Region Specific Cardiology Perspectives on the Cardiorenal Syndrome – Challenges and Solutions

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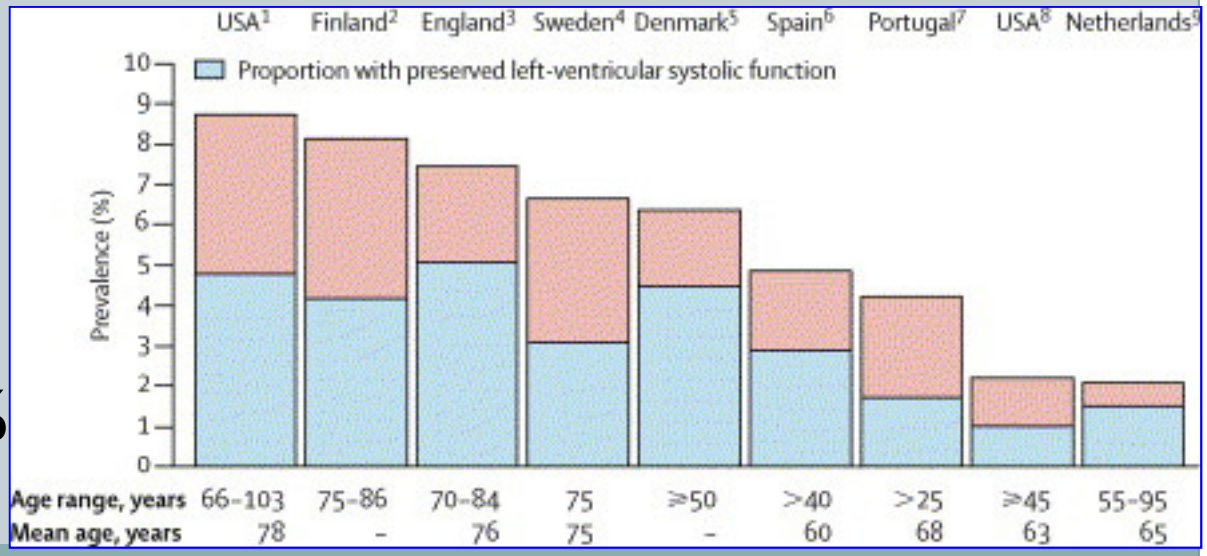
Introduction

- Top 3 causes of mortality in OECD
- Mortality greater than most cancers
  - 30-40% 1yr
  - 60-70% 5yr
- Most common admitting diagnosis > 65yo
- Prevalence:
  - 1-2% Australia
  - 6-10% > 65yo
  - Australia NT 40%
- Lifetime costs 2%



Mc Murray J etal Lancet 2005 Heart Failure

ADHERE DATABASE

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Baseline demographics	*In-hospital clinical outcomes*
1 Only 10,660 (9%) of the study population were classified as stage 1 (normal RF), while 63.6% were classified as either moderate or severe (stage V renal failure).	1 In-hospital outcomes worsened with grade of RI, inclusive of mechanical ventilation, ICU admission, cardiopulmonary resuscitation and new-onset dialysis.
2 Although 59.3% of men and 67.6% of women had at least moderate renal dysfunction at admission, only 33.4% of men and 27.3% of women were reported as having renal insufficiency in the database. Only less than 10% of patients with moderate renal dysfunction (stage III) had a baseline SCr level >2.0 mg/dl.	2 Length of hospital stay correlated with grade of baseline RI, except for stage V, which correlated with moderate RI.
3 MDRD-based eGFR predicts frequency of common risk factors, e.g. hypertension, diabetes and clinical atherosclerosis as manifested by coronary artery disease or peripheral vascular disease.	3 In-hospital mortality increased with severity of baseline RI. GFR remained an independent predictor of mortality (OR with 10 ml/min/1.73 m^2 decrease in GFR was 1.23; 95% CI 1.21–1.25).
4 The mean systolic ejection fraction was similar (37.3–37.8%) for all stages of kidney function except for stage V, where it was 40.3% ($p < 0.0001$).	4 Worsening of RF during hospitalization was also associated with increasingly unfavourable outcomes.

The ADHERE database, which was set up in October 2001, recorded data from 175,000 admissions across 280 participating centres from August 2005.

WHY IS CHD OF UREMIC PATIENTS SO DEVASTATING?

Amman K etal NDT 03

- Evidence of accelerated Atherosclerosis
- Oxidative Stress
- Ischemia Tolerance
- Pump Failure

