**Objectives**

1. Identify the types of albumin and normal vs. abnormal levels
2. Highlight albumin testing and lab deviations with emphasis on patient care
3. Discuss methods of decreasing proteinuria with an eye on the outcome of CKD progression
4. Using sample patients, discuss who/when/how to treat the proteinuric diabetic patient

**Alexis**

24 y/o obese female here to establish care. No PMH. Strong FH of DM, HTN, CKD
PE: 132/78, 240 lbs, no edema, no sx
Labs: SCr 0.9mg/dL, UA + albuminuria, A1C 6.8%
Worried if she has DM, HTN, and CKD

**What is the next step?**

A. Stage her CKD
B. Reassure her that the albuminuria and A1C are not significant
C. Repeat the UA in 6 weeks and if present quantify
D. Refer for kidney biopsy
E. Refer to endocrinologist
### Stages of CKD 2002

#### Table 10. Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or ↑ GFR</td>
<td>&gt;90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60-80</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>20-50</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-20</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
</tr>
</tbody>
</table>

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m² for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

KDIGO CKD Guidelines, AJKD Supplement, 2002

### Stages of CKD 2013

**Council of Advanced Practitioners**

**Trends in adjusted* ESRD incidence rate (per million/year), by primary cause of ESRD, in the U.S. population, 1996-2014**

![Graph showing trends in ESRD incidence rate](USRDS 2016 Annual Report, Vol 2, ESRD, Ch1)

**Estimated prevalence of self-reported kidney disease by state (%), 2014**

![Map showing prevalence of kidney disease by state](USRDS 2016 Annual Report, Vol 1, CKD, Ch1)

**Ralph**

35 y/o male with Hx HTN and DM well controlled with meds X 10 years. Father had CKD 2/2 ESRD requiring dialysis 2/2 HTN and DM. Ralph is worried he is at increased risk for developing CKD and needing dialysis.

PE: 120-125/70 X 3 readings, no edema, no SOB

**What is your next step?**

A. Refer for more lab work*
B. Refer to kidney biopsy
C. Add ACEi or ARB
D. Refer for genetic testing APOL1
CKD Risk Factors

- Diabetic
- Hypertensive/CVD
- Older age (>60y/o)
- Recurrent UTI
- Kidney stones
- History of AKI
- Polycystic Kidney Disease
- Genetics

- Autoimmune disease: Lupus, Sjogrens, RA, MCTD...
- Family history of CKD
- Neoplasm: multiple myeloma, Wilms, kidney cancer
- Previous transplant
- Previous kidney donor

1. KDOQI guidelines 2002

CKD Screening & Evaluation

- Screening:
  - Renal function panel (S Cr, albumin)
  - Proteinuria assay
  - UA with microscopy
- Follow up with:
  - Renal Ultrasound
  - Blood borne Pathogens (at least once)
  - Vitamin D, iPTH

CKD Screening for Proteinuria

- Urine Protein to Creatinine ratio
  - Used when you expect higher degrees of proteinuria
  - Usually lab gives you a Random Total Protein (mg/dL), Random Creatinine (mg/dL)
  - Protein/Creatinine = UPCR
  - Usually represented as g/g (0.5 g/g, 2 g/g, etc)
- Urine Albumin to Creatinine ratio
  - More accurate when there is <1-2 g proteinuria; BEST SCREENING LAB
  - Usually lab gives you Random Albumin (mcg/mL), Random Creatinine (mg/dL), and UACR
  - Usually represented as mg/g

24 hour urine - Gold Standard?
Lois
65 y/o with HTN, HLD, DM
PMH: retinopathy, nephropathy, neuropathy
PE: 150/88, trace edema, RRR, CTA
Labs: Scr 2.3mg/dL (GFR 29ml/min), K 4.5
BUN 45, BG 142, A1C 6.5%, UACR 1700mg/g
Meds: glargine (Lantus), lispro (Humalog), lisinopril, furosemide (Lasix), atorvastatin

What adjustments would you make to her management?
A. None, she is stable
B. Increase the lispro
C. Increase the lisinopril*
D. Increase the atorvastatin

