Cardio-Renal Syndrome.

“To be a good doctor one has to be a good physiologist.”
W Hall.

Objectives:

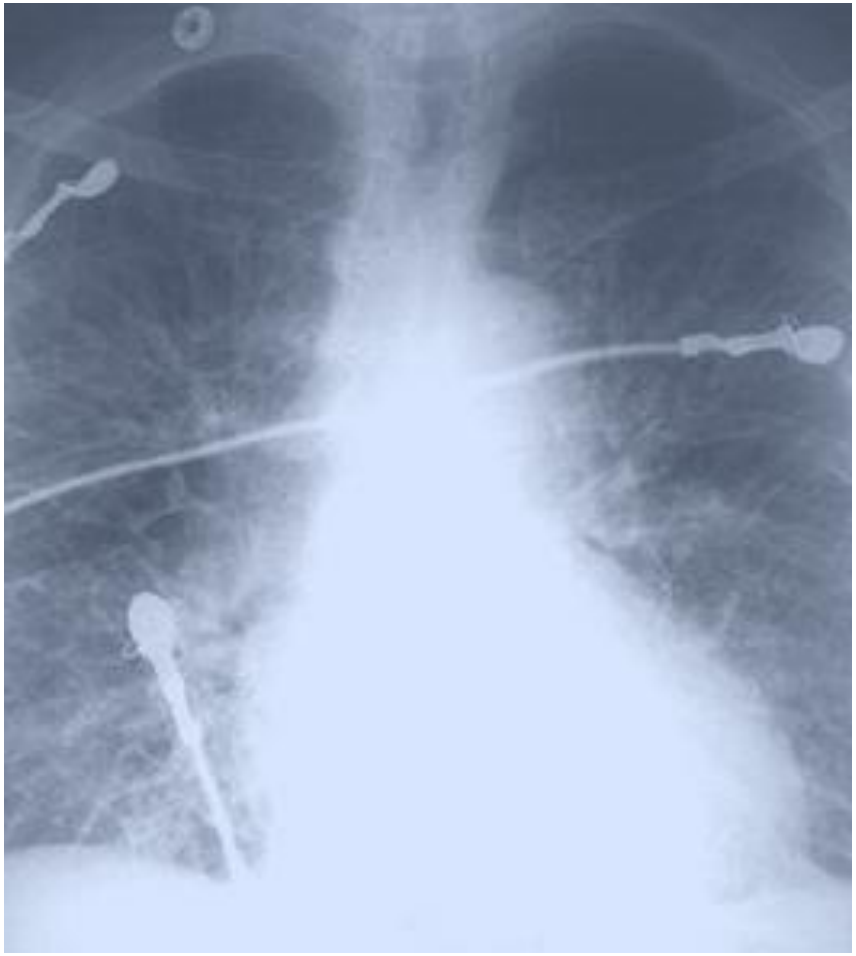
- Recognise the importance of close interaction between cardiac and renal pathophysiology.

ASIAN PACIFIC SOCIETY OF NEPHROLOGY

Case Presentation

- 68 year male with a long history of hypertension, previous MI 2 years ago, presents with progressive orthopnea and paroxysmal nocturnal dyspnea.
- O/E.
  P=88/min, BP 90/80, JVP 6 cm, dilated cardiomegaly, 3rd heart sound and Mitral regurgitation, pulmonary oedema and peripheral oedema

Case Presentation



- Biochemistry.
  Na = 130, K = 5.4
  creatinine = 186 umol/l
  (was 144 umol/l)
  Hb = 98g/l

Cardio-Renal Syndromes

- “Disorders of the heart and kidney where by acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other”

Acute Dialysis Quality Initiative 2008

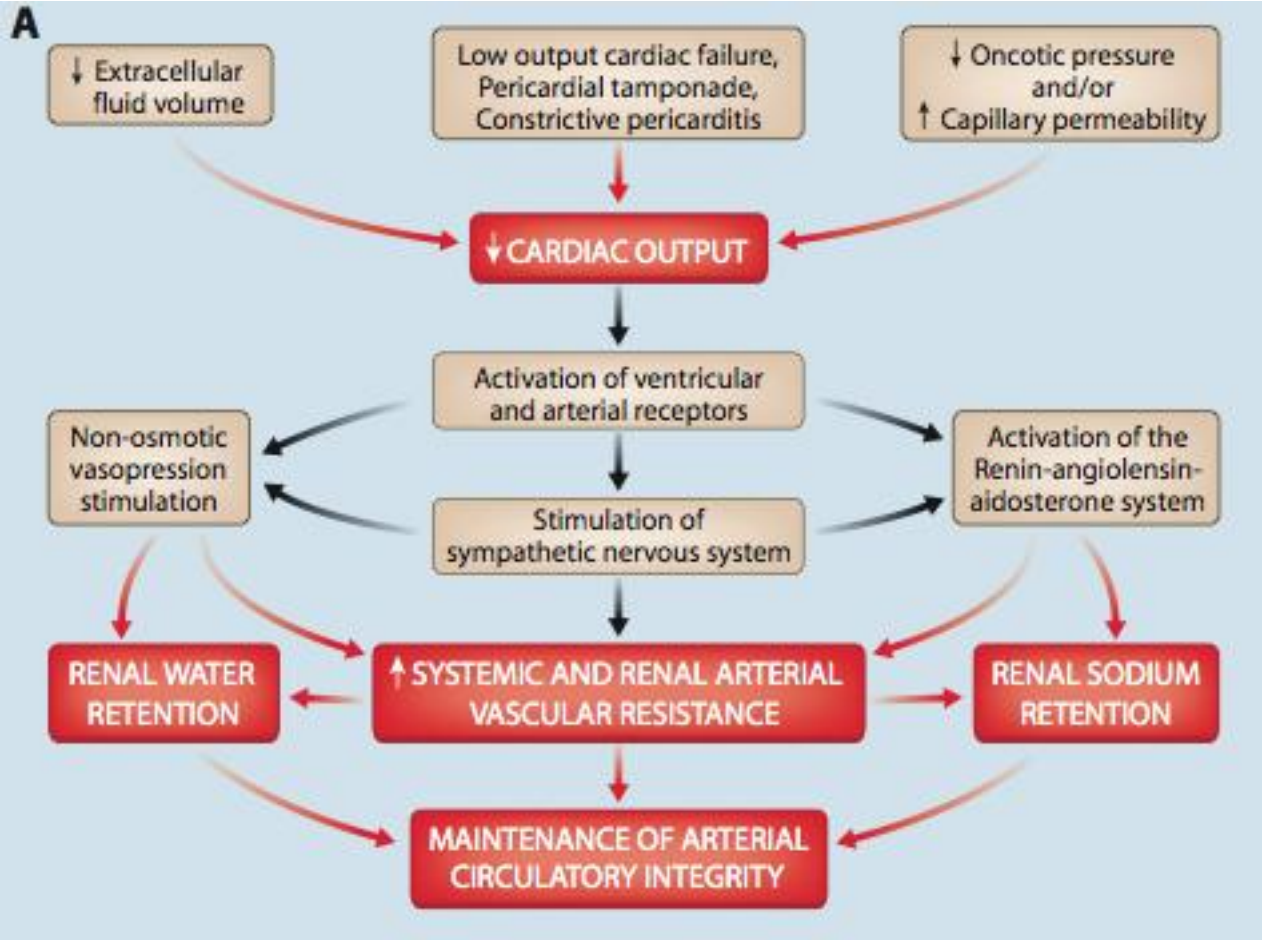
5 groups.
1&2 relate to changes in heart failure leading to a reduction in kidney function.

Pathophysiology

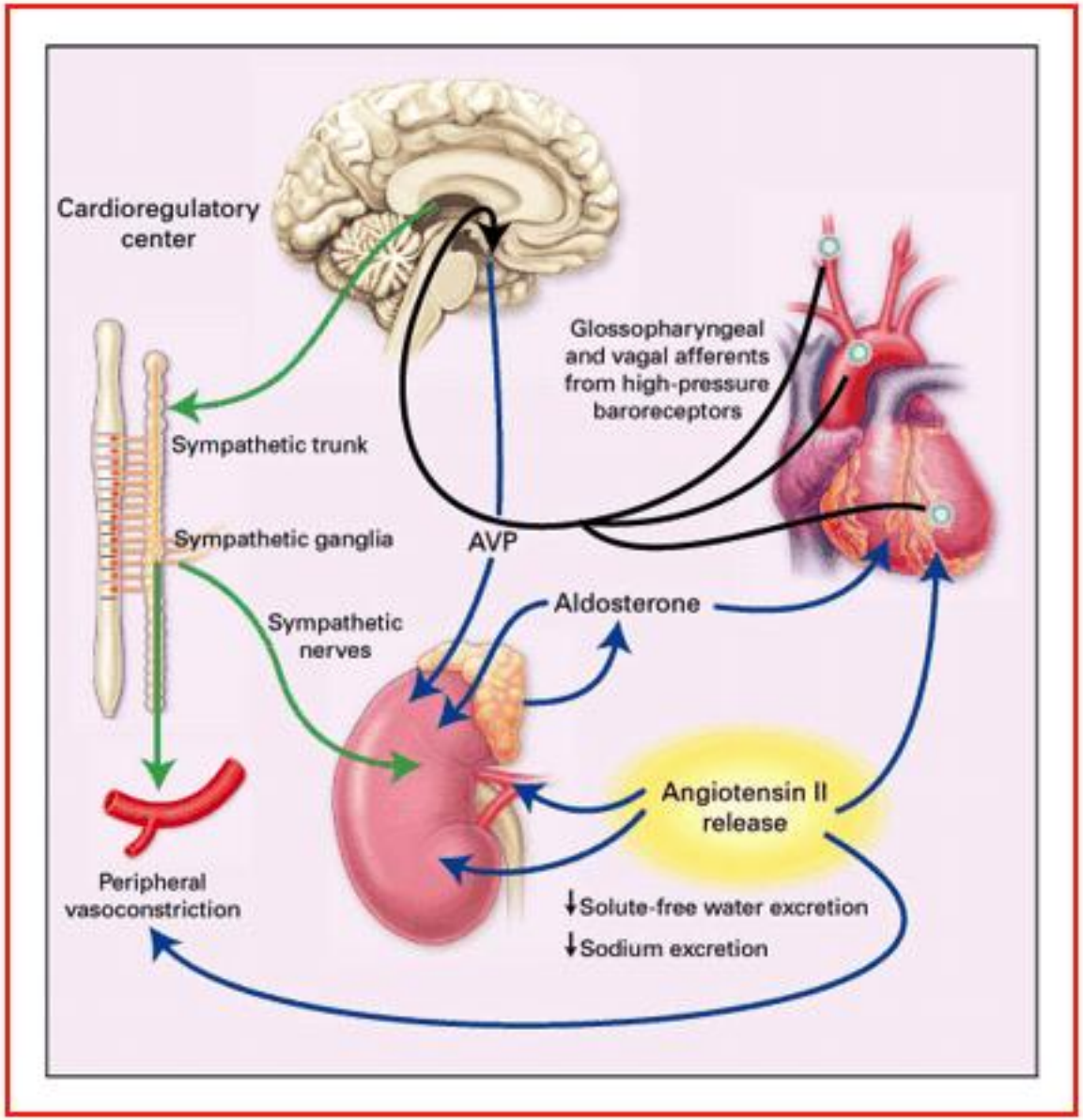
Key component is
“Threat to arterial blood pressure”

Severe decrease in left ventricular function causes a reduction in cardiac output which threatens arterial blood pressure, activating a cascade of compensatory mechanisms.

