Outpatient Management of Chronic Kidney Disease for the Internist

Annual Meeting of Maryland Chapter of the American College of Physicians
February 3, 2018

MARY (TESSIE) BEHRENS, MD, FACP, FASN, FNKF
MID-ATLANTIC NEPHROLOGY ASSOCIATES, P.A.
I. Goal of CKD Management
II. Definition & Staging of CKD
III. Epidemiology
IV. Slowing Progression of CKD
V. Safety Features
VI. Complications of CKD
VII. Referral & Co-Management with Nephrology
Goal of CKD Management

- Prevent or Slow Progression
- Minimize Complications
- Improve Quality of Life
- Lower cost burden on health care system
Primary Care Physicians – First Line of Defense Against Chronic Kidney Disease (CKD)

- Early Detection is essential
- Early management can improve outcomes
- Approximately 14.8% of adults in the U.S. meet the definition of CKD
- PCPs are essential in the management of this population
Definition of Chronic Kidney Disease

- Duration of $\geq$ 3 months
- Glomerular Filtration Rate (GFR) $< 60 \text{ ml/min/1.73 m}^2$
- Kidney damage defined as structural abnormalities or functional abnormalities other than decreased GFR
  - Pathologic abnormalities
  - Kidney transplantation
  - Albuminuria
  - Urinary sediment abnormalities
  - Imaging abnormalities
Classification of Chronic Kidney Disease Staging

- **Causes**
  - Presence or absence of systemic disease
  - Location in the kidney of pathologic or anatomic findings
- **Glomerular Filtration Rate**
  - Based on CKD Epi Equation
- **Albuminuria**
Assign cause of CKD based on presence or absence of systemic disease and the location within the kidney of observed or presumed pathologic-anatomic findings

<table>
<thead>
<tr>
<th>Cause</th>
<th>Examples of systemic diseases or conditions affecting the kidney</th>
<th>Examples of primary kidney diseases (absence of systemic diseases affecting the kidney)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glomerular disease</td>
<td>Diabetes, systemic autoimmune diseases, systemic infections,</td>
<td>Diffuse, focal or crescent proliferative glomerulonephritis; focal and segmental</td>
</tr>
<tr>
<td></td>
<td>drugs, neoplasia (including amyloidosis)</td>
<td>glomerulosclerosis; membranous nephropathy; minimal change disease</td>
</tr>
<tr>
<td>Tubulointerstitial disease</td>
<td>Systemic infections, autoimmune, sarcoidosis, drugs, urate,</td>
<td>Urinary-tract infections, stones, obstruction</td>
</tr>
<tr>
<td></td>
<td>environmental toxins (lead, aristolochic acid), neoplasia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(myeloma)</td>
<td></td>
</tr>
<tr>
<td>Vascular disease</td>
<td>Atherosclerosis, hypertension, ischemia, cholesterol emboli,</td>
<td>ANCA-associated renal limited vasculitis; fibromuscular dysplasia</td>
</tr>
<tr>
<td></td>
<td>systemic vasculitis, thrombotic microangiopathy, systemic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>sclerosis</td>
<td></td>
</tr>
<tr>
<td>Cystic and congenital disease</td>
<td>Polycystic kidney disease, Alport's syndrome, Fabry's disease</td>
<td>Renal dysplasia, medullary cystic disease, podocytopathies</td>
</tr>
</tbody>
</table>

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; CKD, chronic kidney disease; GN, glomerulonephritis.
Genetic diseases are not considered separately because some diseases in each category are now recognized as having genetic determinants.
*Note that there are many different ways in which to classify CKD. This method of separating systemic diseases and primary kidney diseases is only one, proposed by the KDIGO Work Group, to aid in conceptual approach.*

Assign GFR categories

<table>
<thead>
<tr>
<th>GFR category</th>
<th>GFR (ml/min/1.73 m²)</th>
<th>Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>≥90</td>
<td>Normal or high</td>
</tr>
<tr>
<td>G2</td>
<td>60-89</td>
<td>Mildly decreased*</td>
</tr>
<tr>
<td>G3a</td>
<td>45-59</td>
<td>Mildly to moderately decreased</td>
</tr>
<tr>
<td>G3b</td>
<td>30-44</td>
<td>Moderately to severely decreased</td>
</tr>
<tr>
<td>G4</td>
<td>15-29</td>
<td>Severely decreased</td>
</tr>
<tr>
<td>G5</td>
<td>&lt;15</td>
<td>Kidney failure</td>
</tr>
</tbody>
</table>

