Pathophysiology of Cardio-Renal Interactions
Pathophysiology of Cardio-Renal Interactions

- Heart-Kidney Interactions:
  - Bidirectional
  - Temporally regulated
  - Mediated by different mechanisms
  - Different consequences in specific individuals
  - Functional vs structural damage
  - They may affect other organs

- Cardio Renal Syndrome and its consequences

- The importance of an early diagnosis
• Acute Kidney Injury leading to AHF
  • Volume/uremia-induced ADHF
  • Renal ischemia-induced ADHF
  • Sepsis/cytokine induced AKI and HF

• AdHF leading to AKI
• Cardiac Surgery
• Cardiac procedures
  • CIN
  • CPB
  • Valve replacement

• Chronic HF (systolic or diastolic) leading to :
  • CKD
  • CKD progression
  • Diuretic resistant oliguria

• CKD increasing cardiovascular mortality
• CKD increasing cardiovascular morbidity
• Chronic HF progression due to CKD
  • Uremia related HF
  • Volume related HF
Cardio-Renal Interactions
Basically a vicious circle

Primary Insult

ADHF - CHF

Physiological derangements

AKI - CKD

Renal dysfunction

Primary Insult

AKI - CKD

ADHF - CHF

Physiological derangements

Heart dysfunction
Heart-Kidney Interactions

- CKD secondary to chronic heart failure (HF)
- AKI secondary to coronary angiography contrast induced nephropathy (CIN)
- AKI secondary to cardiopulmonary bypass (CPB)
- AKI secondary to acute or acute on chronic heart failure

Cardiovascular mortality increased by end stage renal dysfunction (ESRD)
Cardiovascular risk increased by chronic kidney dysfunction
Chronic HF progression due to kidney dysfunction
  - Uremia related HF
  - Volume related HF
Acute HF due to acute kidney dysfunction
  - Volume/uremia-induced AHF
A widely accepted classification

Cardiorenal Syndrome

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Definition and classification of Cardio-Renal Syndromes: workgroup statements from the 7th ADQI Consensus Conference

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Cardio-renal syndromes: report from the consensus conference of the Acute Dialysis Quality Initiative

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The Cardiorenal Syndrome

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Cardio-Renal syndromes

General Definition:

*Pathophysiologic disorder of the heart and kidneys whereby acute or chronic dysfunction in one organ induces acute or chronic dysfunction in the other*

CRS Type I (Acute Cardiorenal Syndrome)

*Abrupt worsening of cardiac function leading to acute kidney injury*

CRS Type II (Chronic Cardiorenal Syndrome)

*Chronic abnormalities in cardiac function causing progressive and permanent chronic kidney disease*

CRS Type III (Acute Renocardiac Syndrome)

*Abrupt worsening of renal function causing acute cardiac disorders*

CRS Type IV (Chronic Renocardiac Syndrome)

*Chronic kidney disease contributing to decreased cardiac function, cardiac hypertrophy and/or increased risk of adverse cardiovascular events*

CRS Type V (Secondary Cardiorenal Syndrome)

*Systemic condition (e.g. diabetes mellitus, sepsis) causing both cardiac and renal dysfunction*
Markers of Function
- BUN, Creatinine, GFR/eGFR

Markers of Damage
- NGAL, Cystatin C, KIM 1

AKI
- CRS Type 1
- CRS Type 2

CKD
Cardio-Renal Syndrome Type 1

Hemodynamically mediated damage

Exogenous Factors
- Contrast media
- ACE inhibitors
- Diuretics

- Decreased CO
- Decreased perfusion
- Increased venous pressure
- Toxicity
- Vasoconstriction

Exogenous Factors
- RAA activation, Na + H2O retention, vasoconstriction

- Sympathetic Activation

- BNP

Hormonal factors

- Natriuresis
- Cytokine secretion

Immune mediated damage

- Caspase activation
- Apoptosis

Cytokine secretion

- Monocyte activation
- Endothelial activation

Acute Heart Disease

- Acute decompensation
- Ischemic insult
- Coronary angiography
- Cardiac surgery

Acute Kidney Injury

- Renal hypoperfusion
- Reduced oxygen delivery
- Necrosis / apoptosis
- Decreased GFR
- Resistance to ANP/BNP
• Upon initial recognition, AKI induced by primary cardiac dysfunction implies inadequate renal perfusion until proven otherwise. This should prompt clinicians to consider the diagnosis of a low cardiac output state (LCOS) and/or marked increase in venous pressure leading to kidney congestion.