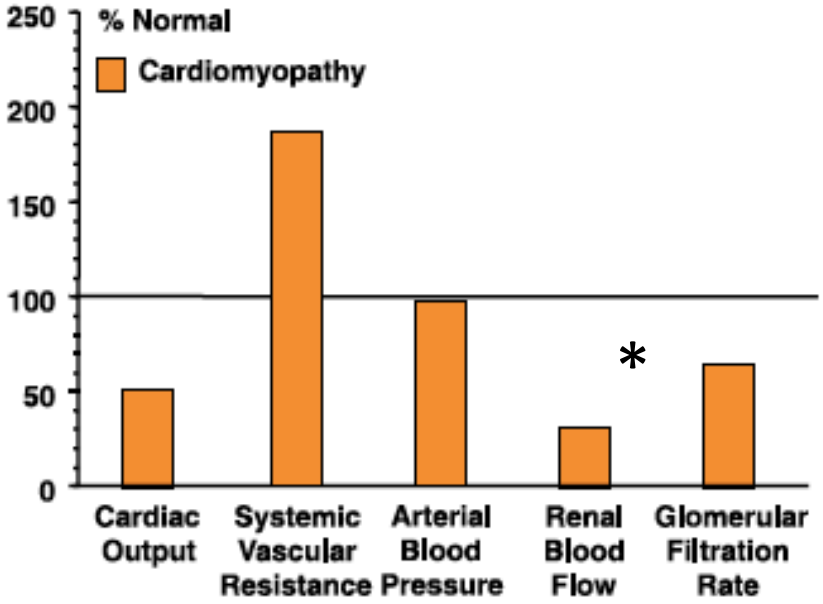
Figure 1. Clinical conditions in which a decrease in cardiac output (A) and systemic arterial vasodilation (B) causes arterial underfilling with resultant neurohumoral activation and renal sodium and water retention

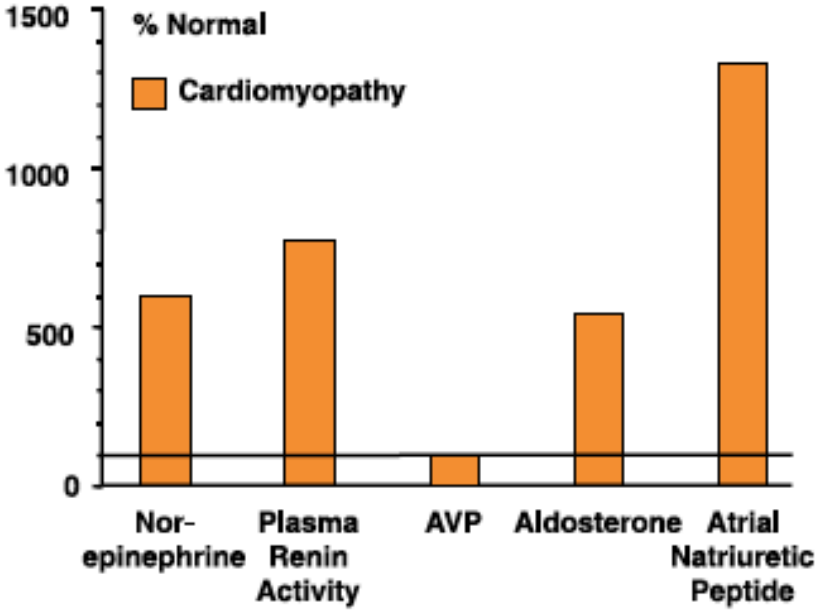


Schrier, R. W. J Am Soc Nephrol 2007;18:2028-2031



Schrier R. NEJM 1999.





* Marked vasoconstriction splanchnic bed

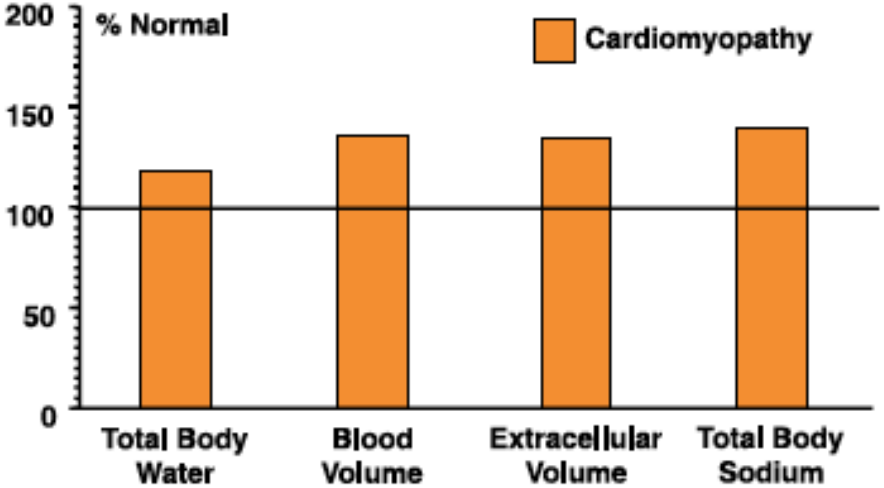


Figure 1. | Bar graphs showing hemodynamic, renal function, plasma hormones, and body fluid compartment data expressed as percent of normal in a group of patients with untreated congestive heart failure. Data are from reference 27. AVP, arginine vasopressin.

Anand IS. Clin J Am Soc Nephrol 2013; 8: 1800-7

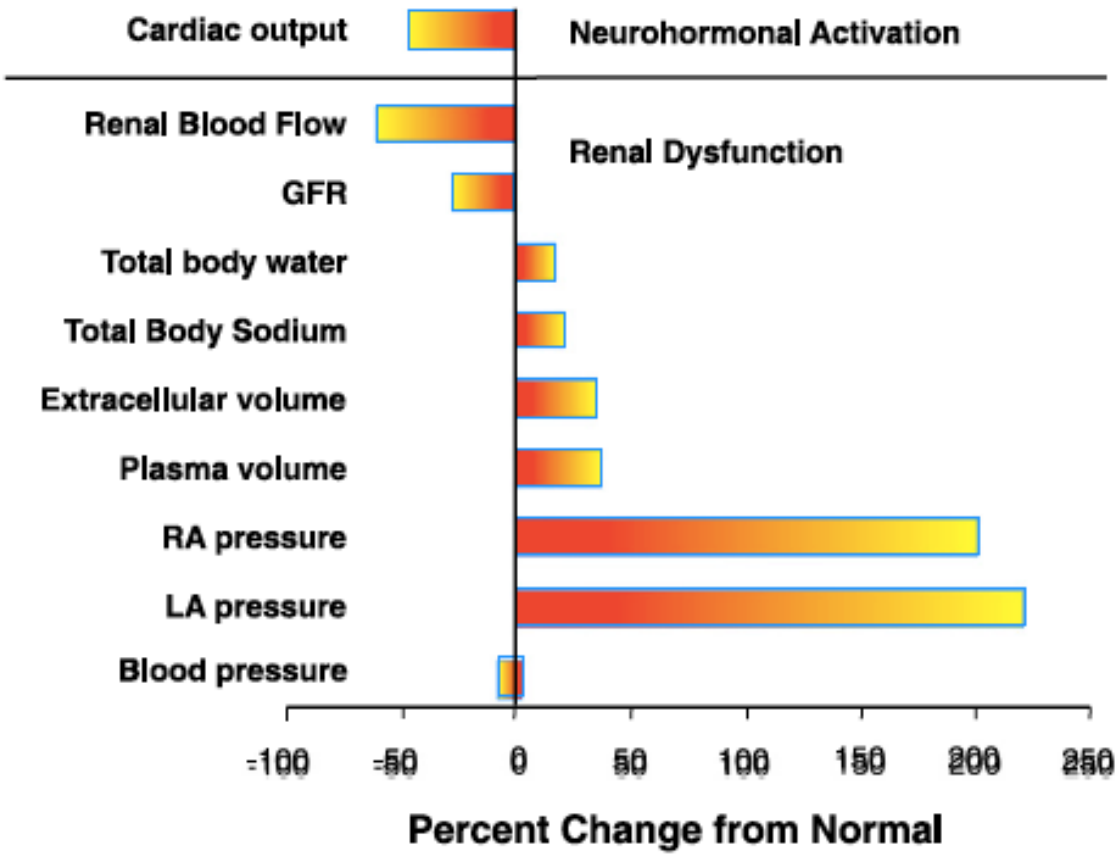
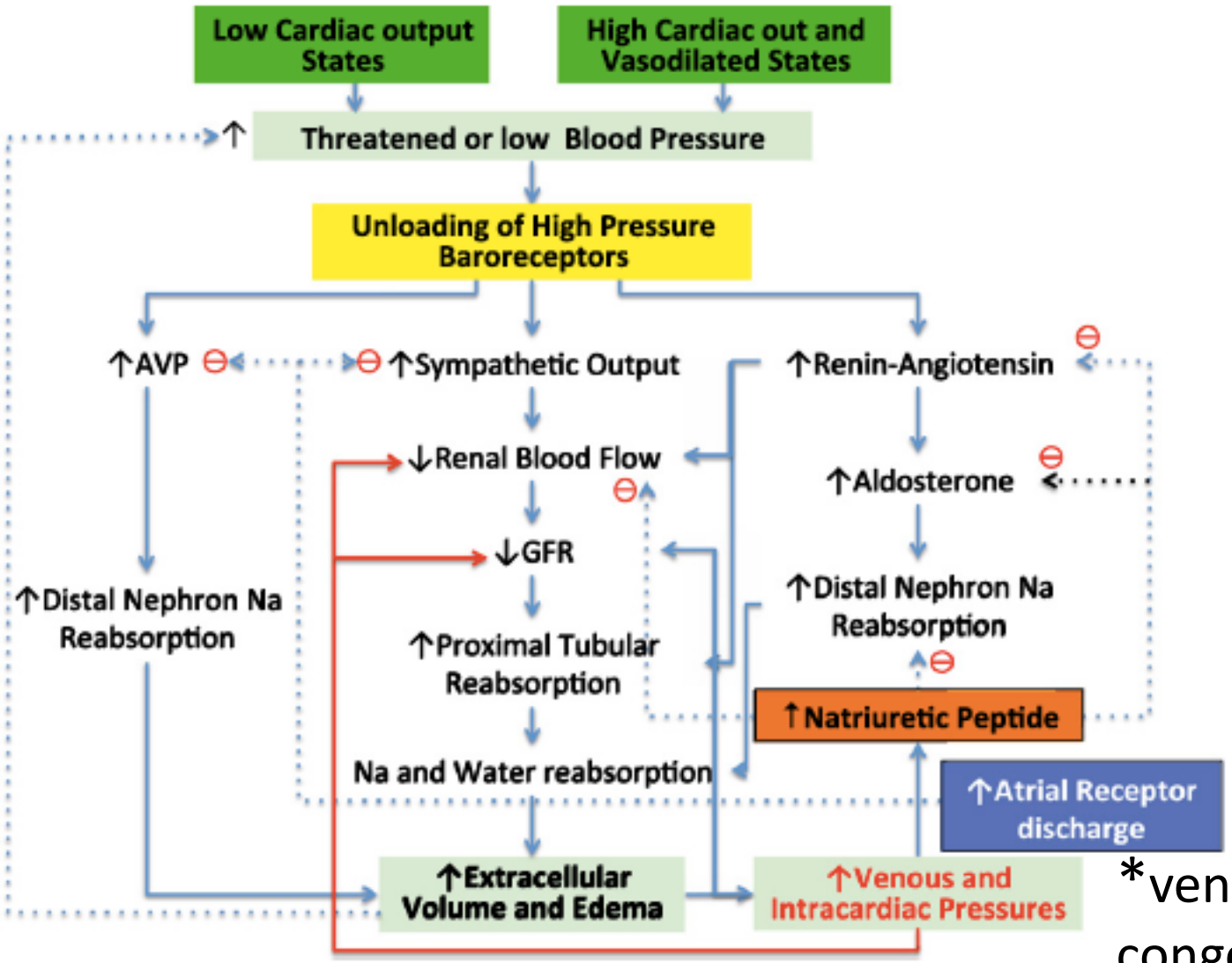


Figure 2. | Compensatory changes in a number of hemodynamic and body fluid compartment parameters help to maintain a normal arterial BP in patients with untreated congestive heart failure. This change occurs at the expense of renal dysfunction. Modified from reference 32, with permission. LA, left atrial; RA, right atrial.

