Management of CKD and Complications in Primary Care

Denise K Link, MPAS, PA-C
The University of Texas Southwestern Medical Center
American Academy of Nephrology PAs
National Kidney Foundation Council of Advanced Practitioners
American Academy PA liaison to Renal Physicians Association and American Society of Nephrology
Denise.Link@utsouthwestern.edu

Nothing to Disclose
Objectives

• Recognize treatment goals for preventing the progression of CKD toward ESRD by lowering blood pressure and proteinuria to current guidelines through dietary changes and initiating RAAS blockade medication(s)

• Interpret the most recent guidelines for blood pressure of CKD patients, goals for DM with CKD, treatments for CKD with and without proteinuria, age of a CKD patient, and co-morbidities of CKD

• Discuss how to manage the complications associated with the treatment of CKD, including hyperkalemia, fluid overload, metabolic acidosis and proteinuria
ARS #1

Which patient has a worse prognosis for CKD progression to ESRD?

a) 75yo HTN eGFR 40ml/min, UACR 150mg/g
b) 22yo SLE eGFR 80ml/min, UACR 3000mg/g
c) 35yo ADPKD eGFR 65ml/min, UACR 100mg/g
d) 55yo T2DM eGFR 50ml/min, UACR 1500mg/g
ARS #2

45yo obese, T2DM, DLD, CAD, HTN, hyperuricemia, CKD presents with worsening of renal function. SCr increased to 2.0mg/dl. eGFR decreased from 58 to 42ml/min. UACR 2000mg/g. A1C 8.5%. You would ______ and refer to endocrinology.

a) Continue metformin 1000mg BID
b) Decrease metformin 500mg BID
c) Discontinue metformin
ARS #3

65yo male with T2DM, uncontrolled HTN and CKD presents with BP 175/60, P80, BMI 35. Scr 2.4 mg/dl, eGFR 32ml/min, K 4.8 mEq/L A1 c 9.8%, UACR 2,550 mg/g Meds: Metoprolol XL 50mg daily, HCTZ 25mg daily and insulin

- What blood pressure medication change(s) would you initially make to achieve optimal BP goal to <130/80?
  a) Discontinue HCTZ and start furosemide
  b) Increase metoprolol based on HR
  c) Start ACEI or ARB
  d) All of the above. Is this a trick question?
Numerous, sometimes conflicting CKD guidelines → challenges providing appropriate care

**Making Sense of CKD**

- Designed to help PCPs manage adult CKD patients
- Emphasizes key considerations for evaluating and managing CKD patients:
  - Identifying patients at highest risk for progression to kidney failure
  - Slowing progression among these high-risk patients
- Highlights useful resources:
  - Patient education materials
  - Clinical tools
  - Professional reference materials
Role of PCP in CKD Management

Nephrology workforce (n=7020) insufficient
PCPs care for majority of patients with CKD providing opportunities for:

• Identification of patients at risk for CKD
• Early recognition of CKD and its severity
• Identification and management of CKD risks
• Engagement of patients in risk factor modification
• Timely referral to nephrology and effective care coordination

“The better the primary care, the greater the cost savings, the better the health outcomes, and the greater the reduction in health and health care disparities”  Barbara Starfield, MD, MPH
TRANSFORMING Healthcare in Texas

SEPTMBER 7-10, 2017
HILTON AUSTIN | AUSTIN, TEXAS
Public Health Burden of ESRD

• Over 600,000 US adults have ESRD

• Cost of treatment:
  - $75,000 per person/year
  - ESRD cost takes up 6% of Medicare budget despite making up 1% of Medicare population

• Associated with poor survival and quality of life

USRDS 2013 /14 Annual Data Report
Public Health Burden of CKD

• Average estimated all-cause cost per patent in 2016: Comparing standard of care with RAAS in those without CKD to those with CKD. 93,912 <65yo and 81,829 >65yo

<table>
<thead>
<tr>
<th></th>
<th>Commercial Insurance</th>
<th>Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>No CKD</td>
<td>$7500</td>
<td>$8100</td>
</tr>
<tr>
<td>Stage 3a CKD (GFR 45-59ml/min)</td>
<td><strong>$27,200</strong></td>
<td>$20,500</td>
</tr>
<tr>
<td>Stage 4-5 CKD GFR (0-29ml/min)</td>
<td><strong>$77,000</strong></td>
<td>$46,100</td>
</tr>
</tbody>
</table>

• New research shows that the all-cause costs to Medicare and private insurers for treating CKD patients rapidly increase as the disease progresses.

