Session Content

1. Recommendations for commonly used medications in CKD
   - Basic principles/patient safety of medication prescribing in CKD
   - Is it ok to continue metformin in CKD?
   - What is the story with PPI and CKD?
   - What are commonly used nephrotoxins to avoid?

2. CKD screening and referral
   - Recommendations for screening in high risk populations
   - Evaluation of CKD in patients with DM: Is work-up necessary?
   - Nephrology referral: What to do with a creatinine elevation?

3. Strategies to slow CKD progression
   - Traditional strategies: RAAS blockade (Should I continue or stop ACE inhibitors in patients with CKD?)
   - Logical strategies: Avoid AKI
   - Unconventional strategies: Treat metabolic acidosis
Building a Practical Approach to Detection and Management of CKD

1. Patient Safety
   - GFR < 60 = Vascular Safety Risk
   - Drug therapy and GFR
   - Reduce dose of all drugs, especially those causing toxicity
   - Contrast-induced AKI prevention
   - Patient education and adherence

2. CKD Progression/Compliance
   - Blood Pressure Goal < 140/90
   - Consider BP goal < 130/80 only if ACR > 300
   - ACEI or ARB for HTN if ACR > 30
   - Avoid ACE-I and ARB in general
   - Diuretics usually required
   - Dietary sodium < 2000 mg/day

CKD Patient Safety Issues

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

- Fluid management
  - Hypotension/Hypertension
  - Diuretics
  - Concomitant heart failure management

- Pharmacology
  - Drug dosing and frequency
Metformin and Renal Impairment: T or F?

T • 1. Evaluate eGFR prior to treatment with metformin and annually thereafter (base assessment on eGFR and NOT serum creatinine)
• More frequent checks in those at risk for renal impairment

FDA Drug Safety Communication: FDA revises warnings regarding use of the diabetes medicine metformin in certain patients with reduced kidney function

T • 4. In those on metformin, assess risk/benefit of continuing if eGFR falls < 45 ml/min

T • 5. Do not administer for 48 hrs after iodinated contrast imaging procedure in patients with eGFR 30-60 ml/min or h/o liver disease, alcoholism or heart failure or in those receiving intra-arterial contrast; restart if eGFR stable.

April 2016

PPIs in the news

PPIs users (compared to users of H2 blockers or non-users) have increased risk of
• AKI (including AIN)
• CKD development
• CKD progression to ESRD

PPI associated kidney disease association is not causality

<table>
<thead>
<tr>
<th>Association</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR &lt; 60</td>
<td>1.19</td>
<td>1.15-1.24</td>
</tr>
<tr>
<td>Incident CKD</td>
<td>1.26</td>
<td>1.20-1.33</td>
</tr>
<tr>
<td>eGFR decline &gt;30%</td>
<td>1.22</td>
<td>1.16-1.28</td>
</tr>
<tr>
<td>ESRD or &gt;50% ↓ eGFR</td>
<td>1.30</td>
<td>1.15-1.48</td>
</tr>
</tbody>
</table>

Xie et al. Kidney Int 2017; 1-13
PPI: Indigestion for Nephrologists

- Twice daily dosing of PPI associated with higher risk of CKD and AKI.
- Higher risk with higher cumulative exposure but risk present even at > 30 days.
- >50% of patients with AIN developed CKD, despite discontinuation of the drug.

Reflection on practical strategy:
- Discuss PPI use with my patients and encourage alternative when possible if no clear indication for the medication exists.
- Wean down and then off medication.
- Discuss concomitant strategies: avoiding known food triggers; using H2 blockers instead.

Common Medications Requiring Dose Reduction in CKD

- **Antimicrobials**
  - Trimethoprim/Sulfamethoxazole
  - SS tablets and adjust frequency!

- **Antifungals**
  - Fluconazole
  - CKD 4 and 5: 50%

- **Antivirals**
  - Acyclovir
  - CKD stage 4, 5: adjust frequency!

- **GI cocktails**
  - Avoid Mg containing agents
  - Avoid Fleets (P containing)

- **Antihypertensive medications**
  - Atenolol
    - CKD 4: 50%
    - CKD 5: 25%

- **Analgesics**
  - Gabapentin
    - CKD 4: Max dose 200-700 mg qd
    - CKD 5: Max dose 300mg qd or qod

Munar et al. JPS 2011; 10: 57-70

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Building a Practical Approach to Detection and Management of CKD