Proteinuria
- BEST PREDICTOR OF PROGRESSION
- Check at least annually in DM patients to screen
- Check every 6-12 months in CKD patients
- Goal: as low as possible
  - Ideally <0.5 g/g
  - Partial remission: 0.2-2 g/g
  - Complete remission: <0.2 g/g

Albuminuria As Risk Factor
The relationship between magnitude of proteinuria reduction and the risk of ESRD: Results of the AASK study of kidney disease and hypertension. Arch Intern Med 2001
Proteinuria and Rate of Change in Kidney Function in a Community Based Population, JASN 2013
Combining GFR and albuminuria to classify CKD improves prediction of ESRD, JASN 2009
Alberta Kidney Disease Network: Relation between kidney function, proteinuria, and adverse outcomes, JAMA 2010
Renin-Angiotensin-Aldosterone System (RAAS)

Inhibition of RAAS: leads to less proteinuria

1. ACEIs
   - Block conversion of angiotensin I to angiotensin II
   - Increase availability of bradykinin

2. ARBs
   - Selectively antagonize angiotensin II
   - May also modulate the effects of angiotensin II breakdown products

RAAS inhibition provides nephroprotection independent of blood pressure lowering

Main Diabetic CKD Goals

- Blood Pressure Control
  - ACCORD: 140/90
  - SPRINT: 120/80
  - KDIGO: <140/90, <130/80 with proteinuria
  - Keep the patient and the med list in mind!
- Glycemic Control
- Proteinuria Reduction
- CVD management
  - Kills more than CKD
  - SHARP trial: Vytorin benefits CKD patients
  - Lipid panel less indicative of true CV risk - set it and forget it

Name of the Game: Slow it down, delay progression of CKD!

Sherman

55 y/o with family history of HTN and DM
BP trending up into the 140-165/85-90 range
S Cr 1.6mg/dL (GFR 58) & UACR 400mg/g

Which of the following is the best HTN medication for Sherman?

A. Loop diuretics
B. Thiazide diuretics
C. ACE inhibitors*
D. ARB inhibitors*
E. Calcium channel blockers
F. Beta blockers
Rose

74 y/o routine visit, PMH: PVD, HL, HTN, Meds: metoprolol, HCTZ, amlodipine, ASA, atorvastatin
PE: 168/98, home 150-160s
Labs: Scr 1.2mg/dL, UACR 50mg/dL, GFR 56ml/min
2 weeks ago, lisinopril added for BP/UACR lowering
F/U labs: 2 weeks later reveal Scr 1.4mg/dL with K 5.4mEq/L, BP 150/90

What is the cause of the rise in Scr?
A. Medication induced AIN
B. Renovascular Disease (RAS)
C. Rhabdomyolysis from statins
D. Usual rise from ACE inhibitor
E. Essential hypertension

Acceptable rise in Scr due to RAAS is 20-25%

Fred

81 y/o poorly controlled DM x 20 years, bilateral BKA, often forgets meds, has passing ‘acquaintance’ with diabetic diet, has issues w/exercise due to chronic leg ulcers
Labs: A1C historically 11.5-12% most recent A1C 7.5%, GFR 20ml/min
Meds: metformin, lisinopril, furosemide, ASA, atorvastatin

Why is his A1C closer to goal now?
A. McDonald's has changed their menu
B. A1C is not reliable at lower GFRs
C. He doubled his metformin
D. He has taken up marathon running
KDOQI Goals in 2014

Evidence that intensive treatment has an effect on loss of glomerular filtration rate (GFR) is sparse*

2.1: We recommend a target HbA1c of 7.0% to prevent or delay progression of the microvascular complications of diabetes, including DKD. *(1A)*

2.2: We recommend not treating to an HbA1c target of <7.0% in patients at risk of hypoglycemia. *(1B)*

2.3: We suggest that target HbA1c be extended above 7.0% in individuals with co-morbidities or limited life expectancy and risk of hypoglycemia. *(2C)*

*NKF-KDOQI Clinical Practice Guideline for Diabetes and CKD, Guideline 2: Management of Hyperglycemia and General Diabetes Care in CKD, AJKD, Vol 60, #5, Nov 2012*

Sadie

85 y/o Type 2 DM, HTN, CKD.