Prevalence of CKD in the US by GFR Stage
Cross-Sectional Data (NHANES III)

CKD Stage: eGFR (mL/min)

<table>
<thead>
<tr>
<th>Stage</th>
<th>eGFR Range</th>
<th>Number of People (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥90</td>
<td>5.9</td>
</tr>
<tr>
<td>2</td>
<td>60-89</td>
<td>5.3</td>
</tr>
<tr>
<td>3</td>
<td>30-59</td>
<td>7.6</td>
</tr>
<tr>
<td>4</td>
<td>15-29</td>
<td>0.4</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>0.3</td>
</tr>
</tbody>
</table>

CV death?

CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate.

Public Health Burden of CKD Associated with Poor Clinical Outcomes

1,120,295 Ambulatory Adults

Death

<table>
<thead>
<tr>
<th>Estimated GFR (ml/min/1.73 m²)</th>
<th>No. of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60</td>
<td>25,803</td>
</tr>
<tr>
<td>45-59</td>
<td>11,569</td>
</tr>
<tr>
<td>30-44</td>
<td>7,802</td>
</tr>
<tr>
<td>15-29</td>
<td>4,408</td>
</tr>
<tr>
<td>&lt;15</td>
<td>1,842</td>
</tr>
</tbody>
</table>

Rate of Death from Any Cause (per 100 person-yr)

CV Events

<table>
<thead>
<tr>
<th>Estimated GFR (ml/min/1.73 m²)</th>
<th>No. of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60</td>
<td>73,108</td>
</tr>
<tr>
<td>45-59</td>
<td>34,690</td>
</tr>
<tr>
<td>30-44</td>
<td>18,580</td>
</tr>
<tr>
<td>15-29</td>
<td>8,809</td>
</tr>
<tr>
<td>&lt;15</td>
<td>3,824</td>
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</table>

Rate of Cardiovascular Events (per 100 person-yr)

Hospitalization

<table>
<thead>
<tr>
<th>Estimated GFR (ml/min/1.73 m²)</th>
<th>No. of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥60</td>
<td>366,757</td>
</tr>
<tr>
<td>45-59</td>
<td>106,543</td>
</tr>
<tr>
<td>30-44</td>
<td>49,177</td>
</tr>
<tr>
<td>15-29</td>
<td>20,581</td>
</tr>
<tr>
<td>&lt;15</td>
<td>11,593</td>
</tr>
</tbody>
</table>

Rate of Hospitalization (per 100 person-yr)

Patient Awareness of CKD is low

USRDS 2014 Annual Data Report
Lifetime Incidence of CKD Stages 3-5 in the US is 59%*

A 60% chance of have CKD is equivalent to saying that 80% of Americans will develop old age. Tough but true.

Paul W. Eggers, PhD
Program Director for Kidney and Urology Epidemiology
National Institute of Diabetes and Digestive and Kidney Diseases

Disease Progression of CKD

- ESRD = Kidney Failure
- Progressive Kidney Disease
- 30 year old
- Normal (0.8 ml/min/yr)

Glomerular Filtration Rate

ml/min/1.73 m²

Time (yrs)

2 4 6 8 10
Sadie

CKD or AGING?

85 y/o
NIDDM
eGFR 45ml/min

If you lose 1%/yr above the age of 30,
85y/o= 55years of GFR loss

Or

100-55 or 45ml/min
ESRD Treatments
Dialysis and Transplantation

Peritoneal Dialysis (PD) uses the peritoneal lining to filter the blood

Hemodialysis (HD) uses a machine and filters the blood outside the body
“Patients with CKD, particularly those with ESRD are among the most symptomatic of any chronic disease group.”

The ESRD Patient

• Substantial impaired health-related quality of life
• Tremendous symptom burden
• The number and severity of physical and mental symptoms are similar to those of many cancer patients hospitalized in palliative care settings
• Symptoms include pain, insomnia, nausea, anorexia, pruritus, severe fatigue and SOB

• Unlike many cancer patients, these symptoms are often present for several YEARS
Predictors of Adverse Renal and Cardiovascular Outcomes

- Age
- Hyperglycemia
- Hypertension
- Albuminuria
- Activation of RAAS
- Family History (renal)
- Ethnicity
- Race
- Hypoalbuminemia
- NT-proBNP/Troponin T
- C-reactive protein
- Smoking

Criteria for CKD
Where is the SCr?

