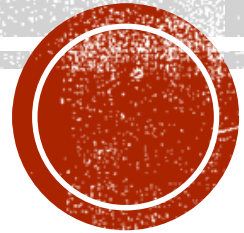
CARDIORENAL SYNDROME

- HOW NEPHROLOGISTS COPE WITH A BROKEN HEART -

Kelly Li

RSC Symposium 2017

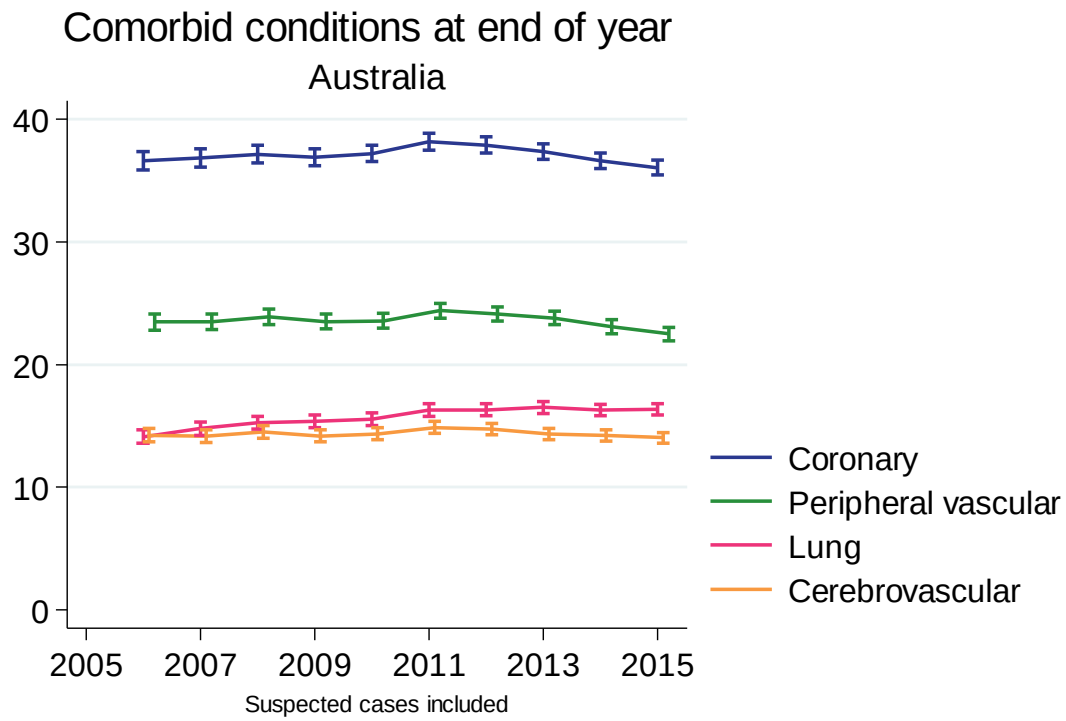


HEART AND KIDNEYS → IS THERE A RELATIONSHIP?

- 40-50% of patients with HF have co-existing CKD (GFR<60)
- Reductions in GFR strongly affect all-cause mortality in HF patients
- CKD is a powerful independent risk factor for the development and progression of CVD and outcomes
- >60% CKD patients have CVD, and degree of CVD correlates with CKD severity
- Patients with stage 3 or higher CKD have a threefold higher risk of HF
- Systemic disorders can cause both cardiac and renal dysfunction

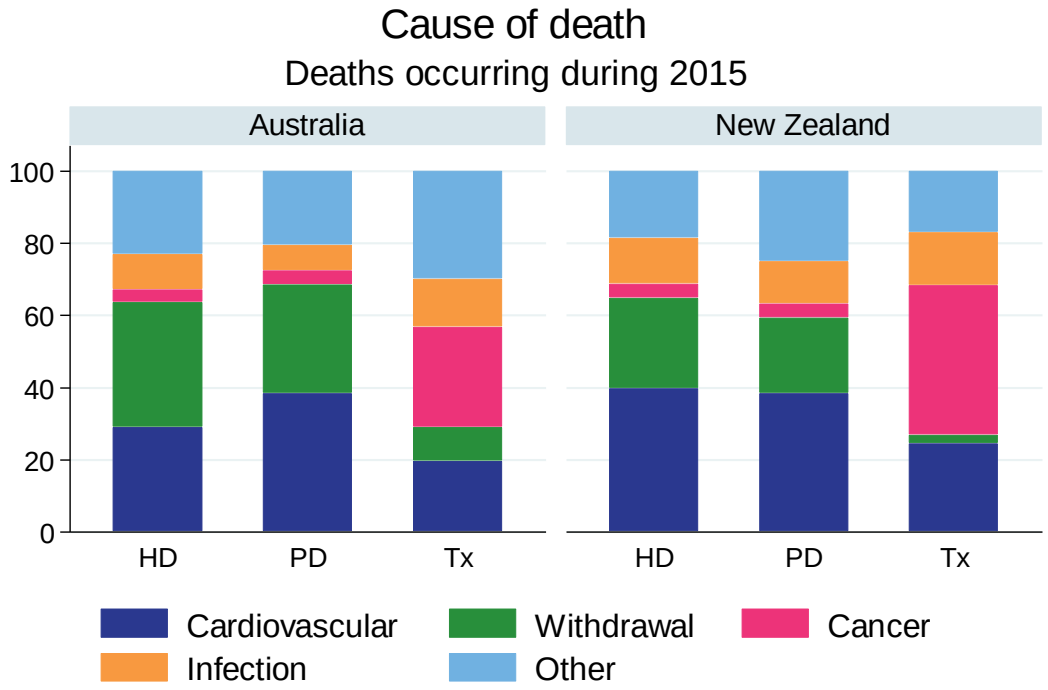
Schefold et al *Nature Reviews Nephrology* 2016

PREVALENCE OF CAD IN ESKD



2016 ANZDATA Annual Report, Figure 2.10

CVD MORTALITY IN ESKD



2016 ANZDATA Annual Report, Figure 3.5

EFFECT OF GFR ON LVEF

Table 1. Description of the Left Ventricular Ejection Fraction (LVEF%) at Different Time Periods: At the Time of Transplant Evaluation, While on the Waiting List to be Transplanted, and During the Follow-Up After Kidney Transplantation

		Groups Based on Post-Transplant LVEF%			p Value		
	All Patients (N = 103)	LVEF ≥50% Group 1 (n = 72)	LVEF ≥40% to <50% Group 2 (n = 16)	LVEF <40% Group 3 (n = 15)	Group 1 vs. 2	Group 2 vs. 3	Group 3 vs. 1
Pretransplant evaluation							
LVEF% (initial transplant evaluation)							
Mean ± SD	31.6 ± 6.7	31.7 ± 6.7	31.6 ± 7.6	31.2 ± 6.1	1.00	0.98	0.98
(95% CI)	(30.3–32.9)	(30.1–33.3)	(27.5–35.6)	(27.7–34.6)			
LVEF% (repeat evaluation before transplant surgery)*							
Mean ± SD	29.3 ± 6.2	29.0 ± 6.0	30.5 ± 8.0	29.6 ± 5.3	0.87	0.97	0.98
(95% CI)	(28.1–30.6)	(27.6–30.5)	(26.2–34.8)	(26.6–32.5)			
Post-transplant evaluation							
Post-transplant LVEF% (at six months)							
Mean ± SD	47.2 ± 10.7	52.5 ± 6.9	39.2 ± 6.1	30.6 ± 6.5	<0.0001	0.002	<0.0001
(95% CI)	(45.1–49.3)	(50.8–54.1)	(35.9–42.5)	(26.9–34.2)			
Post-transplant LVEF% (at 12 months)†							
Mean ± SD	52.2 ± 12.0	58.8 ± 6.8	42.1 ± 2.4	31.6 ± 4.9	<0.001	0.001	<0.001
(95% CI)	(49.9–54.6)	(57.2–60.4)	(40.8–43.4)	(28.9–34.4)			

The groups are based on the LVEF % obtained during the post-transplant period. *Repeat LVEF% (second pretransplant measurement) while on the waiting list for more than 12 months was obtained in 61 patients. †Repeat LVEF% (second post-transplant measurement) was obtained in 101 patients.
CI = confidence interval; LVEF = left ventricular ejection fraction.

