Heart and Kidney

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Why should we learn about heart disease if you have kidney disease?

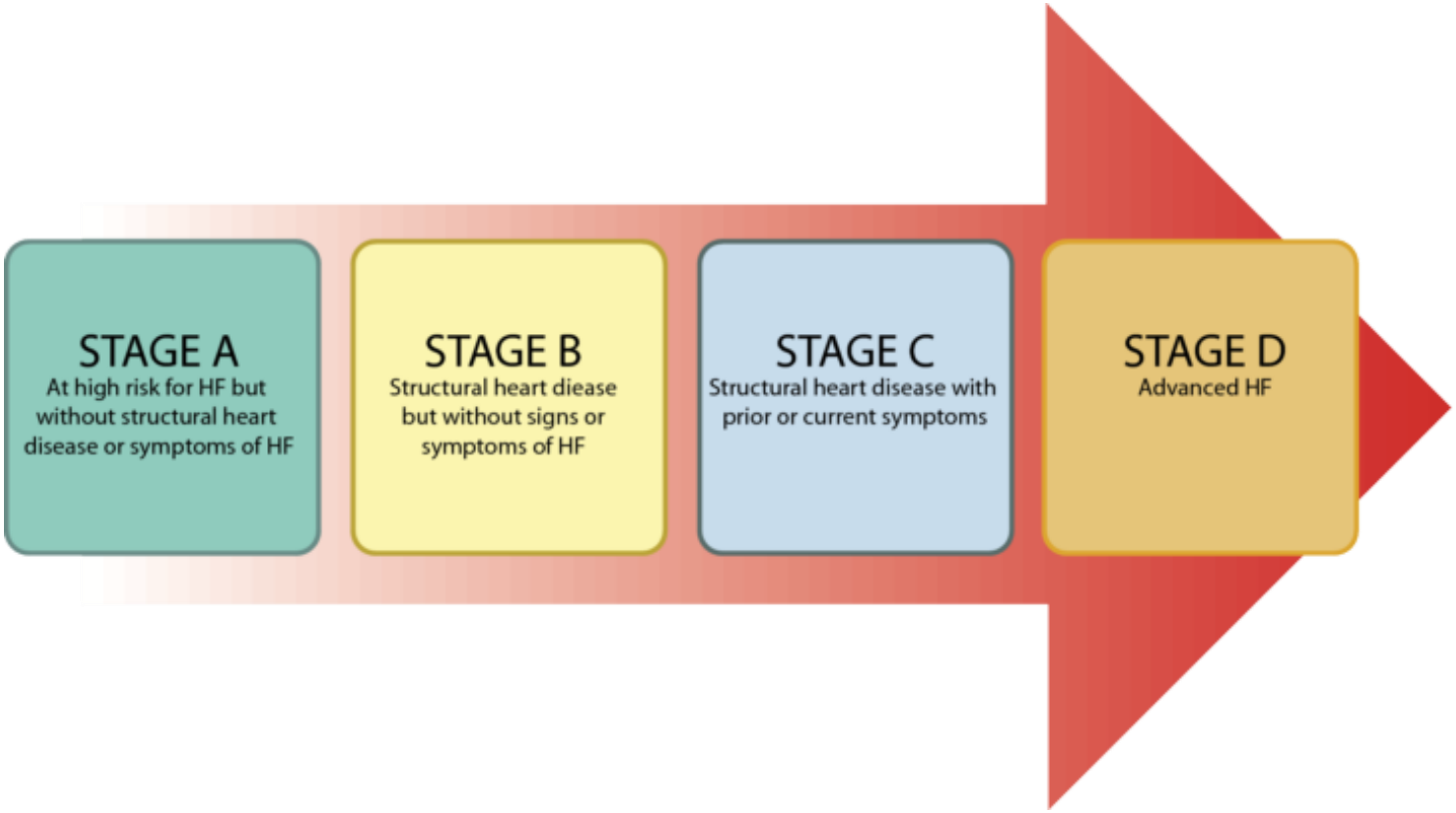
- If you have kidney disease, you are more likely to get heart disease.
- Heart disease is the most common cause of death among people who have kidney disease

