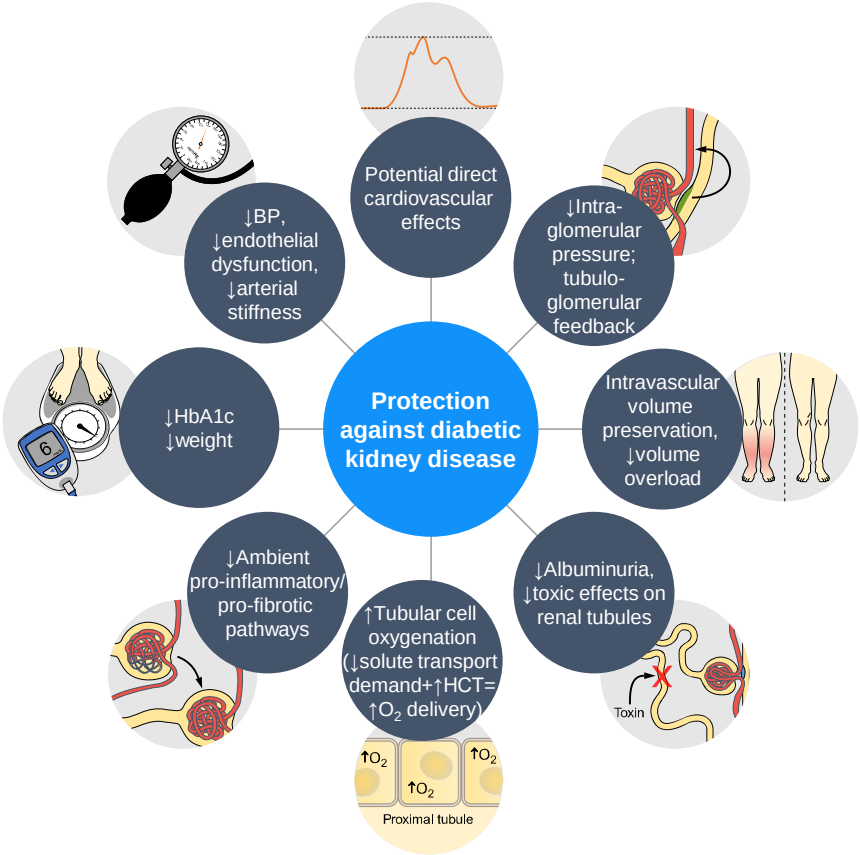
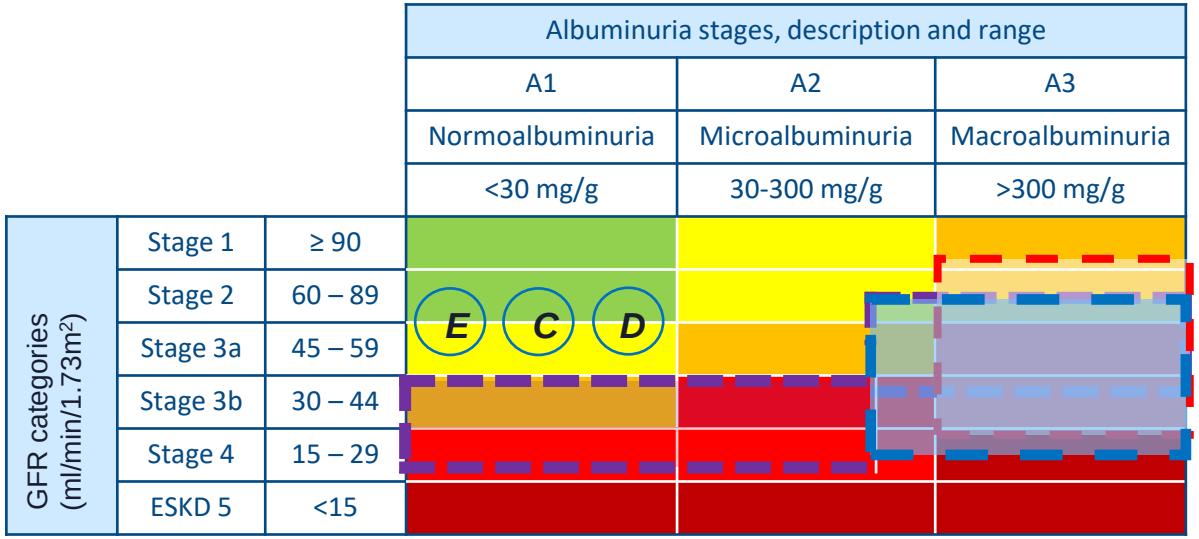
Jankowska E *et al. Eur Heart J* 2010;31:1872–80.
Belonje A *et al. Circulation* 2010; 121:245–51.

Proposed renal protective pathways with SGLT2 inhibitors



BP, blood pressure; CKD, chronic kidney disease; HbA1c, glycated haemoglobin; HCT, hematocrit; SGLT2, sodium-glucose cotransporter 2.
Reproduced from Heerspink HJL, et al *Kidney International* 2018;94:26–39

Kidney outcome trials with SGLT2 inhibitors address the spectrum of CKD



CREDENCE (DKD only)
eGFR ≥30 to <90 ml/min/1.73m²
and UACR ≥300 mg/g

DAPA-CKD (CKD)
eGFR ≥25 to <75 ml/min/1.73m²
and UACR ≥200 mg/g

EMPA-KIDNEY (CKD)
eGFR ≥45 to <75 ml/min/1.73m²
and UACR ≥200 mg/g
OR
eGFR ≥20 to <4 ml/min/1.73m²

E=EMPAREG-Outcome; C=CANVAS; D=DECLARE TIMI-58

CKD, chronic kidney disease; DKD, diabetic kidney disease, eGFR, glomerular filtration rate; GFR, glomerular filtration rate
Heerspink HJL, et.al. *Nephrol Dial Transplant* 2020;35:274–282

Summary

The cardiorenal syndrome refers to a complex interaction between heart and kidney causing reciprocal damage through hemodynamic, neurohumoral and metabolic mechanisms including

- -disturbed calcium/phosphate metabolism
- -anemia and increased red cell turn over
- -iron deficiency
- -inflammation
- -?

Summary

Mechanisms responsible for true reciprocal augmentation of damage are of utmost importance, warrant further studies and may allow development of new treatment approaches