• It is important to remember that central venous pressure translated to the renal veins is a product of right heart function, blood volume, and venous capacitance which is largely regulated by neuro-hormonal systems.

• Specific regulatory and counter-regulatory mechanisms are activated with variable effects depending on the duration and the intensity of the insult.
Cardio-Renal Syndrome Type 1

Hemodynamic mechanisms

- Increased preload
- Decreased cardiac output
- Venous congestion
- Arterial underfilling
- Vasocostriction
- Decreased perfusion pressure
- Functional (Pre-renal)
- A K I
- Parenchymal
- Increased venous pressure
- Compensatory mechanisms
- Vasodilatation
Cardio-Renal Syndrome Type 1
Compensatory mechanisms in HF

HF

Natriuresis
Afterload

Vasodilatation

Natriuretic Peptides
Chinin-kallicrein System
Prostaglandins
Endothelial Relaxin Factor

Vasocostriction

Sympathetic Nervous System
R-A-A System
Arginin Vasopressin
Endothelin

Compensatory Mechanisms

Water excretion
Sodium excretion
Urea readsorption

Water excretion
Sodium excretion
Urea readsorption

Natriuresis
Afterload
AVP in normal and failing heart

Normal Heart

Failing Heart

INCREASED ATRIAL PRESSURE

- Sympathetic tone decrease
- Vasodilat. RAA
- Non-osmotic AVP release
- \( V_1a \)-mediated vasocostriction
- Urea readsorption

- Water excretion
- Sodium excretion
OVERHYDRATION
Time windows for AKI management

- Fluids
- Drugs
- Diuretics
- Nephroprotection?
RIFLE max and AKI outcomes

Cumulative Survival

Non ARD
Risk
Injury
Failure

P<0.001 (Log Rank)

Days after hospital admission

The RIFLE criteria and mortality in acute kidney injury: A systematic review

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¹Department of Pediatric Cardiosurgery, Bambino Gesù Hospital, Rome, Italy; ²Department of Nephrology, Dialysis and Transplantation, S Bortolo Hospital, Vicenza, Italy and ³International Renal Research Institute Vicenza (IRRIV), Vicenza, Italy

Increase in All-Cause Mortality with worse RIFLE Class

N=71,527 patients
Biology of AKI by Time-Zones

Multiple Timezone Organ Damage Clock Display

Ischemia/reperfusion → Toxicity → Damage → Necrosis → Apoptosis → Cell death

↓ GFR

Delayed biomarkers for kidney injury

↑ Serum creatinine
↑ Blood urea nitrogen

The clinical clock is always late
BIOMARKERS

- Sensitive (early appearance)
- Easy to detect
- Specific (typical of organ injury)
- Correlate with severity (prognosis)
- Quantitatively describing the level of injury
- Capable to indicate treatment initiation and discontinuation
- Predicting organ recovery
- Predicting progression to CKD

Management of Cardio-Renal Syndromes
Structural AKI Biomarkers

• Early diagnosis of evolving AKI could result in prevention and/or earlier changes in management:
  – Prevention of disease progression either stopping harmful interventions or mitigating/avoiding exposure to the insult
  – Early therapeutic interventions designed to protect the kidney

• More accurate differential diagnosis of AKI could direct appropriate therapy of AKI (pre-renal vs renal)

• More accurate staging of AKI could help prognostic stratification and therapy of AKI
  – Serial staging of phases of AKI (evolution of the syndrome)
  – Assessment of current and future severity of injury
AKI Biomarkers

Mcllroy et al, Anesthesiology 2010; 112: 998-1004
Cardio-Renal Syndrome Type 1

- **Diuretics & UF**
  - Hemodynamically mediated damage
  - Decreased CO
  - Decreased perfusion
  - Increased venous pressure

- **Humorally mediated damage**
  - Sympathetic Activation
  - RAA activation, Na + H2O retention, vasoconstriction

- **Humoral signalling**
  - BNP
  - Caspase activation
  - Apoptosis
  - Monocyte Activation
  - Endothelial activation

- **Immune mediated damage**
  - Natriuresis
  - Cytokine secretion
  - Caspase activation
  - Apoptosis

- **Acute Heart Disease**

- **Acute Kidney Injury**
  - Renal hypoperfusion
  - Reduced oxygen delivery
  - Necrosis / apoptosis
  - Decreased GFR
  - Resistance to ANP/BNP

- **Hormonal factors**
  - Increased toxicity
  - Vascocostriction
Time Course of worsening of renal function (Creatinine increase) in hospitalized HF patients