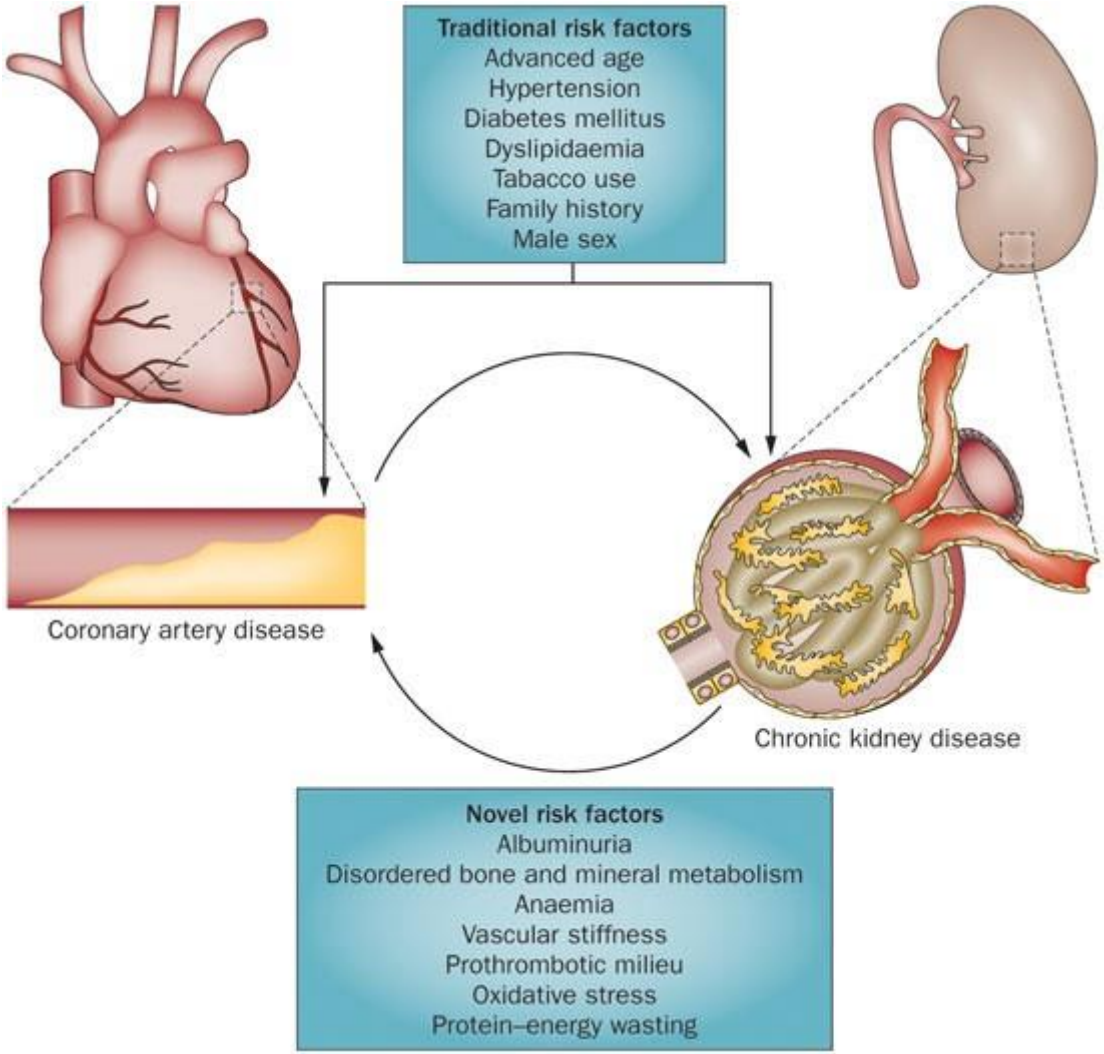
What is kidney disease?

- Kidney disease means that the kidneys are damaged and can't filter blood as they should.
- This damage can cause wastes to build up in the body. For most people, kidney damage occurs slowly over many years. This gradual loss of kidney function is called chronic kidney disease (CKD).
- Most patients with CKD have no symptoms until kidney damage is advanced.
- After many years, you may start to feel sick or tired all the time.
- Kidney failure is when you need a kidney transplant or a blood filtering treatment called dialysis
- Before you reach that stage, other health problems may develop. One of these problems is heart disease.

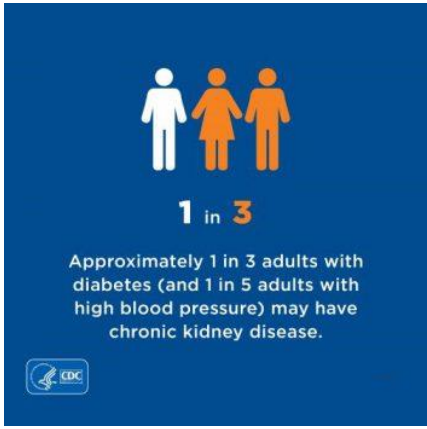
Stages of Kidney Disease

Stages of Congestive Heart Failure




Traditional risk factors
Advanced age
Hypertension
Diabetes mellitus
Dyslipidaemia
Tabacco use
Family history
Male sex
Coronary artery disease
Chronic kidney disease
Novel risk factors
Albuminuria
Disordered bone and mineral metabolism
Anaemia
Vascular stiffness
Prothrombotic milieu
Oxidative stress
Protein–energy wasting

Risk factors



Heart disease

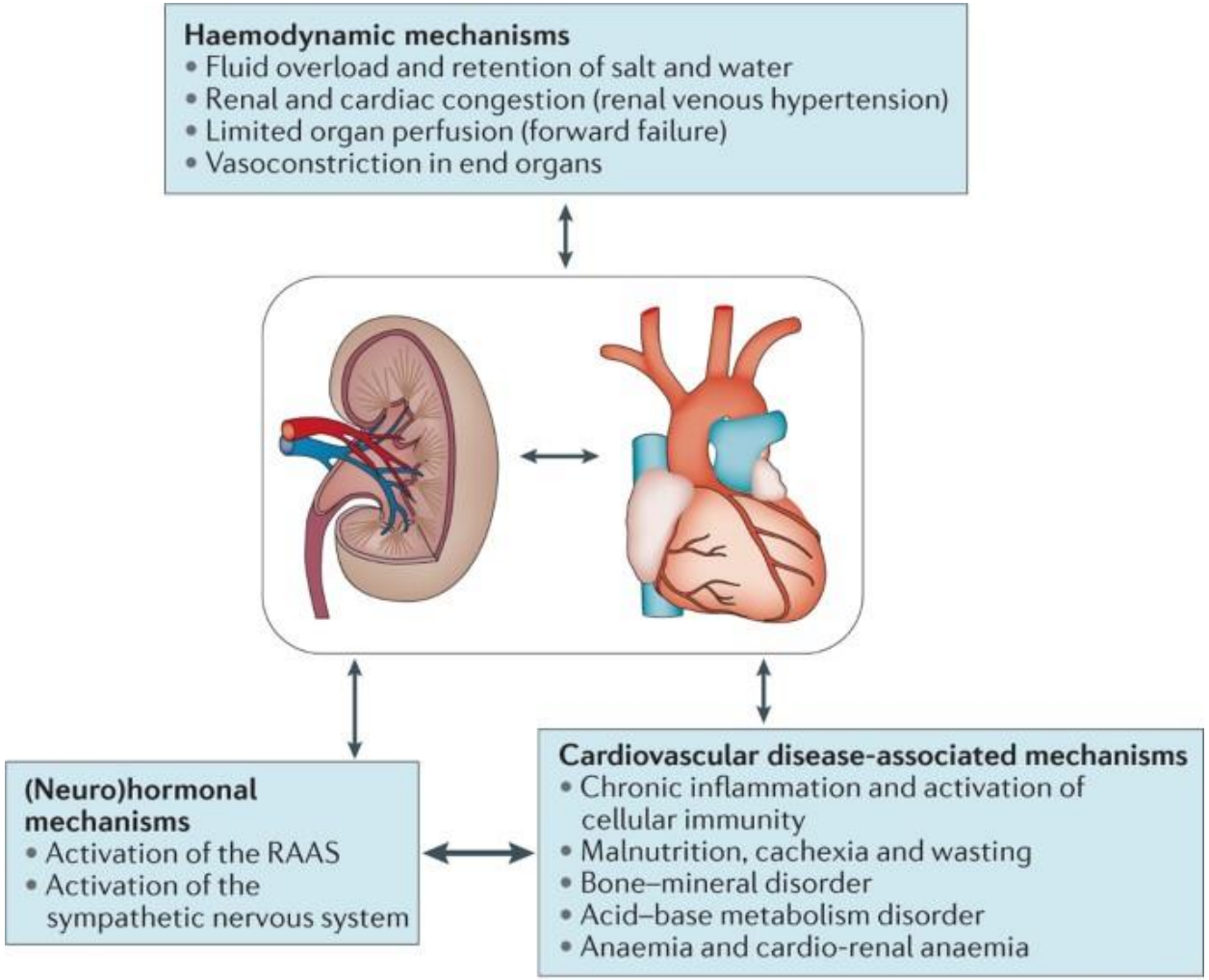
- HTN
- Diabetes Mellitus
- Smoking
- Kidney disease
- FH of heart disease
- High cholesterol
- Smoking
- Inflammatory disease

