Implementing the AADE Practice Advisory for Diabetic Kidney Disease

Advancements in Diabetes, IHS Division of Diabetes
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Implementing AADE DKD Practice Advisory

• Describe the burden of kidney disease due to diabetes in US.
• Definition of DKD and assessing risk for progression.
• Interventions to slow progression of DKD.
• AADE Advisory Recommendations.
• NKDEP curriculum for diabetes educators.
Disclosure of ABIM Service: Andrew Narva, MD

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CKD is Reduced Kidney Function or Kidney Damage

- Chronic Kidney Disease:
  - Kidney Function:
    - Glomerular filtration rate (GFR) < 60 mL/min/1.73 m² for ≥ 3 months with or without kidney damage.
  - AND/OR
  - Kidney Damage:
    - ≥ 3 months, with or without decreased GFR, manifested by either:
      - Pathological abnormalities.
      - Markers of kidney damage, i.e., proteinuria (albuminuria):
        - Urine albumin-to-creatinine ratio (UACR) > 30 mg/g

CKD Usually Means Fewer Functioning Nephrons.
Each Kidney has about 1 Million Nephrons; Slow Loss may not be Noticeable

- Large physiologic reserve.
- Slow, progressive loss of functioning nephrons may not be noticeable.
- The person with CKD may not feel different until more than three quarters of kidney function is lost.
What is the Glomerular Filtration Rate?

• GFR is equal to the sum of the filtration rates in all of the functioning nephrons.
• GFR is not routinely measured in clinical settings.
• Estimation of the GFR (eGFR) gives a rough measure of the number of functioning nephrons.
• eGFR *estimates* the measured GFR.
• eGFR *is not* the measured GFR.
What is the GFR?

- Cardiac output (CO) = 6 L/min
- x 20% of CO goes to kidneys = 1.2 L/min
- x Plasma is 50% blood volume = 600 mL/min
- x Filtration Fraction of 20% = 120 mL/min
Serum creatinine levels reflect muscle mass, age, gender, race.

A typical normal reference range of 0.6–1.2 mg/dL listed on many lab reports does not account for muscle mass, age, gender, and race.

A 28–year–old African American man with serum creatinine of 1.2 has an eGFR > 60.

A 78–year–old white woman with serum creatinine of 1.2 has an eGFR of 43.
Use an Estimating Equation for eGFR

- The Modification of Diet in Renal Disease (MDRD) study equation is widely used for estimating GFR.
- The variables are serum creatinine, age, race, and gender.
- The estimate is normalized to body surface area.

\[
eGFR \text{ (mL/min/1.73 m}^2) = 175 \times (S_{cr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if } \text{female}) \times (1.212 \text{ if African American})
\]

eGFR Estimates the Measured GFR

- eGFR is not the measured GFR.
- Estimating equations are derived from population-based studies.
- The performance measurement of the estimating equation is the P30.
- P30 refers to the percent of GFR estimates that are within 30% of mGFR.
What does this Mean?

• MDRD: There is an 77.2% chance that the estimated GFR (for patients with eGFR <60) is +/- 30% of the measured GFR:
  • e.g., a patient with an eGFR of 59 has an 77.2% chance of having a measured GFR between 42 and 78

  VS

• CKD–Epi: There is an 79.9% chance that the estimated GFR (for patients with eGFR <60) is +/- 30% of the measured GFR:
  • e.g., a patient with an eGFR of 59 has an 79.9% chance of having a measured GFR between 42 and 78.
What does this Mean? (cont.)

- The eGFR is not the actual GFR.
- The eGFR is a good estimate of the risk of having decreased kidney function.
- Like other risk predictors, when it is the solitary indicator it should be used cautiously, especially when diagnosing disease.
Decreased Kidney Function vs. Kidney Disease

- Estimating equations are less reliable at higher GFR.
- Kidney function declines with age.
- While there is an association between decreased eGFR and morbidity, even in elderly, this association does not mean causality.
- Use diagnostic terms denoting disease with caution, especially in older people without evidence of kidney damage (e.g. elderly with eGFR 55).
Creatinine–based Estimates of Kidney Function have Limitations

• Do not use with:
  • Rapidly changing creatinine levels:
    • Example: acute kidney injury
  • Extremes in muscle mass, body size, or altered diet patterns.
  • Medications that interfere with the measurement of serum creatinine.
How to Explain eGFR Results to Patients

- Normal: $\geq 60 \text{ mL/min/}1.73 \text{ m}^2$
- Kidney disease: 15–59 mL/min/1.73 m$^2$
- Kidney failure: < 15 mL/min/m$^2$
Kidney Damage

• Use urine albumin-to-creatinine ratio (UACR) to assess and monitor.
Urine Albumin Results are used for Screening, Diagnosing, and Treating DKD