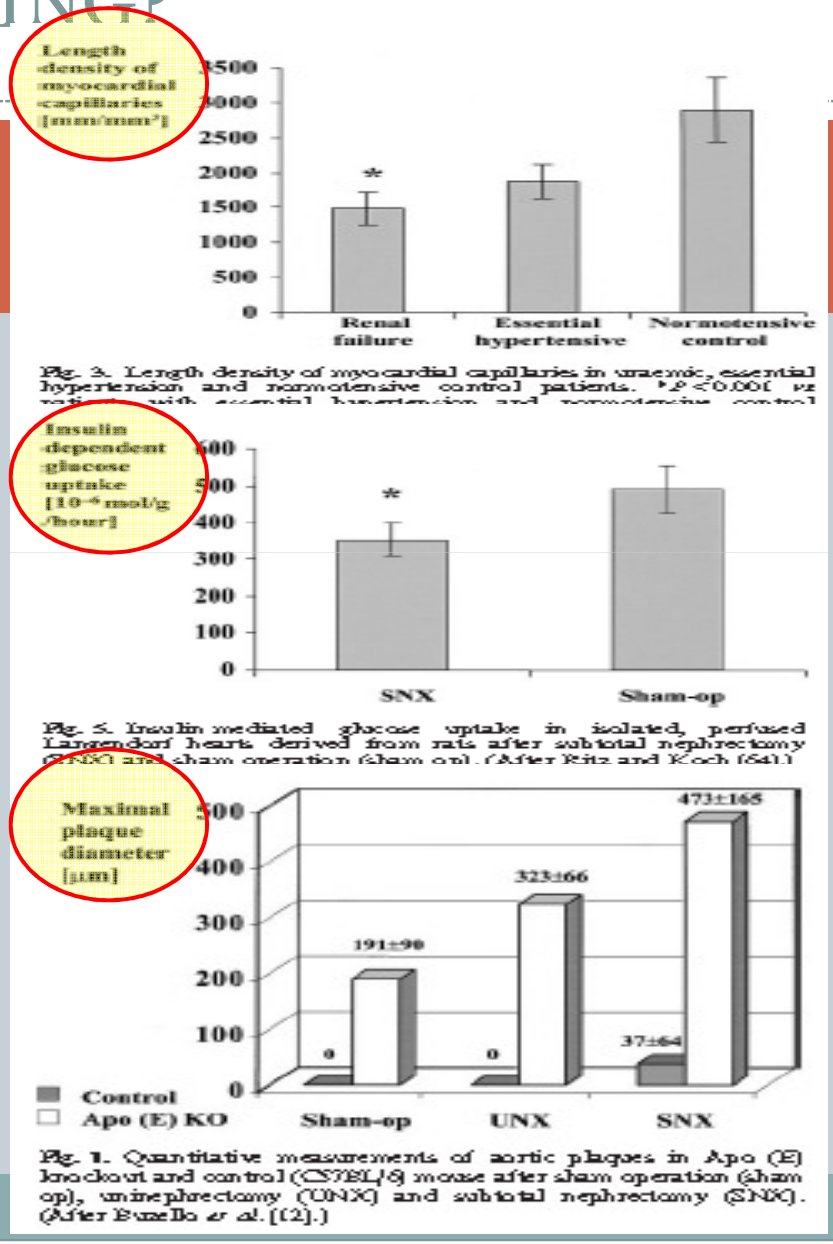


Fig. 3. Length density of myocardial capillaries in uraemic, essential hypertension and normotensive control patients. *$P < 0.001$ vs

Fig. 5. Insulin mediated glucose uptake in isolated, perfused Langendorf hearts derived from rats after subtotal nephrectomy (SNX) and sham operation (sham op). (After Ritz and Koch [64])

Fig. 1. Quantitative measurements of aortic plaques in Apo (E) knockout and control (C57BL/6) mouse after sham operation (sham op), uninephrectomy (UNX) and subtotal nephrectomy (SNX). (After Bonello *et al.* [12].)

ELEMENTARY CARDIORENAL PATHOPHYSIOLOGY

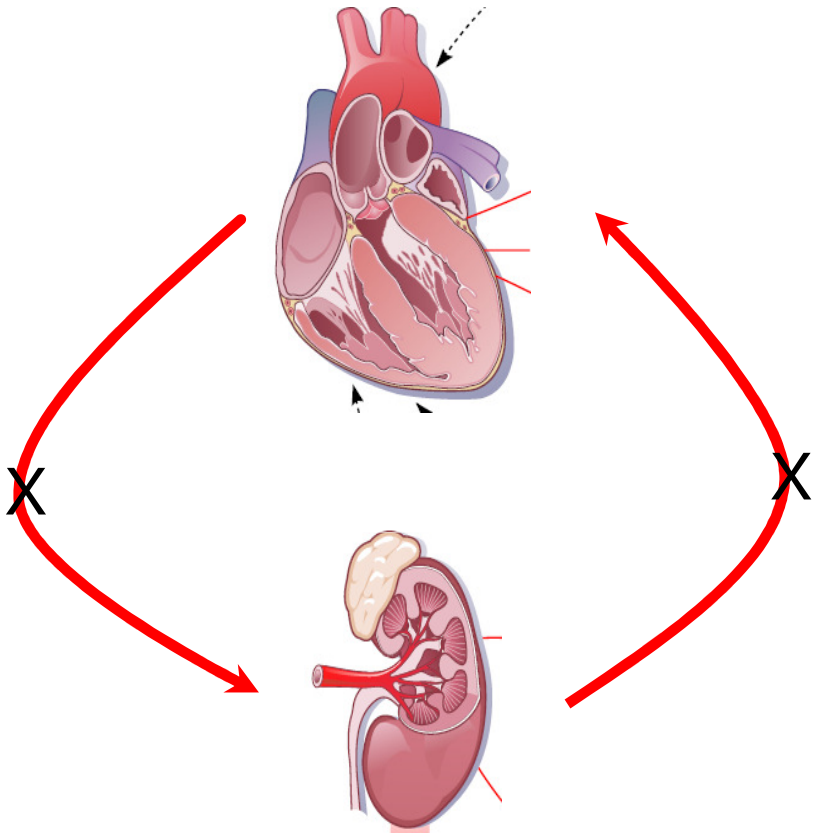
The heart and kidney are connected by primary (continuous) circulatory system and secondary by humoral, autocrine and immune systems.

This understanding is critical in CRS pathophysiology and in planning steps to break the cycle.

Is it?

- RENOCARDIAC
- CARDIORENAL
- BOTH

WHERE DO WE BREAK THE CYCLE?



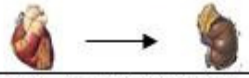
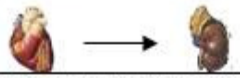
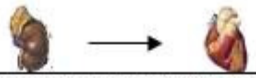
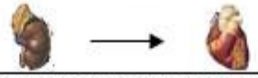
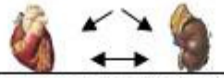
DEFINING THE CARDIORENAL SYNDROME

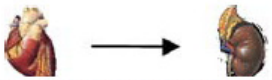
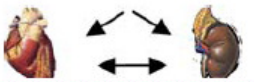
Exp Clin Card 08

- There is no single definition
- Definition should incorporate the bidirectional nature of heart and kidney interaction. (Organ Cross talk)
- No organ predominates. Severity of underlying dysfunction "Cardiorenal" or "Renocardiac" define predominant failing organ.
- Chronology "acute" and "chronic" and further divided by primary organ – *"Primary CRS"*
- If neither of the organs is primary source e.g. systemic disorders such as sepsis than it is labeled *"Secondary CRS"*
- Ronco etal 5 subtypes of CRS considering clinical presentation, pathophysiology and diagnosis

Table 1

Cardio-Renal Syndromes (CRS): Classification, definitions and work group statements

