Cardiorenal Syndromes and their Relationship to Heart Failure

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Outline

- Heart and kidney disease trends
- Acute and chronic disease phenotypes
- Prognosis
- Intercurrent events
- Management
- Conclusions
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Deaths Due to Cardiovascular Disease

- 1958: Coronary arteriography developed (Sones)
- 1962: First beta-blocker developed (Black)
- 1969: First description of CABG (Favalaro)
- 1976: First HMG CoA reductase inhibitor described (Endo)
- 1980: First implantable cardioverter-defibrillator developed (Mirowski)
- 1985: TIMI 1
- 1979: Coronary angioplasty developed (Grüntzig)
- 1983: CASS
- 1985: NCEP
- 1986: GISSI and ISIS-2
- 1993: Superiority of primary PCI vs. fibrinolysis in acute MI noted
- 1992: SAVE
- 2002: ALLHAT
- 2002: Efficacy of drug-eluting vs. bare-metal stents determined
- 2007: Benefit of cardiac resynchronization therapy in heart failure demonstrated
- 2009: Genomewide association in early-onset MI described
- 2009: Deep gene sequencing for responsiveness to cardiovascular drugs performed
- 2009: Left-ventricular assist device as destination therapy in advanced heart failure shown to be effective
- 2009: KDIGO
Epidemiology of Heart Failure in the United States

- 5.0 million patients\(^1\); estimated 10 million in 2037\(^2\)
- Incidence: about 550,000 new cases each year\(^1\)
- Prevalence is 2% in persons aged 40 to 59 years, progressively increasing to 10% for those aged 70 years and older\(^3\)
- Sudden cardiac death is 6 to 9 times higher in the heart failure population\(^1\)

Trends in Death rates per 1000 pt yrs & Annual % Change 1996 to 2014
Projected dialysis population growth
2013 TO 2025

Dialysis 2013: 468,386
Dialysis 2025: 649,392

Projected Growth
2013 to 2025
181,006 (+38.6%)

Data source: USRDS 2015 ADR Reference table D.1; Projection simple auto regression with annual growth 2.5-3%
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# Five Cardiorenal Syndromes

<table>
<thead>
<tr>
<th>Cardiorenal Syndrome (CRS) General Definition:</th>
</tr>
</thead>
<tbody>
<tr>
<td>A pathophysiologic disorder of the heart and kidneys whereby acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRS Type I (Acute Cardiorenal Syndrome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrupt worsening of cardiac function (acutely decompensated congestive heart failure) leading to acute kidney injury</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRS Type II (Chronic Cardiorenal Syndrome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic abnormalities in cardiac function (chronic congestive heart failure) causing progressive and permanent chronic kidney disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRS Type III (Acute Renocardiac Syndrome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrupt worsening of renal function (acute kidney ischaemia or tubular injury) causing acute cardiac disorder (new or decompensated heart failure)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRS Type IV (Chronic Renocardiac Syndrome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic kidney disease (diabetic nephropathy) contributing to decreased cardiac function, cardiac hypertrophy and/or increased risk of adverse cardiovascular events</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CRS Type V (Secondary Cardiorenal Syndrome)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic condition (e.g. sepsis) causing both cardiac and renal dysfunction</td>
</tr>
</tbody>
</table>

Common Signs and Symptoms of Heart and Kidney Failure

- Fatigue
- Effort intolerance/weakness/inanition
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Dyspnea at rest and during exertion
- Jugular vein distention
- Peripheral pitting edema
- Sinus tachycardia
- Basal rales or coarse bubbling rales throughout both lung fields
- Cardiomegaly
- S3 gallop sound
- Liver enlargement

Proposal for a Functional Classification System of Heart Failure in Patients With End-Stage Renal Disease
Proceedings of the Acute Dialysis Quality Initiative (ADQI) XI Workgroup