• An abnormal urine albumin level is often the earliest marker for kidney disease complicating diabetes.
• It is an important prognostic marker, especially in diabetes.
• It is used to monitor and guide therapy.
• It is a tool for patient education and self-management (such as A1C or eGFR).
Use Urine Albumin–to–Creatinine Ratio for Urine Albumin Assessment

• UACR uses a spot urine sample.
• In adults, ratio of urine albumin to creatinine correlates closely to total albumin excretion:
  • Ratio is between two measured substances (not dipstick).
  • UACR of 30 mg/g is generally the most widely used cutoff for normal.

\[
\frac{\text{Urine albumin (mg per dl)}}{\text{Urine creatinine (g per dl)}} = \text{UACR (mg per g)} \approx \text{Albumin excretion in mg per day}
\]

Reference:
http://nkdep.nih.gov/resources/uacr_gfr_quickreference.htm
UACR Quantifies all Levels of Urine Albumin

- UACR is a continuous variable.
- The term *albuminuria* describes all levels of urine albumin.
- The term *microalbuminuria* describes abnormal urine albumin levels *not* detected by dipstick test.
  - 30 mg/g – 300 mg/g
- The term *macroalbuminuria* describes urine albumin > 300 mg/g.
Explaining Urine Albumin

Your urine albumin result on __________ was __________.

Date

☐ A urine albumin result below 30 is normal.

☐ A urine albumin result above 30 may mean kidney disease.

What is urine albumin?

Albumin is a protein found in the blood. A healthy kidney does not let albumin pass into the urine. A damaged kidney lets some albumin pass into the urine. The less albumin in your urine, the better.

Inside a healthy kidney

- blood
- filter
- urine

Inside a damaged kidney

- blood
- filter
- urine
- albumin
More than 10% of U.S. Adults may have CKD

- More than 20 million, aged 20 years or older.
- Kidney function declines with age.

Reference:
Diabetes is the Leading Cause of ESRD, Followed by Hypertension

Natural History of Diabetic Nephropathy

• Hyperglycemia causes hyperfiltration, may be followed by albuminuria

Reference: Adapted from Friedman, 1999
Prevalence of Diabetes; United States, 2005–2008

- 25.8 million people with diabetes; 8.3% of the US population

References:
- 2005-2008 National Health and Nutrition Examination Survey
- 2011 National Diabetes Fact Sheet
Prevalence of Diabetic Kidney Disease Among Adults with Diabetes; United States, 2005–2008

- Albuminuria = ACR ≥30 mg/g
- Impaired GFR = eGFR <60 ml/min/1.73m²

JAMA 305:2532–2539, 2011
Mortality in persons without diabetes or kidney disease.
*Standardized to age, sex, and race of study population.

ESRD Patient Counts, by Modality 2008

- Prevalent dialysis population:
  - Increased 3.6% in 2008
  - Up 34.7% since 2000
- Transplant population:
  - Increased 4.4% in 2008
- Incident population:
  - Increased 1.4% in 2008

Delaying the need for Renal Replacement Therapy may be Cost–effective.

- Total Medicare ESRD expenditures, per person per year (PPPY).
Reference: USRDS Annual Data Report (NIDDK, 2009)
Key Issues in Managing DKD

• Ensure the diagnosis is correct.
• Monitor progression.
• Implement appropriate therapy to slow progression.
• Avoid acute kidney injury (e.g. NSAIDs).
• Screen for CKD complications.
• Educate the patient about CKD.
• Prepare appropriately for kidney failure.
Therapy to Slow Progression

- Hypertension
- Diabetes
- Urine Albumin
- CVD Risk Factors
Blood Pressure is Poorly Controlled in People with CKD

Systolic Blood Pressure ≥ 140 mm Hg

NHANES 1999–2006
Reference: Adapted from USRDS 2009 Annual Data Report
Individualized Blood Pressure Goals in CKD

- Target of $< 140/90$ mmHg endorsed by JNC8.
- Uncontrolled hypertension (systolic blood pressure $> 160$) is a major challenge.
- Issue of BP goal with elevated albuminuria unresolved.

Reference: Chobanian et al., 2003; Jafar et al., 2003
The DASH Diet may Help Prevent CKD, but it is not Generally Used with CKD

• The lower the sodium intake, the lower the blood pressure.
• Combining the DASH pattern and lowest sodium intake (1,150 mg) provided the greatest reduction in blood pressure.
• The DASH pattern may be too high in protein, potassium, and phosphorus for CKD.