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
Primary events	Acute heart failure (AHF) or Acute Coronary Syndrome (ACS) or Cardiogenic Shock	Chronic heart disease (LV remodeling and dysfunction, diastolic dysfunction chronic abnormalities in cardiac function, cardiomyopathy)	Acute Kidney Injury (AKI)	Chronic Kidney Disease (CKD)	Systemic Disease (Sepsis, amyloidosis etc)
Criteria for primary events	ESC, AHA/ACC	ESC, AHA/ACC	RIFLE - AKIN	KDOQI	Disease-specific criteria
Secondary events	Acute Kidney Injury (AKI)	Chronic Kidney Disease (CKD)	AHF, ACS, arrythmias, shock	CHD (LV remodeling and dysfunction, diastolic dysfunction, abnormalities in cardiac function), AHF, ACS	AHF, ACS, AKI, CHD, CKD
Criteria for secondary events	RIFLE - AKIN	KDOQI	ESC, AHA/ACC	ESC, AHA/ACC	ESC, AHA/ACC, RIFLE / AKIN ESC, AHA/ACC KDOQI
Cardiac biomarkers	**Troponin, CK-MB, BNP, NT-proBNP, MPO, IMA**	**BNP, NT-proBNP, CRP**	**BNP, NT-proBNP**	**BNP, NT-proBNP, CRP**	**CRP, procalcitonin, BNP**
Renal biomarkers	**Serum Cystatin C, Creatinine, NGAL. Urinary KIM-1, IL-18, NGAL, NAG**	**Serum Creatinine, Cystatin C, Urea, Uric Acid, CRP, Decreased GFR**	**Serum Creatinine, Cystatin C, NGAL. Urinary KIM-1, IL-18, NGAL, NAG**	**Serum Creatinine, Cystatin C, Urea, Uric Acid, Decreased GFR**	**Creatinine, NGAL, IL-18, KIM-1, NAG**
Prevention strategies	Acutely decompensated heart failure and acute coronary syndromes are most common scenarios. Inciting event may be acute coronary ischemia, poorly controlled blood pressure, and noncompliance with medication and dietary sodium intake. Randomized trials improving compliance with heart failure care management have reduced rates of hospitalization and mortality, and a reduction in the rates of Acute Cardio-Renal (Type 1) can be inferred.	A common pathophysiology (neurohumoral, inflammatory, oxidative injury) could be at work to create organ dysfunction. Drugs that block the renin angiotensin system reduce the progression of both heart failure and chronic kidney disease. It is unknown whether other classes of drugs can prevent Chronic Cardio-Renal (Type 2).	Acute sodium and volume overload are part of the pathogenesis. It is unknown whether sodium and volume overload is prevented with different forms of renal replacement therapy and if this will result in lower rates of cardiac decompensation.	The chronic processes of cardiac and renal fibrosis, left ventricular hypertrophy, vascular stiffness, chronic Na and volume overload, and other factors (neurohumoral, inflammatory, oxidative injury) could be at work to create organ dysfunction. A reduction in the decline of renal function and albuminuria has been associated with a reduction in cardiovascular events. The role of chronic uremia, anemia, and changes in CKD-mineral and bone disorder on the cardiovascular system is known in Chronic Reno-Cardiac S.	Potential systemic factors negatively impact function of both organs acutely. It is uncertain if reduction/elimination of key factors (immune, inflammatory, oxidative stress, thrombosis) will prevent both cardiac and renal decline.
Management strategies	Specific – depends on precipitating factors. General supportive – oxygenate, relieve pain & pulmonary congestion, treat arrhythmias appropriately, differentiate left from right heart failure, treat low cardiac output or congestion according to ESC guidelines* ; avoid nephrotoxins, closely monitor kidney function	Treat CHF according to ESC guidelines*, exclude precipitating pre-renal AKI factors (hypovolemia and/or hypotension), adjust therapy accordingly and avoid nephrotoxins whilst monitoring renal function and electrolytes. Extracorporeal ultrafiltration.	Follow ESC guidelines for acute CHF* specific management may depend on underlying etiology, may need to exclude renovascular disease and consider early renal support, if diuretic resistant	Follow KDOQI guidelines for CKD management, exclude precipitating causes (cardiac tamponade). Treat heart failure according to ESC guidelines*, consider early renal replacement support.	Specific – according to etiology General – see CRS management as advised by ESC guidelines* 2008

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					
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Primary events	Acute heart failure (AHF) or acute coronary syndrome (ACS) or cardiogenic shock	Chronic heart disease (LV remodelling and dysfunction, diastolic dysfunction, chronic abnormalities in cardiac function, cardiomyopathy)	AKI	CKD	Systemic disease (sepsis, amyloidosis, etc.)
Criteria for primary events	ESC, AHA/ACC	ESC, AHA/ACC	RIFLE–AKIN	KDOQI	Disease-specific criteria
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Criteria for secondary events	RIFLE–AKIN	KDOQI	ESC, AHA/ACC	ESC, AHA/ACC	ESC, AHA/ACC, RIFLE/AKIN ESC, AHA/ACC KDOQI
Cardiac biomarkers	Troponin, CK-MB, BNP, NT-proBNP, MPO, IMA	BNP, NT-proBNP, C-reactive protein	BNP, NT-proBNP	BNP, NT-proBNP, C-reactive protein	C-reactive protein, procalcitonin, BNP
Renal biomarkers	Serum cystatine C, creatinine, NGAL. Urinary KIM-1, IL-18, NGAL, NAG	Serum creatinine, cystatin C, urea, uric acid, C-reactive protein, decreased GFR	Serum creatinine, cystatin C, NGAL. Urinary KIM-1, IL-18, NGAL, NAG	Serum creatinine, cystatin C, urea, uric acid, decreased GFR	Creatinine, NGAL, IL-18, KIM-1, NAG
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CRS classification, definition and working group statement EHJ 09