Wali et al *JACC* 2005

EFFECT OF GFR ON MORTALITY AND HOSPITALISATION

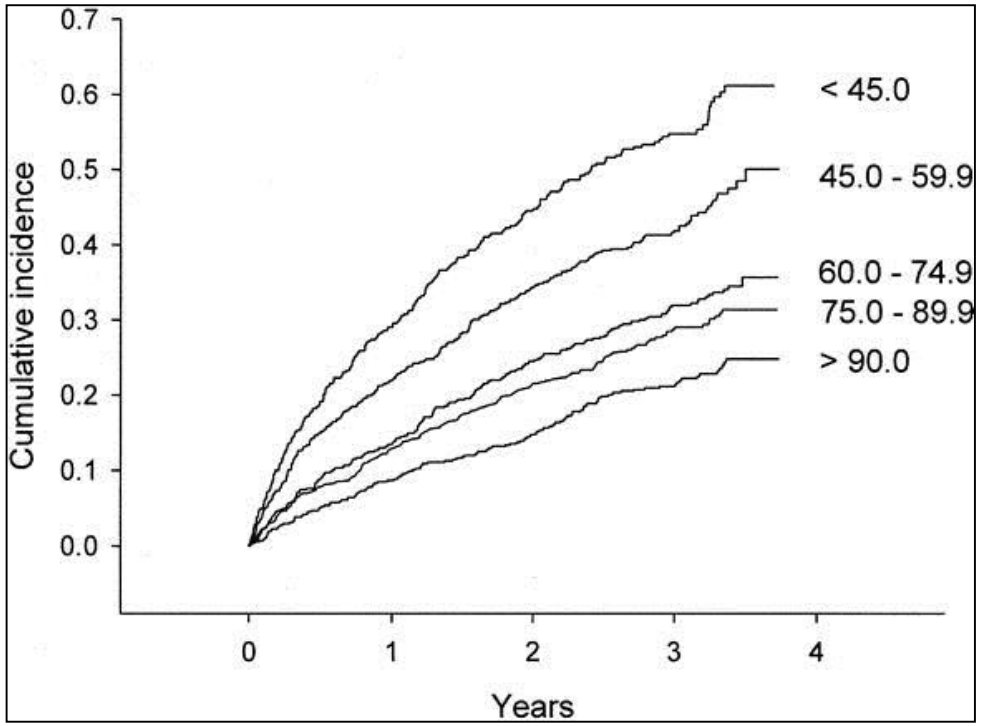
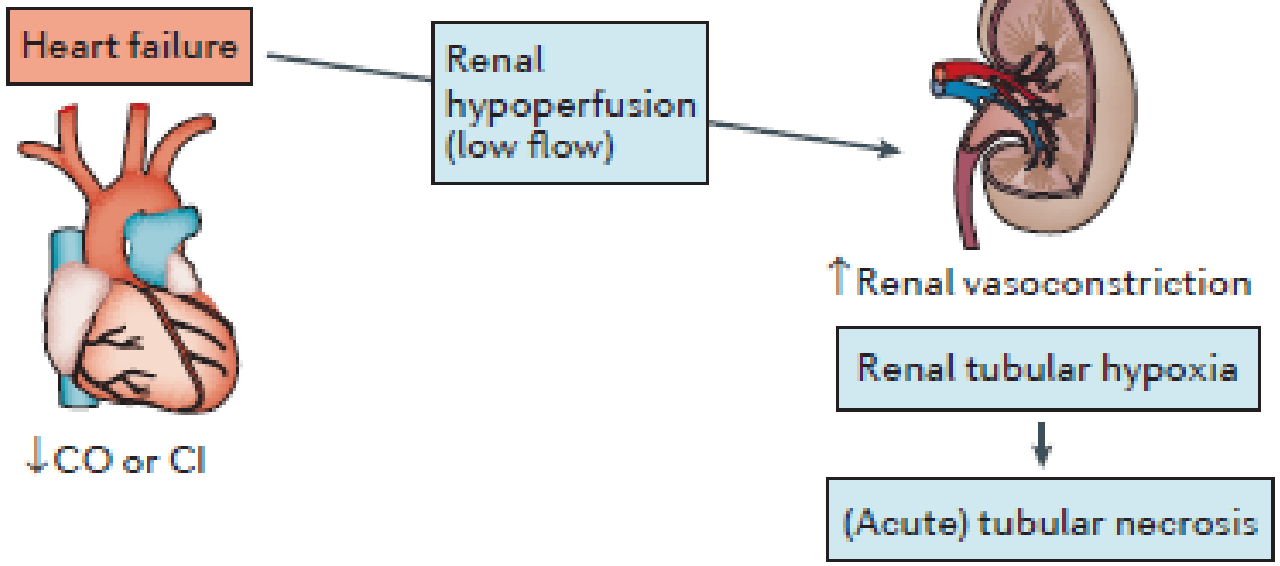


Figure 2. Kaplan-Meier plot of cumulative incidence of cardiovascular death or unplanned admission to hospital for the management of worsening CHF stratified by approximate quintiles of eGFR in mL/min per 1.73 m2 (time in years).

Hillege et al *Circulation* 2016

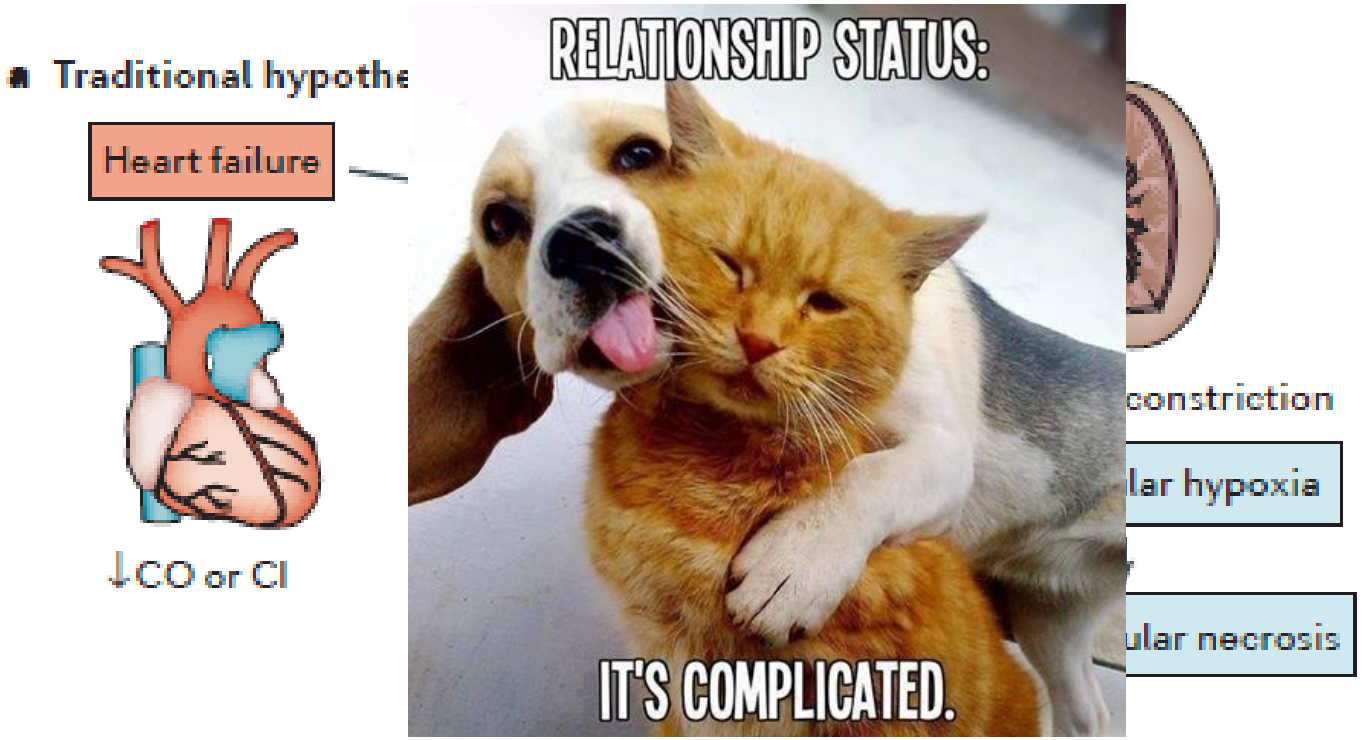
IS THIS THE RELATIONSHIP?