Anand IS. Clin J Am Soc Nephrol 2013; 8: 1800-7

Cardiac Failure and Kidney response .



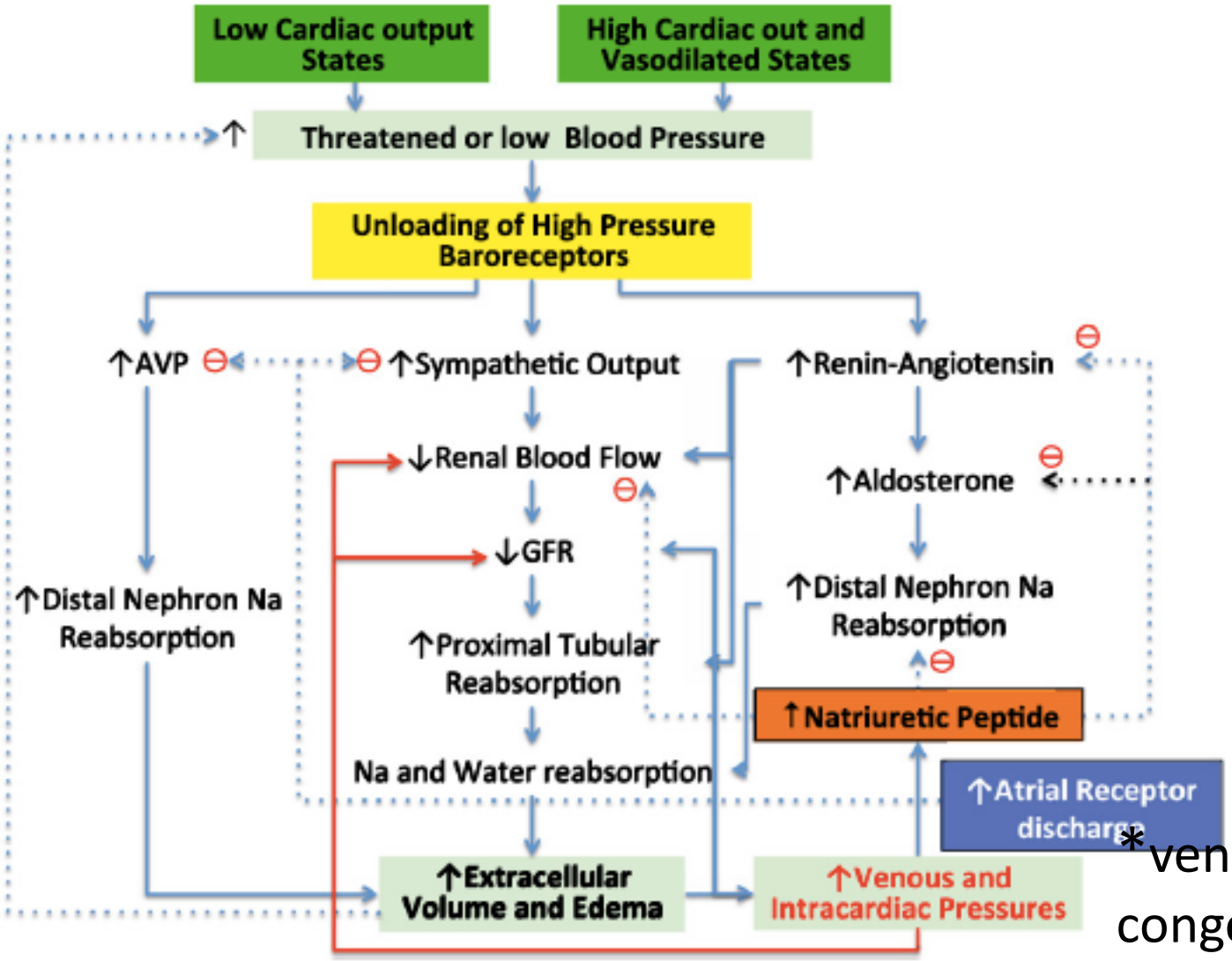
*venous congestion

Anand IS. Clin J Am Soc Nephrol 2013; 8: 1800-7

Pathophysiology cardio-renal syndrome

Compelling mechanisms initially to maintain or protect arterial blood pressure
“at the expense of kidney function”

Cardiac Failure and Kidney response .



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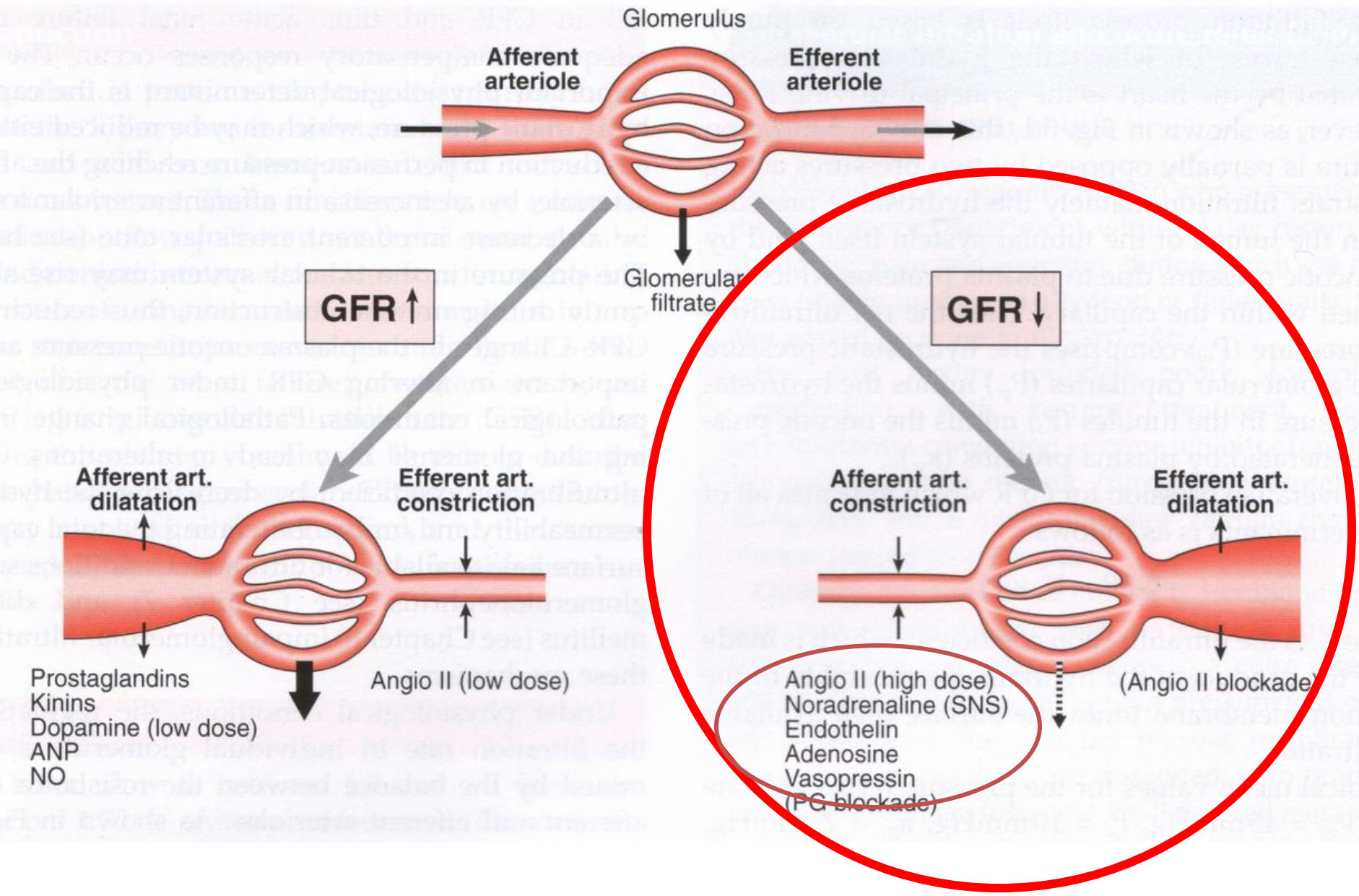
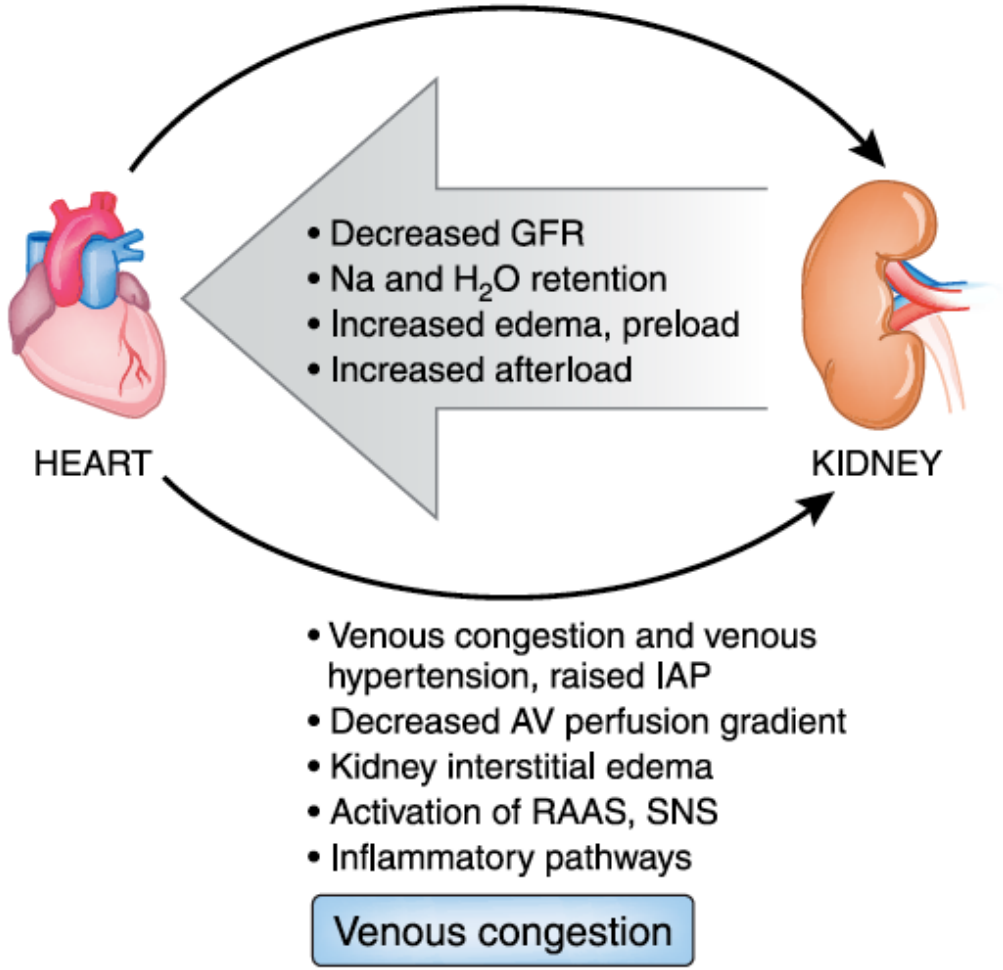

Glomerulus
Afferent arteriole
Efferent arteriole
Glomerular filtrate
GFR ↑
GFR ↓
Afferent art. dilatation
Efferent art. constriction
Prostaglandins
Kinins
Dopamine (low dose)
ANP
NO
Angio II (low dose)
Afferent art. constriction
Efferent art. dilatation
Angio II (high dose)
Noradrenaline (SNS)
Endothelin
Adenosine
Vasopressin
(PG blockade)
(Angio II blockade)



Impact of venous congestion in acute cardiorenal syndrome.