1. Decreased GFR ≤ 60ml/min for > 3 months

   or

2. Markers of Kidney Damage for > 3 months
   - Albuminuria ≥ 30mg/g (UACR)
   - Urinary sediment abnormalities
     Ex: microhematuria
   - Electrolyte and other abnormalities due to tubular disorders
   - Structural abnormalities detected by imaging
     Ex: ADPKD (polycystic kidney disease)
   - History of kidney transplantation
Which GFR?

- Glofil = true/accurate GFR
- eCrCl using Cockcroft-Gault formula
- eGFR using Modification of Diet in Renal Disease (MDRD) formula
- eGFR using the CKD-EPI formula
- eGFR using the Mayo Quadratic formula
- eGFR for children using Schwartz formula
- Cystatin C
- Creatinine Clearance (CrCl)

Not enough variability to change Stage of Kidney Disease
CKD Stages with Prognosis

Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)

<table>
<thead>
<tr>
<th>GFR stages, description and range (ml/min per 1.73 m²)</th>
<th>G1</th>
<th>G2</th>
<th>G3a</th>
<th>G3b</th>
<th>G4</th>
<th>G5</th>
</tr>
</thead>
<tbody>
<tr>
<td>High and optimal</td>
<td>&gt;105</td>
<td>75–89</td>
<td>45–59</td>
<td>30–44</td>
<td>15–29</td>
<td>&lt;15</td>
</tr>
<tr>
<td>90–104</td>
<td></td>
<td>60–74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild-moderate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate-severe</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Albuminuria stages, description and range (mg/g)</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal and high-normal</td>
<td>&lt;10</td>
<td>10–29</td>
<td>30–299</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td></td>
<td>300–1999</td>
</tr>
<tr>
<td>Very high and nephrotic</td>
<td></td>
<td></td>
<td>≥2000</td>
</tr>
</tbody>
</table>

Decline in GFR varies by Disease State, From Patient to Patient and is **Accelerated** in those with **Albuminuria**

Albuminuria Is a Prognostic Indicator

The relationship between magnitude of proteinuria reduction and the risk of ESRD: Results of the AASK study of kidney disease and hypertension Ach Intern Med 2001

Proteinuria and Rate of Change in Kidney Function in a Community Based Population, JASM 2013

The Progression of CKD: A 10-year population-based study of the effects of gender and age. KI 2006

Combining GFR and albuminuria to classify CKD improves prediction of ESRD, JASN 2009

Alberta Kidney Disease Network: Relation between kidney function, proteinuria, and adverse outcomes, JAMA 2010
Prevalence of CKD Complications

Signs and Symptoms

- Decreasing GFR
- Increasing albuminuria
- Uncontrolled HTN
- Improved DM management (Why?)
- Hyperkalemia
- Metabolic acidosis
- Anemia
- Hyperphosphatemia
- Hyperparathyroid
- Hypovitaminosis D

- Nausea, vomiting, poor appetite, weight loss
- Trouble sleeping
- Fatigue
- Nocturia
- Dry, itchy skin
- Leg cramping (night?)
- Skin color changes
- SOB
- Edema
- Confusion
Management of CKD

1. Screen at risk patients
2. Determine level of renal function with eGFR
3. Determine prognosis with albuminuria
4. Add RAAS blockade if albuminuria is present
5. Blood pressure to goal?
6. Diabetes A1C?
7. Smoking cessation
8. Weight loss
9. Limiting future AKI
CKD Risk Factors

- Diabetic
- Hypertensive
- Older age (>60y/o)
- Recurrent UTI
- Kidney stones
- History of AKI
- Autoimmune disease: Lupus, Sjogrens, RA, MCTD...
- Family history of CKD
- CVD
- Neoplasm: multiple myeloma, Wilms, kidney cancer
- Previous transplant
- Previous kidney donor

1. KDOQI guidelines 2002
Management of CKD

1. Screen at risk patients
2. Determine and trend renal function with eGFR
3. Determine prognosis with albuminuria
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5. Blood pressure to goal?
6. Diabetes A1C?
7. Smoking cessation
8. Weight loss
9. Limiting future AKI
What is the GFR?