- Traditional hypothesis of cardio-renal interactions



Schefold et al *Nature Reviews Nephrology* 2016

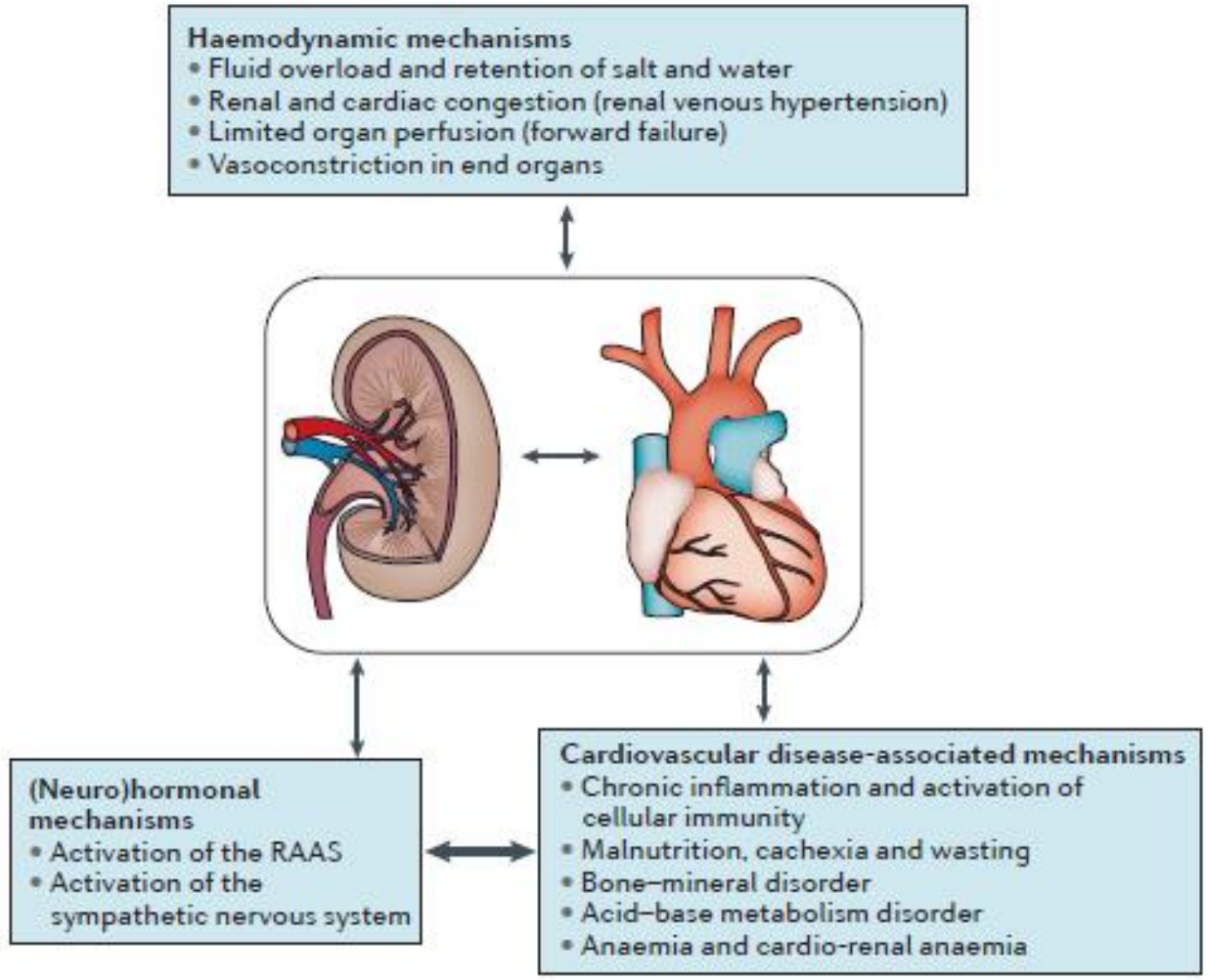
IS THIS THE RELATIONSHIP?



Schefold et al *Nature Reviews Nephrology* 2016

IT'S COMPLICATED!

- Cardiorenal syndrome → complex and bi-directional
  - Haemodynamic interactions
  - Neurohormonal dysregulation
  - Inflammation and other metabolic changes



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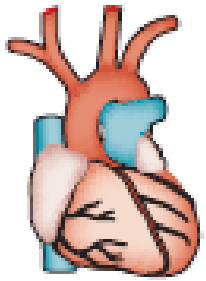
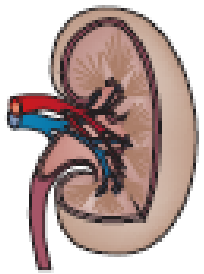
Type 1:
acute cardio-renal syndrome

Acute HF leading to AKI

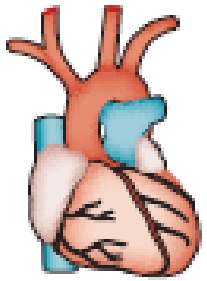


Altered cardiac and/or renal haemodynamics might be of particular importance

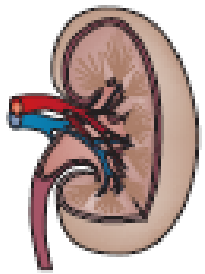


Type 2:
chronic cardio-renal syndrome

Chronic HF leading to progressive and permanent CKD

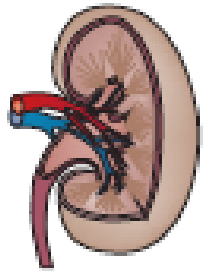


Accelerated renal cell apoptosis and replacement fibrosis might be of particular importance

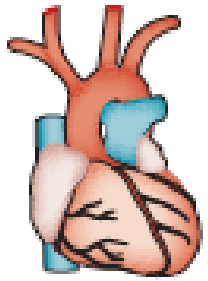


Type 3:
acute reno-cardiac syndrome

AKI causing acute HF

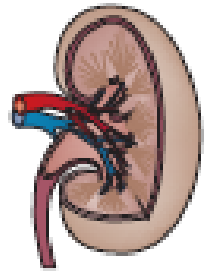


Salt and water imbalance, uraemia-induced effects and neuro-hormonal dysregulation might be key in this setting

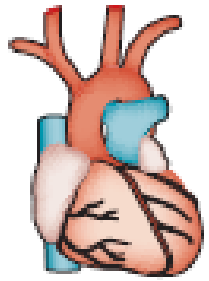


Type 4:
chronic reno-cardiac syndrome

CKD leading to chronic HF and CKD progression



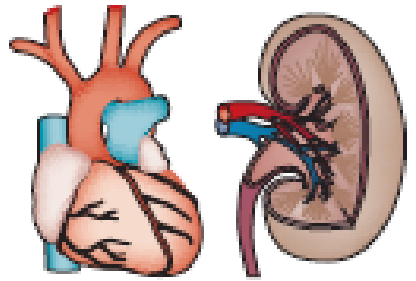
CKD-induced myopathy might be of particular importance in this setting