References:
Good Glycemic Control Early may Reduce CKD Later

• There is evidence that control of newly diagnosed diabetes may help prevent CKD:
  • Type 1 diabetes (DM 1):
    • Diabetes Control and Complications Trial (DCCT)
  • Type 2 diabetes (DM 2):
    • United Kingdom Prospective Diabetes Study (UKPDS)
Treating Hyperglycemia in Patients with Chronic Kidney Disease

- Hyperglycemia harms kidneys.
- Intensive glycemic control increases the risk of severe hypoglycemia.
- Evidence that intensive glycemic control reduces the kidney complications of diabetes is based almost exclusively on prevention of micro- and macroalbuminuria.
- The benefits of intensive glycemic control must be balanced against the potential harm of this intervention.
- Hypoglycemia may be a sign that kidney disease has progressed.
A1C Goal is Individualized in CKD

• Goal for the general population:
  • A1C < 7%
• Less stringent goal may be appropriate for:
  • Frequent severe hypoglycemia
  • Limited life expectancy
  • Advanced microvascular (CKD) or macrovascular complications
• Spontaneous improvement and/or increased frequency of hypoglycemia may indicate CKD is progressing.
Reference: Diabetes Care, (supplement 1) 2011
Dietary protein may increase GFR and renal blood flow rates. Animal protein may have greater effect than plant protein.

Dietary protein is a source of nitrogen, phosphorus, potassium, and metabolic acids that need to be filtered and excreted by the kidneys.

Animal protein intake may be a risk factor for increased urine albumin excretion in hypertension and diabetes.

References: Friedman, 2004; Bernstein et al., 2007; Wrone et al., 2003
Effect of DKD on the Risk of Renal Events in ADVANCE

HR = 22.2 (95% CI 7.6–64.7)
Elevated UACR is Associated with risk of Renal Events

• Lowering UACR may lower risk of progression
• Renal events = loss of half of eGFR, dialysis, or death

Reference: NIH, February 2010; De Zeeuw et al., 2004
Interventions for Reducing Urine Albumin

- Control blood pressure.
- Reduce sodium intake.
- Achieve good control of diabetes early; may help prevent albuminuria.
- Reduce weight (if obese).
- Reduce protein intake, if excessive.
- Achieve tobacco cessation.
ACEi and ARBs are Kidney-protective

- Their effects are beyond blood pressure control.
- They also reduce protein in the urine.
- Sometimes these medications are prescribed to lower urine albumin levels in normotensive people.
- Small increase in creatinine may reflect efficacy.

Reference: Chobanian et al., 2003; Strippoli et al., 2010; Kunz et al., 2008
Cardiovascular Disease

• CVD is the leading cause of morbidity and mortality in people with CKD.
Effect of DKD on the Risk of Cardiovascular Disease in ADVANCE


HR = 3.2 (95% CI 2.2-4.7)
HR = 5.9 (95% CI 3.5-10.2)
Lipid Abnormalities may Increase as eGFR Declines

Reference: Adapted from Astor et al., 2008
Statins are Used in Patients with CKD

• Statins reduce hepatic cholesterol synthesis.
• Statins significantly reduce all-cause and CVD mortality in persons with CKD.
• Use of statins does not appear to slow CKD progression but may reduce proteinuria.

Reference: Navaneethan et al., 2009
Complications of CKD

- Anemia:
  - Inadequate erythropoietin and iron
  - Hemoglobin and iron indices

- Hyperkalemia:
  - Limit dietary potassium when serum level is elevated.

- Hypoalbuminemia:
  - Poor oral intake (spontaneous reduction in protein)
  - Inflammation
Complications (cont.)

• Metabolic Acidosis:
  • Maintaining serum CO2 > 22 mEq/L may be beneficial.
  • Animal protein is a source of metabolic acids.
  • Acidosis may be treated with supplemental bicarbonate.

• Bone Disease in CKD:
  • Calcium, phosphorus, vitamin D, parathyroid hormone:
    • Use corrected calcium with hypoalbuminemia
  • Vitamin D supplementation may increase risk of hypercalcemia and hyperphosphatemia.
  • Calcium based binders may increase vascular calcification.
Community–Acquired Acute Kidney Injury: Common and Preventable

- AKI is a rapid loss of kidney function:
  - An absolute increase in serum creatinine of $\geq 0.3$ mg/dl
  - OR a percentage increase in serum creatinine of $\geq 50\%$
- Drug–induced AKI accounts for 18% of AKI hospital admissions from the outpatient setting.
- There is a 3– to 8–fold age–dependent increase in the frequency of community acquired AKI in patients $>60$ years old.

References:
Who is at High Risk for AKI?