Figure 1 ADQI Heart Failure in ESRD Classification System

Classification is determined by a dyspnea assessment before and after renal replacement therapy (RRT)/ultrafiltration (UF). When patients have the same class assessment before and after RRT/UF, they are scored by their post-treatment assessment. The classification scheme assumes that the class assignment represents the patient’s achievement of optimized UF and is representative of the patient’s usual level of dyspnea before and after RRT/UF. *If dyspnea symptoms improve to class II levels, the patient would be classified as class 3R. ADQI = Acute Dialysis Quality Initiative; ESRD = end-stage renal disease; NYHA = New York Heart Association.
Etiology of Chronic Kidney Disease

Causes of Chronic Kidney Disease:

- Type 2 diabetes: 42%
- High blood pressure: 28%
- Glomerular diseases: 6%
- Miscellaneous: 6%
- Unknown: 4%
- Type 1 diabetes: 4%
- Cystic/Hereditary: 3%
- Nephritis: 3%
- Tumors: 3%
Physicians and Nephrologists in CKD

- Grade I: Structural damage, normal function
- Grade II: Structural damage, impaired function
- Grade III: Moderately impaired function
- Grade IV: Severely impaired function

At increased risk

Primary Health Provider

Nephrologist

eGFR, ml/min/1.73 sqm
Heart Failure Phenotypes

All Heart Failure

- LVEF
- LV Chamber size
- LVH
- Other chambers
- Valve function
- Estimate PA pressure
- Diastolic FXN
  - ASE Gr 1
  - ASE Gr 2
  - ASE Gr 3
  - ASE Gr 4
  - Strain/strain rate

50% Reduced LVEF
Systolic Dysfunction
LVEF<45%

50% Preserved LVEF
Diastolic Dysfunction
LVEF>45%

67% Ischemic Etiology
33% Non-ischemic Etiology

50% No Ischemia
50% Ischemic Contribution but ??? importance
CENTRAL ILLUSTRATION  Mode of Death Distribution in HFrEF and HFpEF

**HFrEF**

- Cardiovascular (80%-85%)
  - Worsening HF
  - Cardiogenic Shock
  - Low Output State
  - Sudden Cardiac Death
  - Ventricular Tachyarrhythmia +++
  - Bradyarrhythmia +

- Other Cardiovascular or Noncardiovascular (15%-20%)

**HFpEF**

- Cardiovascular
  - Worsening HF
  - Restrictive Cardiomyopathy
  - Right Heart Failure
  - Sudden Death
  - Nonarrhythmic Sudden Death
  - Tachyarrhythmia
  - Bradyarrhythmia
  - Myocardial Infarction
  - Vascular
    - Aortic Aneurysm
    - Pulmonary Embolism
  - Cerebrovascular
    - Intracranial Hemorrhage
    - Ischemic Stroke

- Noncardiovascular
  - Renal
    - End-stage Renal Disease
    - Renal Venous Congestion
  - Respiratory
    - Respiratory Failure
    - Pulmonary Hypertension
    - Chronic Obstructive Pulmonary Disease
  - Infection/Sepsis
  - Malignancy

- Multisystem Disease
  - Multisystem Organ Failure

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- Prognosis
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- Conclusions
Confirmation of a Heart Failure Epidemic: Findings From the Resource Utilization Among Congestive Heart Failure (REACH) Study

Peter A. McCullough, MD, MPH, FACC, FACP,* Edward F. Philbin, MD, FACC,† John A. Spertus, MD, MPH, FACC,‡ Scott Kaatz, DO, FACP,§ Keisha R. Sandberg, BS,|| W. Douglas Weaver, MD, FACC||

Kansas City, Missouri; Albany, New York; and Detroit, Michigan
10-year CHD Mortality
A Continuum in Risk

Per 1000 Person-Years

- Actual with 3 RF's: 10.2
- Framingham Predicted in CRD: 25
- DM + Micro-Albuninuria: 58.3
- DM + Gross Proteinuria: 85.5
- Actual USRDS: 107

Chicago Heart Detection Project, Arch Int Med, 1998
ACC/AHA Scientific Statement, Grundy et al, Circulation, 1999
USRDS, Am J Kid Dis 1998

FIGURE 88-3 Relative risks of heart and kidney outcomes in cohorts where eGFR and ACR were measured.