17 y/o non-white Male
eGFR 80
Stage 1

45 y/o white Female
eGFR 39
Stage 3b

70 y/o non-white Male
eGFR 60
Stage 2

70 y/o white Female
eGFR 30
Stage 3b/ borderline 4

Hold SCr stable at 1.5
R.K. is a 53yo male who has advanced liver disease and nephrotic proteinuria

<table>
<thead>
<tr>
<th>Scr</th>
<th>eGFR</th>
<th>Year</th>
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<tbody>
<tr>
<td>0.55mg/dl</td>
<td>177ml/min</td>
<td>2003</td>
</tr>
<tr>
<td>0.63mg/dl</td>
<td></td>
<td>2004</td>
</tr>
<tr>
<td>0.77mg/dl</td>
<td></td>
<td>2005</td>
</tr>
<tr>
<td>0.86mg/dl</td>
<td></td>
<td>2006</td>
</tr>
<tr>
<td>1.2mg/dl</td>
<td>63ml/min</td>
<td>2008</td>
</tr>
</tbody>
</table>
Management of CKD

1. Screen at risk patients
2. Determine and trend renal function with eGFR
3. Determine prognosis with albuminuria
4. Add RAAS blockade if albuminuria is present
5. Blood pressure to goal?
6. Diabetes A1C?
7. Smoking cessation
8. Weight loss
9. Limiting future AKI
Proteinuria vs Albuminuria

<table>
<thead>
<tr>
<th>Level</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>negative</td>
<td>0 mg/dL</td>
</tr>
<tr>
<td>trace</td>
<td>15-30 mg/dL</td>
</tr>
<tr>
<td>1+</td>
<td>30-100 mg/dL</td>
</tr>
<tr>
<td>2+</td>
<td>100-300 mg/dL</td>
</tr>
<tr>
<td>3+</td>
<td>300-1000 mg/dL</td>
</tr>
<tr>
<td>4+</td>
<td>&gt;1000 mg/dL</td>
</tr>
</tbody>
</table>
Quantifying ALBUMINURIA: Where is the UA dipstick?

Special Thanks to Scott and White of Temple TX for use of their kidney comic
Evaluation of Albuminuria

Morning UACR

- UACR > 30 and < 300 mg/g
  - Moderate albuminuria

- UACR 300 mg/g
  - Severe albuminuria

Unconfirmed

- Monitor annually

Confirmed within 3 months

Intervention → Tx:
1. Add ACEi OR ARB
2. Lower BP <130/80
3. Begin low Sodium diet

- Monitor q 3-6 months
Management of CKD

1. Screen at risk patients
2. Determine and trend renal function with eGFR
3. Determine prognosis with albuminuria
4. Add RAAS blockade if albuminuria is present
5. Blood pressure to goal?
6. Diabetes A1C?
7. Smoking cessation
8. Weight loss
9. Limiting future AKI
Albuminuria more detrimental to hypertensive black patients
Long acting ARB more effective than short. Cost vs side effects
Taking the medication works better than not, NO matter which drug!
Renin-Angiotensin-Aldosterone System (RAAS)

Inhibition of RAAS: leads to less proteinuria

1. ACEIs
   - Block conversion of angiotensin I to angiotensin II
   - Increase availability of bradykinin

2. ARBs
   - Selectively antagonize angiotensin II
   - May also modulate the effects of angiotensin II breakdown products

RAAS inhibition provides nephroprotection independent of blood pressure lowering

Blockade of the RAAS Slows or Prevents Onset and Progression of Diabetic Kidney Disease in Hypertensive Type 2 Diabetics

ACEi or ARBs even with Advanced CKD

20-30% bump in SCr is normal. This should be expected. Repeat labs in 2 weeks
ACEI + ARB ≠ Dual Blockade

Efficacy and safety of dual blockade of the renin-angiotensin system: meta-analysis of randomized trials Jan 2013

Increased risk of AKI with ACEi+ARB

Dual Blockade means- Increased risk of Complications And No decrease in mortality

Complications include: Hyperkalemia, hypotension, and kidney failure

ACE Inhibitor and Angiotensin Receptor-II Antagonist Prescribing and Hospital Admissions with Acute Kidney Injury: A Longitudinal Ecological Study
Strategies to Lower Albuminuria
Multi-Risk Factor Interventions

1. Control BP to goal of <130/80. (MDRD, ABCD AASK)
   Lowering BP by itself will reduce albuminuria by ~50% or prevents the 2-3x ↑ in albuminuria observed in patient with usual BP goal