The NT Demographics

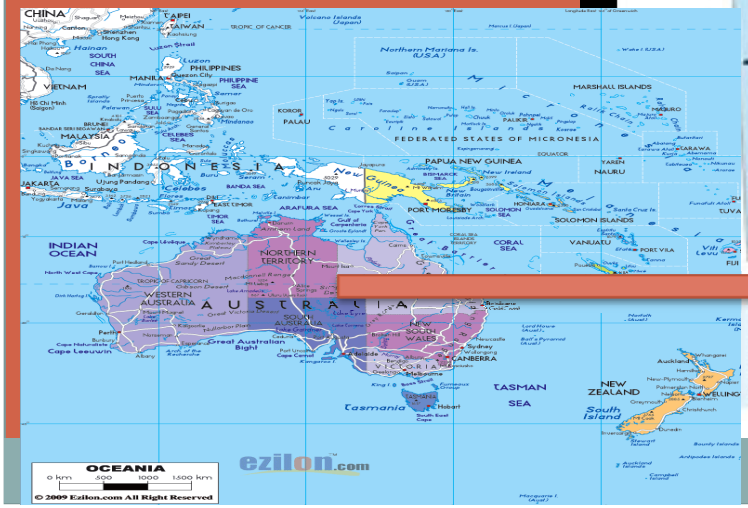
Population: 230K

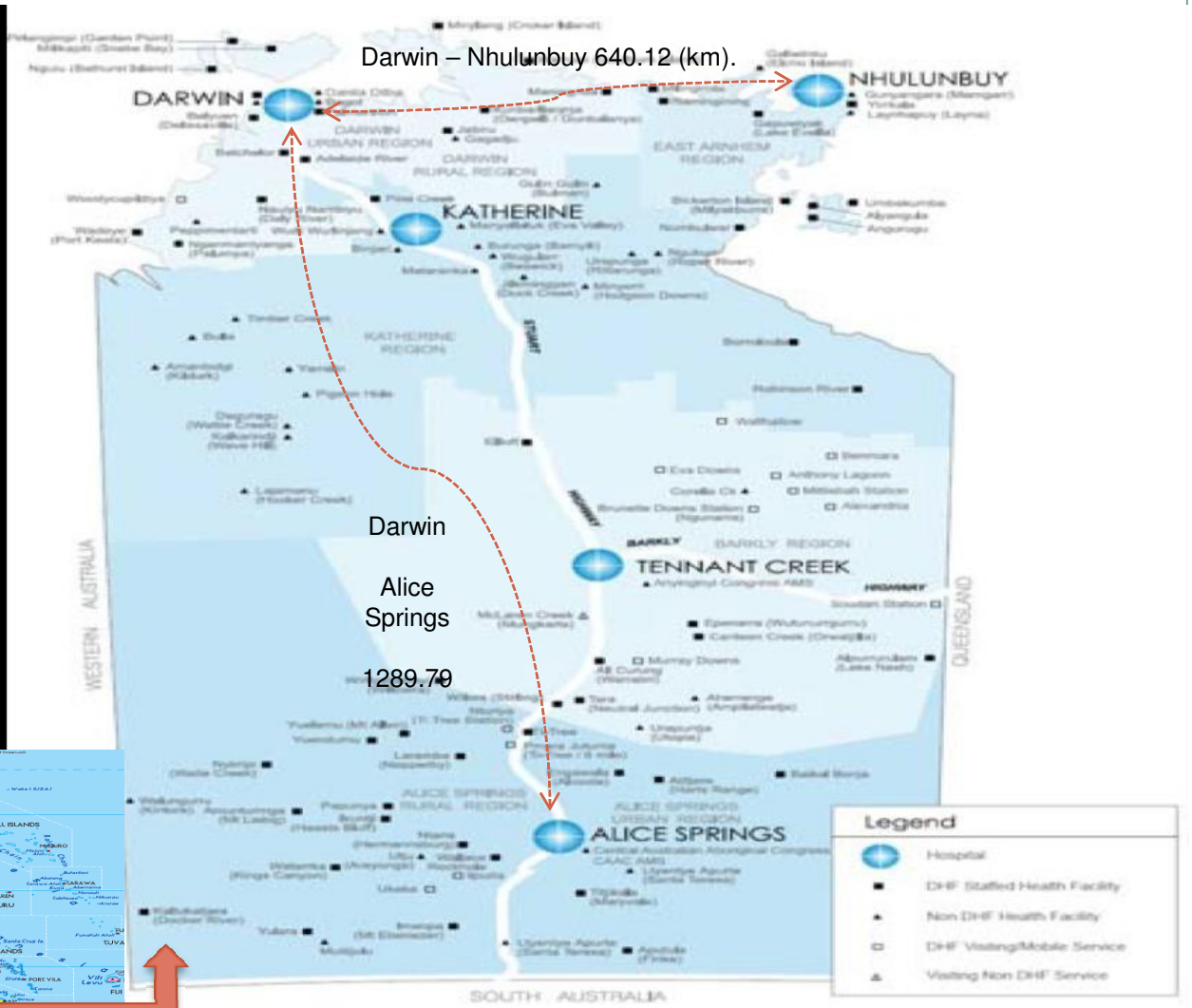
Urban: 2 major cities 150K

Remote: 30%

Indigenous: 30%; 60% remote

Health services: see next page





NOTE:
Other DHF services including Northern Territory Families and Children (NTFC) offices are located within main towns and provide visiting regional services.

KPMG 2011 Health Services Report

What is the problem?

- 1) *High burden of CHF that cannot be explained by traditional risk factors alone.*
- 2) Greater burden of CHF related to rheumatic and *non-ischemic aetiology,*
- 3) Greater burden of CHF with *co-morbidities*
- 4) *Barriers and differentials in access to appropriate,*
- 5) *Delay in presentation and receipt of acute care during periods of decompensation*
- 6) Poor *uptake of post-discharge services such as cardiac rehabilitation*
- 7) Unique *geography -*
- 8) *External validity - adherence to guidelines early in hospital admission can improve outcomes*

THERAPEUTICS

Common Comorbidities

Condition	Prevalence	RAAS	SNSA	NO	ROS	AGE	Notes IyngkaranP HCCR 2013
HT	>55	+	+	P	P	S	• Most important comorbidity and contributor to CHF • >50 are IR • Untreated >50% develop CHF
DM	>40	+	+	P	P	P	• Overrepresented and under recognized • IR rates probably 2-3x more • >70% will have another metabolic comorbidity • Every 1% increase HbA1c >8% increase mortality
IHD	>30	+	+	P	P	S	• Most important cause for CHF mortality • Underreported as sicker patients excluded from trials
MetS	30-40	+	+	P	P	P	• Constellation of central obesity, HT, IR/DM, sleep apnea • Control of individual components of MetS improves HT and CHF • OSA important association and cause for worsening HT, AF, CCF and is often sub optimally treated
Chol	>30	~	~	P	P	S	• Common association in CHF trials • Role of hypertriglyceridemia in Indigenous populations uncertain
CRF	30-50	+	+	P	P	S	• Underrepresented in HF RCT • Stronger predictor of mortality greater even than LVEF
RHD	?	+	+	P	P	S	• Important cause in Indigenous clients • Importance cause of early CCF
AF	>40	+	+	P	P	S	• Rhythm strategy preferred but often given less importance • All beta-blockers similar for rate control
Mood	13-77	+	+	P	P	S	• Under recognized and undertreated