### Summary of Relative Risks from Categorical Meta-Analysis (dipstick included [-, ±, +, ++])

<table>
<thead>
<tr>
<th>Kidney Failure (ESRD)</th>
<th>All-Cause Mortality</th>
<th>Cardiovascular Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACR &lt;10</td>
<td>ACR 10-29</td>
</tr>
<tr>
<td>eGFR &gt;105</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>eGFR 90-105</td>
<td>Ref</td>
<td>11</td>
</tr>
<tr>
<td>eGFR 75-90</td>
<td>Ref</td>
<td>3.8</td>
</tr>
<tr>
<td>eGFR 60-75</td>
<td>Ref</td>
<td>7.4</td>
</tr>
<tr>
<td>eGFR 45-60</td>
<td>5.2</td>
<td>22</td>
</tr>
<tr>
<td>eGFR 30-45</td>
<td>56</td>
<td>74</td>
</tr>
<tr>
<td>eGFR 15-30</td>
<td>433</td>
<td>1044</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Acute Kidney Injury (AKI)</th>
<th>ACR &lt;10</th>
<th>ACR 10-29</th>
<th>ACR 30-299</th>
<th>ACR ≥300</th>
<th>ACR &lt;10</th>
<th>ACR 10-29</th>
<th>ACR 30-299</th>
<th>ACR ≥300</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR &gt;105</td>
<td>Ref</td>
<td>Ref</td>
<td>2.7</td>
<td>8.4</td>
<td>Ref</td>
<td>Ref</td>
<td>0.4</td>
<td>3.0</td>
</tr>
<tr>
<td>eGFR 90-105</td>
<td>Ref</td>
<td>2.4</td>
<td>5.8</td>
<td></td>
<td>Ref</td>
<td>Ref</td>
<td>0.9</td>
<td>3.3</td>
</tr>
<tr>
<td>eGFR 75-90</td>
<td>Ref</td>
<td>3.3</td>
<td>6.4</td>
<td></td>
<td>Ref</td>
<td>Ref</td>
<td>1.9</td>
<td>5.0</td>
</tr>
<tr>
<td>eGFR 60-75</td>
<td>3.1</td>
<td>4.0</td>
<td>9.4</td>
<td>67</td>
<td>Ref</td>
<td>Ref</td>
<td>3.2</td>
<td>8.1</td>
</tr>
<tr>
<td>eGFR 45-60</td>
<td>3.0</td>
<td>19</td>
<td>15</td>
<td>22</td>
<td>Ref</td>
<td>Ref</td>
<td>4.0</td>
<td>12</td>
</tr>
<tr>
<td>eGFR 30-45</td>
<td>17</td>
<td>17</td>
<td>21</td>
<td>29</td>
<td>Ref</td>
<td>Ref</td>
<td>4.0</td>
<td>12</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Progressive CKD</th>
<th>ACR &lt;10</th>
<th>ACR 10-29</th>
<th>ACR 30-299</th>
<th>ACR ≥300</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR &gt;105</td>
<td>Ref</td>
<td>Ref</td>
<td>0.4</td>
<td>3.0</td>
</tr>
<tr>
<td>eGFR 90-105</td>
<td>Ref</td>
<td>Ref</td>
<td>0.9</td>
<td>3.3</td>
</tr>
<tr>
<td>eGFR 75-90</td>
<td>Ref</td>
<td>Ref</td>
<td>1.9</td>
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<td>9.4</td>
<td>67</td>
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<tr>
<td>eGFR 45-60</td>
<td>3.0</td>
<td>19</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>eGFR 30-45</td>
<td>17</td>
<td>17</td>
<td>21</td>
<td>29</td>
</tr>
<tr>
<td>eGFR 15-30</td>
<td>4.0</td>
<td>12</td>
<td>21</td>
<td>7.7</td>
</tr>
</tbody>
</table>