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

*Relative to young adult level

In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

## Assign albuminuria† categories

<table>
<thead>
<tr>
<th>Category</th>
<th>AER (mg/24h)</th>
<th>ACR (mg/mmol)</th>
<th>Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1</td>
<td>&lt;30</td>
<td>&lt;3</td>
<td>Normal to mildly increased</td>
</tr>
<tr>
<td>A2</td>
<td>30-300</td>
<td>3-30</td>
<td>Moderately increased*</td>
</tr>
<tr>
<td>A3</td>
<td>&gt;300</td>
<td>&gt;30</td>
<td>Severely increased**</td>
</tr>
</tbody>
</table>

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease  
*Relative to young adult level.  
**Including nephrotic syndrome (albumin excretion usually >2200 mg/24 hours [ACR >2220 mg/g; >220 mg/mmol])

†Note that where albuminuria measurement is not available, urine reagent strip results can be substituted.

Importance of Staging

- Guide management of CKD
- Identify those at highest risk for complications
- Guides when to intensify monitoring of patients
- Guides when to refer to Nephrologist
- Guides content of patient education
Epidemiology
Percentage of NHANES Participants in KDIGO Risk Categories (2011-2014)

<table>
<thead>
<tr>
<th>Albuminuria categories</th>
<th>A1 Normal to mildly increased</th>
<th>A2 Moderately increased</th>
<th>A3 Severely increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 mg/g</td>
<td>54.7</td>
<td>4.3</td>
<td>0.4</td>
</tr>
<tr>
<td>&lt;3 mg/mmol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-300 mg/g 3-30 mg/mmol</td>
<td>30.4</td>
<td>2.6</td>
<td>0.3</td>
</tr>
<tr>
<td>&gt;300 mg/g &gt;30 mg/mmol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GFR categories (ml/min/1.73 m²)</th>
<th>G1 Normal to high</th>
<th>G2 Mildly decreased</th>
<th>G3a Mildly to moderately decreased</th>
<th>G3b Moderately to severely decreased</th>
<th>G4 Severely decreased</th>
<th>G5 Kidney failure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥ 90</td>
<td>60-89</td>
<td>45-59</td>
<td>30-44</td>
<td>15-29</td>
<td>&lt; 15</td>
</tr>
<tr>
<td></td>
<td>54.7</td>
<td>30.4</td>
<td>3.9</td>
<td>1.0</td>
<td>0.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>4.3</td>
<td>2.6</td>
<td>0.9</td>
<td>0.5</td>
<td>0.1</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>0.3</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.01</td>
</tr>
<tr>
<td>14.8% of US Population Meets Definition of CKD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Summary of Relative Risks from Categorical Meta-Analysis
(reagent strip included [-, ±, +, ≥++]

#### Kidney Failure (ESRD)

<table>
<thead>
<tr>
<th>eGFR</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>&gt;105</td>
<td>Ref</td>
<td>7.8</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>90-105</td>
<td>Ref</td>
<td>11</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>75-90</td>
<td>Ref</td>
<td>3.8</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>60-75</td>
<td>Ref</td>
<td>7.4</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>45-60</td>
<td>5.2</td>
<td>22</td>
<td>40</td>
<td>147</td>
</tr>
<tr>
<td>30-45</td>
<td>56</td>
<td>74</td>
<td>294</td>
<td>763</td>
</tr>
<tr>
<td>15-30</td>
<td>433</td>
<td>1044</td>
<td>1056</td>
<td>2286</td>
</tr>
</tbody>
</table>

#### Acute Kidney Injury (AKI)

<table>
<thead>
<tr>
<th>eGFR</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>&gt;105</td>
<td>Ref</td>
<td>2.7</td>
<td>8.4</td>
<td></td>
</tr>
<tr>
<td>90-105</td>
<td>Ref</td>
<td>2.4</td>
<td>5.8</td>
<td></td>
</tr>
<tr>
<td>75-90</td>
<td>Ref</td>
<td>2.5</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>60-75</td>
<td>Ref</td>
<td>3.3</td>
<td>6.4</td>
<td></td>
</tr>
<tr>
<td>45-60</td>
<td>2.2</td>
<td>4.9</td>
<td>6.4</td>
<td>5.9</td>
</tr>
<tr>
<td>30-45</td>
<td>7.3</td>
<td>10</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>15-30</td>
<td>17</td>
<td>17</td>
<td>21</td>
<td>29</td>
</tr>
</tbody>
</table>