Kidney disease

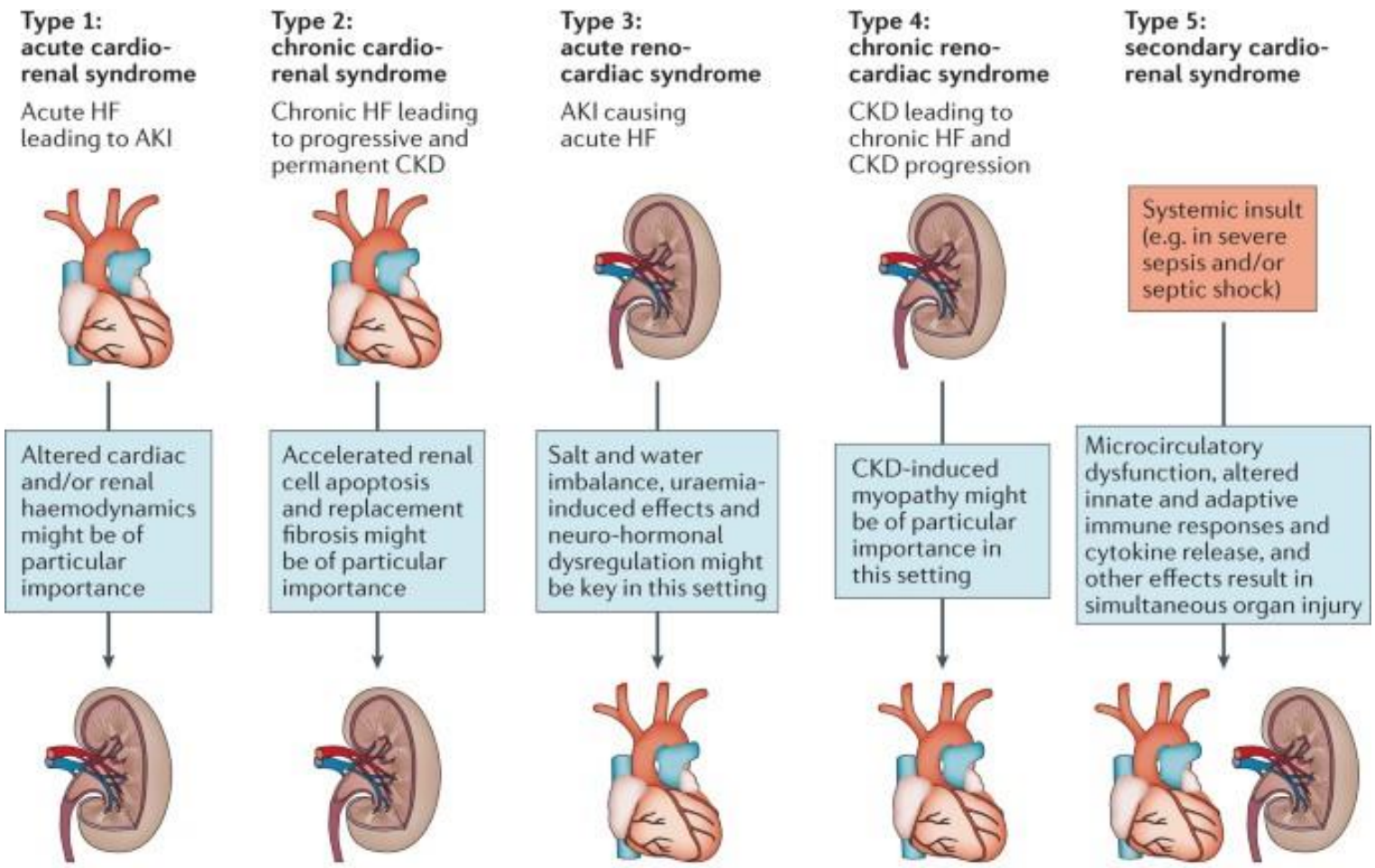
- HTN
- Diabetes Mellitus
- Heart disease
- FH of heart disease
- NSAIDs
- Inflammatory disease