Type 5:
secondary cardio-renal syndrome

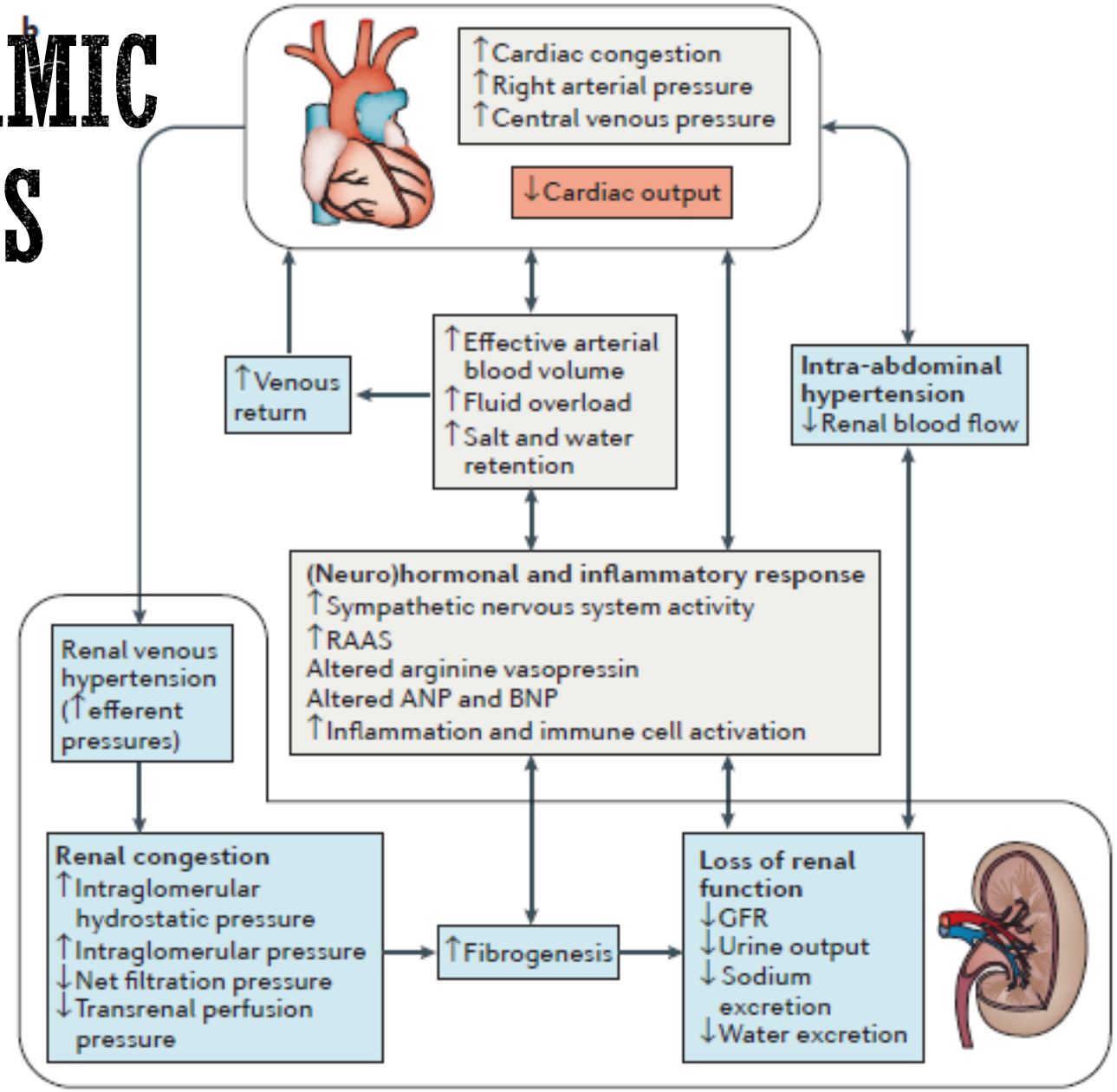
Systemic insult (e.g. in severe sepsis and/or septic shock)

Microcirculatory dysfunction, altered innate and adaptive immune responses and cytokine release, and other effects result in simultaneous organ injury



Schefold et al *Nature Reviews Nephrology* 2016

HAEMODYNAMIC MECHANISMS



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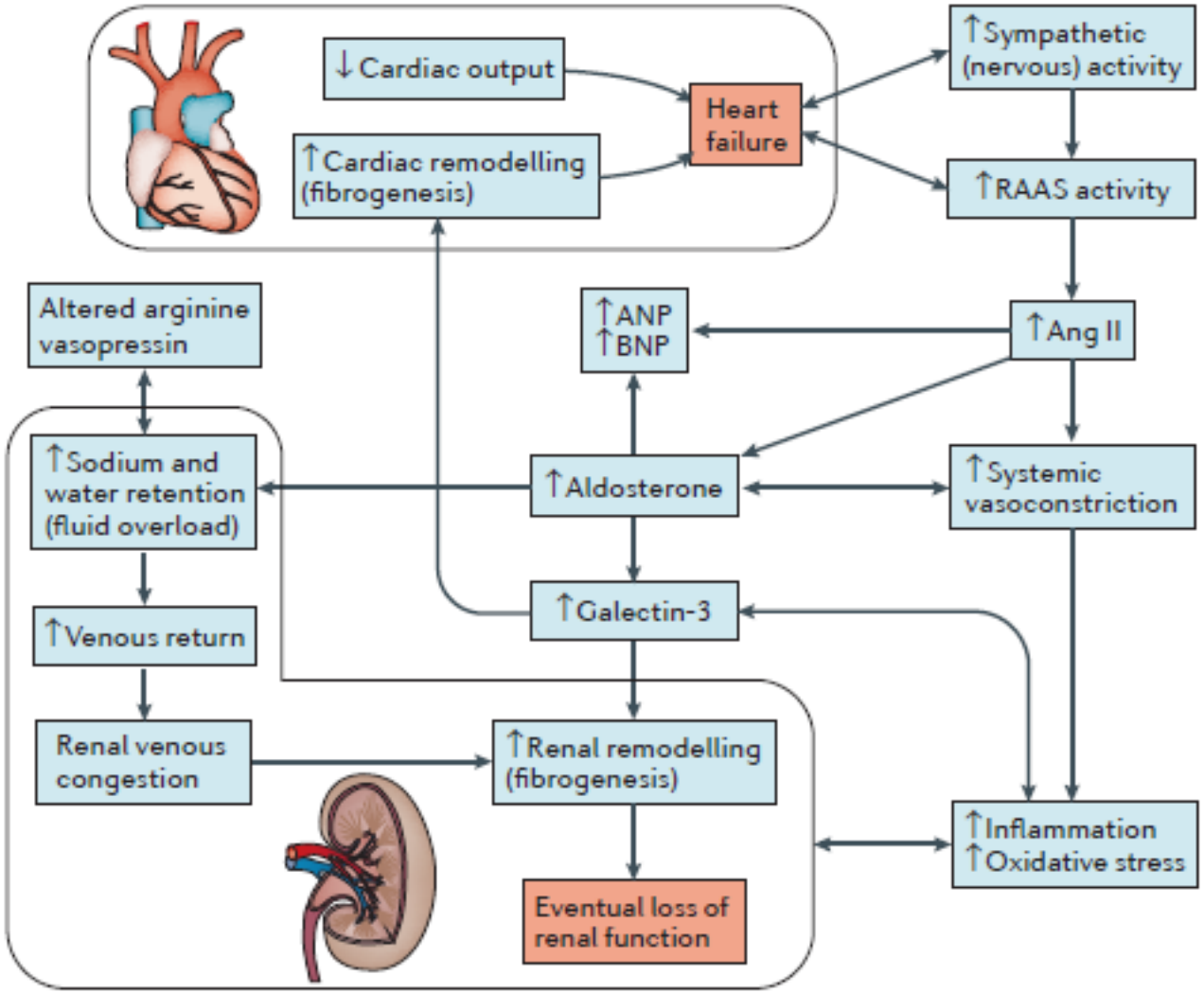
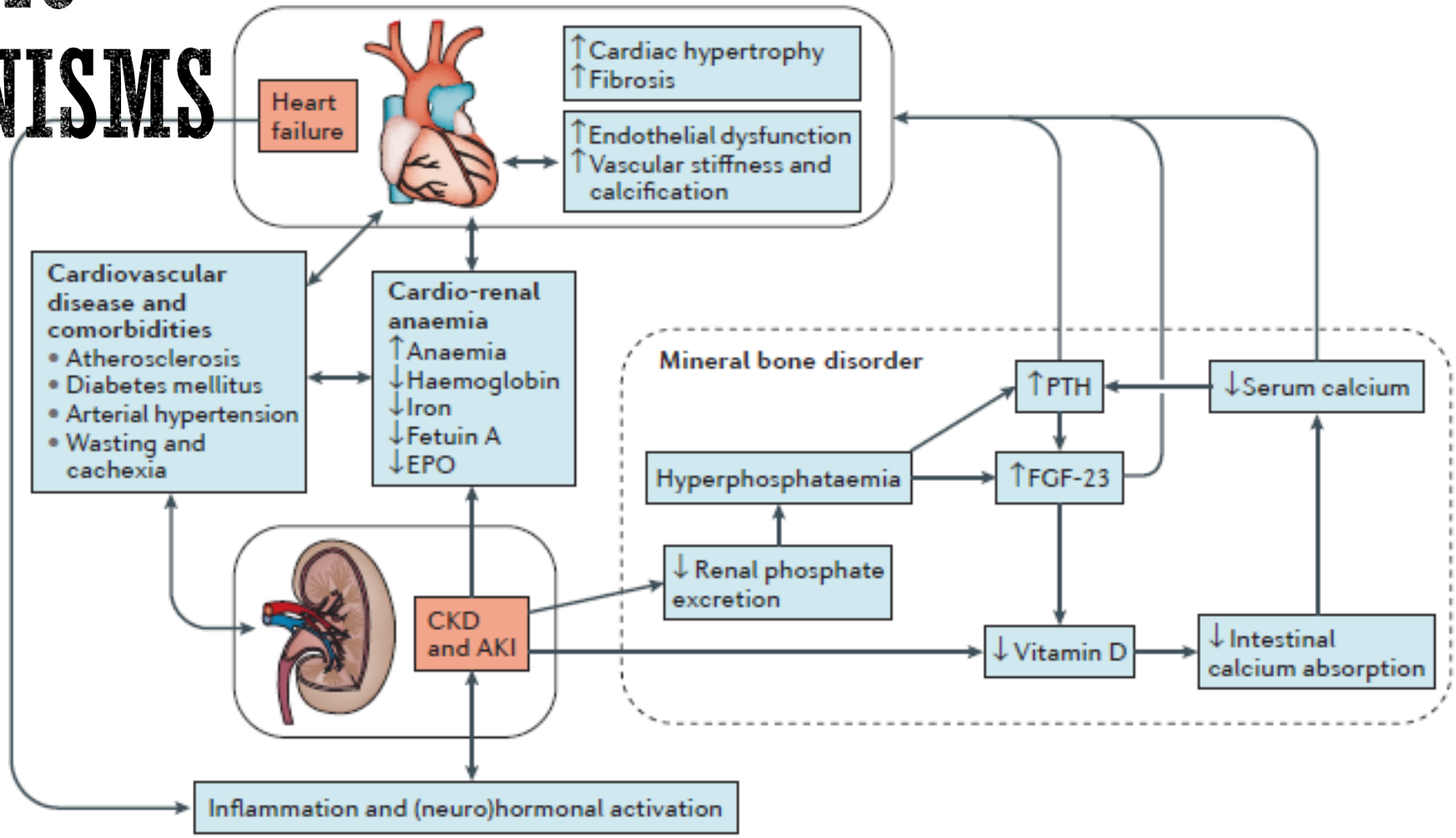
NEUROHORMONAL RESPONSES



