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 Factors\textsuperscript{1*}

**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

\textsuperscript{1} Harjutsalo 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 1-3

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 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 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 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 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 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>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
<td>≥90</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased</td>
<td>60-89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased</td>
<td>45-59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>30-44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased</td>
<td>15-29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<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 &lt; 3 mg/mmol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-299 mg/g 3-29 mg/mmol</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥300 mg/g ≥30 mg/mmol</td>
<td></td>
<td></td>
<td></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

Improved diagnosis creates opportunity for strategic preservation of kidney function.

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.
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
Slowing CKD Progression: ACEi/ARB

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**¹

- 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**³,⁴

- Risk of adverse events
  - Impaired kidney function
  - Hyperkalemia

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¹Reasonable 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

Lipid Disorders in CKD

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></td>
<td>Consider the need for dose adjustment of medications</td>
</tr>
<tr>
<td>&lt;30</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 Foundation: www.kidney.org
- United States Renal Data Service: www.usrds.org
For more information visit www.jjdi.com. Become a member and opt in to be notified about our new programs, publications and more!

Follow us on Twitter @JJDiabetesInst to receive timely and important updates about diabetes!