#### Progressive CKD

<table>
<thead>
<tr>
<th>eGFR</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>&gt;105</td>
<td>Ref</td>
<td>0.4</td>
<td>3.0</td>
<td></td>
</tr>
<tr>
<td>90-105</td>
<td>Ref</td>
<td>0.9</td>
<td>3.3</td>
<td></td>
</tr>
<tr>
<td>75-90</td>
<td>Ref</td>
<td>1.9</td>
<td>5.0</td>
<td></td>
</tr>
<tr>
<td>60-75</td>
<td>Ref</td>
<td>3.2</td>
<td>8.1</td>
<td></td>
</tr>
<tr>
<td>45-60</td>
<td>3.1</td>
<td>4.0</td>
<td>9.4</td>
<td>57</td>
</tr>
<tr>
<td>30-45</td>
<td>3.0</td>
<td>19</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>15-30</td>
<td>4.0</td>
<td>12</td>
<td>21</td>
<td>7.7</td>
</tr>
</tbody>
</table>

Slowing Progression
Interventions to Delay Progression in CKD

I. Hypertension Management
II. Albuminuria should use ACE1 or ARB
III. Diabetes – target A1C 7%
IV. Correct Metabolic Acidosis
Hypertension Management

- Blood Pressure (BP) Goal <140/90
- Consider BP Goal <130/80 if spot UACR > 300 mg/g
  - Use ACEI or ARB if spot UACR > 30 mg/g
    - Do not use ACEI and ARB together (Risk Acute Kidney Injury (AKI) & Hyperkalemia)
- Diuretics usually required
  - Thiazide – stage G1-G3b
  - Loop diuretic - stage G4-G5
- Dietary sodium restriction < 2g/day
Complications of ACEI or ARBs

A. Hyperkalemia

- Low K diet
- Diuretics
- Potassium binding resins (i.e., Veltassa, Patiromer)
- Correct metabolic acidosis if present
- Discontinue RAAS blockers
B. Acute Kidney Injury

- Stable increase in creatinine up to 25% within 2 months of starting ACEI or ARB can be considered normal and not need to discontinue RAAS blockers

- Increase in creatinine over 25%
  - Discontinue RAAS blockers
  - Evaluate for renal artery stenosis or overdiuresis
Glycemic Control

- Target HgbA1C < 7%
  - Higher target for patients at high risk of hypoglycemia or a limited life expectancy

- Benefits
  - Reduction of cardiovascular risk
  - Renal Protection
    - Decreased progression of albuminuria
    - Preservation of renal function
Metabolic Acidosis

- Some evidence to suggest correction slows progression of CKD
- Treat if serum bicarbonate level is less than 22 mmol/L
  - Sodium bicarbonate - 650 mg tid
  - Sodium citrate – 30 cc daily

Susantitaphong et al American Journal of Nephrology, 2012; 35 : 540-547
Safety Features
Patient Safety in CKD

- Dose drugs for level of eGFR if they are predominantly excreted by the kidney
- Decrease risk of AKI from volume depletion
- Prevent contrast-induced AKI
  - Avoid contrast if possible or use minimal volume of low osmolality contrast
  - Consider isotonic saline infusion before, during and after procedure
  - Withhold Metformin, RAAS blockers, and diuretics
Patient Safety in CKD

- **Stage G3a (eGFR 45-59)**
  - Avoid prolonged use of NSAIDs
  - Can continue Metformin

- **Stage G3b (eGFR 30-44)**
  - Avoid use of NSAIDs
  - Reduce dose of Metformin by 50% and monitor patient closely
Patient Safety in CKD – cont’d

- Stage G4-G5 (eGFR < 30)
  - Avoid NSAIDs
  - Avoid Bisphosphonates
  - Avoid Metformin
  - Avoid PICC lines
    - Protect veins for future dialysis access
  - Monitor for increased risk of bleeding with Warfarin
Complications
Complications of CKD