Schefold et al *Nature Reviews Nephrology* 2016

SYSTEMIC MECHANISMS



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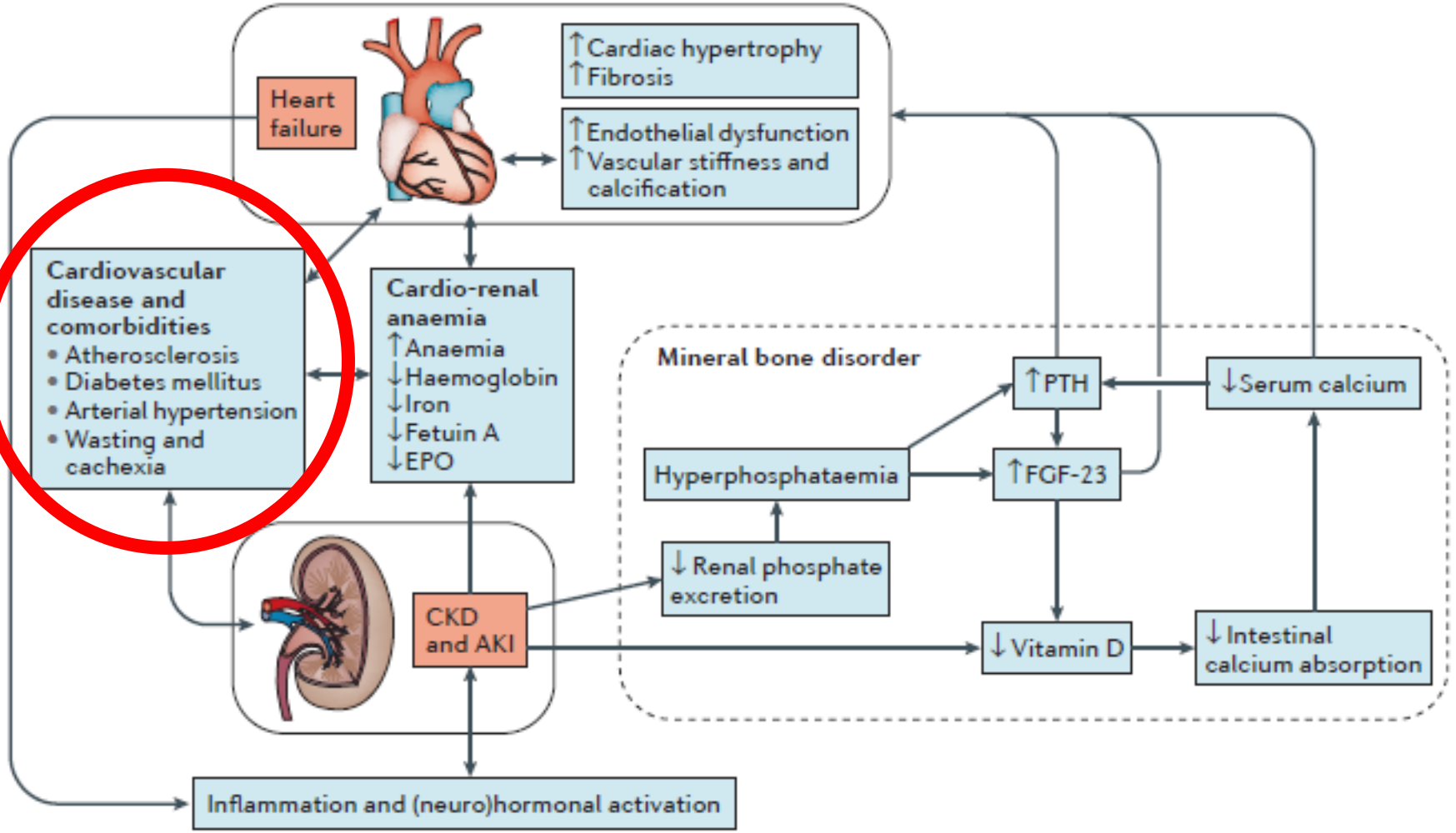

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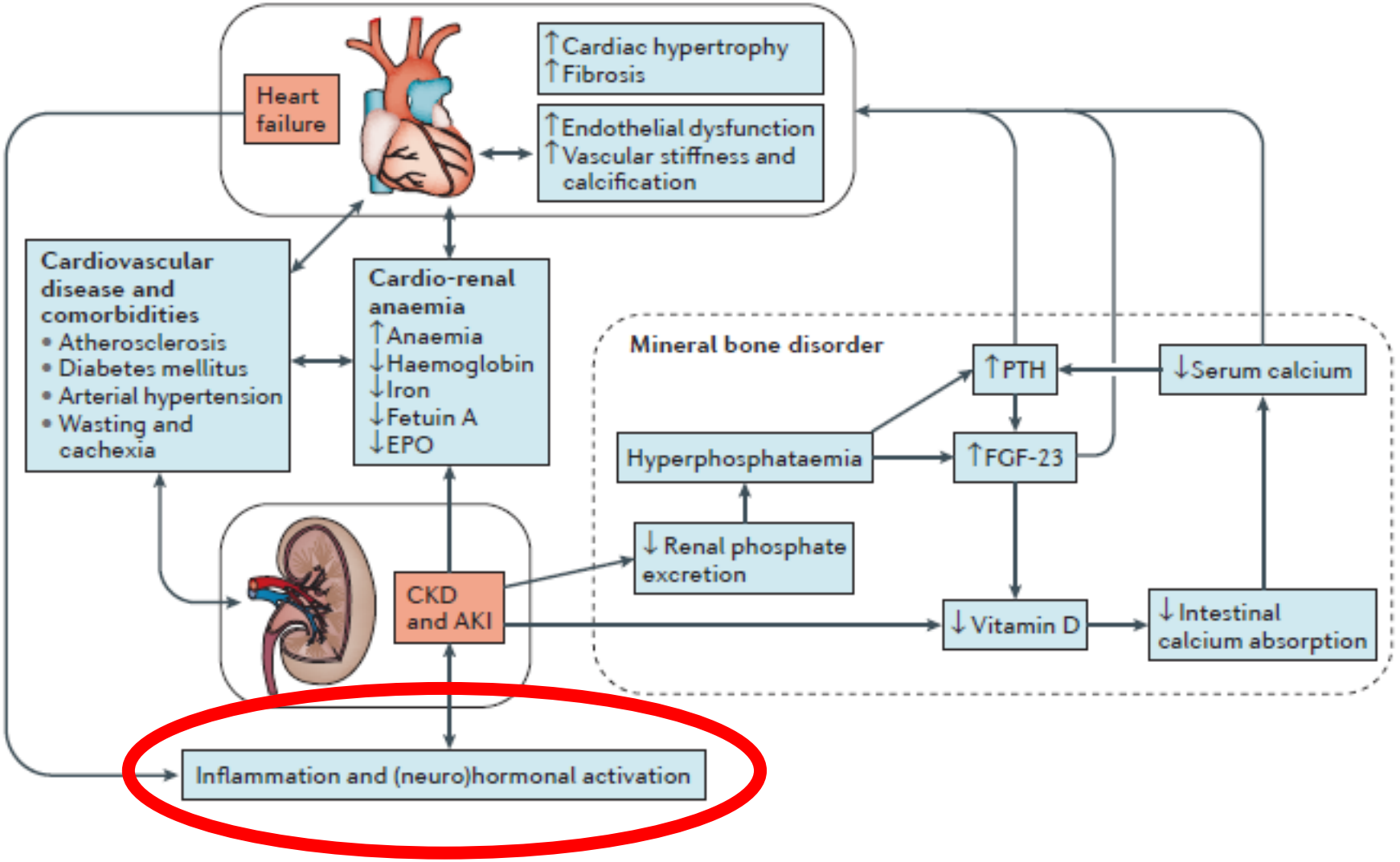