Clinical Scenarios

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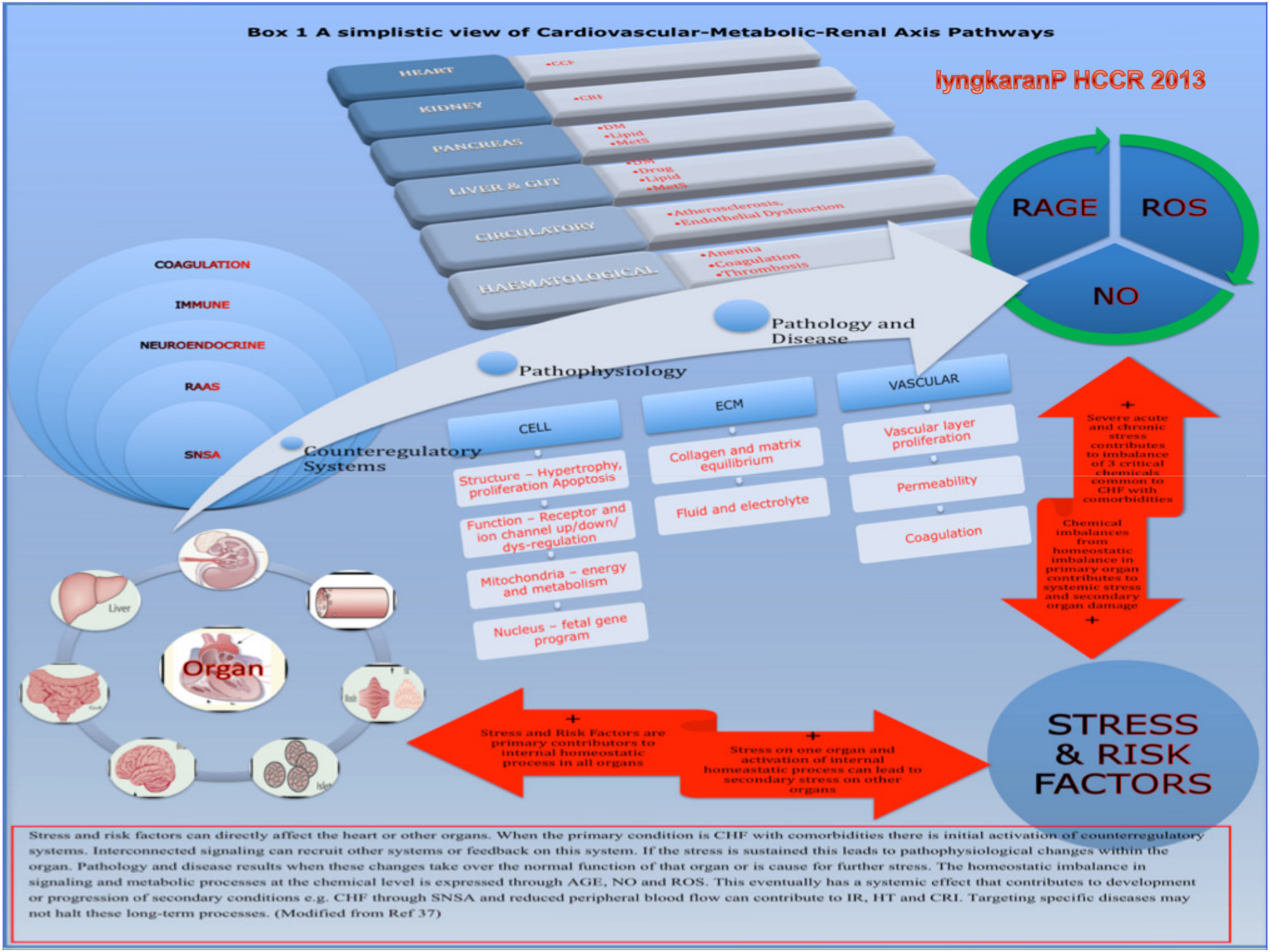
Client	LVEF	Comorbid Conditions	Smoking Alcohol Nutrition	Regime 1	Regime 2	Pill Burden/ Dosing Interval
55 yo Indigenous Male (Remote)	35%	DM HT Chol IHD OSA Obesity (BMI>35) CRF Stage 3-4 Sexual dysfunction Chronic cough	+ + -	Carvedilol 25bd Ramipril 10 od Frusemide 40 od Metformin 2 tds Amlodipine 5 od Aspirin 100 od Lipitor 80 od Viagra (PRN)	Nebivolol 10 od Telmisartan/Thiazide 40/25 od Frusemide 40 od Metformin 1gm XR od Omacor 1g od Coplavix 75/100 od Vytorin 10/40 od Viagra (PRN)	2 1 1 1 1 1 3 or 6 1 or 2 1 1 1 1 1 1 1 1 15/3 9/1
45 yo Indigenous Female (Remote)	45%	RHD HT OSA Obesity IGT Dilated LA (? PAF) CRF Stage 3	+ + -	Metoprolol 25bd Ramipril 10 od Thiazide 25 od Aspirin 100 od Lipitor 40 od	Nebivolol 5od Perindopril/Amlodipine 10/5 od Omacor 1g od Coplavix 100 od Vytorin 10/20 od	2 1 1 1 1 1 1 1 1 1 5/2 4/1
65 yo Caucasian Male (Urban)	30 %	HT Chol CRF Stage 2 Sexual dysfunction	- - +	Metoprolol 195 od Lipitor 80 od Ramipril 10 od Thiazide 25 od Spironolactone 25od	Carvedilol 25 bd or Nebivolol 10 od Lipitor 80od or Vytorin 10/40od Ramipril 10od + Thiazide 25 od or Perindopril/Amlodipine 10/5od Spironolactone or Aldactone 25/25od	1 2 or 1 1 1 1 2 or 1 1 1 1 4 /1 6 or 4/1



Stress and risk factors can directly affect the heart or other organs. When the primary condition is CHF with comorbidities there is initial activation of counterregulatory systems. Interconnected signaling can recruit other systems or feedback on this system. If the stress is sustained this leads to pathophysiological changes within the organ. Pathology and disease results when these changes take over the normal function of that organ or is cause for further stress. The homeostatic imbalance in signaling and metabolic processes at the chemical level is expressed through AGE, NO and ROS. This eventually has a systemic effect that contributes to development or progression of secondary conditions e.g. CHF through SNSA and reduced peripheral blood flow can contribute to IR, HT and CRI. Targeting specific diseases may not halt these long-term processes. (Modified from Ref 37)

Box 1 Study Design, Interpretations and Implications for Remote CHF Clients

Internal Validity

- Lack of blinding of recruiters and outcome assessment
- Scales used to measure outcomes
- Inadequate duration of treatment and follow-up
- Sample size

External Validity

- Setting of Trial
- Selection of Patients
- Characteristics of Randomized Patients
- Differences between trial protocol and routine practice
- Outcome measures and Follow-up
- Adverse effects of treatments

