Transforming Diabetes Care

Diabetic Kidney Disease: Prevention, Detection and Treatment

Alexis Chettiar, ACNP-BC, PhD(c)
Polling Question - 1
What is your role as a healthcare provider?

a) Dietitian  
b) Nurse  
c) Nurse Practitioner  
d) Pharmacist  
e) Physician  
f) Physician Assistant  
g) Other
Polling Question - 2

What type of healthcare setting do you work in?

a) Health plan
b) Hospital
c) Outpatient specialty care
d) Pharmacy
e) Primary care
f) Other
Primary Care Providers—The First Line of Defense Against Chronic Kidney Disease (CKD)

Primary care professionals provide
- Early diagnosis
- Early-stage CKD Treatment
- Patient education

Early detection of CKD
- Improves management
- Improves patient outcomes

CKD is part of primary care
CKD Risk Factors¹*

Modifiable
- Diabetes
- Hypertension
- Acute kidney injury
- Frequent NSAID use

Non-Modifiable
- Family hx of
  - Kidney disease
  - Diabetes
  - Hypertension
- Age >60 (GFR normally declines with age)
- Race

*partial list

¹Harjutsalo V., Groop PH. Advances in Chronic Kidney Disease. 2014;21(3): 260-266
Diagnosing CKD ...

Changes clinician behavior
• Increased urinary albumin testing
• Increased appropriate use of ACEi or ARB
• Avoidance of NSAIDs
• Appropriate nephrology consultation

Results in significantly improved outcomes for patients with CKD 1-3¹-³

Screening Tools: eGFR

- Best overall index of kidney function
- Normal GFR varies by
  - Age
  - Sex
  - Body mass
- **CKD-EPI** tool recommended to estimate GFR
- Other eGFR calculators
  - MDRD
  - Cockcroft-Gault
- Online eGFR calculator

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>eGFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage* with normal or increased eGFR</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage* with mildly decreased eGFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderately decreased eGFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severely decreased eGFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

* Kidney damage is defined as UACR persistently ≥30 mg/g Cr or other abnormalities on pathological, urine, blood, or imaging tests. Adapted from Levey et al. (4).
# eGFR, SCr Comparison

<table>
<thead>
<tr>
<th>Age</th>
<th>Weight in lbs</th>
<th>Height in Ft/in</th>
<th>Sex</th>
<th>Race</th>
<th>SCr mg/dl</th>
<th>eGFR ml/min per CKD-EPI</th>
<th>eGFR Adj for BSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>285</td>
<td>6’</td>
<td>M</td>
<td>AA</td>
<td>1.6</td>
<td>68</td>
<td>97</td>
</tr>
<tr>
<td>49</td>
<td>180</td>
<td>5’4”</td>
<td>F</td>
<td>Hispanic</td>
<td>1.6</td>
<td>38</td>
<td>41</td>
</tr>
<tr>
<td>67</td>
<td>155</td>
<td>5’8”</td>
<td>M</td>
<td>Asian</td>
<td>1.6</td>
<td>44</td>
<td>46</td>
</tr>
<tr>
<td>92</td>
<td>98</td>
<td>5’1”</td>
<td>F</td>
<td>Caucasian</td>
<td>1.6</td>
<td>28</td>
<td>22</td>
</tr>
</tbody>
</table>
Polling Question - 3
How often do you screen people with diabetes for proteinuria?

a) Only if secondary indication is present
b) Annually
c) Semiannually
d) Quarterly
e) Every visit
Screening Tools: ACR

Urinary albumin-to-creatinine ratio (ACR)

- Albumin concentration in milligrams/creatinine concentration in grams
- Creatinine adjusts for varying urine concentrations
- More accurate results versus albumin alone
- Spot test; easy to collect
- First morning void preferable
- 24hr proteinuria test rarely necessary
Abnormalities of kidney structure or function, present for >3 months, with implications for health

Either of the following must be present for >3 months:
- ACR >30 mg/g
- GFR <60 mL/min/1.73m²

Only 12% of people with diabetes with CKD 1-5 are diagnosed by their primary care provider¹

# CKD Heat Map

Risk for CKD Progression Based on eGFR and Albuminuria

## Prognosis of CKD by GFR and Albuminuria Categories

<table>
<thead>
<tr>
<th>GFR categories (mL/min/1.73m²)</th>
<th>Description and range</th>
<th>Albuminuria categories Description and range</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
<td>A1: Normal to mildly increased</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A2: Moderately increased</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A3: Severely increased</td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased</td>
<td>&lt;30 mg/g &lt;3 mg/mmol</td>
</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased</td>
<td>30-299 mg/g 3-29 mg/mmol</td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>≥300 mg/g ≥30 mg/mmol</td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased</td>
<td>≥30 mg/g</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