2. Blockage of RAAS

3. Restrict NaCl intake. High sodium intake will override anti-albuminuric effects of ACEi/ARBs

4. Aldosterone antagonistic Tx: spironolactone

5. Smoking cessation

6. Reduce obesity
Management of CKD

1. Screen at risk patients
2. Determine and trend renal function with eGFR
3. Determine prognosis with albuminuria
4. Add RAAS blockade if albuminuria is present
5. **Blood pressure to goal?**
6. Diabetes A1C?
7. Smoking cessation
8. Weight loss
9. Limiting future AKI
Lowering Blood Pressure Slows Progression of Chronic Kidney Disease

Trials included: MDRD, RENAAL, IDNT, AIPRI, Captopril Trail, REIN, AASK

Incidence of all **Renal Events** according to achieved **BP levels**: ADVANCE TRIAL

Renal Event = New onset or worsening albuminuria, Doubling serum creatinine and ESRD
The Prevalence of Hypertension Increases with Worsening Kidney Function (NHANES)

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>Percent with HTN (BP 140/90 mmHg or Drug Use)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall...</td>
<td>30</td>
</tr>
<tr>
<td>Non CKD</td>
<td>40</td>
</tr>
<tr>
<td>CKD I</td>
<td>50</td>
</tr>
<tr>
<td>CKD II</td>
<td>60</td>
</tr>
<tr>
<td>CKD III</td>
<td>70</td>
</tr>
<tr>
<td>CKD IV/V</td>
<td>90</td>
</tr>
</tbody>
</table>

1. *JAMA* 2010; 303: 2043

*Slide courtesy of Dr. Van Buren*
What BP Targets should we Strive to Achieve?
## Comparison of BP Guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Population</th>
<th>Goal BP mmHg</th>
<th>Initial drug treatment option</th>
</tr>
</thead>
<tbody>
<tr>
<td>JNC 8</td>
<td>General &gt;60 yo</td>
<td>&lt;150/90</td>
<td>NB: thiazide, ACEi, ARB or CCB</td>
</tr>
<tr>
<td></td>
<td>General &lt;60yo</td>
<td>&lt;140/90</td>
<td>BL: thiazide or CCB</td>
</tr>
<tr>
<td></td>
<td>DM</td>
<td>&lt;140/90</td>
<td>DM: thiazide, ACEi, ARB or CCB</td>
</tr>
<tr>
<td></td>
<td>CKD</td>
<td>&lt;140/90</td>
<td>CKD: ACEi or ARB</td>
</tr>
<tr>
<td></td>
<td><strong>NB</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KDIGO 2012</td>
<td>CKD no proteinuria</td>
<td>&lt;140/90</td>
<td>ACEi or ARB</td>
</tr>
<tr>
<td></td>
<td>CKD + proteinuria</td>
<td>&lt;130/80</td>
<td>ACEi or ARB</td>
</tr>
<tr>
<td></td>
<td>DM &amp; CKD no proteinuria</td>
<td>&lt;140/90</td>
<td>ACEi or ARB</td>
</tr>
<tr>
<td></td>
<td>DM &amp; CKD + proteinuria</td>
<td>&lt;130/80</td>
<td>ACEi or ARB</td>
</tr>
<tr>
<td>KDOQI 2004</td>
<td>DM+CKD</td>
<td>&lt;130/80</td>
<td>ACEi/ARB</td>
</tr>
<tr>
<td></td>
<td>CKD with proteinuria</td>
<td>&lt;130/80</td>
<td>ACEi</td>
</tr>
<tr>
<td></td>
<td>CKD without proteinuria</td>
<td>&lt;130/80</td>
<td>No preference</td>
</tr>
</tbody>
</table>

**NB**-nonblack, **BL**-black, **ACEi**-angiotensin converting enzyme inhibitors, **ARB**-angiotensin receptor blocker, **CCB**-calcium channel blocker
# Lifestyle Modification

<table>
<thead>
<tr>
<th>Modification</th>
<th>Approximate SBP reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>5–20 mmHg/10 kg wt loss</td>
</tr>
<tr>
<td>Adopt DASH diet</td>
<td>8–14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium</td>
<td>2–8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>4–9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>2–4 mmHg</td>
</tr>
</tbody>
</table>

