Screening and Monitoring of Chronic Kidney Disease (CKD) in Diabetes

Frequently-Asked Questions

1. **Q**: Why are kidney function issues so important in diabetes care?

   A: Diabetic nephropathy (the term for kidney disease caused by diabetes) occurs in 20-40% of patients with diabetes. It is the single leading cause of end-stage renal disease (ESRD) in the United States.

2. **Q**: What is the difference between "Chronic Kidney Disease "and "diabetic nephropathy"?

   A: These two terms are often used interchangeably by providers, however there are some differences. Diabetic nephropathy refers generally to the damage to the kidneys caused by diabetes. Chronic Kidney Disease (CKD) has a clinical definition (see #4 below) and may be caused by diabetes or by other diseases. They both reflect damage not only to the kidneys but to the systemic vasculature as well (see #6 below).

3. **Q**: Why is it important to screen for CKD in people with diabetes?

   A: In this high-risk population, early CKD detection and treatment of the underlying risk factors reduce the development of kidney failure by 30-70%. It has been shown in Pima Indians that half of the patients with macroalbuminuria (see #9 below) progress to ESRD within the next ten years, although it is hoped that improved treatment will reduce this.

4. **Q**: How is CKD defined?

   A: CKD is defined as ≥ three months duration of <u>either</u>:

   - **Decreased kidney function:** GFR < 60 mL/min/1.73 m2
   - **Evidence of kidney damage:** albuminuria (e.g. UACR ≥ 30 mg/g) or abnormalities on kidney blood tests, imaging or biopsy

   GFR = <u>G</u>lomerular <u>F</u>iltration <u>R</u>ate

   UACR = <u>U</u>rine <u>A</u>lbumin to <u>C</u>reatinine <u>R</u>atio

5. **Q**: What tests should be used to screen for and monitor CKD? What should be done once CKD is diagnosed?

   A: Given the definition of CKD above, it follows that the two tests which should be used together to give the best assessment of how the kidneys are doing are the **GFR and UACR**. In the clinical setting, GFR is **e**stimated using a calculation and so is often referred to as **eGFR**.

   Screening: Both the eGFR and UACR should be checked at diagnosis of type 2 diabetes and then annually thereafter.

   - **eGFR**: If the **eGFR** is < 60 mL/min/1.73 m2, it should be repeated in three months to confirm a diagnosis of CKD.
   - **UACR**: Because of variability in urinary albumin excretion, two out of three UACR specimens collected within a three–six month period should be abnormal to diagnose CKD.
     - As they may elevate urine albumin excretion, avoid screening if infection, fever, congestive heart failure (CHF), marked hyperglycemia, marked hypertension or if significant exercise within 24 hours.

   Link to urine albumin screening card:

   http://www.ihs.gov/MedicalPrograms/Diabetes/HomeDocs/Resources/DiabetesTopics/Treatment/DM_urine_albumin_screening.pdf

   Monitoring: Once CKD has been diagnosed, the eGFR and UACR should be checked at least annually if stable. They should be checked more frequently if they are rising rapidly and as needed to assess the effect of therapeutic interventions. Once a patient has started dialysis, they no longer need to be checked.

   The diagnosis of CKD should prompt the provider to initiate or intensify treatment:

   - Delay CKD progression: ACE inhibitor/ARB use, glucose control, blood pressure control, dietary protein restriction
   - Reduce associated CVD risk: lipid control, smoking cessation, consider ASA
   - When eGFR is < 60 mL/min/1.73 m2, begin screening for complications of CKD
     - Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, iPTH at least yearly
   - Consider nephrology referral
     - if uncertainty about the etiology of CKD (e.g. if heavy proteinuria, active urine sediment, absence of retinopathy, rapid decline in eGFR, abnormal renal ultrasound or resistant hypertension)
     - if difficulty managing any CKD issue or complication
     - when advanced kidney disease (e.g. by Stage 4 CKD)

Link to CKD algorithm card:
http://www.ihs.gov/MedicalPrograms/Diabetes/HomeDocs/Resources/DiabetesTopics/Treatment/DM_CKD_algorithm.pdf

6. **Q**: Staging of CKD is based only on GFR, so why is urine albumin testing important?

   A: Recent studies have made it clear that both kidney function (GFR) and albuminuria are independent risk factors for progression to kidney failure. Because of this evidence, the CKD staging criteria will be changing in the future. Also, albuminuria is often detected long before the eGFR drops below 60 mL/min/1.73 m2, thus allowing for earlier CKD diagnosis and intervention.

   Further, albuminuria is a risk factor for coronary heart disease (CHD) and is a component of the Strong Heart Calculator, which calculates ten-year risk for having CHD in American Indian adults: http://strongheart.ouhsc.edu/CHDcalculator/calculator.html Patients with CKD in even the earliest stages are at increased risk for subsequent CHD and their providers should intensify interventions that reduce those risks.

7. **Q**: Why is UACR the test of choice for evaluating proteinuria?

   A: The American Diabetes Association, National Institutes of Health (NIH)/National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the National Kidney Foundation (NKF) all recommend using the UACR. UACR has the following advantages over other urine protein tests:

   - UACR is a quantitative test which is reliable for CKD screening, diagnosis, monitoring and clinical decision-making.
     - Even though the result from a semi-quantitative POC (point of care) test strip may look like a UACR result (mg albumin/g creatinine), these strips should only be used for urine albumin *screening*, if used at all in the clinic setting. When the test strip indicates an elevated level of urine albumin, the result should be confirmed with a quantitative method (UACR). If the result is confirmed and persists for at least three months, the diagnosis of CKD is made. Thereafter, only UACRs should be used to monitor the patient's urine albumin.
   - UACR measures albumin, the major protein excreted in diabetic nephropathy
     - Urine albumin measurement and reporting is in the process of being standardized nationally so it will be even more accurate and reproducible.
   - UACR accounts for urine concentration through the ratio to creatinine.
   - UACR can reliably be done on a spot ("random") urine sample—there is no longer a routine need for 24-hour urine collections to assess proteinuria.