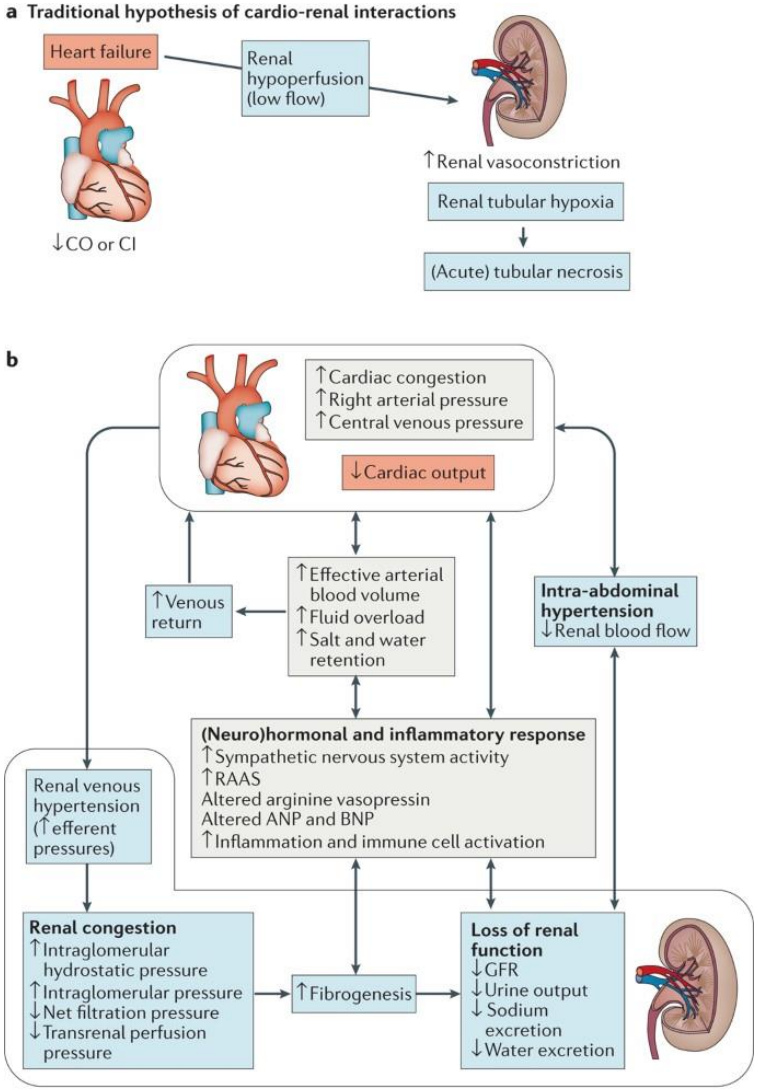
Heart Failure and Kidney Disease

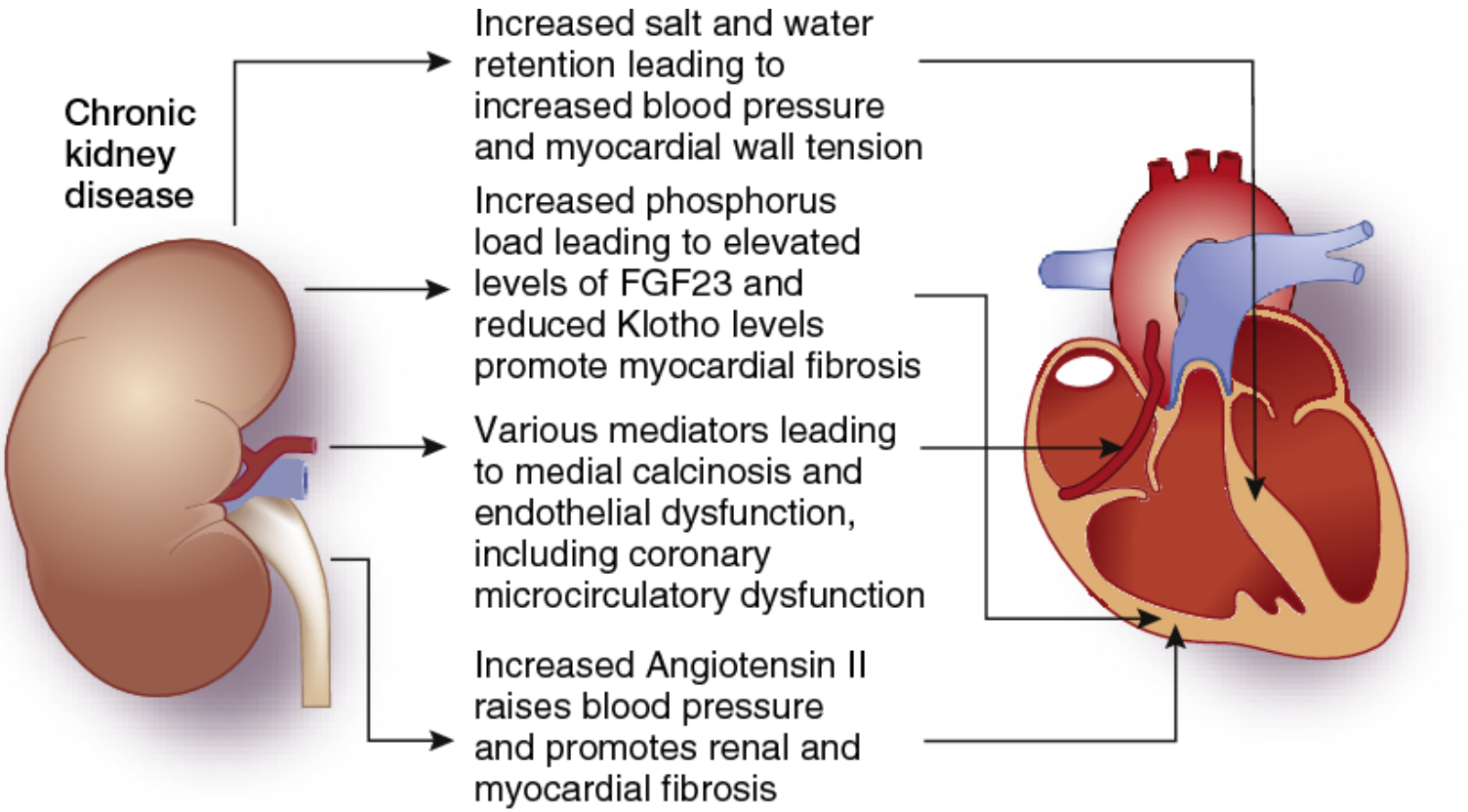
- Heart failure (HF) interacts with kidney disease via numerous pathophysiological pathways in both the acute and chronic setting
- Mounting data indicate that the complex interplay between the heart and the kidneys involves hemodynamic, (neuro)hormonal and cardiovascular disease-associated mechanisms
- Acceleration of HF or kidney dysfunction is driven by impairment of either the heart or kidneys via mechanisms including induction of inflammation, activation of the cellular immune system, metabolic disorders, anemia and mineral and bone disorder