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Proportion of AKI Cases

- Primary Care
- Outpatient Procedures
- Inpatient

Among 11,683 qualifying AKI hospitalizations, 2954 patients (25%) were hospitalized with recurrent AKI within 12 months of discharge. Median time to recurrent AKI was 64 days.
Combined Angiotensin Inhibition for the Treatment of Diabetic Nephropathy

A. Acute Kidney Injury

Percent of Patients (95% CI)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Percent (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Losartan + Placebo</td>
<td>5.2 (3.8–7.2)</td>
<td></td>
</tr>
<tr>
<td>Losartan + Lisinopril</td>
<td>11.2 (8.8–14.1)</td>
<td>15.4 (12.4–19.1)</td>
</tr>
<tr>
<td>Losartan + Placebo</td>
<td>16.6 (13.8–20.0)</td>
<td>23.7 (20.0–28.0)</td>
</tr>
<tr>
<td>Losartan + Lisinopril</td>
<td>40.8 (28.2–56.4)</td>
<td></td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Months since Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Losartan + Placebo</td>
<td>724</td>
</tr>
<tr>
<td>Losartan + Lisinopril</td>
<td>724</td>
</tr>
</tbody>
</table>
Combined Angiotensin Inhibition for the Treatment of Diabetic Nephropathy

K > 6.0 mEq/L that required ED visit or hospitalization
Severe Hyperkalemia (≥6.5 mEq/L)

- 36% on chronic ACE, ARB, or MRA
- 22% had AKI with baseline normal eGFR
- 52% had AKI superimposed on CKD
- 20% presented with cardiac arrest
- 31% in-hospital mortality

Acute kidney injury (AKI) in patients with normal baseline renal function was a strong predictor of mortality, compared with AKI superimposed on CKD.

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical ward</td>
<td>244 (44.0)</td>
</tr>
<tr>
<td>Emergency room</td>
<td>28 (5.1)</td>
</tr>
<tr>
<td>Multi-organ failure at admission</td>
<td>108 (11.7)</td>
</tr>
<tr>
<td>Multi-organ failure at the time of diagnosis</td>
<td>226 (24.5)</td>
</tr>
<tr>
<td>Diagnosis at the time of cardiac arrest</td>
<td>187 (20.3)</td>
</tr>
<tr>
<td>Symptoms pertinent to hyperkalemia</td>
<td>432 (46.8)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>187 (43.3)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>152 (35.2)</td>
</tr>
</tbody>
</table>
Cardio-Pulmonary-Renal Interactions
A Multidisciplinary Approach

Faeq Husain-Syed, MD,*† Peter A. McCullough, MD, MPH,*‡ Horst-Walter Birk, MD,‡ Matthias Renker, MD,‡ Alessandra Brocca, MSc,* Werner Seeger, MD,† Claudio Ronco, MD*
**Increased FGF23 levels**

**Klotho-dependent effects**
- Stimulation of phosphate excretion and inhibition of 1α-hydroxylase

**Klotho-independent effects**
- Inhibition of PTH secretion
- Induction of hypertrophy of cardiomyocytes

**Decreased Klotho-FGFR1 expression**

**Nonfunctioning kidney**

**Hyperplastic parathyroid gland**

**Left ventricular hypertrophy**
Diabetes
Obesity
Metabolic syndrome
Smoking
Genetic predisposition
Increasing age
Acute injury

Chronic Kidney Disease

Genetics

Mediators
- Inflammation
  - CD8+ cells
  - TNFα, IL-1β, IL-8
- Endothelial dysfunction
  - Uric acid
  - L-arginine synthesis
  - NO signalling
  - Renin-angiotensin-system
  - ox-LDL
- Redox perturbations
  - ROS, RNS
  - Antioxidant enzyme activity
  - Mitochondria
  - Nrf2/keap1/ARB pathway