Gotlieb et Al, JACC 2008
HF, Diuretics and NGAL

Stop Diuretics «5B»

NGAL Warning

Creatinine

Diuretics

Day 0 Day 1 Day 2 Day 3 Day 4 Day 5

NGAL BNP Diuresis
Blood Volume

Extracorporeal UF

Vascular Space

Interstitium

Osmolality

Transcellular water flux

Intravascular Refilling

Starling Forces
Cardiovascular Conditions

Blood Volume

Extracorporeal UF
Cardio-Renal Syndrome Type 1

Hemodynamically mediated damage

Decreased CO

Exogenous factors
Contrast media
ACE inhibitors
Diuretics

Increased venous pressure

Toxicity
Vasocostriction.

Humorally mediated damage

RAA activation, Na + H2O retention, vasoconstriction

Hormonal factors

BNP

Natriuresis

Immuno mediated damage

Humoral signalling

Caspase activation
Apoptosis

Monocyte Activation

Endothelial activation

Cytokine secretion

Inflammation

Acute Heart Disease

Acute Kidney Injury

Renal hypoperfusion
Reduced oxygen delivery
Necrosis / apoptosis
Decreased GFR
Resistance to ANP/BNP

Decreased perfusion

Sympathetic Activation

INFLAMMATION
Current issues in AKI management

- Repair and differentiation
- Apoptosis
- Inflammation
- ATP depletion
  - Cellular injury
- Hemodynamic

GFR

Prerenal  Initiation  Extension  Maintenance  Recovery

Days

0  2  4  6
APOPTOSIS STUDY IN CRS T.1 and CONTROLS

Evaluation of percentage of apoptosis in U937 cells after incubation with plasma from CRS Type 1 patients and healthy volunteers for 72h and 96h.
Cardio-Renal Syndrome Type 1
Inflammation/humoral theory

- Plasma
- Monocyte Cell Culture
- Supernatant
- RTC Culture
- Cytokines
- Apoptosis

Heart Failure Patient
Evaluation of percentage of apoptosis in U937 cells after incubation with plasma from Heart Failure Patients developing CRS Type 1 (HF/AKI) or not (HF/No AKI)
Cardio-Renal Syndrome Type 1

- Occurs in ~25% of unselected patients admitted with ADHF.
- Among these patients, pre-morbid CKD is common and predisposes to AKI in approximately 60% of cases.
- AKI is an independent risk factor for 1-year mortality in ADHF patients including in patients with ST-elevation myocardial infarction who develop signs and symptoms of heart failure or have a reduced left ventricular ejection fraction. This independent effect might be due to an associated acceleration in cardiovascular pathobiology due to kidney dysfunction through the activation of neurohormonal, cell signaling, oxidative stress, or exuberated repair (fibrosis) pathways.
Cardio-Renal Syndrome: possible pathophysiological mechanisms of AKI following HF

Hemodynamic deterioration (congestion, ↓CO, ↓ perfusion)

Hemodynamic deterioration

Myocardial damage injury

Renal dysfunction (AKI)

HF progression

Neurohormonal & cytokine activation

Gheorghiade M et al. Am J Cardiol. 2005
# Cardiorenal Syndrome

## Risk Factors

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P Value</th>
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<tr>
<td>Women</td>
<td>1.41</td>
<td>(1.12-1.77)</td>
<td>.003</td>
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<tr>
<td>HTN</td>
<td>1.64</td>
<td>(1.12-2.40)</td>
<td>.003</td>
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<tr>
<td>Rales&gt;Bases</td>
<td>1.28</td>
<td>(1.02-1.61)</td>
<td>.03</td>
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<tr>
<td>HR &gt;100 bpm</td>
<td>1.34</td>
<td>(1.06-1.68)</td>
<td>.01</td>
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<tr>
<td>SCr ≥1.5 mg/dL</td>
<td>1.77</td>
<td>(1.42-2.22)</td>
<td>&lt;.001</td>
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<tr>
<td>SBP &gt;200 mm Hg</td>
<td>1.63</td>
<td>(1.13-2.35)</td>
<td>.009</td>
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</table>

N=1,681

CARDIO-RENAL CACHEXIA SYNDROMES

**CRS TYPES 1-2**
- Low Cardiac output
- Na and fluid overload
- Chronic hypoperfusion
- Embolism
- Venous Congestion
- Chronic inflammation
- Cardiac Remodeling
- Endothelial Dysfunction
- Acceler. Atherosclerosis

**CRS TYPES 3-4**
- Na and fluid overload
- Chronic inflammation
- Uremic Toxins
- Malnutrition
- Anemia
- EPO resistance
- pH abnormalities
- Ca-P abnormalities
- Lack of VDR activation
- Soft Tissue calcifications

Non-oedematous weight loss of >6% of total body weight over a period of 6 or more months.