**Total= ↓21 mmHg**
Management of CKD

1. Screen at risk patients
2. Determine and trend renal function with eGFR
3. Determine prognosis with albuminuria
4. Add RAAS blockade if albuminuria is present
5. Blood pressure to goal?
6. Diabetes A1C?
7. Smoking cessation
8. Weight loss
9. Limiting future AKI
A1C Goal 7%

CKD 4, 5, 5D = 7.5%
Metformin Dosing

<table>
<thead>
<tr>
<th>SCr</th>
<th>Race</th>
<th>Age</th>
<th>eGFR</th>
<th>CKD Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1.5</td>
<td>17</td>
<td>78</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.5</td>
<td>70</td>
<td>46</td>
<td>3a</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.5</td>
<td>17</td>
<td>48</td>
<td>3a</td>
</tr>
<tr>
<td></td>
<td>African American</td>
<td></td>
<td></td>
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<tr>
<td>Female</td>
<td>1.5</td>
<td>70</td>
<td>35</td>
<td>3b</td>
</tr>
<tr>
<td></td>
<td>White</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

GFR calculator available at NKF.org

US Food and Drug Administration Prescribing Guidelines for Metformin as Related to Kidney Function

Metformin is contraindicated in “renal disease or renal dysfunction (eg, as suggested by serum creatinine levels $\geq 1.5$ mg/dL [males], $\geq 1.4$ mg/dL [females]) or abnormal creatinine clearance (CrCl).”

Metformin “should not be initiated in patients $\geq 80$ years of age unless measurement of creatinine clearance demonstrates that renal function is not reduced.”
The New FDA Metformin Dosing

- PI states metformin can be used until GFR of 30ml/min (4/11/16)
- Based on studies showing little chance of lactic acidosis
- Very few reports of lactic acidosis in ‘real practice’
  - Collected via MedWatch (FDA Safety Information and Adverse Event Reporting Program)
  - Do you report known side effects of medications?
### Table 2. Possible Approach to Metformin Prescribing in the Setting of CKD

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>eGFR, mL/min per 1.73 m²</th>
<th>Maximal Total Daily Dose, mg</th>
<th>Other Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥90</td>
<td>2550</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>60 - &lt;90</td>
<td>2550</td>
<td></td>
</tr>
<tr>
<td>3A</td>
<td>45 - &lt;60</td>
<td>2000</td>
<td>Avoid if kidney function is or expected to become unstable&lt;br&gt;Consider more cautious follow-up of kidney function</td>
</tr>
<tr>
<td>3B</td>
<td>30 - &lt;45</td>
<td>1000</td>
<td>Do not initiate therapy at this stage but drug may be continued&lt;br&gt; Avoid if kidney function is or expected to become unstable&lt;br&gt;Consider more cautious follow-up of kidney function</td>
</tr>
<tr>
<td>4</td>
<td>15 - &lt;30</td>
<td>Do not use</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
<td>Do not use</td>
<td></td>
</tr>
</tbody>
</table>
Management of CKD

1. Screen at risk patients
2. Determine and trend renal function with eGFR
3. Determine prognosis with albuminuria
4. Add RAAS blockade if albuminuria is present
5. Blood pressure to goal?
6. Diabetes A1C?
7. Smoking cessation
8. Weight loss
9. Limiting future AKI
Management of CKD

1. Screen at risk patients
2. Determine level of renal function with eGFR
3. Determine prognosis with albuminuria
4. Add RAAS blockade if albuminuria is present
5. Blood pressure to goal?
6. Diabetes A1C?
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9. Limiting future AKI
Iatrogenic AKI
Preventable events $\rightarrow$ AKI $\rightarrow$ CKD progression $\rightarrow$ ESRD
Complications of CKD

1. Hyperkalemia
2. Fluid overload
3. Metabolic acidosis
4. Anemia
5. Hyperparathyroid/hyperphosphatemia
6. Depression
7. Malnutrition
Complications of CKD

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Case Presentation

65yo female with CKD stage 4, CAD, DM with retinopathy, HTN, CHF and obesity who presents for 3 month follow up on diabetes management.