Barriers to Conducting Studies in NT

- Funding scarcity for audit and investigator initiated research
- Conflict of interest in freedom of design from pharmaceutical funding
- Lack of acknowledgement for observational studies

Limitations & Barriers

Internal Validity

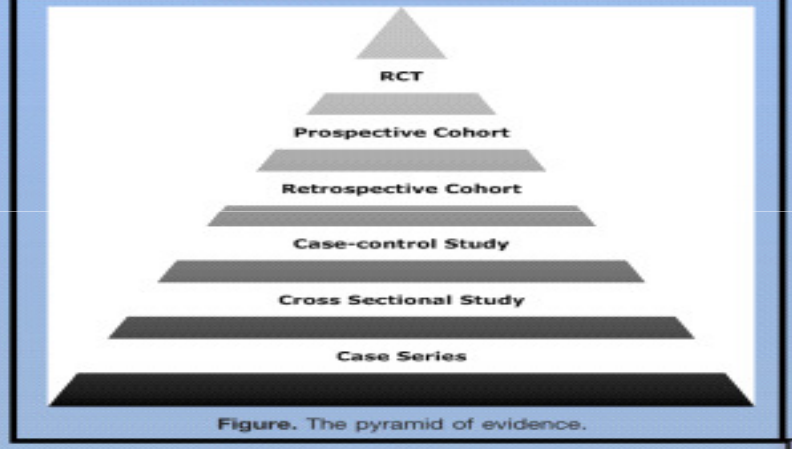


Figure. The pyramid of evidence.

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External Validity

Lesson on Interpretation

Key Terminology

- Target Population
- Eligibility Fraction
- Enrolment fraction
- Recruitment fraction
- Number of patients needed to be screened

Interpretation	
i) Is the Trial's design valid?	• Was randomization technique described adequately? • Were all enrolled patients accounted for? • Were patients, health and study staff blind to treatment? • Were the groups equally treated? • Were study outcomes appropriate?
ii) Is the analysis valid?	• Was primary analysis appropriate? • Was a power calculation performed?
iii) What are the results?	• How Large was the treatment effect? • How precise was the treatment effects?
iv) Will the results help care for my patients?	• Can the results be applied to my patient care? • Are the benefits worth the potential harms and costs?

Table 3. Therapeutics in HF and chronic renal failure

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Therapy	Number of studies including sub-studies	Number of participants	Number of trials with information on method of RF assessment					Age years	Race[a]	Sex[b]	CKD as exclusion criterion[c]	Contra-indication in CRF	AKI or ↑K+ as adverse event	Post hoc analysis
			SCr	BUN	MDRD	C-G	NA							
Beta-blockers	10	19,687	6	0	1	0	4	49–64	2 (5–23)	17–27	7 (SCr >245.5 to >300)	No	No	1 – SENIORS
ACE-I	7	14,810	5	0	1	0	1	59–75	1 (9.5–15)	18–57	7 (SCr >151 to >300)	Relative	Marginal	2 – SOLVD, ATLAS, CONSENSUS
ATRA	6	15,713	2	0	4	0	0	62–71	6 (1–7)	20–60	6 (SCr >177 to >220)	Relative	Marginal	2 – V-HEFT, CHARM
Aldosterone antagonist	2	7,895	1	0	1	0	0	65	2 (1–13)	27–30	2 (SCr >220)	Relative	Yes	1 – RALES
A-HEFT	1	1,050	NA					56	1 (100)	59	NA – prevalence RI 16–18	No	No	No
Inotropes[d]	2	1,530	2	1	0	0	0	67	1 (<6)	12–28	1 (SCr >450)	No	No	No
Device	10	10,306	4	2	0	0	4	63–67	2 (8–23)	8–27	1 (SCr >265)	No	No	1 – MADIT

	CHF	DHF	IHD	DM	Chol	CRF	Mood	Race	Additional properties	Combination Dose	Notes
ACE-inhibitor											
CaptoprilϒCaptopril	+	~	+	+	+	+	-	+	-	6.25-50tds NA	Some concern of ACE-I effect as a class on blacks due to baseline renin levels. Newer agents more costly.
Enalapril**	++	~	++	+	+	+	-	+	-	2.5-20bd C	
Lisinopril*	+	~	+	+	+	+	-	~	-	2.5-35od NA	
Ramipril**	++	~	++	+	+	+	-	+	-	2.5-10od/5bd C	
TrandolaprilϒTrandolapril	+	~	+	+	+	+	-	+	-	0.5-4od C	
Perindopril	~/+	~	+	+	+	+	-	+	-	1.25-10od CD	
Beta Blockers											
Carvedilol**	++	~/+	+	~/+	~/+	+	~	~	α1	3.125-25-50bd	Vasodilatory ββ are preferred in the MetS.
Bisoprolol	+	~	+	~	~	~	-/~	~	-	1.25-10 od	
Metoprolol XL	+	~	~/+	-/~	-/~	-/~	-/~	~	-	12.5-200od	
Nebivolol$	+	~/+	+	~/+	~/+	+	~	~	NO	1.25-10od	
ARB											
Candersartan**	++	~/+	+	+	+	+	-	+	-	4-32od D	Candersatan has strongest evidence. Telmisartan most potent 24 hr BP and prevention. Cost higher for newer agents.
Valsartan**	+	~	++	+	+	+	-	+	-	40-160bd D	
Losartan*$	+	~	+	+	+	+	-	~	-	50-150od NA	
Irbesartan	+	~	+	+	+	+	-	+	-	75-300od D	
Telmisartan	~/+	~/+	+	+	+	+	-	+	PPAR-γ activation	20-80od CD	
MRA											
Spironolactone	+	~/+	?	-/~	+	-	-	+	-	25-50od	Gynecomastia 10%
Eplerenone	+	~/+	+	~	+	-	-	+	Receptor specificity	25-50od	Cost; ADI more likely
OTHER AGENTS											
Co-plavix	++	N/A	++	+	+	+	N/A	+	Dual antiplatelet	75/100od	Mulitiinfarct dementia
Metformin XR	+	N/A	+	++	+	+	N/A	+	Once daily	500-2god	CRF, Severe HF CI
Omacor	~/+	?	+	~/+	~/+	~/+	~/+	+	Tryglyceride AF Inflammation	1god	Apart from GISSI most studies have been equivocal. External validity issues in RCT. Anti-inflammatory for arthritis. Cost. PBS unavailability.
Vytorin	+	N/A	+	+	+	+	N/A	+	Ezetemibe Bypass liver	10/10-10/80od	Pill size. Half statin dose for equal efficacy. Simvastatin 80 mg suicide, myopathy
Fluvastatin XR	+	N/A	+	+	+	~	N/A	+	Novel action XR reduces myopathy	20-80od	Low potency in LDL reduction at high doses.