House AA. Clin J Am Soc Nephrol. 2013; 8: 1808 -15

Management and outcomes

- Interventions may change kidney function
- Most studies use surrogate markers of outcome such as plasma creatinine or eGFR, but these parameters will have haemodynamically related changes that do not necessarily reflect a true deterioration in kidney function.

Case progress

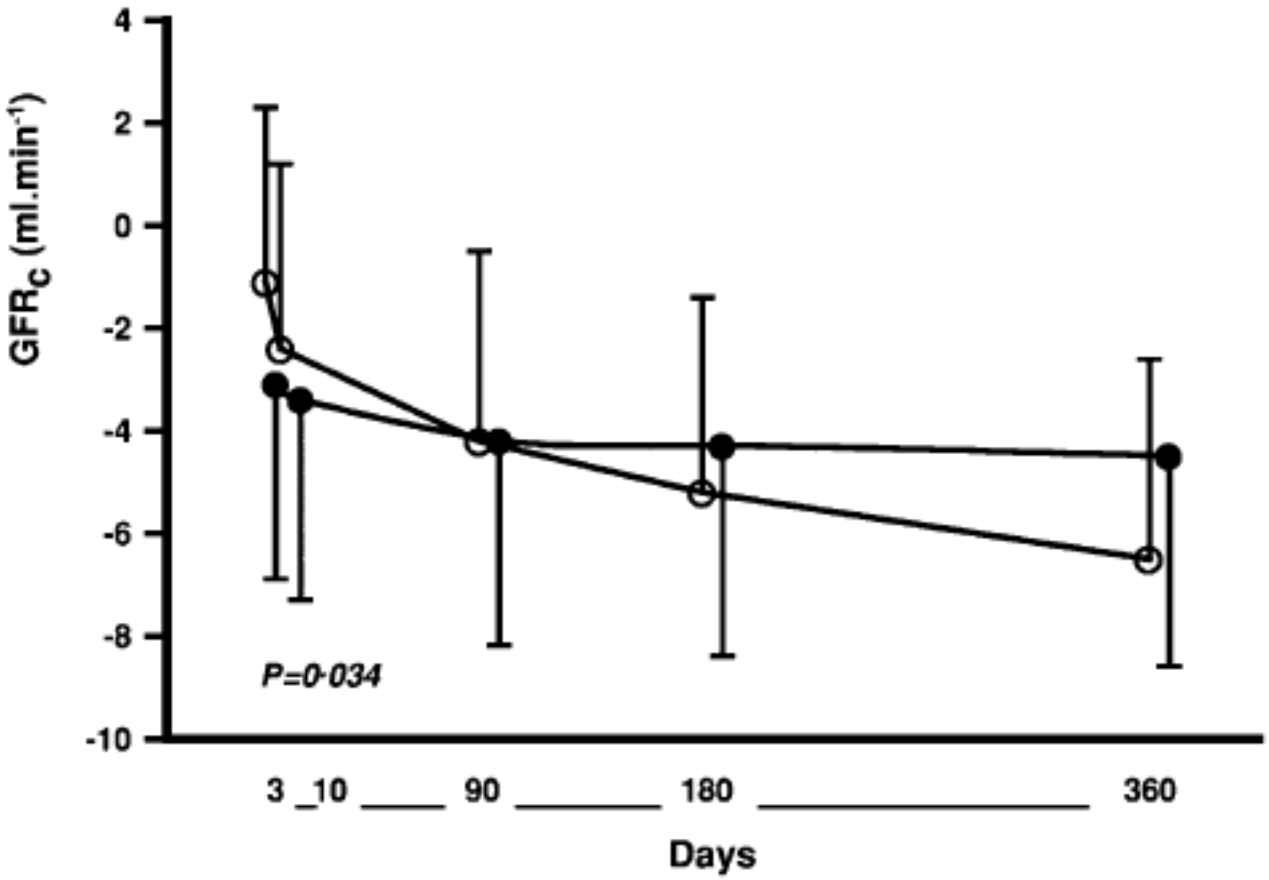
- On admission, he is given IV frusemide 120 mg initially and repeated 6 hours later.
- He is commenced on quinapril (ACEI).

- Acute LVF improves, blood pressure improves. BP 118/82, JVP 3 cm, pulmonary oedema improves
- Plasma creatinine rises to 206 umol/l over the next 48 hours
- What do you do?

Changes in renal perfusion

Consider:

- Rapid diuresis – impact on intravascular volume
- ACEI – may produce initial reduction GFR Improvement in cardiac output will subsequently restore – improve renal perfusion.
- Remember majority of patients with CHF will also have CKD.

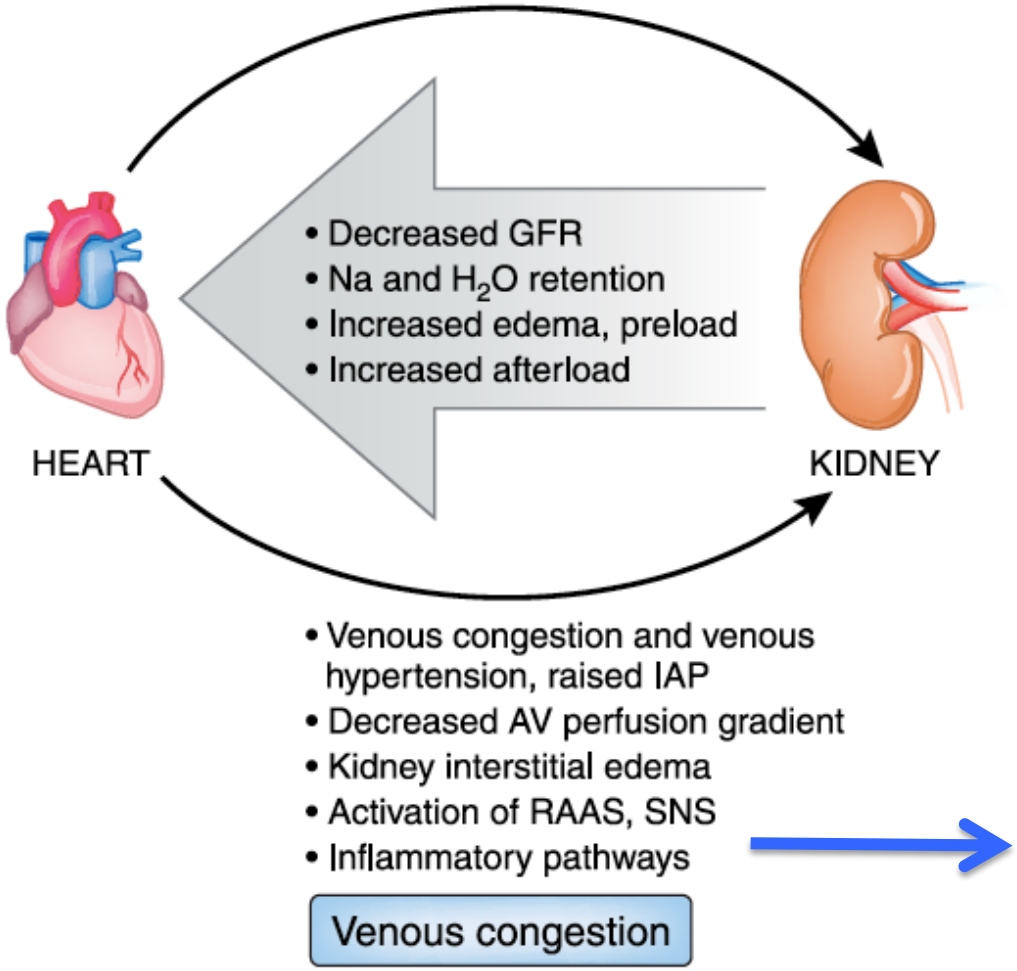


Captopril and Thrombolysis Study
Changes in GFR over a year.
Placebo 5.5ml/min. Captopril 0.5 ml/min.

House AA. CJASN 2013. Hilege H et al. Eur Heart Journal 2003

6 months later

- Haemodynamically stable
- Congestive heart failure controlled.
- Plasma creatinine = 174 umol/l
- Pre-CHF creatinine was 144 umol/l
- Why evidence of impaired kidney function?

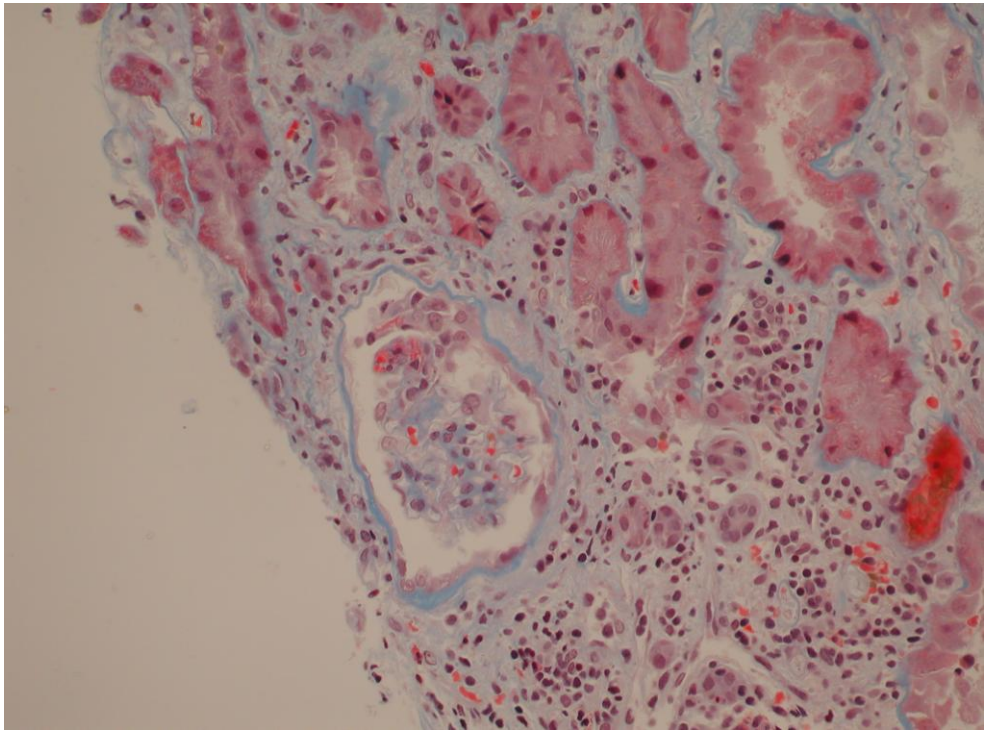


Impact of venous congestion in acute cardiorenal syndrome.