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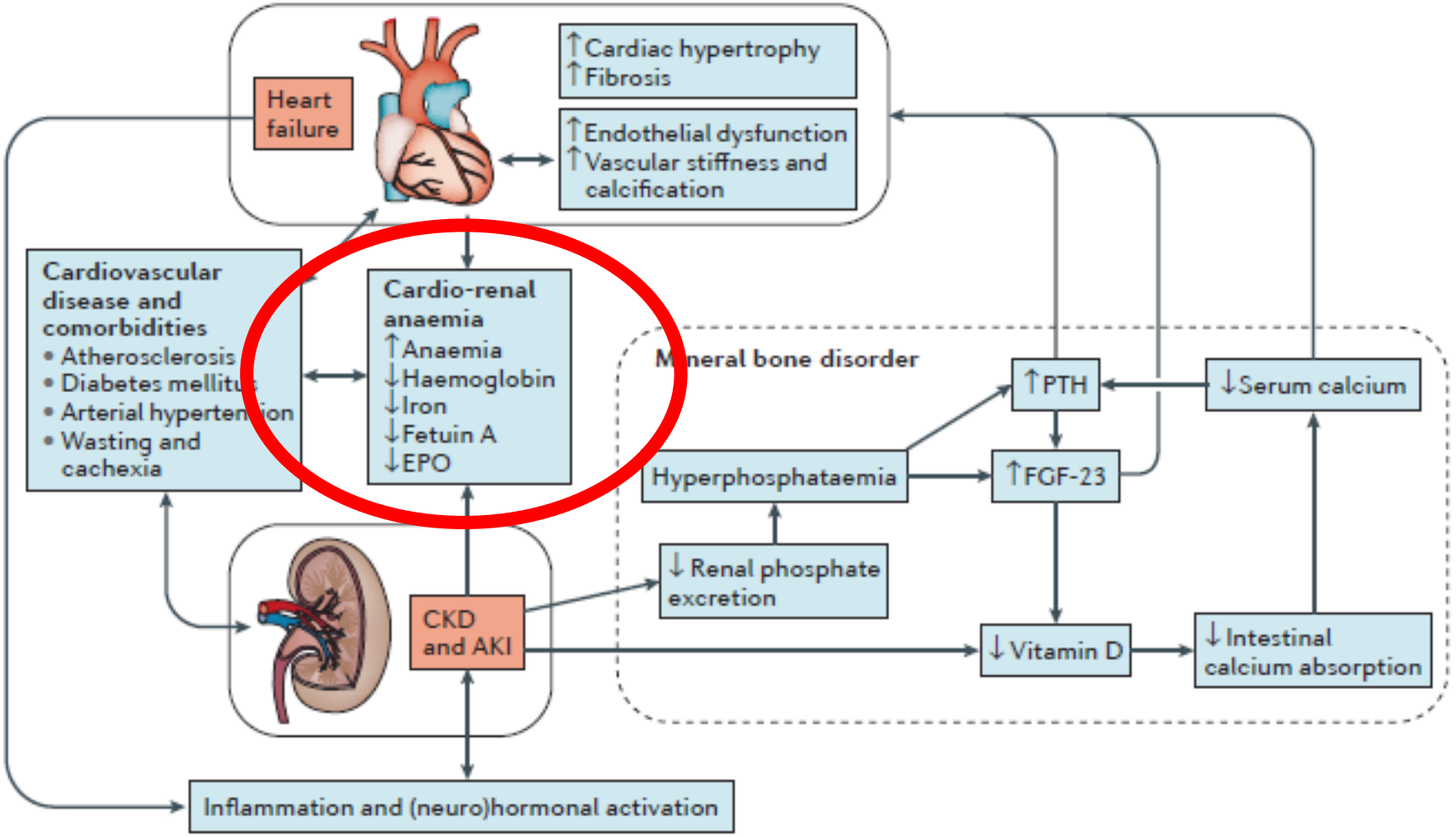

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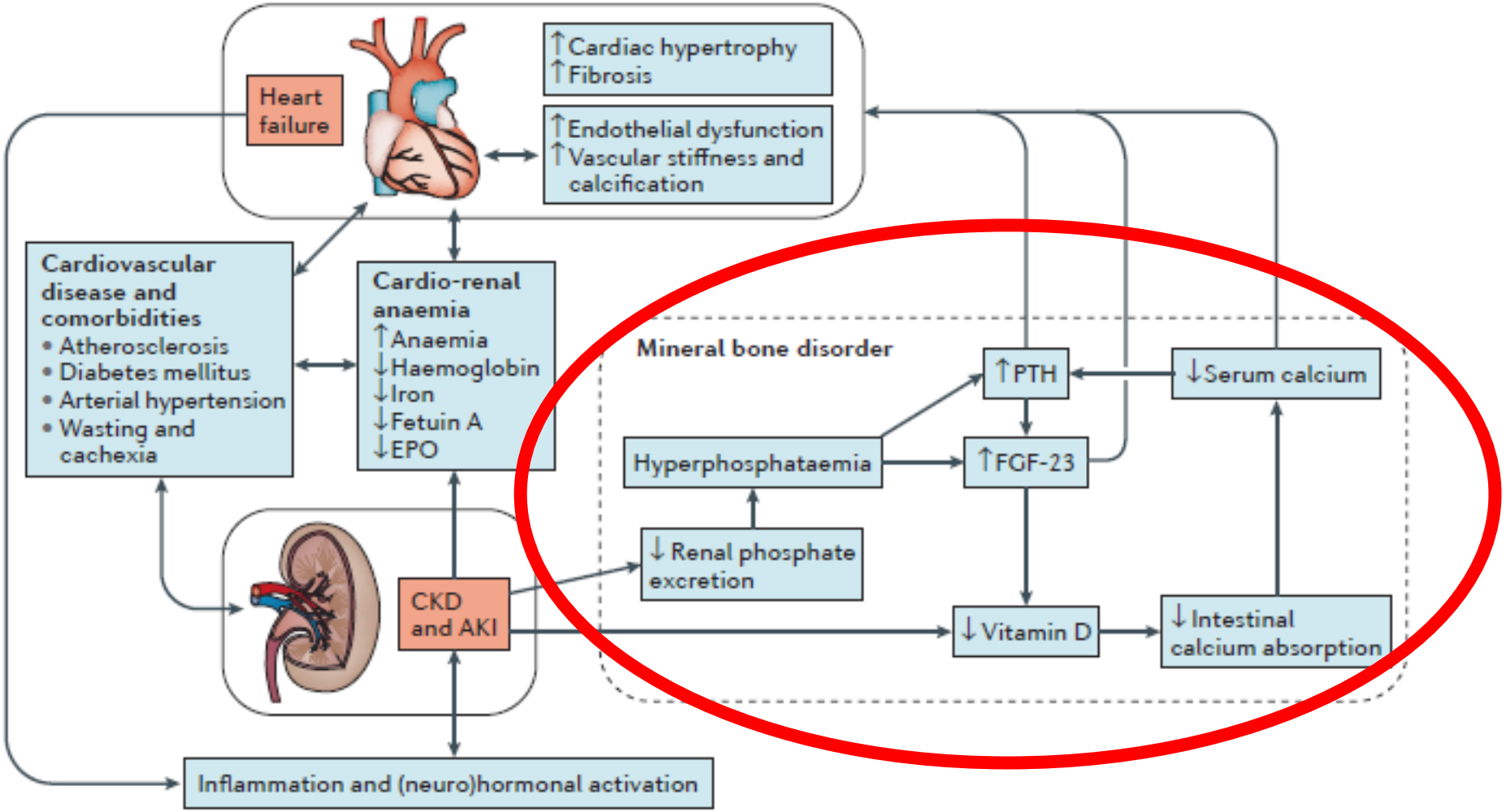