DIAGNOSTICS

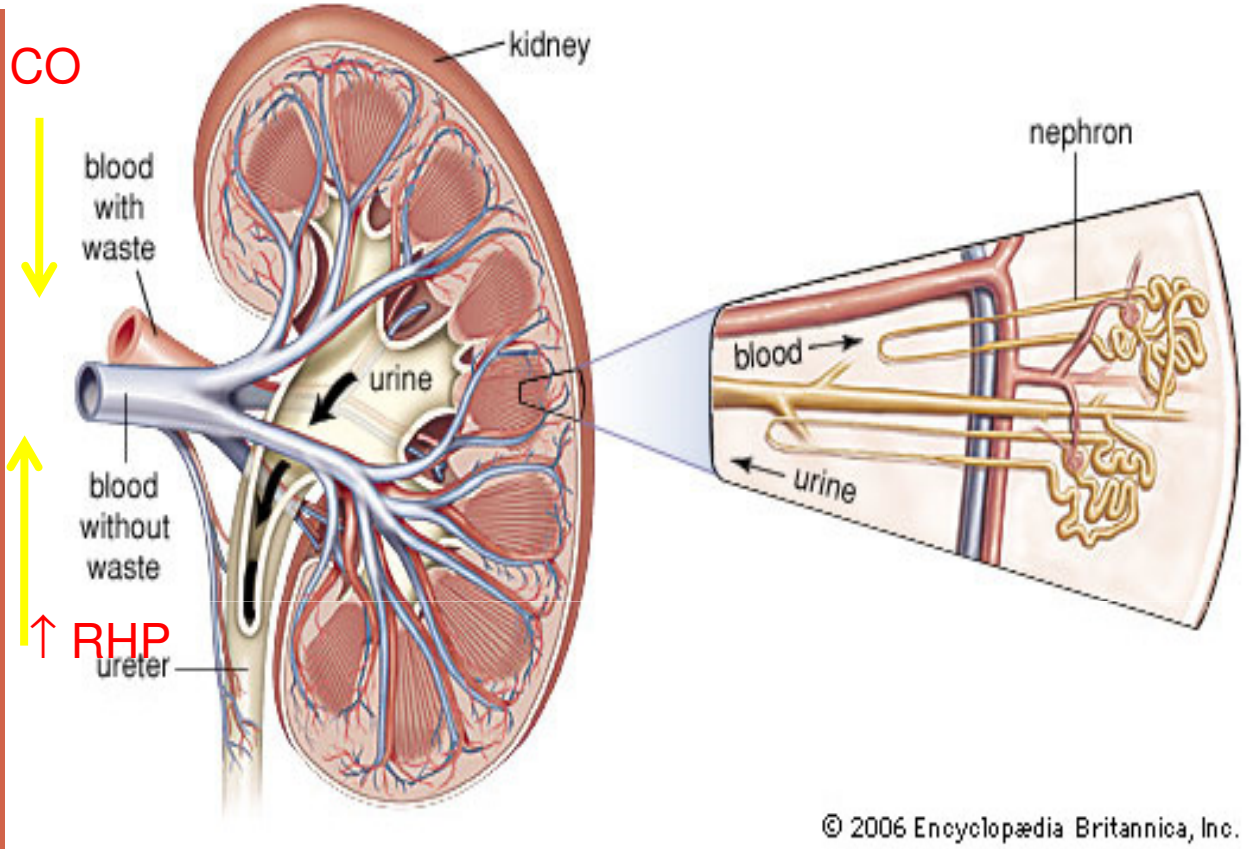
RENAL BLOOD AND PHYSIOLOGY

RBF is the single most important contributor of GFR

All nephrons contribute to total GFR via SNGFR

$SNGFR = k_f \times \Delta P$

Thus changes in afferent, intraglomeruli and efferent blood flow can alter GFR independent of CO



Biomarker	Source	Sample Source Blood Urine	Conditions CPB CN ICU/ Sepsis	Type AKI	Elevation
Creatinine	Amino acid derived from metabolism of muscle enzyme	√ √	ALL ↔ ↔	All	Young, male, body size, meat, drugs, exercise
Urea	Low molecular weight by-product of protein metabolism	√ √	ALL ↔ ↔	All	Dehydration, diet protein, illness, GIT bleed, drugs
NGAL	25KD Protein bound to gelatinase on neutrophils	√ √	2hr 2-4 48	Ischemic Cisplatin Septic	Inflammation Malignancy sepsis
KIM-1	Cell membrane glycoprotein in proximal tubule	× √	12-24 NT NT	Ischemic Prox tubule ATN	
IL-18	Pro inflammatory cytokine Distal tubule	× √	4-6 NT 48	Ischemic/ ATN	Inflammation
Cystatin-C	Extracelular cysteine protease inhibitor, nucleated cells, constant	√ ×	12 8 48		Sex, old age, smoker, inflamation, ↑ T4,

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HEART ATTACK*							KIDNEY ATTACK						
	Sym	Bio	EKG	Th	EF	MI		Sym	UO	SCr	Bio	RF	RI
STEMI	++	↑	↑	+++	↓↓	++	Clinical AKI with Kidney Dysfunction						
							➢ AKI KDIGO Stage 1	-	↓	↑	↑	↓	+
							➢ AKI KDIGO Stage 2	-	↓↓	↑↑	↑↑	↓	++
							➢ AKI KDIGO Stage 3	-	↓↓↓	↑↑↑	↑↑	↓	++
NSTEMI	++	↑	↓	++	N/↓	±	Subclinical AKI with damage biomarker positive but dysfunction biomarker negative						
							➢ Damage Biomarker Trend	-	N	±	↗	±	±
							➢ Damage Biomarker Rise	-	N/↓	±	↑	±	+
UNSTABLE ANGINA	+	-	±/↓	+	N/↓	-	Renal Angina Recognition of renal stressors (e.g. hypotension)	+	↓	N/↑	N	↓	-