Tissue injury Interstitial fibrosis

House AA. Clin J Am Soc Nephrol. 2013; 8: 1808 -15

Chronic interstitial fibrosis.
- Inflammatory response
- Underlying CKD
- Hypertensive injury

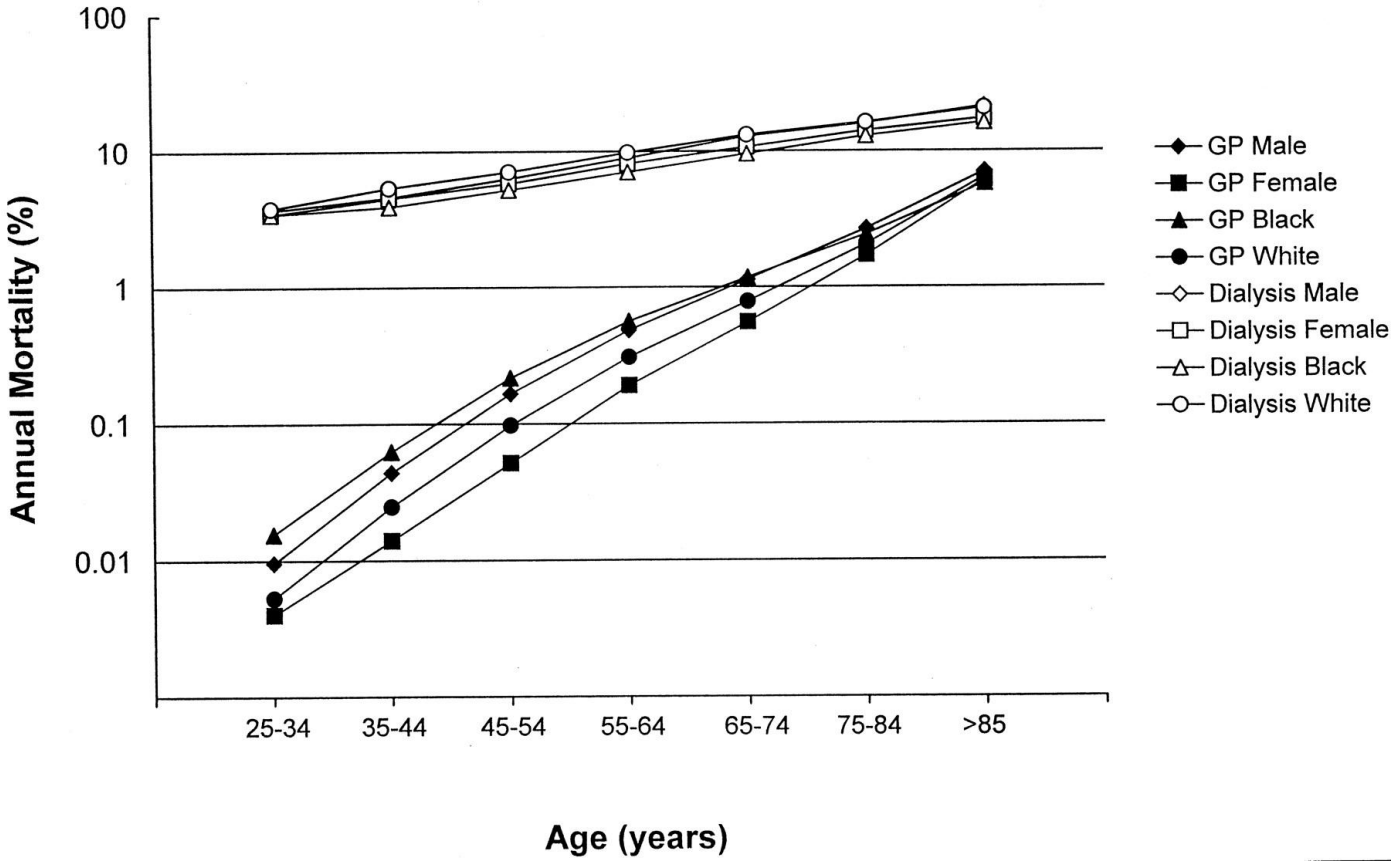


Summary

- Cardio – renal syndrome
- Response to ‘threat to arterial blood pressure’ at ‘the expense of the Kidney’
- Activation of a cascade of compensatory mechanisms.
- Longer term may be left with kidney injury despite improvement in cardiac function.

Reno – Cardiac Syndromes

Cardiovascular disease mortality by age, race, and gender in the general population and dialysis population



PARFREY, P. S. et al. J Am Soc Nephrol 1999;10:1606-1615

JASN

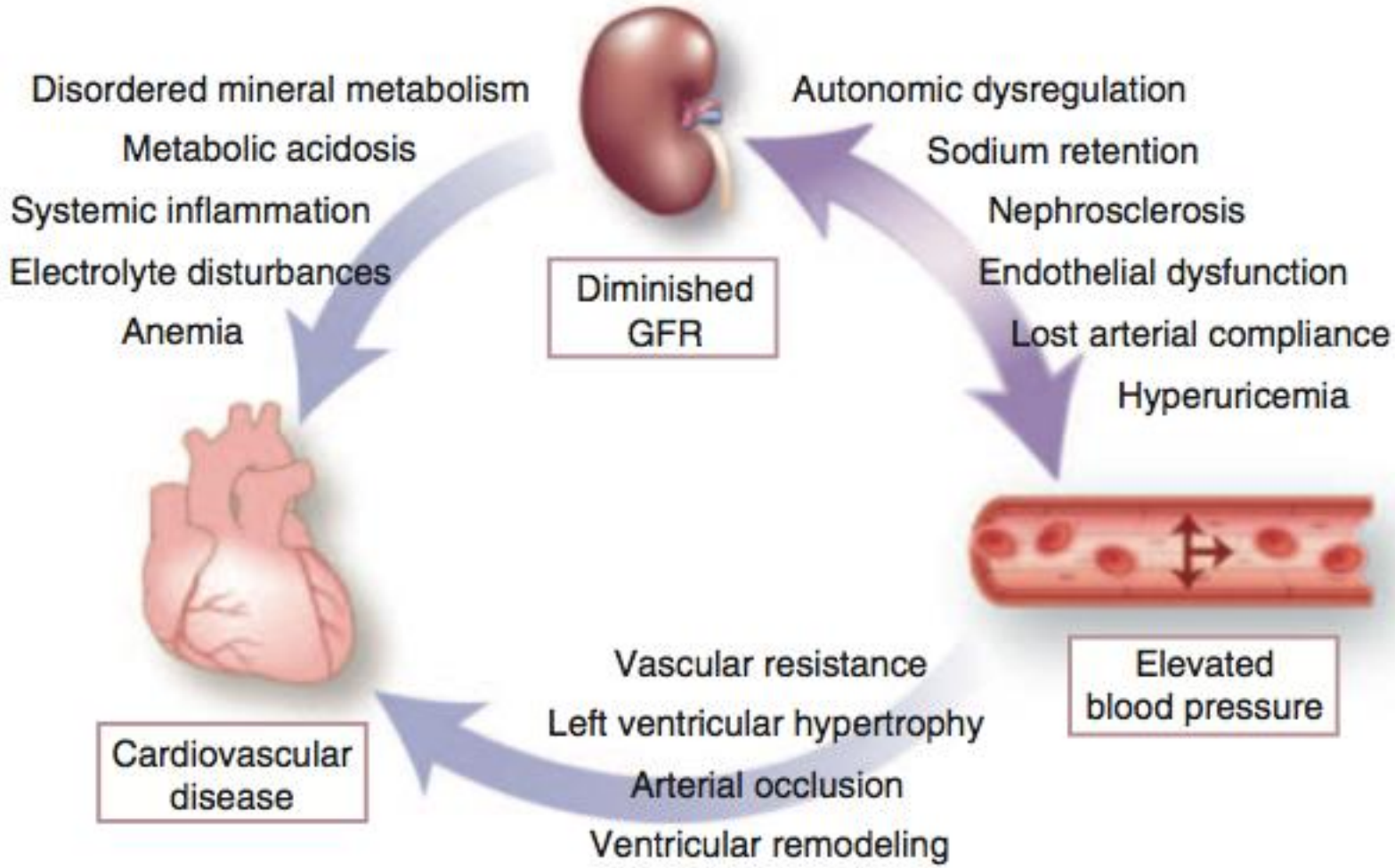


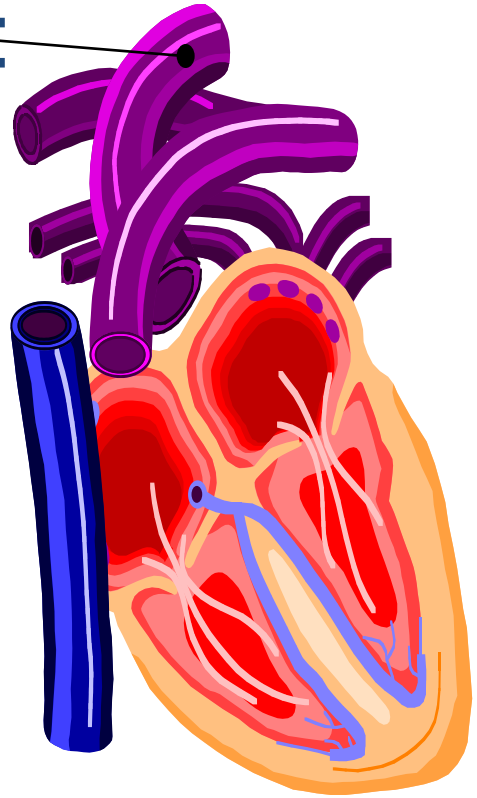
Figure 1 | Joint contribution of CKD and hypertension to cardiac risk. CKD, chronic kidney disease; GFR, glomerular filtration rate.

Middleton & Pun. Kidney Int 2010; **77,** 753–755

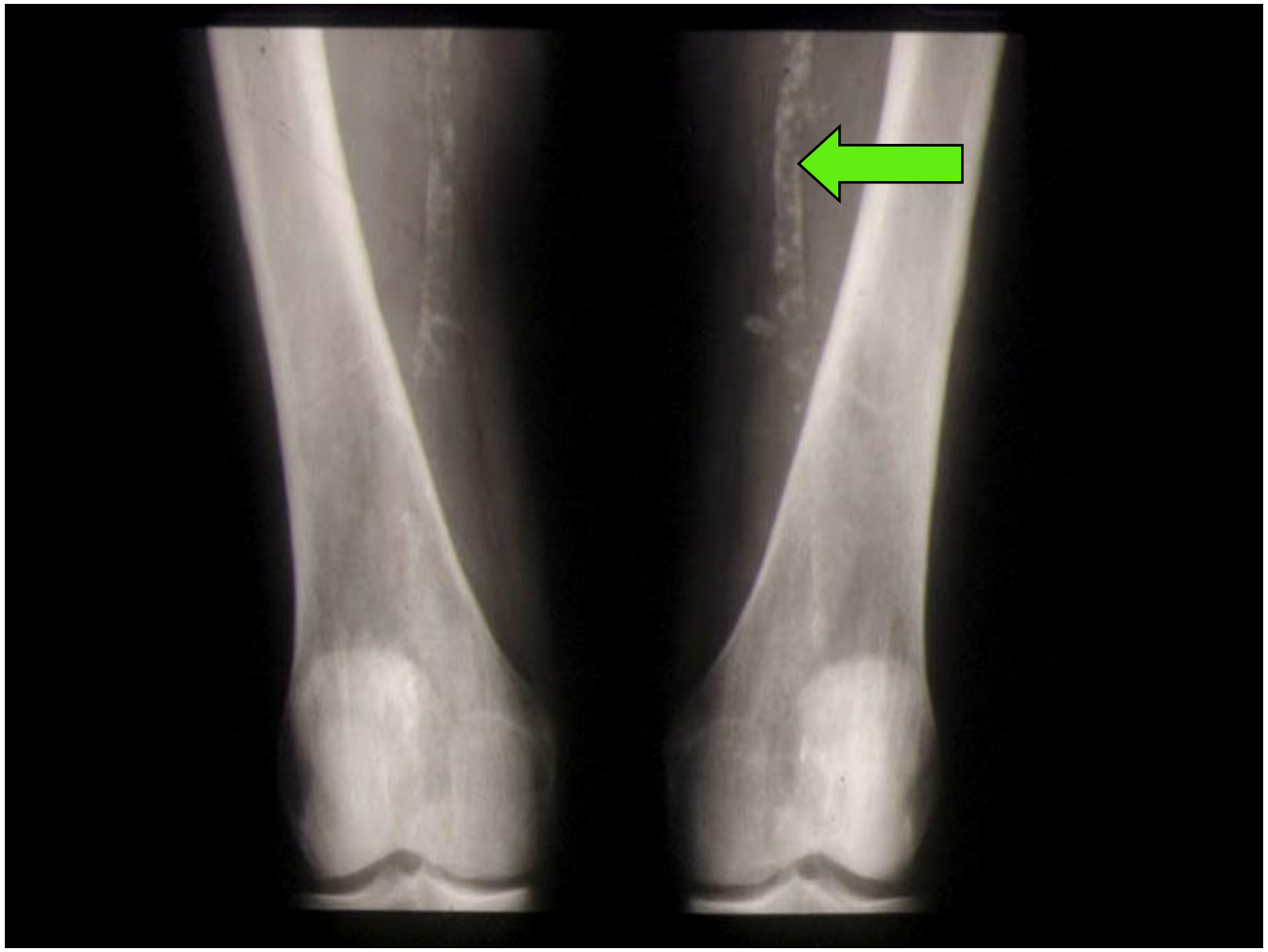
Cardiovascular complications of CKD

Vascular disease:

- ↑ Stiffness
- ↑ Calcification

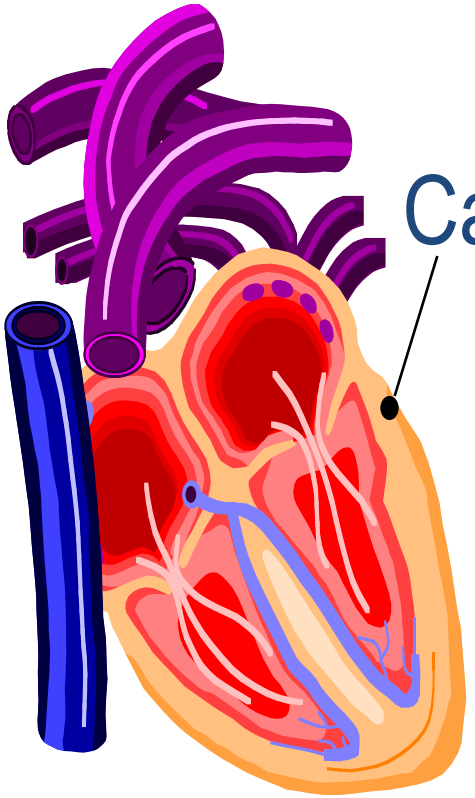


Femoral artery calcification



Cardiovascular complications of CKF

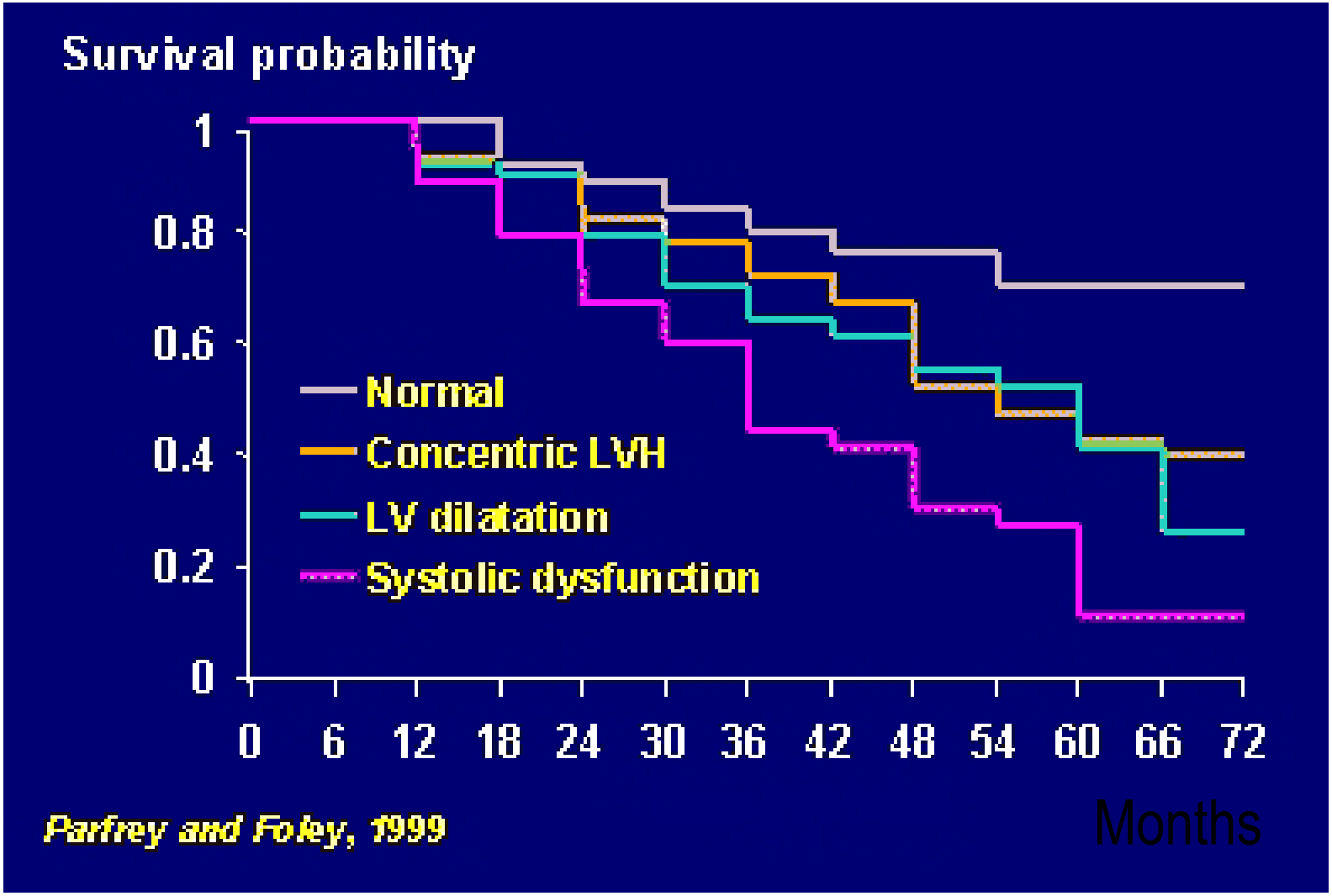
Vascular disease:



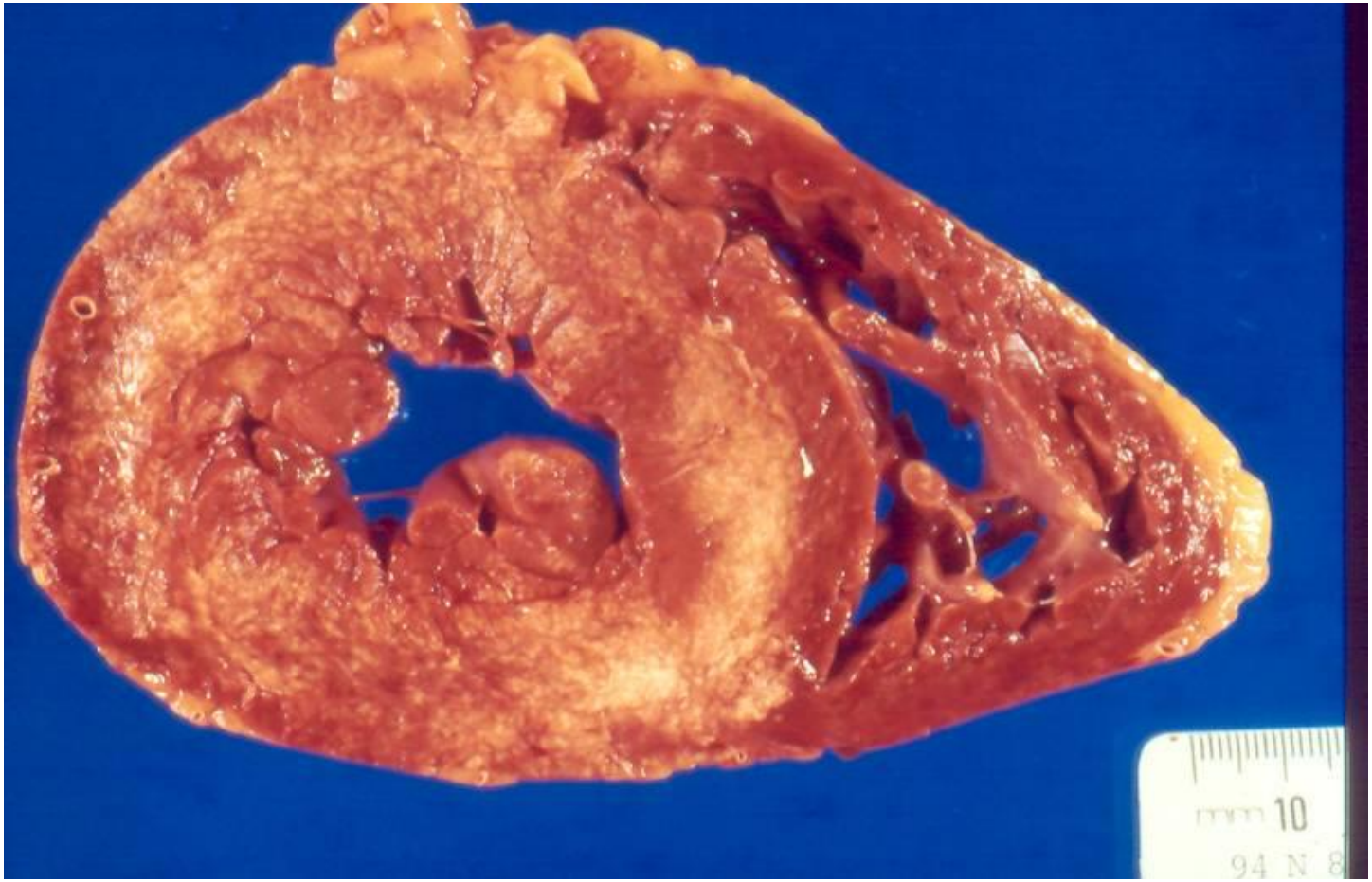
Cardiomyopathy:

- ↑ LV wall thickness
- ↑ Cavity volume
- ↓ Microvasculature
- ↑ Fibrosis

LV disease predicts survival on dialysis



Intramyocardial fibrosis and calcification



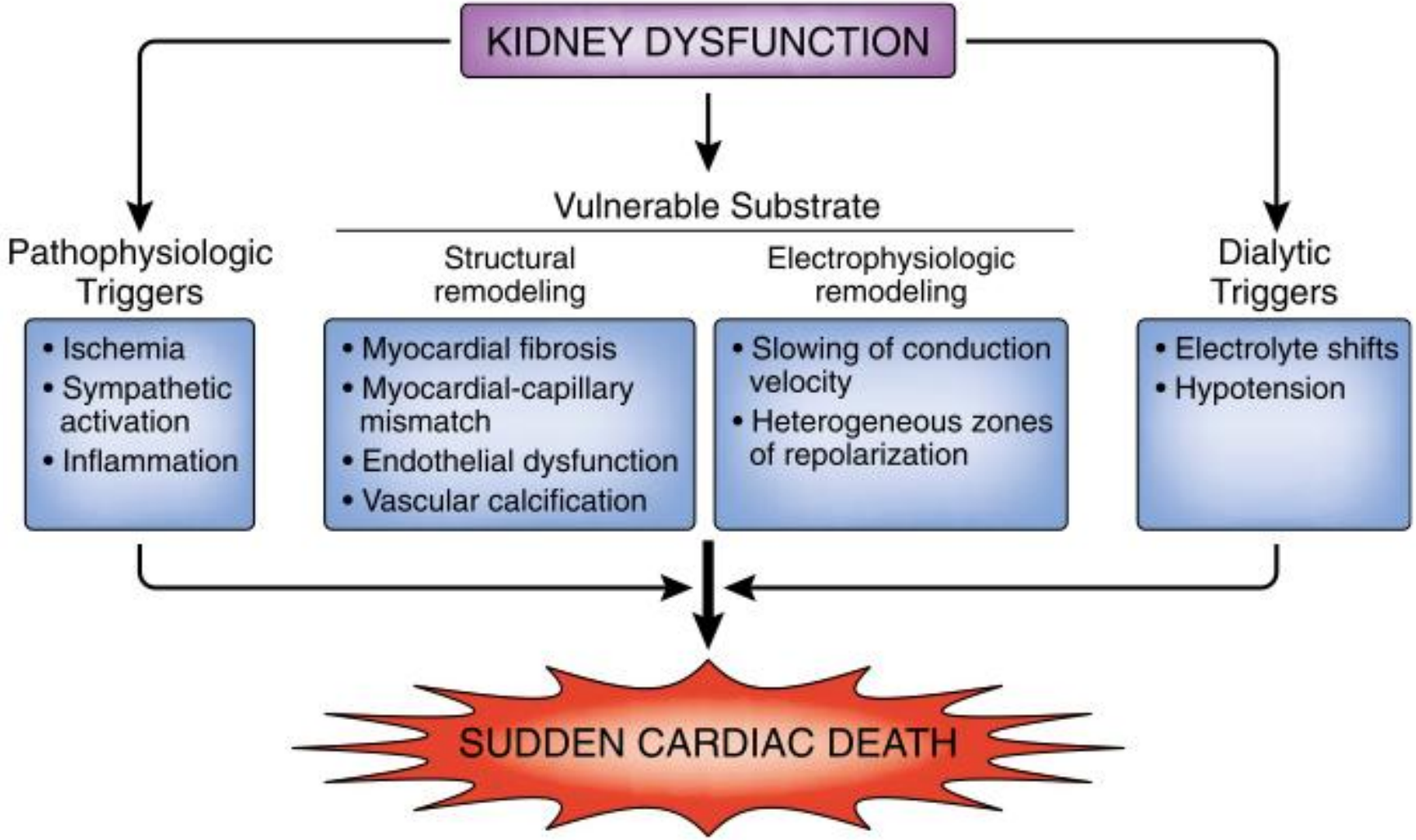
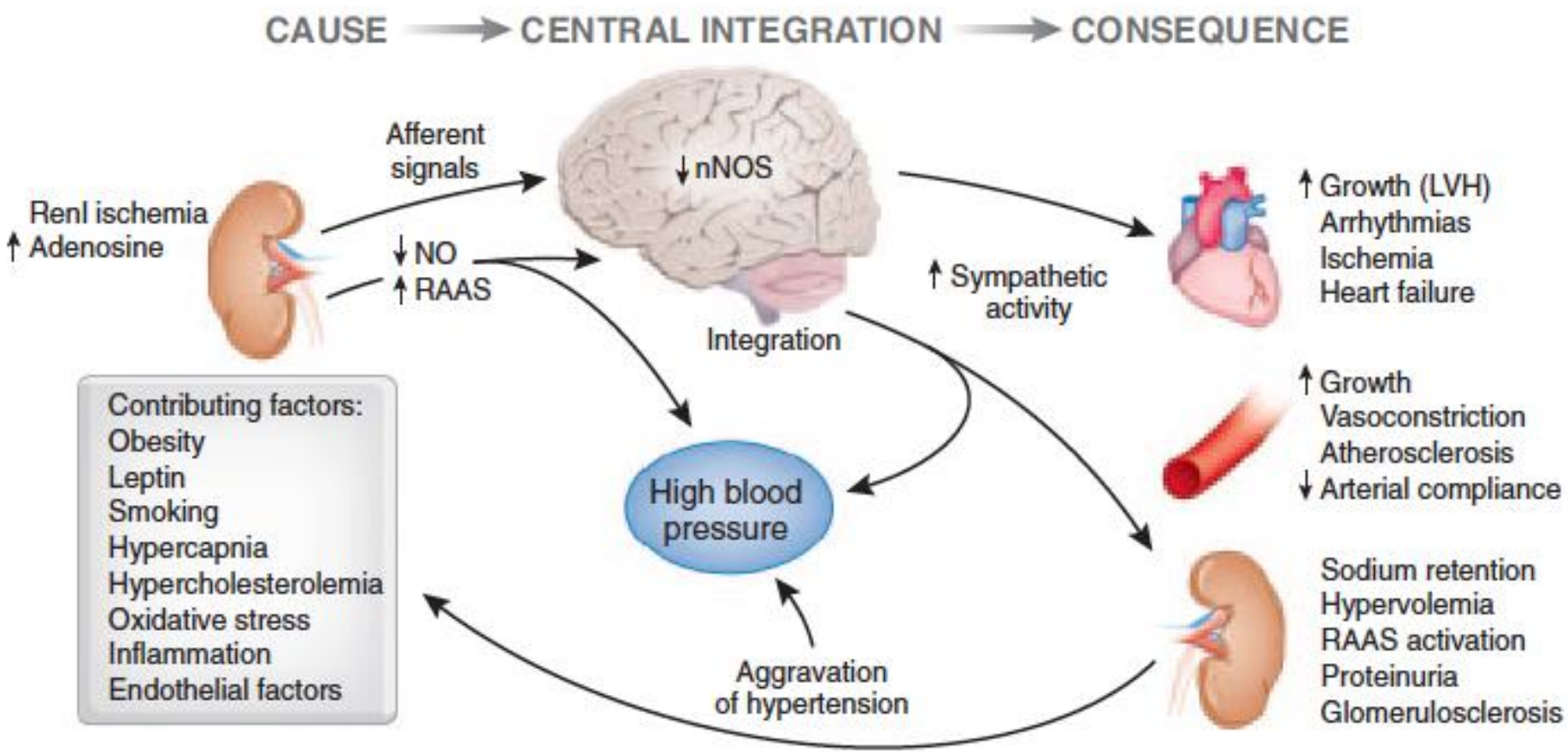


Figure 2. Overview of SCD and kidney dysfunction.

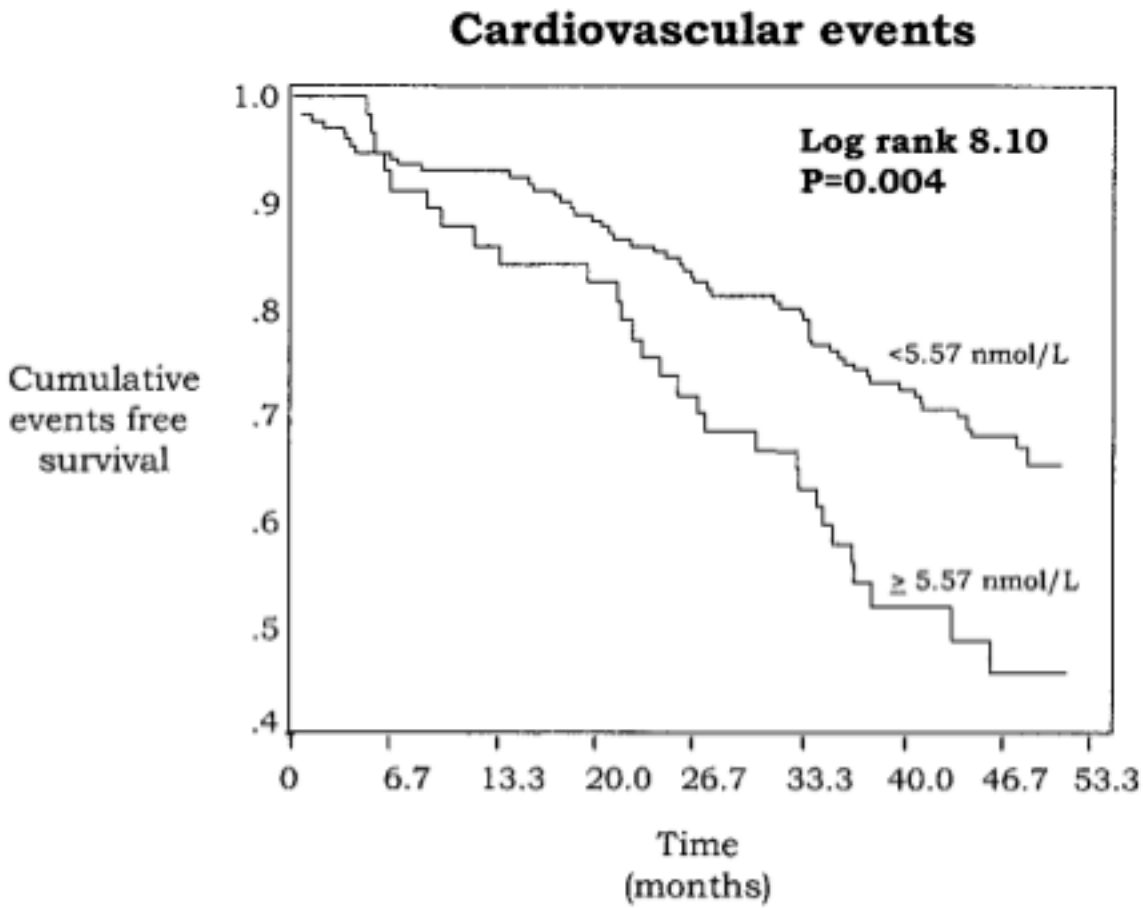
Whitman IR et al. J Am Soc Nephrol 2012; 23: 1929–39

Background

- Increased cardiovascular risk can not be explained by increased atheroma.
- CKD is characterized by sympathetic nerve over-activity, which increases in severity as the disease progresses[1]
- Pathological changes in sympathetic nervous activity contribute to the higher incidence of sudden cardiac death in CKD and ESKD patients:
  - Plasma norepinephrine predicts survival and incident cardiovascular events in patients with ESKD[2]
  - Heart-rate variability predicts ESKD- and CKD-related hospitalisation[3] as well as haemodialysis patient mortality[4]