8. **Q**: Why is it important to have an accurate, quantified assessment of urine albumin?

   A: Even mildly elevated urine albumin levels should prompt clinical interventions such as improving blood pressure control, starting or maximizing ACE inhibitors/ARBs, improving blood sugar control, and re-emphasizing smoking cessation. The UACR should then be rechecked to assess whether the intervention has succeeded in reducing the level of urine albumin—this is clinically significant as the most recent UACR result is the one that predicts that patient's future kidney status. Further, both the absolute amount as well as the "rate of rise" of urine albumin have clear prognostic value as well. Assessing this important indicator over time requires an accurate, quantified test.

9. **Q**: How are UACR results interpreted?

   A: Urine albumin is a continuous variable, meaning that there is increasing risk for every incremental increase in the result—there is no threshold above which risk abruptly changes. As such, the categories of "microalbuminuria" and "macroalbuminuria" are somewhat arbitrary and national organizations are discussing adopting new terms which better reflect the continuous nature of this risk variable. In the meantime, the current categorizations are used both clinically and in the medical literature to provide a quick view of risk for progression to ESRD in individuals as well as patient populations.

   The current definitions are:

   - Normal = < 30 mg/g
   - Microalbuminuria = 30-300 mg/g
   - Macroalbuminuria ≥ 300 mg/g

10. **Q**: Can UACR and eGFR be used in children with diabetes as well as in adults?

    A: A recent NIH/NIDDK study in Pima Indians showed that UACR was useful in youth with diabetes and supported the same annual screening recommendation as in adults.

    For adults, eGFR should be calculated using the MDRD equation—this is the equation programmed into the IHS Electronic Health Record (EHR) laboratory packages ["MDRD" refers to "Modification of Diet in Renal Disease"]. However, MDRD is not accurate in children—instead, the Schwartz equation should be used for children; see the National Kidney Disease Education Program (NKDEP) website:

    http://www.nkdep.nih.gov/professionals/gfr_calculators/selecting.htm

    as well as the National Kidney Foundation calculator:

    http://www.kidney.org/professionals/kdoqi/gfr_calculatorPed.cfm

11. Q: What options are available for a clinic to provide the UACR test?

A: UACR can be done in any CLIA-certified laboratory, including those at many Indian Health sites. There is a POC option available but it is not CLIA-waived. If a site doesn't have the capability to provide UACR in-house, the test can be done at whatever reference laboratory is used. Since prices charged by these labs vary widely, it is often cost-effective for sites to establish a contract pricing agreement with their reference lab, either on their own or in collaboration with other sites. In addition to cost considerations, performing UACR in-house is advantageous in terms of something very important to busy clinics: turn-around time for providers to receive the test results. Diabetes providers should talk with their facility's laboratory supervisor to determine the most efficient and cost-effective way to provide UACR testing. It is also important to make sure that UACR is clearly and correctly listed in the local electronic health record's lab orders.

12. Q: This is a change from the tests we have used in the past to screen for and monitor CKD. Will the other urine protein tests still being used in some Indian Health clinics continue to count for the Diabetes Audit?

A: During this current period while many clinics are transitioning to using the UACR, the Diabetes Audit will continue to count other urine protein tests. However, within the next few years, UACR will become the only urine protein test which the Audit will count.

References and Resources

American Diabetes Association. Clinical Practice Recommendations 2011. *Diabetes Care* 2011;34:Supplement 1.

Chronic Kidney Disease Prognosis Consortium. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. *Lancet* 2010, published online May 18, 2010, doi:10.1016/S0140-6736(10)60748-9.

Di Angelantonio E, Chowdhury R, Sarwar N, Aspelund T, Danesh J, Gudnason V. Chronic kidney disease and risk of major cardiovascular disease and non-vascular mortality: prospective population based cohort study. *BMJ* 2010;341:c4986 doi:10.1136/bmj.c4986

Hammelgarn BR, Manns BJ, Lloyd A, James MT, Klarenbach S, Quinn RR, Wiebe N, Tonelli M. Relation between kidney function, proteinuria, and adverse outcomes. *JAMA* 2010;303(5):423-429.

Indian Health Service, Division of Diabetes of Diabetes Treatment and Prevention website resources on CKD:

http://www.ihs.gov/MedicalPrograms/Diabetes/index.cfm?module=toolsCKDQuickGuides

http://www.ihs.gov/MedicalPrograms/Diabetes/index.cfm?module=trainingSeminars

http://www.ihs.gov/medicalprograms/diabetes/index.cfm?module=toolsDTTreatmentAlgorithm

Kim NH, Pavkov ME, Knowler WC, Hanson RL, Weil EJ, Curtis JM, Bennett PH, Nelson RG. Predictive value of albuminuria in American Indian youth with or without type 2 diabetes. *Pediatrics* 2010, doi:10.1542/peds.2009-1230

National Kidney Disease Education Program website:

http://www.nkdep.nih.gov/professionals/index.htm

National Kidney Foundation website:

http://www.kidney.org/professionals

Pakov ME, Knowler WC, Hanson RL, Nelson RG. Diabetic nephropathy in American Indians, with a special emphasis on the Pima Indians. *Current Diabetes Reports* 2008;8:486-493.

Strong Heart Calculator:

http://strongheart.ouhsc.edu/CHDcalculator/calculator.html