Nature Reviews | Nephrology

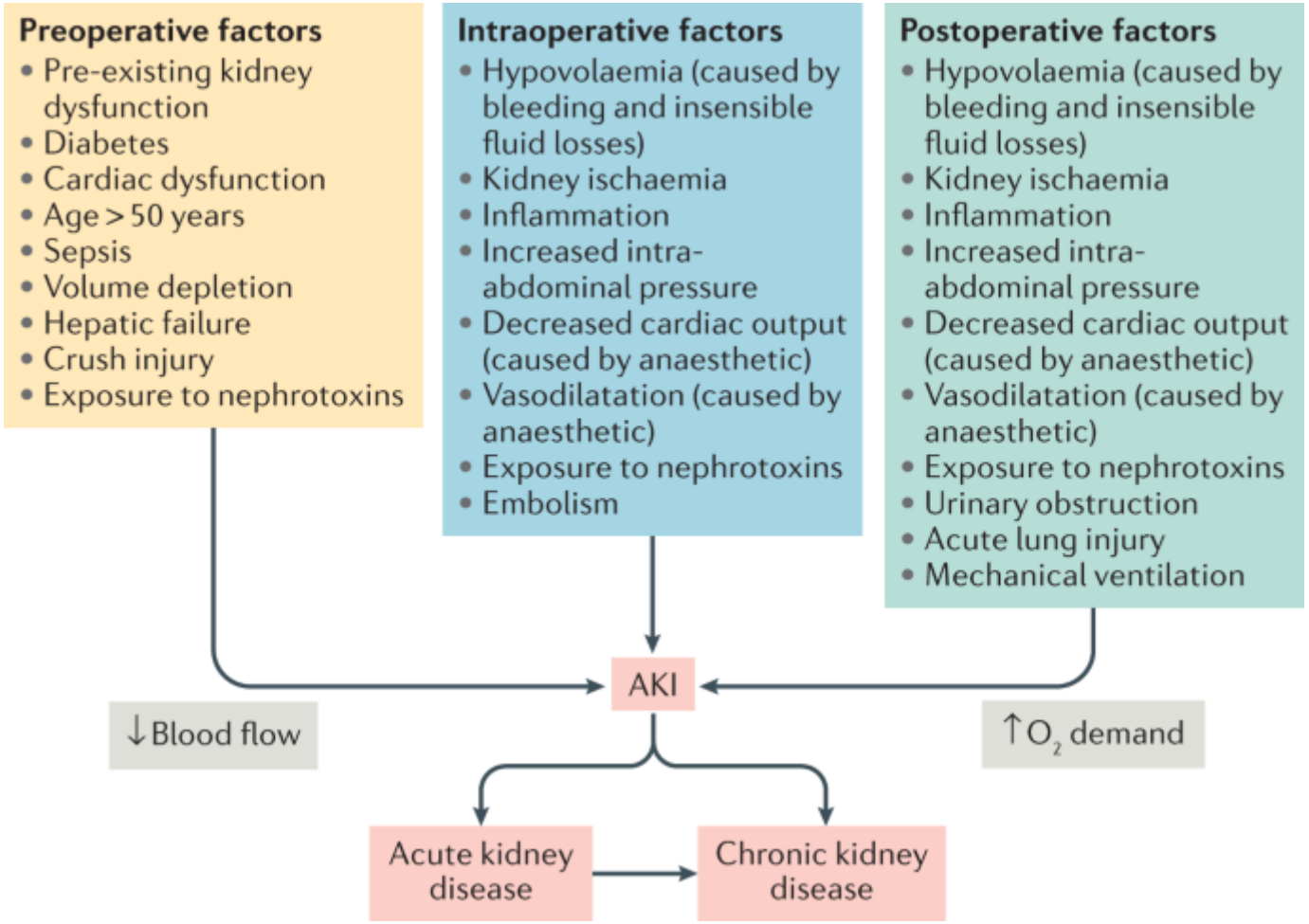

Type 1:
acute cardio-renal syndrome
Acute HF leading to AKI
Altered cardiac and/or renal haemodynamics might be of particular importance
Type 2:
chronic cardio-renal syndrome
Chronic HF leading to progressive and permanent CKD
Accelerated renal cell apoptosis and replacement fibrosis might be of particular importance
Type 3:
acute reno-cardiac syndrome
AKI causing acute HF
Salt and water imbalance, uraemia-induced effects and neuro-hormonal dysregulation might be key in this setting
Type 4:
chronic reno-cardiac syndrome
CKD leading to chronic HF and CKD progression
CKD-induced myopathy might be of particular importance in this setting
Type 5:
secondary cardio-renal syndrome
Systemic insult (e.g. in severe sepsis and/or septic shock)
Microcirculatory dysfunction, altered innate and adaptive immune responses and cytokine release, and other effects result in simultaneous organ injury