Cardiovascular Disease
Outline

- Heart and kidney disease trends
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Loop diuretics in acute heart failure: beyond the decongestive relief for the kidney

Alberto Palazzuoli¹, Gaetano Ruocco¹, Claudio Ronco² and Peter A. McCullough³

**Fig. 3** Strategy for loop diuretic therapy optimization looking for renal dysfunction fluid accumulation and hemodynamic status. AKI acute kidney injury
## Reduced GFR:

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Potential solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal glomerular hemodynamics</td>
<td>Discontinue NSAIDs, consider holding ACEI/ARB</td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>Hemodynamic support</td>
</tr>
<tr>
<td>Chronic kidney disease or functional renal hypoperfusion</td>
<td></td>
</tr>
</tbody>
</table>

## Proximal Tubule Hyperfiltration

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Potential solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuro-hormonal activation</td>
<td>Excessive aldosterone- mediated sodium retention</td>
</tr>
<tr>
<td>Sodium-avid states</td>
<td>Excessive vasopressin-mediated water retention</td>
</tr>
<tr>
<td>Excessive daily sodium intake</td>
<td>Loop diuretics</td>
</tr>
</tbody>
</table>

## Distal Tubule Hypertrophy

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Potential solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebound sodium retention</td>
<td>Sequential nephron blockade (Combination diuretic therapy)</td>
</tr>
</tbody>
</table>

### Diuretic Strategy

**Unguided (inpatient bolus/infusion):** No improvement in outcomes

- Dose HF Trial
- ROSE HF Trial
- DIUR-HF Trial

**Guided (clinic, oral):**

- Biomarkers
- PA pressure → Reduced hospitalization/death

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6 Biomarker Trials Felker 2009
CHAMPION Trial PA Pressure monitor 2011

---

JACC Vol. 56, No. 19, 2010
CHAMPION Trial PA Pressure monitor 2011

November 2, 2010:1527-34
Dialysis Induced Stress on the Heart: Myocardial “Stunning”

Effective fluid management holds the promise of better cardiovascular outcomes.

EFFECTIVENESS VARIES BY MODALITY: LOWER FLOW RATES, LONGER TIMES, MORE FREQUENT RUNS → LESS STUNNING

- CARDIOMYOPATHY
- CARDIOVASCULAR RELATED DEATH
  - Pump Failure
  - Arrhythmic Sudden Death

VOLUME OVERLOAD
PRESSURE OVERLOAD
INTRADIALYTIC MYOCARDIAL STUNNING
Ultrafiltration in Decompensated Heart Failure with Cardiorenal Syndrome

Bradley A. Bart, M.D., Steven R. Goldsmith, M.D., Kerry L. Lee, Ph.D., Michael M. Givertz, M.D., Christopher M. O’Connor, M.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Anita Deswal, M.D., M.P.H., Jean L. Rouleau, M.D., Martin M. LeWinter, M.D., Elizabeth O. Ofili, M.D., M.P.H., Lynne W. Stevenson, M.D., Marc J. Semigran, M.D., G. Michael Felker, M.D., Horng H. Chen, M.D., Adrian F. Hernandez, M.D., Kevin J. Anstrom, Ph.D., Steven E. McNulty, M.S., Eric J. Velazquez, M.D., Jenny C. Ibarra, R.N., M.S.N., Alice M. Mascette, M.D., and Eugene Braunwald, M.D., for the Heart Failure Clinical Research Network
Compelling Evidence for End Organ Benefit

Role of Angiotensin II in the Progression of Cardiovascular Disease

- Brain
  - Atherosclerosis
  - Vasoconstriction
  - Vascular inflammation and hypertrophy
  - Endothelial dysfunction