Meds: metformin 1000mg BID

Labs: Scr 1.7mg/dl (historical 1.3mg/dL), eGFR 31ml/min, A1C 7.0%

What is the next step in management of DM?

A. Decrease metformin*
B. Discontinue metformin
C. Add insulin
D. Discontinue metformin and start insulin

<table>
<thead>
<tr>
<th></th>
<th>SCr</th>
<th>Race</th>
<th>Age</th>
<th>eGFR</th>
<th>CKD Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1.5</td>
<td>African American</td>
<td>17</td>
<td>78</td>
<td>2</td>
</tr>
<tr>
<td>Male</td>
<td>1.5</td>
<td>African American</td>
<td>70</td>
<td>54</td>
<td>3a</td>
</tr>
<tr>
<td>Female</td>
<td>1.5</td>
<td>white</td>
<td>17</td>
<td>50.7</td>
<td>3a</td>
</tr>
<tr>
<td>Female</td>
<td>1.5</td>
<td>white</td>
<td>70</td>
<td>35</td>
<td>3b</td>
</tr>
</tbody>
</table>

GFR using CKD-EPI equation
Metformin in CKD

Now approved by the FDA for lower GFR’s

- eGFR level (mL/min per 1.73 m²) | Action
- >90 | No renal contraindication to metformin
- 60-90 | Monitor renal function annually
- 30-60 | Consider use
- <30 | Increase monitoring of renal function (every 3-6 months)

Prescribe metformin with caution
Use lower dose (e.g., 50%, or half-maximal dose)
Gently monitor renal function (every 3 months)
Do not start new patients on metformin
Stop metformin.

Additional caution is required in patients at risk for acute kidney injury or with unexplained significant deterioration in renal status, based on previous history, other comorbidities, or potentially interacting medications.

Non-Insulin Agents & CKD/Dialysis

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Mild CKD stage 3 (eGFR 45-59 mL/min/1.73 m²)</th>
<th>Moderate CKD stage 4 and 5, eGFR 20-44 mL/min/1.73 m²</th>
<th>ESRD stages 4-5, eGFR &lt;20 mL/min/1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td>Starting dose: 45 mg daily, increase dose until adequate control is achieved.</td>
<td>No dose adjustment necessary</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>Meglitinide</td>
<td>Starting dose: 15 mg daily, increase dose until adequate control is achieved.</td>
<td>No dose adjustment necessary</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>GIP agonists</td>
<td>Incretins mimetics - not recommended for moderate/severe renal impairment (late stage 3 and onward)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucagon-like peptides</td>
<td>GLP-1 receptor agonists - no data</td>
<td>No dose adjustment necessary</td>
<td>No dose adjustment necessary</td>
</tr>
</tbody>
</table>

Incretins and SGLT-2 Inhibitors

- DPP-4 inhibitors - have showed reductions in albuminuria and
  - Victoza - cardioprotection and renoprotection in the LEADER trial
- SGLT-2 - have demonstrated ability to decrease BP, weight, uric acid, and albuminuria beyond what can be explained by its glycemic effect
• EMPA-REG: ~7000 diabetics
• Empagliflozin vs placebo
• Similar use of ACE/ARB in both groups
• Initial drop in GFR seen in empagliflozin group (wk 1-4), then later showed stable GFR with empagliflozin vs declining GFR with placebo
• Significant relative risk reduction in progressing albuminuria

• CANATU-SU: >1000 diabetics
• Canagliflozin vs glimepiride
• Initial drop in eGFR, then stabilized & declines slower with canagliflozin at either dose
• Canagliflozin significantly reduced albuminuria, mostly with patients who started with positive UACR
• Results were independent of A1c reductions


• All types are safe and effective for All Stages of CKD
• Basal Insulin is VERY easy to dose in CKD
• Basal Insulin with Oral Medications is fine
• CKD Patients including Dialysis may use pumps
• Dosing Requirements decrease with decreasing Kidney Function
• Decreasing Dosing Requirements are NOT logarithmic no matter what you may have read...
References