- Standard definition for all spectrum of myocardial ischemia/threat or "Heart Attack" are well established[9-14]. With the advent of diagnostic tools predominately biomarkers the definitions of "Heart Attack" has also evolved[9]. Similarly with the kidneys, the advent of renal injury biomarkers call for a new paradigm in AKI or "Kidney Attack". The lack of symptoms and delays in conventional AKI markers highlight a greater impetus for this term "Kidney Attack" within such a framework as we have highlighted. It is also stressed that injury and function in the renal and cardiac sense or not synonymous. In addition physiological differences highlight that injury is not always associated with loss of function and vice versa. It is thus important we introduce the term "attack" to highlight a heightened risk that may not always be associated with early renal functional decline.
- Bio = cardiac or renal biomarkers; EF = ejection fraction , surrogate for cardiac function. EKG = electrocardiogra; MI = myocardial injury/infarction; N = Normal; RF = Renal Fucntion; RI = renal injury/infarction; ST segments; Th = Thrombus; Sym = symptom; UO = urine output; ↑ increased; ↓ = decreased; ↗ = Trend; + = positive; - negative; ± equivocal

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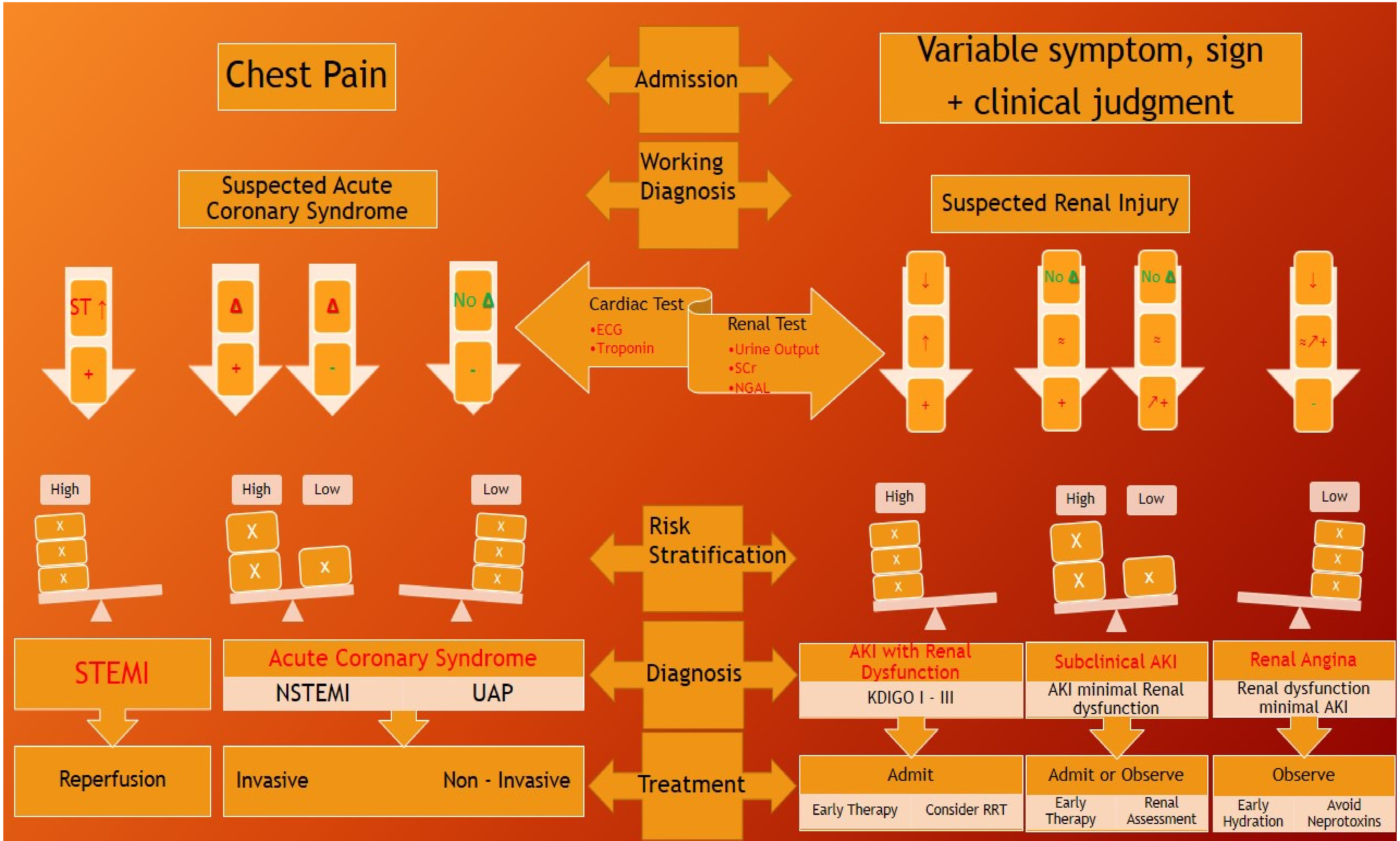

- Two clinical pathways are shown. Chest pain pathways are well established. Renal pathways are less well established. Urine output and SCr provide suurogate information on renal function. With the advent of AKI biomarkers, clinicians now have the ability to anticipate renal injury as early as 2 hours from the insult. With more specific and comprehensive renal injury and function information we also begin the paradigm of reclassification the spectrum of "acute kidney syndromes". We have chosen the term "Kidney Attack" as it highlights firstly the urgency involved and secondly there are correlations with the lessons learnt from the heart. We emphasize that the role of AKI biomarkers are still partly in the research domain, and so to our understanding of "*acute kidney syndromes*". As such the schema proposed, has a degree of conjecture, however we feel that significant impetus is needed to highlight the renal injury risk and as such the severity of the "Kidney Attack". We have chosen NGAL from the spectrum of renal biomarkers as it remains the most likely candidate for a "Renal Troponin". (Diagram and concepts modified from ref 14, 15)
- ***ABBREVIATIONS: AKI*** = acute kidney injury; ECG = electrocardiogram; EF = ejection fraction , surrogate for cardiac function. EKG = electrocardiogram; NGAL = neutrophil gelatinase associated lipocalin; NSTEMI = non ST elevation myocardial infarction; ST segments; STEMI = ST elevation myocardial infarction; Sym = symptom; UAP = unstable angina pectoris; UO = urine output;
- ***SYMBOLS:*** ↑ increased; ↓ = decreased; ↗ = Trend; + = positive; - negative; ± equivocal; Δ = changes; [illegible]

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CONCLUSION

- CARDIORENAL SYNDROME REMAINS A MAJOR ISSUE
- DIAGNOSTIC AND THERAPEUTIC MEASURES COULD MAKE SOME INROADS

THANK YOU