**3.** CKD G Stage

<table>
<thead>
<tr>
<th>eGFR &lt;60 ml/min/1.73 m²</th>
<th>A Stage ACR &gt; 30 mg/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>45 – 59 = 3a</td>
<td>30 – normal or mild</td>
</tr>
<tr>
<td>30 – 44 = 3b</td>
<td>30.399 – moderately 1</td>
</tr>
<tr>
<td>15 – 29 = 4</td>
<td>&gt; 300 = severely</td>
</tr>
<tr>
<td>&lt; 15 = 5</td>
<td></td>
</tr>
</tbody>
</table>

**4.** Magnifiers Fatora

- eGFR < 60 ml/min/1.73 m²
- ESRD (end-stage renal disease)
- Presence of proteinuria
- Hypertension
- Diabetes
- Family history of kidney disease
- Age > 60 or older
- Obesity

A 5-step plan for CKD evaluation and referral:

1. Recognize the criteria for CKD
   - Abnormalities in kidney structure or function, present for > 3 months, with implications for health
   - Either of the following must be present for > 3 months:
     - Proteinuria (persistent or intermittent)
     - Serum creatinine > 1.5 mg/dl

2. Intervene prior to AKI risk factors:
   - Diabetes
   - Hypertension
   - Family history of kidney disease
   - Age > 60 or older
   - Obesity

3. Start treatment:
   - Assess CKD severity
   - Adjust antihypertensive therapy
   - Patients with stage 3 CKD:
     - Start with a ACE inhibitor or ARB
   - Patients with stage 4 or 5 CKD:
     - Start with a potassium-sparing diuretic

4. Consider referral to a nephrologist:

5. Follow-up:
   - Review patient progress and adjust therapy as needed
   - Monitor for progression or improvement in kidney function

References for CKD with race-specific tests:

- Test should be selected on the basis of the patient's race
- Consider race-specific or population-specific CKD classification
- Consider race-specific or population-specific CKD classification

Additional information:

- Consider race-specific or population-specific CKD classification
- Consider race-specific or population-specific CKD classification

Gaps in CKD Diagnosis

Studies demonstrate that clinician behavior changes when CKD diagnosis improves. Significant improvements realized in:1,2,3

- Increased urinary albumin testing
- Increased appropriate use of ACE I or ARB
- Avoidance of NSAIDs prescribing among patients with low eGFR
- Appropriate nephrology consultation

Screening for CKD

High Risk Patients

- HTN
- DM
- CV disease
- Certain ethnicities
- Prior AKI
- Autoimmune disease
- Reduced renal mass (solitary kidney)
- Nephrotic exposure
- Obstruction

eGFR, microalbuminuria or proteinuria

3/26/2019
Screening Tools: eGFR

- Considered the best overall index of kidney function.
- Normal GFR varies according to age, sex, and body size, and declines with age.
- Equations can be misleading with "normal" kidney function, obesity, advanced age

**MDRD equation**
1. Determinant of body size is pre-packaged into this equation
2. Developed in patients with GFR < 60

Summary of the MDRD Study and CKD-EPI Estimating Equations:

eGFR tools: case 1
- 25 yo healthy male, exercises, BMI satisfactory but creatinine was elevated and eGFR by MDRD was 67

Average Measured GFR by Age in People Without CKD

Kidney function and eGFR decline with age

Reference Table for Population Mean eGFR from NHANES III

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean-eGFR (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-34</td>
<td>158</td>
</tr>
<tr>
<td>35-44</td>
<td>135</td>
</tr>
<tr>
<td>45-54</td>
<td>107</td>
</tr>
<tr>
<td>55-64</td>
<td>81</td>
</tr>
<tr>
<td>65-74</td>
<td>60</td>
</tr>
<tr>
<td>75+</td>
<td>37</td>
</tr>
</tbody>
</table>
Age related declines in eGFR
- Should not be considered a disease
- “Normal” may be eGFR 60-89 ml/min/1.73 m²
- May not need referral to nephrology if
  - No proteinuria
  - No hematuria
  - No structural lesion
  - Stable serum creatinine

Microalbuminuria and Proteinuria

Microalbuminuria
- Stage of Nephropathy
  - Urinary Albumin Level
    - Normal
    - Microalbuminuria
    - Macroalbuminuria

<table>
<thead>
<tr>
<th>Category</th>
<th>Spot (mg/g creatinine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normoalbuminuria</td>
<td>&lt; 30</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>30-300</td>
</tr>
<tr>
<td>Macroalbuminuria</td>
<td>&gt; 300</td>
</tr>
</tbody>
</table>

Screening for CKD

High Risk Patients
- HTN
- DM
- FH of CKD
- Autoimmune disease
- Obstructive
- Reduced renal mass (solitary kidney)
- Nephrotoxin exposure
- Certain ethnicities

If eGFR is abnormal and + proteinuria: refer to nephrology

If eGFR is normal and no microalbuminuria, repeat kidney check tests in 1-2 years annually for DM and HTN
Should other causes of CKD be considered in patients with DM?