Malnutrition, loss of >10% of lean tissue or percent of ideal weight <90%.

CKD Progression, Apoptosis, Necrosis, Fibrosis, Sclerosis

Heart Failure, Systolic/diastolic dysfunction, Myoc.Remodelling
Cardio-Renal Syndrome

Anemia and Iron deficiency

AKI

↑ Arterial diameter and volume
↑ Arterial wall tension
Eccentric remodelling of the arterial system

CKD

↑ Left ventricle hypertrophy
↑ Left Ventricle wall tension
Left ventricle eccentric remodelling

Reduced Blood Viscosity
Decreased Oxygen Delivery
Increased Sympathetic Activity
Hyperdynamic circulation

Cardiac Work
Cardiac Output
Cardio-Renal Syndrome
CKD and UREMIA

Acquired Risk factors
Primary nephropathy

- Anemia
- Uremic toxins
- Ca/P abnormalities
- Nutritional status, BMI
- Na – H₂O overload
- Chronic Inflammation

Anemia & malnutrition
Ca/P abnormalities
Na – H₂O overload
Unfriendly milieu
Inflammation

Glomerular-interstitial damage

Sclerosis - Fibrosis
Cardio-Renal Syndrome
The unfriendly uremic milieu

Uremia retention products

↑ Insulin resistance
↓ Fetuin-A

↑ Acute phase reactants

↑ Adipocytokine production

↓ Appetite
↑ REE

↑ Endothelial dysfunction
↑ Monocyte adhesion
↑ Smooth muscle cell proliferation
↑ LDL oxidation
↑ Vascular calcification
↑ Oxidant stress

↑ Bone remodeling
↑ Muscle catabolism
Risk of Cardiorenal Syndrome by Number of Risk Factors

- ≤ 1: 16%
- 2: 24%
- 3: 29%
- 4: 38%
- ≥ 5: 53%

Chronic Cardio-Renal Syndrome (Type 2) a condition close to veterinary pathophysiology

Chronic Heart Disease
- Anemia
- Sodium and H2O retention
- Uremic solute retention
- Ca and P abnormalities
- Hypertension

Anemia, hypoxia
- RAA and sympathetic activation
- Na and H2O retention
- Ca and P abnormalities
- Hypertension, LVH

Low cardiac output (CO)
- Subclinical inflammation
- Endothelial dysfunction
- Accelerated atherosclerosis

Genetic risk factors
- Acquired Risk factors
- Low cardiac output (CO)

Insult and Initiation of kidney damage
- Increased susceptibility to insults
- Chronic hypoperfusion
- Apoptosis

Insult and Initiation of kidney damage
- Sclerosis - Fibrosis

Progression of CKD
- Anemia, hypoxia
- RAA and sympathetic activation
- Na and H2O retention
- Ca and P abnormalities
- Hypertension, LVH

Chronic hypoperfusion
- Increased renal vascular resistance
- Increased venous pressure
- Embolism
The Continuum of Renal Damage

Hypovolemic? (functional)  Renal (damage)  Renal (damage + functional)

Normal  ↑Risk  Damage  ↓GFR  Failure  Death
CRS Type II

• **Common scenario**: longstanding HF leading to progressive CKD (possibly via episodes of AKI)

• **Key concept**: management of sodium and extracellular fluid volume

• Therapies that influence the natural history of HF (effect on CRS?)
  – Optimal Na and volume management (diet control)
  – ACEI, ARB, BB, Aldo blockers, nitrates, hydralazine
  – Loop diuretics (lower doses have better outcomes)
  – Optimal hemodynamic control (avoid hyper- and hypotension)
  – Treatment of anemia and anemia-associated inflammation
  – Cardiac resynchronization mildly favorable

• Avoidance of added insults to HF and CKD
  – NSAIDS, Iodinated contrast, Other renal toxic agents
The burden of CHF

In the European Union diseases of the heart and circulatory system account for 4.3 million deaths a year. The major forms of cardiovascular death are attributable to coronary heart disease and stroke. The economic burden of cardiovascular disease (CVD) in the European Union (EU) in 2006 was 110 billion Euros. Furthermore, the production losses due to morbidity and mortality in the working age population amounted to just under 17 billion Euros.