KDIGO 2012

Opportunity for Primary Care Providers to Impact CKD Progression

CKD Patient Safety Issues

Diagnostic tests
- Iodinated contrast media: AKI
- Gadolinium-based contrast: NSF
- Sodium Phosphate bowel preparations: AKI, CKD

CVD
- Missed diagnosis
- Improper management

Fluid management
- Hypotension/hypovolemia: AKI
- CHF exacerbation

AKI = acute kidney injury; CHF = congestive heart failure; NSF = nephrogenic systemic fibrosis.
Indications for Nephrology Referral

- Acute kidney injury or abrupt sustained fall in eGFR
- eGFR <30 mL/min/1.73m² (eGFR categories G4-G5, CKD 4-5)
- Persistent albuminuria (ACR >300 mg/g)*
- Atypical progression of CKD**
- Hypertension refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease

*Significant albuminuria is defined as ACR ≥300 mg/g (≥30 mg/mmol) or AER ≥300 mg/24 hours, approximately equivalent to PCR ≥500 mg/g (≥50 mg/mmol) or PER ≥500 mg/24 hours

**Progression of CKD is defined as one or more of the following: 1) A decline in GFR category accompanied by a 25% or greater drop in eGFR from baseline; and/or 2) rapid progression of CKD defined as a sustained decline in eGFR of more than 5mL/min/1.73m²/year. KDOQI US Commentary on the 2012 KDIGO Evaluation and Management of CKD.
Blood Pressure and CKD Progression

Control of BP more important than exactly which agents are used

Avoidance of side-effects is important

With proteinuria
  • Diuretic + ACEi or ARB

No proteinuria
  • No clear drug preference
  • ACEi or ARB ok to use
Check labs 2 weeks after initiation
- If less than 25% SCr increase, continue and monitor
- If more than 25% SCr increase, stop ACEi and evaluate for RAS

Continue until contraindication arises, no absolute eGFR cutoff

Better proteinuria suppression with low Na diet and diuretics

Avoid volume depletion
Polling Question - 4

Roughly what percentage of patients with diabetic nephropathy will progress to ESRD in spite of ideal medical management?

a) 10
b) 30
c) 50
d) 80
Blood Pressure Targets in CKD

Target blood pressure in non-dialysis CKD

- ACR <30 mg/g: ≤140/90
- ACR 30-300 mg/g: ≤130/80*
- ACR >300 mg/g: ≤130/80

Individualize targets and agents by

- Age
- Coexistent CVD
- Other comorbidities

Avoid ACEi and ARB in combination

- Risk of adverse events
  - Impaired kidney function
  - Hyperkalemia

*Reasonable to select a goal of 140/90 mm Hg, especially for moderate albuminuria (ACR 30-300 mg/g).2
ARBs and Progression of Diabetic Nephropathy

• Most placebo-controlled studies in type 2 DM have been in patients with either moderate albuminuria (A2) or established nephropathy treated with ARB

• ARB and ACEi appear to be equivalent for moderate albuminuria (A2) and proteinuria reduction

Managing Hyperglycemia

• Hyperglycemia is a fundamental cause of vascular complications, including CKD

• Poor glycemic control has been associated with albuminuria in type 2 diabetes

• Risk of hypoglycemia increases as kidney function becomes impaired

• Declining kidney function may necessitate changes to diabetes medications and renally cleared drugs

• Target HbA1c ~7.0%1
  • Can be extended above 7.0% due to
    • Comorbidities
    • Limited life expectancy
    • Risk of hypoglycemia

Lipid Disorders in CKD

- Use statin alone or statin + ezetimibe in adults >50 yrs with CKD 3-5(ND)
- Use statin alone in adults >50 yrs with CKD 1-2
- In adults <50 yrs use statin alone if history of known CAD, MI, DM, stroke
- Treat according to a “fire and forget” rather than “treat to target” strategy
- Treat CKD patients (non dialysis) with statins or statin/ezetimibe combinations without the need for follow up blood tests

http://kdigo.org/home/2013/11/04/kdigo-announces-publication-of-guideline-on-lipid-management/
32% reduction in LDL associated with 17% reduction in primary outcome (nonfatal MI, coronary death, non-hemorrhagic stroke, arterial revascularization)