• Patients with diabetes or hypertension because both cause kidney damage over time.
• Multiple co–morbid conditions which are acquired with age (e.g., congestive heart failure, renal artery disease, severe liver disease).
• Patients with multiple co–morbid conditions who were recently discharged from the hospital.
• Patients with co–morbid conditions that require the use of drugs that affect renal hemodynamics (e.g., ACE Inhibitors, ARBs, diuretics, NSAIDs).
Video on Counseling Patients on NSAID Use to Prevent Kidney Injury
Kidney Failure is an eGFR < 15

- Kidneys cannot maintain homeostasis.
- Kidney failure is associated with fluid, electrolyte, and hormonal imbalances and metabolic abnormalities.
- End-stage renal disease (ESRD) means patient is on dialysis or has a kidney transplant.
Kidney Disease Education is a Medicare Benefit

eGFR < 30

• Medicare B:
  • Individual pays 20%, deductible applies.
  • Qualified providers: physicians, physician assistants, nurse practitioners, and clinical nurse specialists.
  • Up to six sessions covered.
• Delay the need for renal replacement therapy:
  • Recognize and test at-risk patients: monitor eGFR and UACR.
  • Screen for anemia (Hgb), malnutrition (albumin), metabolic bone disease (Ca, Phos., PTH).
  • Treat cardiovascular risk, especially with smokers and hypercholesterolemia.
  • Refer to dietitian for nutritional guidance.
  • Avoid acute injury to the kidney (NSAIDs).
  • Educate patients about CKD and treatment.
Patient Awareness of CKD is Low General U.S. Population

Have you ever been told by a doctor or other health care professional that you had weak or failing kidneys?

- **NHANES 1999–2000:** 4101 participants.
- < 20% of patients with moderate to severe CKD said yes.
- Most had seen a physician within the past year.

*Adapted from: Coresh, et al. JASN 2005*
Awareness & Knowledge about CKD in Patients Seen by Nephrologists

• Low Self–Rating Perceived Knowledge N=676:
  • No Knowledge of Hemodialysis 43%
  • No Knowledge of Peritoneal Dialysis 57%
  • Little or No Knowledge Re: Diagnosis 35%

• Limited Awareness & Objective Knowledge N=401:
  • Unaware of CKD diagnosis 31%
  • Do not understand CKD implications, e.g., heart disease 34%
  • Do not understand kidney functions, e.g., urine production 34%
  • Do not understand terminology, GFR 32%
    Wright, et al. AJKD 2011
Healthy People 2010

- Increase the proportion of treated chronic kidney failure patients who have received counseling on nutrition, treatment choices, and cardiovascular care 12 months before the start of renal replacement therapy.

Reference: USRDS Annual Data Report (NIDDK, 2010)

![Graph showing pre-ESRD counseling and care for greater than 12 months (2008). Target goal: 45%.](image)
AADE Practice Advisory Recommendations

• Identify CKD due to diabetes and educate the patient about their kidney test results.
• Slow progression of DKD: BP, Glucose control, diet.
• Collaborate with PCP to identify and monitor CKD complications.
• Promote self-management:
  • Talk to patients about CKD.
  • Communicate importance of testing.
  • Explain progressive nature of CKD.
  • Begin to speak about dialysis and transplantation.

Managing DKD Training Program

• Training modules to help diabetes educators manage kidney disease patients:
  • **Module 1**: Identify Diabetic Kidney Disease will help you recall the basics of kidney anatomy and physiology, assess kidney function and damage in your diabetes patients, determine whether your patient’s kidney disease may be due to diabetes, and talk to your patients about kidney disease.
  • **Module 2**: Slow Progression of Kidney Disease introduces the three patient cases you will follow through the remainder of the program and provides an overview of blood pressure control, diabetes management, and cardiovascular disease risk in CKD patients through the lens of each case study.
  • **Module 3**: Complications covers common CKD complications—including anemia, hyperkalemia, hypoalbuminemia, metabolic acidosis, and mineral and bone disorders—as well as the lab data for evaluation and monitoring, the medications for treating, and the nutrients involved in these complications.
  • **Module 4**: Treatment Choices for Kidney Failure reviews advantages and disadvantages of treatment options for kidney failure, provides guidance on discussing treatment options with patients, and covers key considerations for managing diabetes patients after transplant or during dialysis.

• Continuing professional education credits will be available through the American Association of Diabetes Educators.
CKD Training Program

Managing Chronic Kidney Disease in the Primary Care Setting

- Designed to help PCPs manage adult CKD patients.
- Emphasizes key considerations for evaluating and managing CKD:
  - 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
Lessons Learned

• CKD is best addressed through population management.
• Improvement in care results from changes implemented by in the community and in the clinic by all health professionals (CCM).
• Implemented through diabetes care delivery system; not specialty clinic based.
• Surveillance and prevention are part of multisystem chronic disease control.
• Emphasis on ensuring that patient received care from competent and interested individual, not referral.
Trends in Adjusted ESRD Incidence Rate

• Per million/year), by race, in the U.S. population, 1996–2013

Data Source: Special analyses, USRDS ESRD Database. *Adjusted for age and sex. The standard population was the U.S. population in 2011. Abbreviations: Af Am, African American; ESRD, end-stage renal disease.
Questions and Comments

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All materials available at: http://nkdep.nih.gov/