- Vessels
  - Stroke
  - Hypertension

- Heart
  - Left ventricular hypertrophy
  - Fibrosis
  - Remodeling
  - Apoptosis
  - \( \uparrow \) Glomerular capillary pressure
  - \( \uparrow \) Proteinuria
  - \( \uparrow \) Aldosterone release
  - Glomerular sclerosis
  - Renal Fibrosis

- Kidney
  - Progression of Heart Failure
  - Progression of CKD

- Death

Effects of withdrawing vs continuing renin-angiotensin blockers on incidence of acute kidney injury in patients with renal insufficiency undergoing cardiac catheterization: Results from the Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker and Contrast Induced Nephropathy in Patients Receiving Cardiac Catheterization (CAPTAIN) trial

Kevin R. Rainey, MD, MSc, Sherali Rahim, MD, Krystal Etherington, BSc, Michael L. Rokoss, MD, Madhu K. Natarajan, MD, MSc, James L. Vellianou, MD, Sonya Brons, RN, and Shamie B. Mehta, MD, MSc, for the CAPTAIN Investigators Alberta, and Ontario, Canada

Figure 1

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Event Rate (%)</th>
<th>Risk Ratio (95% CI)</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>16.4</td>
<td>0.59 (0.30, 1.19)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>&lt;65 Yr</td>
<td>18.2</td>
<td>0.61 (0.12, 2.98)</td>
<td>0.61 (0.12, 2.98)</td>
</tr>
<tr>
<td></td>
<td>&gt;=65 Yr</td>
<td>16.4</td>
<td>0.58 (0.27, 1.20)</td>
<td>0.58 (0.27, 1.20)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>22.0</td>
<td>0.59 (0.26, 1.37)</td>
<td>0.59 (0.26, 1.37)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>12.2</td>
<td>0.67 (0.19, 2.33)</td>
<td>0.67 (0.19, 2.33)</td>
</tr>
<tr>
<td>Mehran risk</td>
<td>0-5</td>
<td>10.6</td>
<td>0.45 (0.04, 4.80)</td>
<td></td>
</tr>
<tr>
<td>score</td>
<td>6-10</td>
<td>19.4</td>
<td>0.60 (0.10, 1.33)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;10</td>
<td>21.7</td>
<td>0.81 (0.33, 2.02)</td>
<td></td>
</tr>
</tbody>
</table>

Risk ratios for the primary end point in prespecified subgroups.
RAASi: Benefit to Risk Balance

Renal Function Stable
Compelling Indication for RAASi
- Post-MI low LVEF or HF
- Progressive HF
- Progressive CKD with proteinuria

Renal Function Unstable
Risk ↑ AKI, Risk ↑ K
Less compelling Indication for RAASi
- HTN
- ASCVD
- Stage 5 CKD

Full Court Press
- Monitor carefully
- Look forward to new agents for potassium control

Select Away from RAASi
- Still have to monitor carefully
- Use fall back drugs with less efficacy
- Expect poor outcomes
<table>
<thead>
<tr>
<th></th>
<th>Heart Failure with Preserved Ejection Fraction (HFP EF)</th>
<th>Heart Failure with Reduced Ejection Fraction (HFr EF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dialysis CKD</td>
<td>Working Group #1</td>
<td>Working Group #2</td>
</tr>
<tr>
<td>Dialysis CKD</td>
<td>Working Group #3</td>
<td>Working Group #4</td>
</tr>
<tr>
<td>Kidney Transplant Patients</td>
<td></td>
<td>Working Group #5</td>
</tr>
</tbody>
</table>
Outline

- Heart and kidney disease trends
- Acute and chronic disease phenotypes
- Prognosis
- Intercurrent events
- Management
- Conclusions
Conclusions

- Both HF and CKD/ESRD prevalence pools will dramatically rise in the years to come
- Both heart and kidney disease phenotypes are important
- Prognosis is impacted by intercurrent events
- Pathophysiological targets include conventionally assessed parameters such as volume status, but also many novel ones
- KDIGO Controversies methods aim to bring bright minds together to consider evidence and arrive at conclusions and help identify gaps in knowledge for future research