An estimated 82.6 million Americans suffer from at least one form of cardiovascular disease. Of those, 5.7 million patients carry a diagnosis of heart failure (HF). Hospitalization for heart disease and acute myocardial infarction (AMI) are higher in males, while women are more commonly hospitalized for HF and stroke. The cost burden of CVD and CHF can be quite substantial, nearing $29 billion in 2004 for 1.1 million CHF hospitalizations.
Renal perfusion pressure is calculated by the equation *mean arterial pressure minus central venous pressure*. Decreases in left ventricular systolic or diastolic function, in HF, result in decreased cardiac output, stroke volume and underfilling of the arterial beds. In HF patients with volume overload, low systemic pressures combined with increased central venous or pulmonary artery pressures can lead to compromise of renal perfusion pressure. This decrease in renal perfusion, coupled with the underlying atherosclerotic changes due to comorbidities such as diabetes and hypertension in this particular population, can rapidly worsen any pre-existing renal dysfunction.
The overall decrease in arterial filling pressures causes release of neurotransmitters, including the RAA cascade and production of vasoconstrictors (epinephrine and endothelin). Vasoactive agents work to increase peripheral and renal vasoconstriction, leading to decreased RBF and GFR. The progressive results of this endogenous neurotransmitter-mediated vasoconstriction are renal hypoxia, cytokine release, inflammation, and over the long course eventual loss of structural integrity and function. Neurohormonal abnormalities are coupled with altered release of endogenous vasodilators like natriuretic peptide and nitric oxide. These processes lead to sodium and fluid retention, along with progressively diminishing renal function leading to irreversible kidney damage.
Water and salt retention. Effective circulating volume increases. Perfusion of the juxtaglomerular apparatus increases.

Decrease in renal perfusion (juxtaglomerular apparatus)

Angiotensinogen → Angiotensin I → Angiotensin II

Sympathetic activity

Tubular Na⁺ Cl⁻ reabsorption and K⁺ excretion. H₂O retention

Aldosterone secretion

Arteriolar vasoconstriction. Increase in blood pressure

ADH secretion

Collecting duct: H₂O absorption

Legend:
- Secretion from an organ
- Stimulatory signal
- Inhibitory signal
- Reaction
- Active transport
- Passive transport
Fluid Balance

**Daily fluid input:**
- 1.5-2.0 L maintenance
- 1.5-2.5 L medications
- 0.8-1.5 L nutrition
- 0.5-1.5 L boluses

**Daily fluid output:**
- 1.0-2.0 L Urine
- 1.0-2.0 L Insensible losses
- 1.0-3.0 L Dialysis/ UF
- 0.5-1.5 L Other

**Body Composition**

- **ECF (20%)**: Plasma volume (4-3%)
- **ICF (40%)**: Interstitial fluid (15-7%)
- **Minerals, protein, glycogen, fat (40%)**

Percentage of body weight vs. body weight range:

- 0: 20%
- 40%
- 60%
- 80%
- 100%
Fluid Balance

Risk of Complications

Restrictive Fluid protocols

- Dehydration
- Hypotension
- Tachycardia
- Shock
- Organ hypoperfusion
- Oliguria
- Renal Dysfunction

Liberal Fluid protocols

- Overhydration
- Hypertension
- Peripheral Edema
- Impaired pulmonary exchanges
- Organ Congestion
- Renal Dysfunction

Normal Heart

Diseased Heart

Optimal Status

Procedures

- Drugs

Dialysis
Acute Reno-Cardiac Syndrome (Type 3)

Acute Kidney Injury
- Glomerular diseases
- Interstitial diseases
- Acute tubular necrosis
- Acute pyelonephritis
- Acute urinary obstruction

Glomerular diseases
- Interstitial diseases
- Acute tubular necrosis
- Acute pyelonephritis
- Acute urinary obstruction

Hypertension
- Sympathetic Activation
- RAA activation, vasoconstriction
- Electrology, acid-base & coagulation imbalances

Humoral Signalling
- Caspase activation
- Apoptosis

Cytokine secretion
- Caspase activation
- Apoptosis

Monocyte Activation
- Endothelial activation

Electrolyte, acid-base & coagulation imbalances
- Volume expansion
- Increased pre-load

Na + H2O retention
- Decreased GFR

Acute decompensation
Acute heart failure
Ischemic insult
Arrythmias
Decreased CO

Acute Heart Dysfunction

BIOMARKERS
- Troponin
- Myoglobin
- MPO
- BNP
Community-based incidence rates of non-dialysis requiring AKI