No reduction in CKD progression, overall or CAD mortality, other individual CAD end-points

Vaccination in CKD

Annual influenza vaccine, unless contraindicated

Pneumococcal vaccine when eGFR <30 ml/min/1.73m² and at high risk of pneumococcal infection
  • Nephrotic syndrome
  • Diabetes
  • Receiving immunosuppression
  • Revaccination within 5 years

Hepatitis B immunization when GFR <30 ml/min/1.73 m²
  • Confirm response with serological testing

Use of a live vaccine should consider the patient’s immune status (e.g., immunosuppression)
Complications of Kidney Failure
Start in Stage 3 and Progress
CKD 4-5 Management

Nephrogenic Anemia
- Erythropoetin Stimulating Agent (ESA)
- Iron supplement (PO or IV)
- Avoid transfusion for transplant candidates
  - If transfused use leukocyte filter to reduce HLA sensitization

CKD-MBD
- Vit D3 supplement
  - 2,000IU OTC cheaper and better absorbed than 50,000IU monthly D2 dosing
  - Limit dietary phosphorous
  - Phosphate binders
  - DEXA doesn't predict fracture risk in CKD 3-5
Metabolic Acidosis

- Becomes apparent at GFR <25-30 ml/min/1.73m²
- More severe with higher protein intake
- Contributes to
  - Bone disease
  - Protein catabolism
  - CKD progression
- Correction of metabolic acidosis may
  - Slow CKD progression
  - Improve functional status¹,²
- Target: Serum bicarbonate > 22 mmol/L
  - Start with 0.5-1 mEq/kg per day
    - Sodium bicarbonate tablets
    - Sodium citrate solution
    - Baking soda

Hyperkalemia

- First try reduction of dietary potassium
- Stop NSAIDs, COX-2 inhibitors
- Stop potassium sparing diuretics (Aldactone)
- Stop or reduce beta blockers
- Avoid salt substitutes that contain potassium
- Stop or reduce ACEi/ARBs
- Add loop or thiazide diuretics
- Treat with laxatives
  - As effective as cation exchange resins
### Summary of Diabetic CKD Management Guidelines

<table>
<thead>
<tr>
<th>eGFR (mL/min/1.73 m²)</th>
<th>Recommended Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>• Yearly measurement of UACR, serum Cr, potassium</td>
</tr>
<tr>
<td>45-60</td>
<td>• Referral to a nephrologist if possibility for nondiabetic kidney disease exists (duration of type 1 diabetes &lt; 10 years, persistent albuminuria, abnormal findings on renal ultrasound, resistant hypertension, rapid fall in eGFR, or active urinary sediment on urine microscopic examination)</td>
</tr>
<tr>
<td></td>
<td>• Consider the need for dose adjustment of medications</td>
</tr>
<tr>
<td></td>
<td>• Monitor eGFR every 6 months</td>
</tr>
<tr>
<td></td>
<td>• Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, and parathyroid hormone at least yearly</td>
</tr>
<tr>
<td></td>
<td>• Assure vitamin D sufficiency</td>
</tr>
<tr>
<td></td>
<td>• Vaccinate against Hep B virus</td>
</tr>
<tr>
<td></td>
<td>• Referral for dietary counseling</td>
</tr>
<tr>
<td>30-44</td>
<td>• Monitor eGFR every 3 months</td>
</tr>
<tr>
<td></td>
<td>• Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, hemoglobin, albumin, and weight every 3-6 months</td>
</tr>
<tr>
<td>&lt;30</td>
<td>• Consider the need for dose adjustment of medications</td>
</tr>
<tr>
<td></td>
<td>• Referral to a nephrologist</td>
</tr>
</tbody>
</table>

Considerations for CKD Management in Older Adult

• More than 36 million adults are now over the age of 65, and ~50% have two or more chronic diseases.¹

• Management requires an individualized approach, with attention to unique considerations for older adults.

• Treatment of hypertension in older adults has been shown to reduce CV morbidity and mortality. However, older frail adults should be monitored for risk of hypotension.²,³

• Less stringent glycemic goals can be appropriate for older adults with other comorbidities, or those at higher risk for hypoglycemia.⁴

• Encourage advance care planning with patient and family. Undertake frank discussion on prognosis and treatment options.

Additional Online Resources for CKD Learning

• CDC’s CKD Surveillance Project: http://nccd.cdc.gov/ckd

• National Kidney Disease Education Program (NKDEP): http://nkdep.nih.gov

• National Kidney Foundation: www.kidney.org

• United States Renal Data Service: www.usrds.org
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