- BP 160/85, P60, weight 250lbs
- PE reveals S4 and +1 edema
- Labs revealed stable SCr 2.5mg/dl, BUN 20, eGFR 20ml/min, Na+ 140, K+ 6.5, CO2 20, spot urine alb/cr 2500mg/g.
- Current meds: HCTZ 25mg daily, potassium chloride 20mEq BID, lisinopril 40mg BID, labetalol 300mg TID, ibuprofen 400mg BID, spironolactone 12.5mg BID

1. What are the possible causes of hyperkalemia?
2. What changes should be made to achieve optimal BP?
Question 1

What are the possible cause(s) of hyperkalemia?

a) Meds
b) CKD
c) Diet
d) K+ supplements
e) Metabolic acidosis
f) All of the above
Question 1b

Which of her medication(s) could have led to hyperkalemia?

a) Lisinopril
b) Labetalol
c) Ibuprofen
d) Spironolactone
e) Potassium chloride
f) a, d, and e
g) All of the above
Question 2

What change(s) should be made to achieve optimal BP?

a) Following low sodium diet
b) Medication compliance
c) OTC meds?
d) Discontinue HCTZ.
e) Start torsemide
f) Start furosemide
g) All of the above
Diuretics: Key to success

• Loop diuretics when eGFR <30-50ml/min
• Do not use thiazide diuretics when eGFR <30-50ml/min. They do not work with ↓ kidney function
• Placebo pill with high NaCl intake
• If patients require potassium supplementation = NOT compliant with low NaCl intake
• Once daily loop
• Torsemide more bioavailable than furosemide
  Use 50% dose of furosemide. Particularly with more albuminuria
  Ex: Furosemide 40mg BID = Torsemide 40mg daily

• Treats MANY complications of CKD
  1. Hyperkalemia
  2. Fluid overload
  3. Elevated BPs
  4. Metabolic acidosis
  5. Usage of ACEi/ARB to ↓ albuminuria
Question 3

After discontinuing HCTZ, ibuprofen and potassium chloride and initiation of torsemide 20mg QAM, repeat labs reveal:

• ↑ in SCr 2.5 to 2.9mg/dl, BUN 24, ↓ in eGFR from 20 to 18ml/min, ↓ SK+ 5.5, ↑ CO2 22, ↓ UACR 1500mg/g.
• BP 145/80, P 60, weight 250lbs
• Trace to +1 LE edema

Meds: lisinopril 40mg BID, labetalol 300mg TID, spironolactone 12.5mg BID and torsemide 20mg QAM

What is your next step?
Question 3

1. Decrease lisinopril to 40mg daily due to ↑ in SCr and ↓ eGFR
2. Decrease torsemide to 10mg due to ↑ in SCr and ↓ eGFR
3. Increase torsemide to 30mg daily to ↓ SK+, ↑ CO2, ↓ LE edema, ↓ BP to goal of <130/80
4. Discontinue spironolactone and start calcium channel blocker
5. Reassess NaCl with 24hr urine sodium to ensure <200mmol/24hr indicating low NaCl intake

*Remember high NaCl renders RAAS blockade and diuretics less efficacious = PLACEBO PILLS
ARS #1

Which patient has a worse prognosis for CKD progression to ESRD?

a) 75yo HTN eGFR 40ml/min, UACR 150mg/g
b) 22yo SLE eGFR 80ml/min, UACR 3000mg/g
c) 35yo ADPKD eGFR 65ml/min, UACR 100mg/g
d) 55yo T2DM eGFR 50ml/min, UACR 1500mg/g
ARS #2

45yo obese, T2DM, DLD, CAD, HTN, hyperuricemia, CKD presents with worsening of renal function. SCr increased to 2.0mg/dl. eGFR decreased from 58 to 42ml/min. UACR 2000mg/g. A1C 8.5%. You would _____ and refer to endocrinology.

a) Continue metformin 1000mg BID  
b) Decrease metformin 500mg BID  
c) Discontinue metformin
ARS #3

65yo male with T2DM, uncontrolled HTN and CKD presents with BP 175/60, P80, BMI 35.
Scr 2.4 mg/dl, eGFR 32ml/min, K 4.8 mEq/L
A1c 9.8%, UACR 2,550 mg/g
Meds: Metoprolol XL 50mg daily, HCTZ 25mg daily and insulin

• What blood pressure medication changes would you initially make to achieve optimal BP goal to <130/80?
  a) Discontinue HCTZ and start furosemide
  b) Increase metoprolol based on HR
  c) Start ACEI or ARB
  d) All of the above. Is this a trick question?
Questions?

Denise.Link@utsouthwestern.edu.

Thank you for your time