> 60% increase from 1996 to 2003

Community-based incidence rates of dialysis requiring AKI


> 50% increase from 1996 to 2003

<table>
<thead>
<tr>
<th>Year Range</th>
<th>Number per 100,000 per years</th>
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<td>1996 – 1997</td>
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<tr>
<td>2000 – 2001</td>
<td>26.7</td>
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<tr>
<td>2002 – 2003</td>
<td>29.5</td>
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AKI is common in dogs too
Acute Renal Failure Represents an Independent Risk Factor

* Mortality of isolated ARF has decreased from 80% in 1974 to 9% in 2003

**Mortality In Acute Renal Failure**

Star RA; Kidney Int (1998); 54: 1817-1831
Acute Interactions

% Mortality

Number of failing organs

Kidney  K + 1  K + 2  K + 3
CRS Type III

• **Common scenario:** AKI leading to HF (probably in patients with an underlying subclinical heart disease), CSAAKI, Contrast-induced AKI leading to LV dysfunction

• **Key Concept:** Na and Water management (other signals such as uremia, cytokines, potassium?)

• Acute Na and volume imbalance (overload or underload)

• If Na and volume overload is avoided, will cardiac decompensation be eliminated?
  – Early intervention with hemofiltration, SCUF,—trials ongoing

• If early bidirectional signaling can be understood, can new preventive targets be developed?
  – ET receptor antagonists
  – Vasopressin receptor antagonists
  – Natriuretic peptides
  – Adenosine receptor antagonists

Disappointing in those without CKD
Chronic Reno-Cardiac Syndrome (Type 4)

CKD Stage 1-2
- Glomerular/interstitial damage

CKD Stage 3-4
- Sclerosis - Fibrosis
- Genetic risk factors
  - Acquired risk factors
  - Primary nephropathy
  - Diabetes mellitus
- Acquired risk factors
  - Smoking
  - Obesity
  - Hypertension
  - Dyslipidemia
  - Homocysteinemia
  - Chronic inflammation

CKD Stage 5- Dialysis
- Anemia & malnutrition
  - Ca/Phos abnormalities
  - Soft tissue calcification
  - Na – H2O overload
  - EPO resistance
  - Uremic toxins
- Artificial surfaces
  - Contaminated fluids
- Chronic Inflammation

Biomarkers
- Cardiac troponin
- Natriuretic peptides
- Asymmetric dimethylarginine
- Ischemia modified albumin
- Acute phase proteins
- Serum amyloid protein A
- C-reactive protein

Cardiac remodeling
- Neurohormonal abnormalities
- Increased ischemic risk
- Left ventricular hypertrophy
- Left diastolic dysfunction
- Decreased coronary perfusion
- Inflammation
- Coronary and tissue calcification

Endothelial dysfunction
- Smooth muscle proliferation
- LDL oxidation
- Vascular calcification
- Oxidant stress
- Accelerated atherosclerosis

Bone remodeling
- ↑ Muscle catabolism
- ↓ Appetite
- Acute phase reactants
- ↑ Adipocytokine production
- ↑ Insulin resistance
CHRONIC INFLAMMATION IN HEMODIALYSIS

Uremia

Comorbid State

Dialysate Purity

Membrane

Access & Procedure
Secondary Cardio-Renal Syndrome (Type 5)

Heart failure

Sympathetic system activation
Neurohumoral stress
Inflammation

Hemodynamic changes
Hypoperfusion
perfusion pressure ↓, RVR ↑
Hemichemia/ reperfusion

hypoxia
oxidative stress
toxemia

Exogenous toxins
heme proteins
antibiotics, contrast media

LPS / endotoxin
Monocyte activation
cytokines

Renal Insufficiency

Systemic diseases
Diabetes
Amyloidosis
Vasculitis
SEPSIS

Organ damage/dysfunction
CRS: Conclusions

- The cardiorenal syndrome is real and we have a new definition available
- There is insufficient awareness of its implications and of what we already know
- A tsunami of cardiorenal patients is coming
- We need to focus our clinical understanding, research agenda and education on how best to help these patients
- Different types of Cardio-Renal Syndrome exist
- The new classification will help consistency in prevention, diagnosis and treatment
- Cardio-Renal Syndrome Type 1 is a leading cause of AKI
- Biomarkers may represent a corner stone in the evaluation of these syndromes and in detecting early organ damage making possible prevention of disease progression