a Traditional hypothesis of cardio-renal interactions
Heart failure
Renal hypoperfusion (low flow)
↑Renal vasoconstriction
Renal tubular hypoxia
(Acute) tubular necrosis
↓CO or CI
b
↑Cardiac congestion
↑Right arterial pressure
↑Central venous pressure
↓Cardiac output
↑Effective arterial blood volume
↑Fluid overload
↑Salt and water retention
↑Venous return
Intra-abdominal hypertension
↓Renal blood flow
(Neuro)hormonal and inflammatory response
↑Sympathetic nervous system activity
↑RAAS
Altered arginine vasopressin
Altered ANP and BNP
↑Inflammation and immune cell activation
Renal venous hypertension (↑efferent pressures)
Renal congestion
↑Intraglomerular hydrostatic pressure
↑Intraglomerular pressure
↓Net filtration pressure
↓Transrenal perfusion pressure
↑Fibrogenesis
Loss of renal function
↓GFR
↓Urine output
↓Sodium excretion
↓Water excretion


Chronic kidney disease
Increased salt and water retention leading to increased blood pressure and myocardial wall tension
Increased phosphorus load leading to elevated levels of FGF23 and reduced Klotho levels promote myocardial fibrosis
Various mediators leading to medial calcinosis and endothelial dysfunction, including coronary microcirculatory dysfunction
Increased Angiotensin II raises blood pressure and promotes renal and myocardial fibrosis

Causes of Kidney Disease

Type	**Mechanism**
Prerenal	renal hypoperfusion (hypovolemia, hypotension)
Intrarenal	Rhabdomyolosis, infection
Post renal	kidney stones, tumors


Preoperative factors
• Pre-existing kidney dysfunction
• Diabetes
• Cardiac dysfunction
• Age > 50 years
• Sepsis
• Volume depletion
• Hepatic failure
• Crush injury
• Exposure to nephrotoxins
Intraoperative factors
• Hypovolaemia (caused by bleeding and insensible fluid losses)
• Kidney ischaemia
• Inflammation
• Increased intra-abdominal pressure
• Decreased cardiac output (caused by anaesthetic)
• Vasodilatation (caused by anaesthetic)
• Exposure to nephrotoxins
• Embolism
Postoperative factors
• Hypovolaemia (caused by bleeding and insensible fluid losses)
• Kidney ischaemia
• Inflammation
• Increased intra-abdominal pressure
• Decreased cardiac output (caused by anaesthetic)
• Vasodilatation (caused by anaesthetic)
• Exposure to nephrotoxins
• Urinary obstruction
• Acute lung injury
• Mechanical ventilation
AKI
↓Blood flow
↑O_2 demand
Acute kidney disease
Chronic kidney disease