Schefold et al *Nature Reviews Nephrology* 2016

TREATING CRS

- Cardiovascular risk factors
- Improving renal function
- Improving cardiac function
- Drugs

CARDIOVASCULAR RISK FACTORS IN CKD

- Traditional interventions less effective in CKD patients
- Traditional risk factors
  - Hypertension
  - Dyslipidaemia
  - Diabetes
  - Obesity
- Non-traditional risk factors
  - Anaemia
  - Chronic inflammation
  - Hyperparathyroidism
  - LVH
  - RAAS/SNS hyperactivity

WHAT RISK FACTORS TO TREAT

- Treatment targets are complicated – U shaped curve in haemodialysis patients associating mortality with
  - BP
  - BMI
  - Dyslipidaemia
  - Hyperphosphataemia

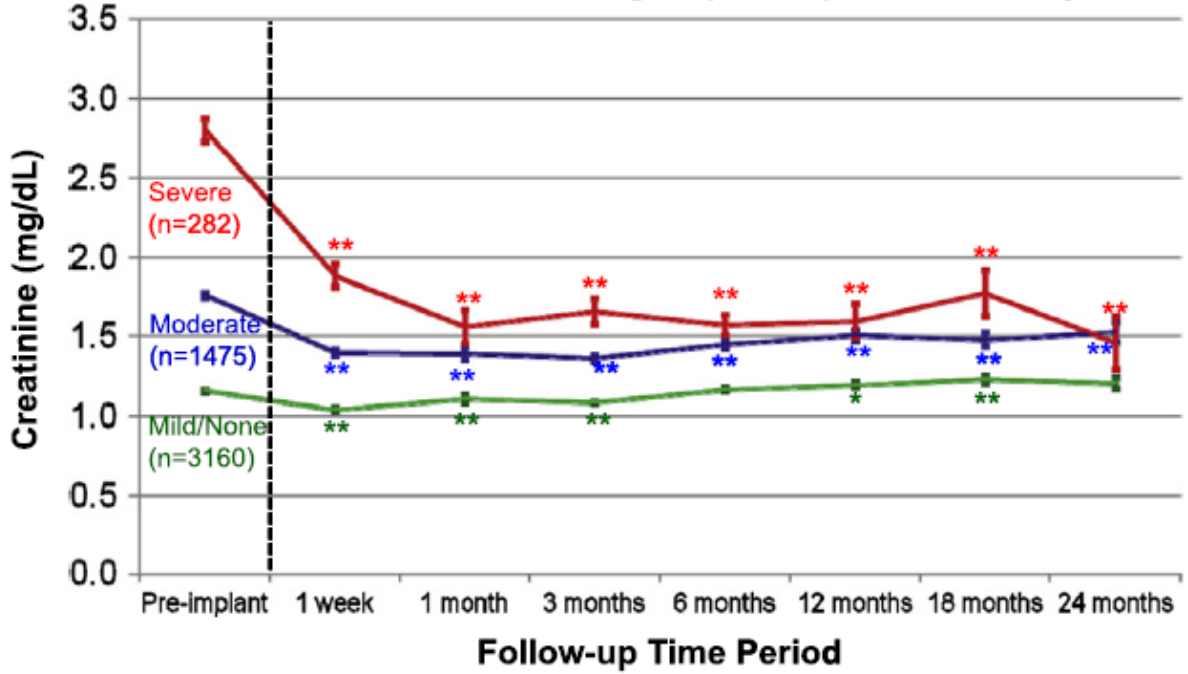
- Secondary hyperparathyroidism
  - EVOLVE in HD patients: cinacalcet did not significantly reduce risk of death or major cardiovascular events in patients with mod to severe hyperparathyroidism
- Dyslipidaemia
  - SHARP in CKD patients: reduction in cardiovascular events (MI/stroke/cath) with combination of simvastatin and ezetimibe
  - Does not apply to those already on dialysis
- Anaemia
  - Clear role for correcting anaemia with iron and EPO

IMPROVING RENAL FUNCTION

- No treatment shown to directly improve renal function in heart failure

IMPROVING CARDIAC FUNCTION

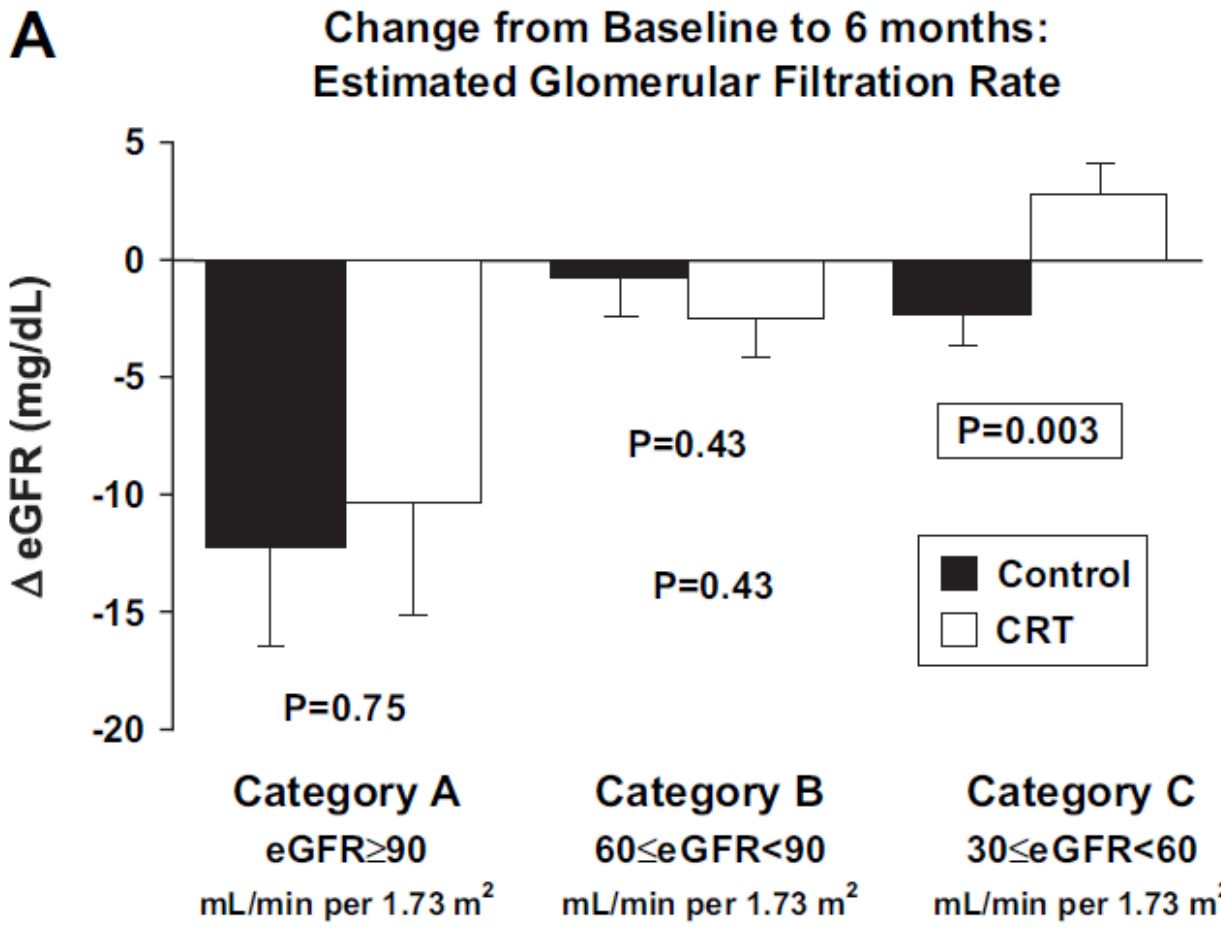
Adult Primary Continuous Flow LVADs & BIVADs, DT and BTT , n=4917
Implants: June 2006 – March 2012: Creatinine
Time course of Creatinine according to pre-implant Renal Dysfunction