Schlaich M et al. J Am Soc Nephrol 2009; 20: 933–9

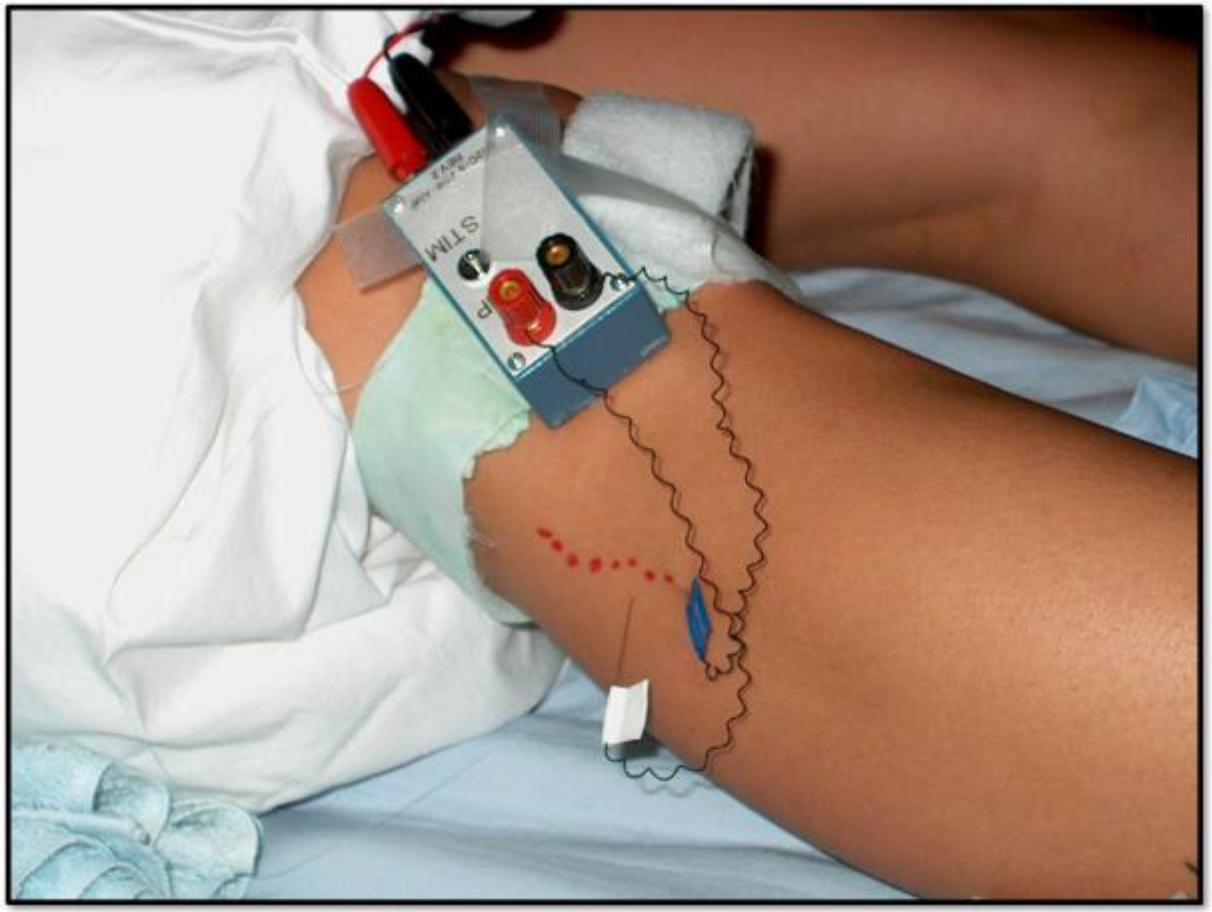


Sympathetic Activity and Survival in ESRD

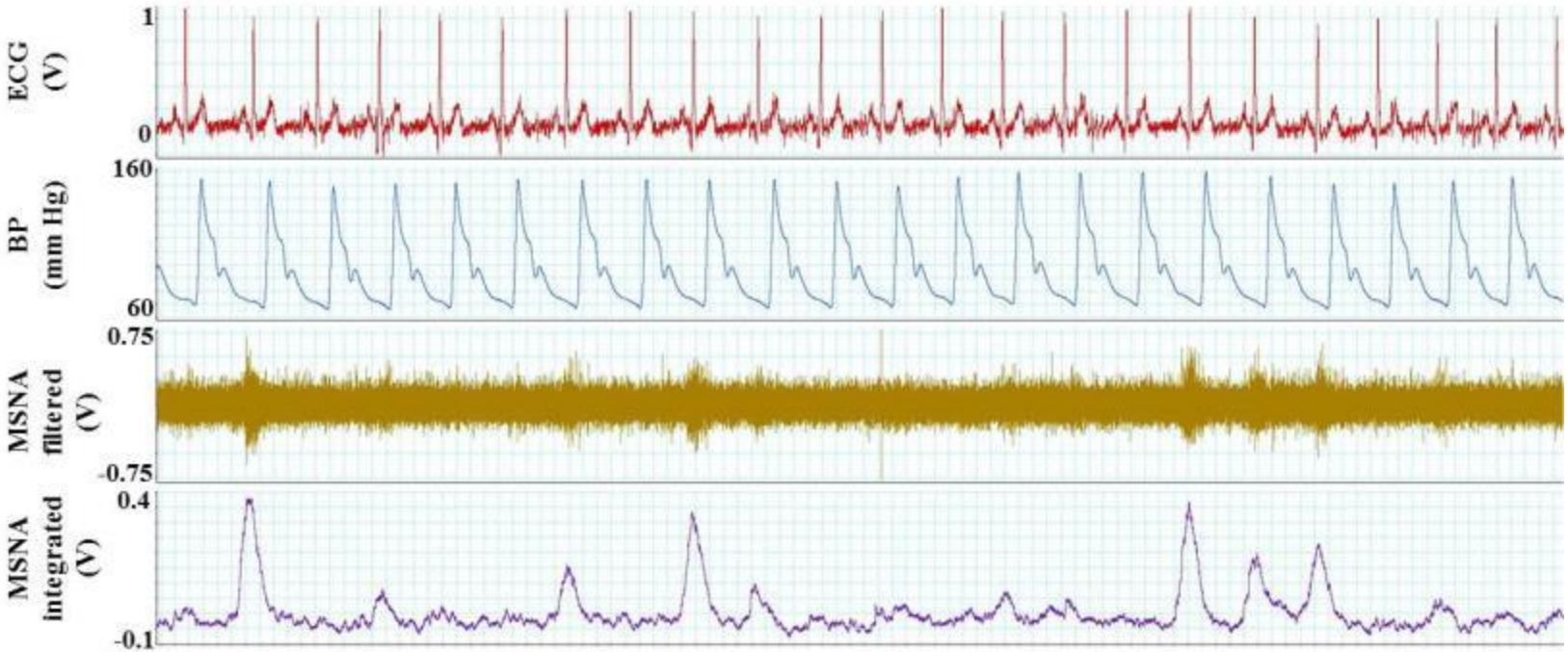
Zoccali et al
Circulation 2002; **105:1354-59**

The adjusted relative risk for cardiovascular complications in patients with plasma NE > 75th percentile was 1.92 (95% CI 1.20 to 3.07) times higher than in those below this threshold ($P < 0.006$).

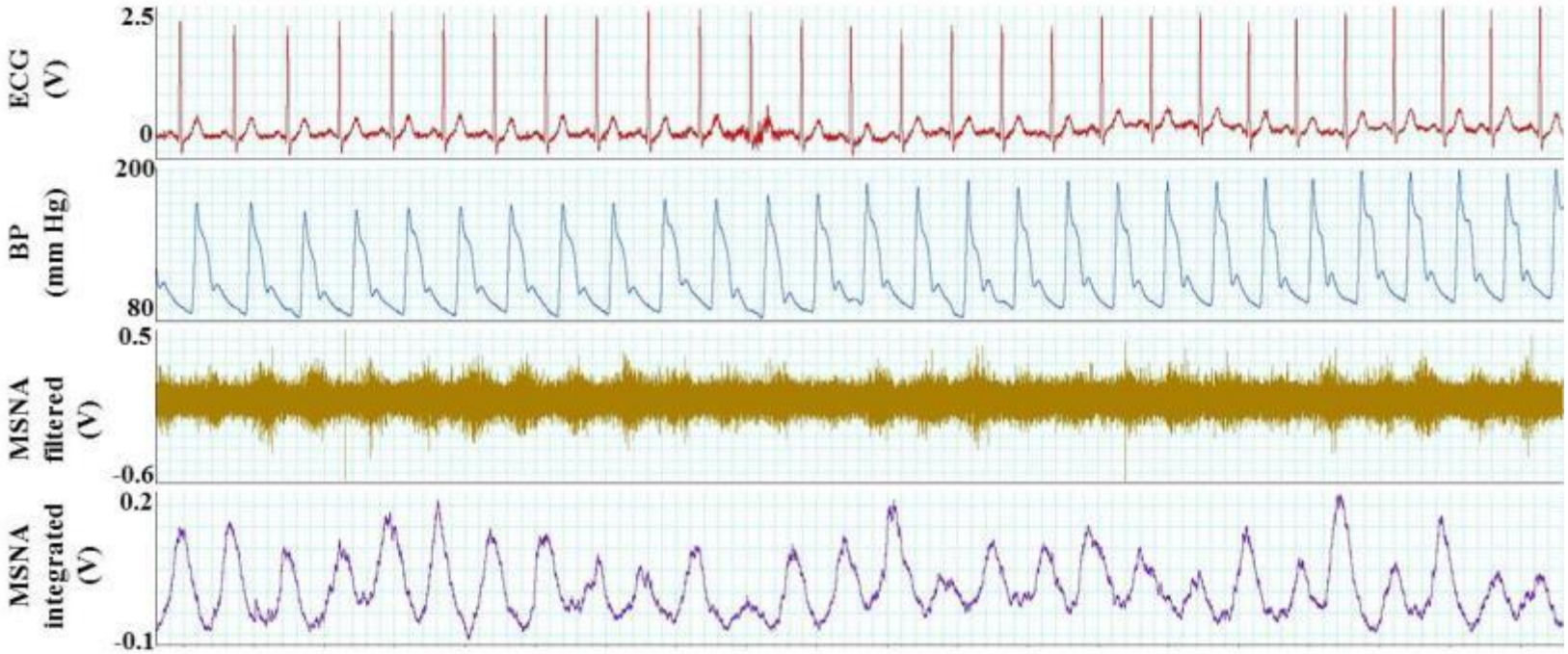
Muscle Sympathetic Nerve Activity (MSNA)



MSNA in Healthy Older Age



MSNA in a Dialysis Patient



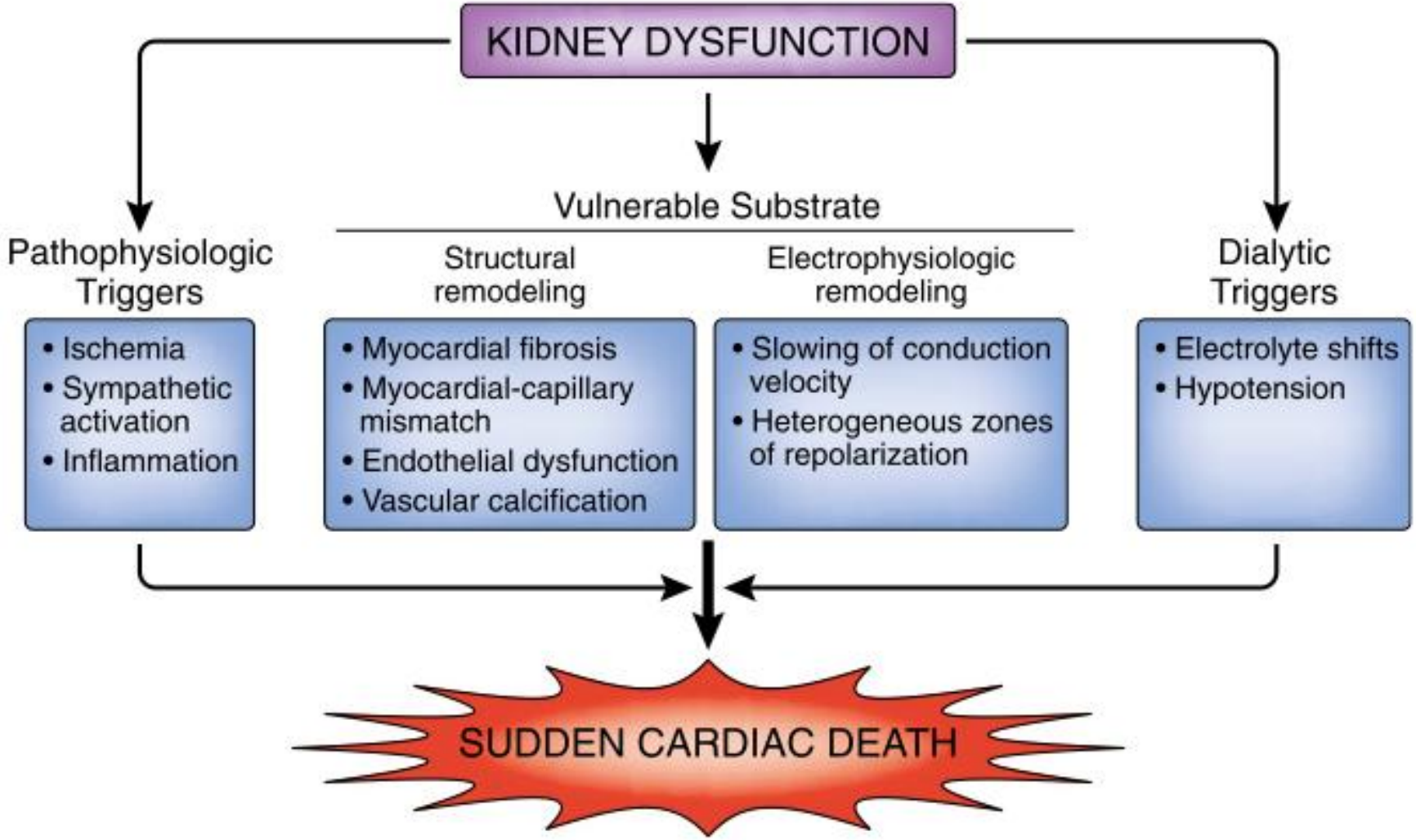


Figure 2. Overview of SCD and kidney dysfunction.

Whitman IR et al. J Am Soc Nephrol 2012; 23: 1929–39

Management

- Bilateral nephrectomies?
- Beta Blockers ?
- Good dialysis
- Control of blood pressure (salt / water balance)
- Other possibilities?

REMEMBER:

THE HEART IS ESSENTIAL TO KEEP THE KIDNEYS FUNCTIONING WELL