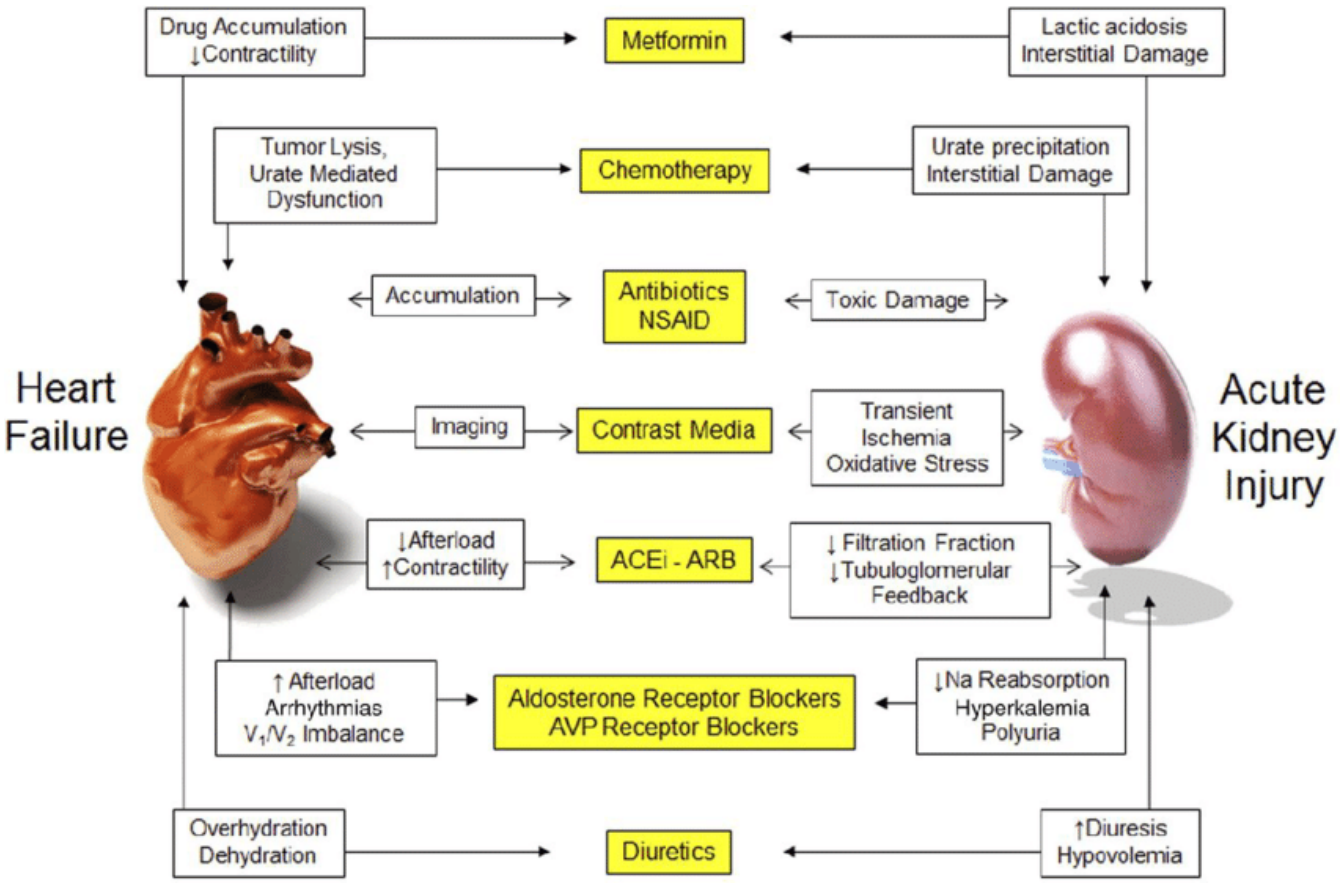
Drugs affecting kidney disease

Noncardiac drugs affecting the kidneys

- Contrast dye
- Metformin
- Antibiotics
- NSAIDS
- Chemotherapy
- Antirejection
- Colchicine

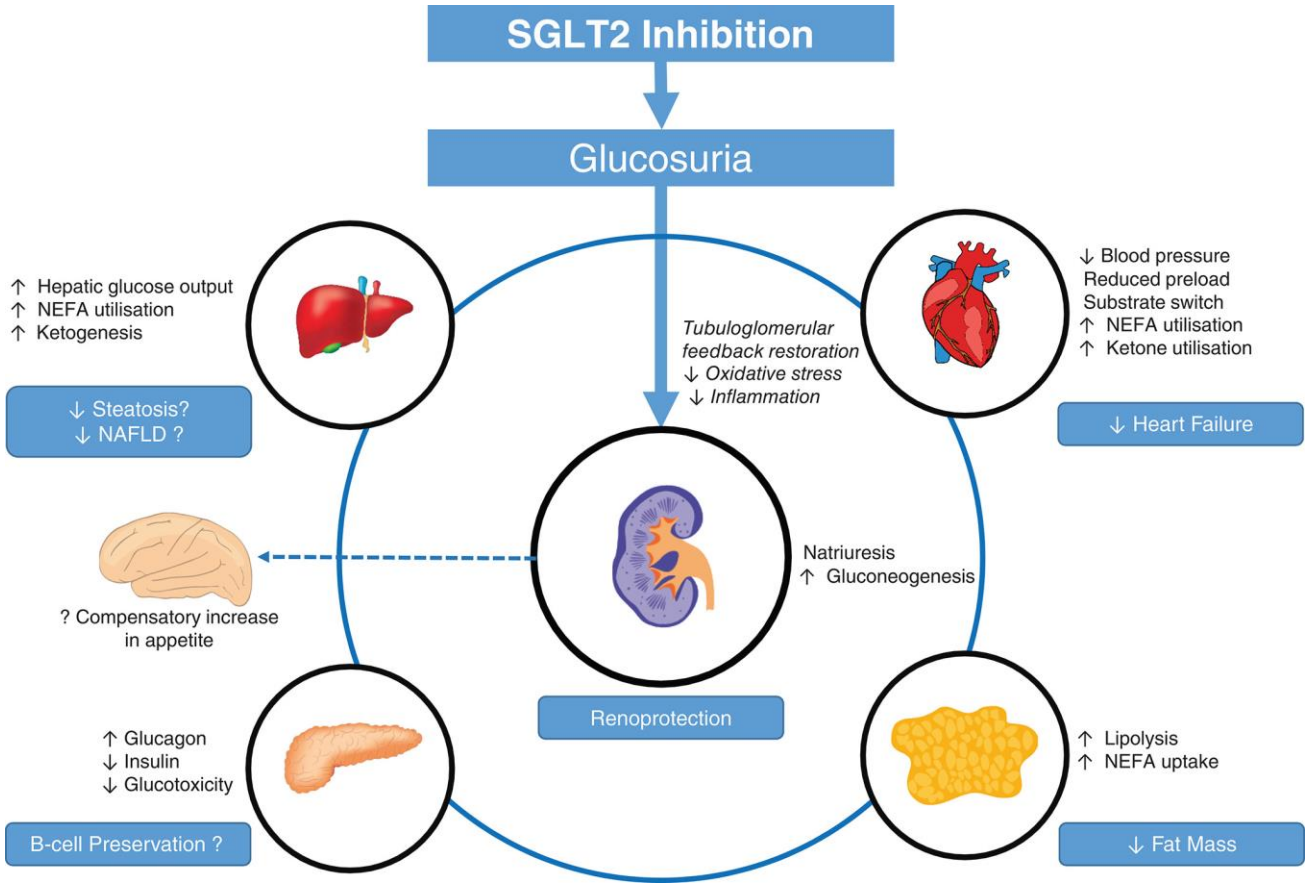
Cardiac Medications affecting kidneys

- Contrast dye
- Diuretics: Lasix, Bumex, Torsemide, HCTX, Aldactone
- Atenolol
- ACEI/ ARBs
- Antibiotics
- Anti-inflammatory drugs
- Anti arrhythmic: Dose adjustment and elimination if low kidney function: Digoxin, Flecainide, Sotalol, Amiodarone, Doefetilide
- Blood thinners: Dose adjustment