* p < .05
** p < .001
Paired comparisons to pre-implant

Brisco et al *Circ Heart Fail* 2014

IMPROVING CARDIAC FUNCTION

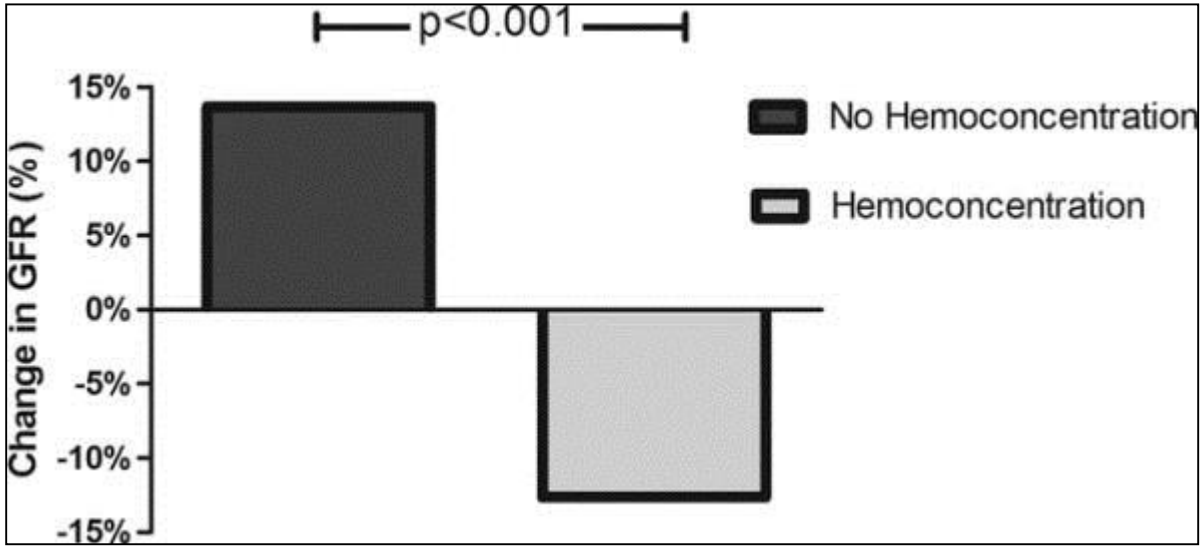


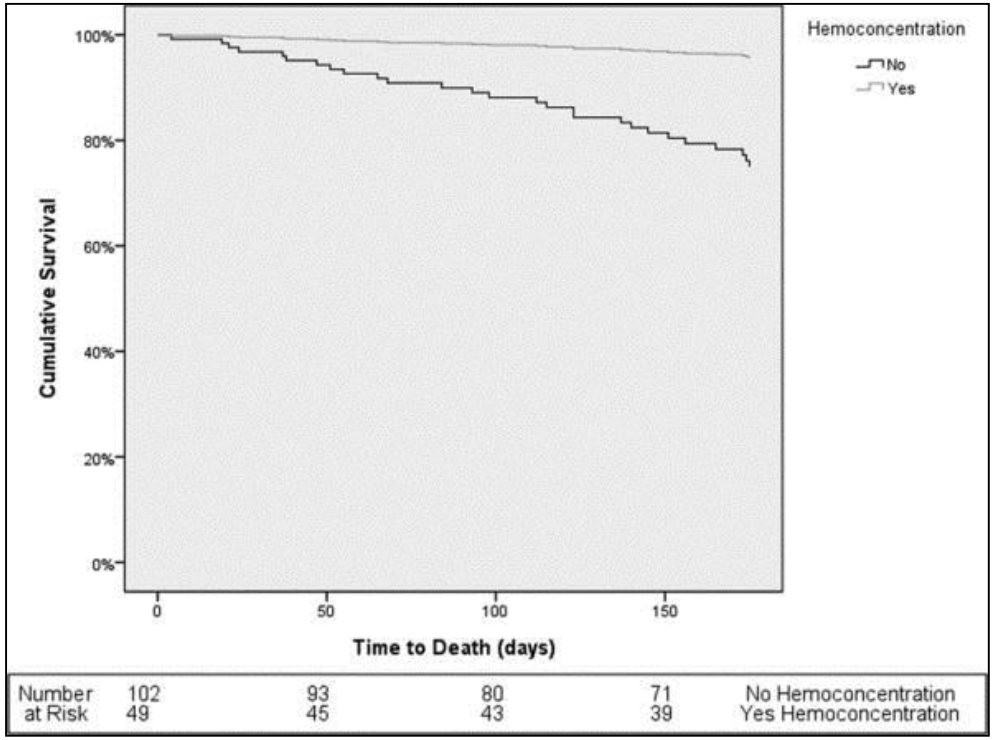
Boerrigter et al *J Card Fail*. 2008

LOOP DIURETICS

- Used for managing volume overload
  - Some patients have increase in Cr, presumed to be due to reduction in renal perfusion from decline in cardiac output
  - Some have stable renal function
  - Some have improved renal function
    - Reduction in intra-abdominal and renal venous pressures
    - Improved LV filling secondary to reduction in RV dilatation

WORSENING RENAL FAILURE WITH DIURETICS





Testani et al *Circulation* 2010

HF WITH REDUCED EF

- B-blockers
  - Meta-analysis of patients with HF and CKD shows b-blockers reduced the risk of all-cause and cardiovascular mortality (Badve et al J Am Coll Cardio 2011)
  - Increased risk of hypotension and bradycardia

- RAAS inhibition
  - ACEI/ARB in HF with reduced EF associated with survival, symptom improvement, and reduced hospitalization
  - Most patients have a reduction in GFR
  - CKD patients at higher risk of hyperkalaemia

- Aldosterone antagonist
  - Evidence of benefit for HF and of safety demonstrated for both spironolactone (RALES) and eplerenone (EMPHASIS-HF)
  - However, risk of hyperkalaemia (esp when used with ACEI/ARB)

VASODILATORS

- Used in treatment of acute decompensated heart failure

- Nitrates
  - Can worsen renal function when used in combination with iv diuretics

- Nesiritide (recombinant BNP)
  - Conflicting results on renal function

INOTROPIC DRUGS

- Used in cardiogenic shock
  - Dobutamine
  - Levosimedan
- Improve renal function in HF by reducing renal venous pressure
- Only problem → increase mortality

DOPAMINE

- Potential role in preserving renal function
- Increase in renal blood flow greater than increase in cardiac output

- Benefit of low dose dopamine not shown in trials

ULTRAFILTRATION

- 3 RCT: UNLOAD, RAPID-CHF, and CARESS-HF
- No improvement in renal function (worse renal function in CARESS)
- More rapid weight reduction and fluid removal
- More adverse events compared to diuretics

- Recommended only in refractory congestion not responding to medical therapy

AICD

- AICD in dialysis patients associated with increased risk for bleeding and infection and does not significantly affect morbidity and mortality

PALLIATIVE CARE – CHALLENGES

- Specific decisions in CRS
- Symptom management
- End of life care

ANTICIPATED DECISIONS

- Medical therapy
  - Cardiac procedures such as CABG or PCI
  - AICD
  - Inotropic support
  - NIV
  - Dialysis
- EOL
  - Hospitalisation
  - Resuscitation
  - Location of death
  - Withdrawing from dialysis/inotropes
  - AICD deactivation

SYMPTOMS

- Dyspnoea
  - Haemodynamic interventions: diuretics, inotropes
  - Fan
  - Opioids
    - Most evidence exist in the use of morphine 10-30mg/day orally
    - In renal failure, substitute with hydromorphone
  - Benzos: especially if dyspnoea accompanied by anxiety
  - Exercise: reduce dyspnoea and improve QOL in HF
  - Supplemental oxygen in those who are hypoxic

SYMPTOMS

- Fatigue
  - Correct anaemia
  - Muscle-strengthening exercises
- Pain
- Nausea and cachexia
- Depression

END OF LIFE CARE

- Location of death
  - Home vs hospice vs hospital
- Intravenous diuretics
  - Limits care in the home or hospice
- AICD deactivation – preserve quality of life during the dying process
  - Discuss early (rarely happens)
  - In emergencies, placing magnet over the device
- Withdrawing from dialysis

THANK YOU