- Anemia
- Metabolic Acidosis
- Metabolic and Bone Disease
- Cardiovascular Disease
Anemia

- Identification is Essential
  - Stage G3a – check Hgb at least annually
- Normocytic, Normochromic
- Be sure not iron deficient before using Erythrocyte Stimulating Agents (ESAs)
  - Replete with oral iron or use IV iron if no response to oral
- Indication for ESA
  - Avoid Transfusion
  - Frequently used for Hgb <9
  - No goal hemoglobin
Metabolic Acidosis

- **Adverse Consequences**
  - Progression of CKD
  - Increased bone resorption
  - Increased protein catabolism
  - Decreased albumin synthesis

- **Treatment**
  - Sodium bicarbonate
  - Sodium citrate
Bone and Mineral Disorders

- Usually see Stage G3b, G4, & G5
- Abnormalities
  - Hyperphosphatemia
  - Hypocalcemia
  - Decreased Vitamin D
  - Increase Parathyroid Hormone
- Goals for PTH vary with Stage of CKD
  - G3  35-70
  - G4  70-110
  - G5  150-300
- Co-Manage with Nephrology
Cardiovascular Disease

- CKD is an independent risk factor for cardiovascular disease and death
- Strategies to employ:
  - Statins
  - Low dose aspirin if bleeding risk is acceptable
  - Weight reduction
  - Exercise
  - Stop smoking
Co-Management of CKD Population with PCPs and Nephrologists

- PCPs essential in early detection
  - Screen high risk patients – Diabetics & Hypertension
  - Number of patients with early stages is too great to be cared for by nephrology
  - Better patient outcomes when issues addressed to slow progression, complications of CKD, & also safety issues
  - Need team approach
Referral & Co-Management with Nephrology
Classification of CKD Based on GFR and Albuminuria Categories: “Heat Map”

CKD is classified based on:
- Cause (C)
- GFR (G)
- Albuminuria (A)

<table>
<thead>
<tr>
<th>Albuminuria categories Description and range</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal to mildly increased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderately increased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severely increased</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 mg/g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3 mg/mmol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-299 mg/g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-29 mg/mmol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥300 mg/g</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥30 mg/mmol</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Colors: Represents the risk for progression, morbidity and mortality by color from best to worst. Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Numbers: Represent a recommendation for the number of times per year the patient should be monitored.

Refer: Indicates that nephrology referral and services are recommended.

*Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referral.

<table>
<thead>
<tr>
<th>PCP</th>
<th>Co-Management</th>
<th>Nephrologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>(G 1- G3b A1/A2)</td>
<td>Early Detection, staging &amp; identification of CKD complications</td>
<td>Hypertension</td>
</tr>
<tr>
<td></td>
<td>Comorbid conditions (CAD, PAD, COPD, DM, Obesity-OSA, Arthritis)</td>
<td>Hypervolemia</td>
</tr>
<tr>
<td></td>
<td>Vaccination (Flu, Pneumococcal, Hep B)</td>
<td>Medication usage &amp; dosing</td>
</tr>
<tr>
<td></td>
<td>Health Screening (appropriate for age and comorbidities)</td>
<td>Patient safety-risk benefit of IV contrast (Iodinated &amp; Gadolinium)</td>
</tr>
<tr>
<td></td>
<td>Guideline based nephrology referral</td>
<td>AKI follow up</td>
</tr>
<tr>
<td></td>
<td>&quot;Save the veins&quot; &amp; avoid PICC lines</td>
<td>Glomerulonephritis including renal biopsy if indicated</td>
</tr>
<tr>
<td></td>
<td>Hyperlipidemia</td>
<td>Refractory Hypertension</td>
</tr>
<tr>
<td></td>
<td>Cardiovascular-Primary &amp; Secondary Prevention</td>
<td>Preparation for Renal Replacement: Modality Selection</td>
</tr>
<tr>
<td></td>
<td>End of Life Planning including decisions to start/terminate dialysis &amp; palliative care</td>
<td>Nutritional CKD counseling</td>
</tr>
<tr>
<td></td>
<td>Renal Transplant follow up</td>
<td></td>
</tr>
</tbody>
</table>

Co-Management of CKD
Impact of primary care CKD detection with a patient safety approach

CKD is a very prevalent problem
CKD is associated with much morbidity
Early detection & treatments is key
Primary Care Providers are essential for this process to be successful