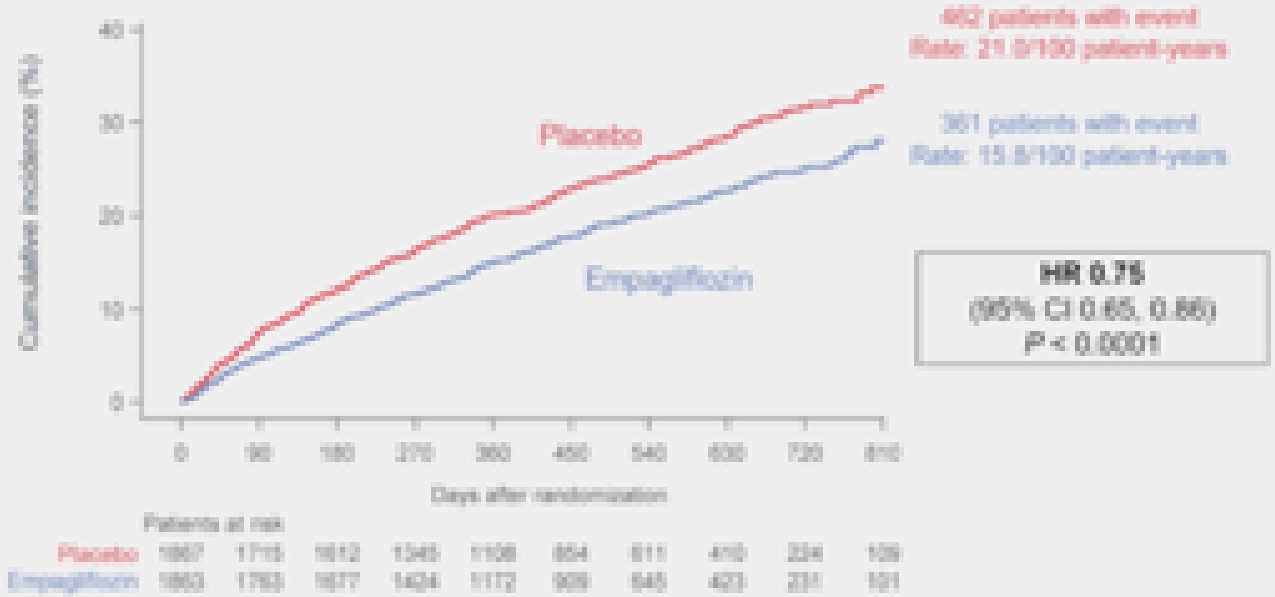

Drug Accumulation
↓Contractility
Metformin
Lactic acidosis
Interstitial Damage
Tumor Lysis,
Urate Mediated
Dysfunction
Chemotherapy
Urate precipitation
Interstitial Damage
Accumulation
Antibiotics
NSAID
Toxic Damage
Heart
Failure
Acute
Kidney
Injury
Imaging
Contrast Media
Transient
Ischemia
Oxidative Stress
↓Afterload
↑Contractility
ACEi - ARB
↓ Filtration Fraction
↓Tubuloglomerular
Feedback
↑ Afterload
Arrhythmias
V1/V2 Imbalance
Aldosterone Receptor Blockers
AVP Receptor Blockers
↓Na Reabsorption
Hyperkalemia
Polyuria
Overhydration
Dehydration
Diuretics
↑Diuresis
Hypovolemia

Dose adjustment in kidney disease

Drug	Dose Adjustment In CKD/Dialysis
Aspirin	None
Clopidogrel	None
Prasugrel	None
Ticagrelor	None
Abciximab	None
Eptifibatide	50% dose reduction with a creatinine clearance <50 ml/min
Tirofiban	50% dose reduction with a creatinine clearance <30 ml/min
Unfractionated heparin	None
Enoxaparin	Reduce by 50% with CKD; contra-indicated in dialysis patients
Warfarin	None
Bivalrudin	No specific guidelines
Fondaparinux	No specific guidelines
Fibrinolytics	No specific guidelines
Beta-and alpha/beta-blockers	None required for metoprolol or carvedilol; possible dose reduction for atenolol, acetbutalol and nadolol
Calcium channel blockers	None required
Nitrates	None required
Ranolazine	Dose reduction required
ACE inhibitors	Initiate low dose and increase as tolerated; observe for deterioration of renal function and hyperkalemia
Angiotensin receptor blockers	Initiate low dose and increase as tolerated; observe for deterioration of renal functions and hyperkalemia
Aldosterone receptor blockers	Safety not well-established in advanced CKD
Statins	No dose adjustment required; efficiency not well-established in dialysis patients


SGLT2 Inhibition
Glucosuria
↑ Hepatic glucose output
↑ NEFA utilisation
↑ Ketogenesis
↓ Steatosis?
↓ NAFLD ?
Tubuloglomerular
feedback restoration
↓ Oxidative stress
↓ Inflammation
↓ Blood pressure
Reduced preload
Substrate switch
↑ NEFA utilisation
↑ Ketone utilisation
↓ Heart Failure
? Compensatory increase
in appetite
Natriuresis
↑ Gluconeogenesis
Renoprotection
↑ Glucagon
↓ Insulin
↓ Glucotoxicity
B-cell Preservation ?
↑ Lipolysis
↑ NEFA uptake
↓ Fat Mass

EMPEROR-Reduced: Time to Cardiovascular Death or Hospitalization for Heart Failure (Primary Endpoint)



Prevention of Heart disease and Kidney disease

Prevention of Heart disease and Kidney disease

- Keep your blood pressure below 140/90.
- Control your blood glucose
- Have your blood and urine checked as your provider instructs.
- Try to keep your cholesterol numbers in a healthy range.
- Control your weight. Be physically active 30 minutes a day most days of the week.
- Avoid smoking, alcohol, drugs

- People with *advanced* chronic kidney disease may need to adjust their diet to avoid high potassium.
- If you have advanced kidney disease, you may need to limit foods such as bananas, oranges, potatoes, and tomatoes and eat apples, berries, grapes, and peaches instead.

Diet

- fruits and vegetables
- whole-grain breads and cereals
- low-fat milk and milk products such as yogurt and cheese
- lean meats or meat substitutes such as tofu
- fish
- unsaturated fats such as olive oil or corn oil
- low-sodium foods

Thank you