- DM frequent single cause of ESRD
- Timeline more consistent in T1DM
- Diabetic Kidney Disease: absence of renal bx

- Without intervention 20-40% patients with T2DM progress from micro to macroalbuminuria, however 20 yrs after developing overt proteinuria only 20% progress to ESRD
- Biopsy can influence therapeutic strategies and prognostication; consider alternative Dx (pre-biopsy clues)

1. Sharma SG et al. CJASN 2013, 8, 1718-1724
2. Fiorentino M. NDT 2017, 32, 97-110

Should other causes of CKD be considered in patients with DM?

- High probability of diabetic nephropathy if overt proteinuria + diabetic retinopathy
- Overt proteinuria, No diabetic retinopathy: 30% other renal disease

- Consider renal referral and biopsy if:
  - Proteinuria and no retinopathy
  - Signs/symptoms of systemic disease
  - AKI/rapid progressive renal failure
  - < 5 yr evolution of DM (type 1 DM)
  - Active urine sediment (hematuria, casts)
  - Regional prevalence of other diseases

- Biopsy may allow better design of clinical trials aimed at delaying progression of renal disease

1. Sharma SG et al. CJASN 2013, 8, 1718-1724
2. Fiorentino M. NDT 2017, 32, 97-110
3. Christensen PK. Kidney Int 2000, 58, 1719-1731
When to refer to nephrology?

- AKI, rapid decline in GFR or unexplained elevation in serum creatinine
- CKD with eGFR < 30
- Evidence of intrinsic renal disease
  - Microscopic hematuria with rbc casts and/or proteinuria
  - Persistent proteinuria
- Hypertension, refractory to treatment
- Electrolyte abnormalities (K, Na)
- Hereditary kidney disease (ADPKD)

**STONE CLINIC REFERRAL:** Recurrent or extensive nephrolithiasis

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Session Content

- 3. Strategies to slow CKD progression
  - Traditional strategies: RAAS blockade (Should I continue or stop ACE inhibitors in patients with CKD?)
  - Logical strategies: Avoid AKI
  - Unconventional strategies: Treat metabolic acidosis

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Slowing CKD Progression: ACE I or ARB

- Benefits clearly demonstrated in proteinuria patients with CKD
- Risk/benefit should be carefully assessed in the elderly and medically fragile
- Avoid ACE I and ARB in combination\(^1,2\)
  - Risk of adverse events (impaired kidney function, hyperkalemia)
- Check labs 1-2 weeks after initiation: If less than 25% SCr increase, continue and monitor
  - If more than 25% SCr increase, stop ACE I and evaluate for RAS
  - Continue until contraindication arises, no absolute eGFR cutoff
- Better proteinuria suppression with low Na diet (< 2 g Na) and diuretics
- Avoid volume depletion
- Avoid NSAIDs

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Slowing CKD Progression: role of AKI

1) Forni et al, Intensive Care Med 2017, 43, 855-866

Metabolic Acidosis: why do we care?
- Apparent when eGFR < 25-30 ml/min
- Increases bone resorption and stimulates bone turnover
- Increases protein degradation
- Associated with muscle wasting and weakness
- Associated with progression of CKD

Metabolic Acidosis: treatment
- Sodium bicarbonate tablets
  - 650 mg tablet = ~8 meq bicarbonate
  - Can start at 1 tab tid
- Baking soda
  - Level tsp = ~50 meq bicarbonate
Key Points on Medications, Patient Safety, Screening and Referral in CKD

- Use eGFR when prescribing medications
- Creatinine can be misleading in elderly, reduced muscle mass
- Any med with >30% renal clearance probably need dose adjustment for CKD
- Avoid NSAIDs
- No Dual RAAS blockade (JNC 8)
- Avoid gadolinium (MRI) for eGFR <30
- Keep up with the news and patient safety issues
- In high risk patients check urine protein and eGFR
- Use the heat-map as a guide to referral to nephrology and monitoring
- Consider nephrology referral in atypical cases of DM
- Consider strategies to slow progression of CKD to ESRD

Slowing CKD Progression: role of AKI

Impact of primary care CKD detection with a patient safety approach

Conditions of CKD Risk

- Apolipoprotein B
- Fasting C-reactive protein
- Family history of CKD
- Obesity
- Hypertension
- Metabolic syndrome
- Diabetes
- Smoking
- Alcohol
- Hyperuricemia
- Anemia

CKD in the Clinic

A joint venture between nephrology and primary care

Thank you!