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?
   - Should I continue or stop ACE inhibitors in patients with CKD?
   - What is the story with PPI and CKD?

2. CKD screening and referral
   - Recommendations for screening in high risk populations
   - Nephrology referral: What to do with a creatinine elevation?
## Building a Practical Approach to Detection and Management of CKD

### 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

NSF = nephrogenic systemic fibrosis.

### Metformin and Renal Impairment: T or F?

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

2. Contraindicated if eGFR < 30 ml/min

3. Not recommended to start if eGFR 30-45 ml/min

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

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.

(FDA April 2016)
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
  - 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 and diuretics
- Avoid volume depletion

PPIs in the news

- Popular medications linked to higher risk of kidney failure

PPI: association with CKD

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

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

PPI associated kidney disease association is not causality

1. Xie et al, Kidney Int 2017; 1-13
2. Lazarus et al, JAMA 2016; 176(2): 238-246
3. Xie et al, JASN 2016; 27: 3153-3163
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!
  - Fluoroquinolones
    - Adjust dose and 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%
- Bisoprolol
  - CKD 4 - 75%
  - CKD 5 - 50%

Analgesics
- Minimize NSAIDs

Gout medications
- Colchicine
- Allopurinol
- NO INDOMETHACIN

Neuropathy medications
- Gabapentin
  - CKD 4 - Max dose 200-700mg qd
  - CKD 5 - Max dose 300mg qd or qod

Munar et al. JFM 2007; 75 (3): 1487-1496

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1. Recommendations for commonly used medications in CKD
   - Guidelines/basic principles of medication prescribing in CKD
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   - Should I continue or stop ACE inhibitors in patients with CKD?
   - What is the story with PPI and CKD?

2. CKD screening and referral
   - Recommendations for screening in DM and HTN (high risk populations)
   - Nephrology referral: What to do with a creatinine elevation?
Gaps in CKD Diagnosis

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

- 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
- Obesity
- Certain ethnicities
- FH of CKD
- Prior AKI
- Autoimmune disease
- Reduced renal mass (solitary kidney)
- Nephrotoxin exposure
- Obstruction

eGFR, microalbuminuria or proteinuria
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

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eGFR tools: case 1

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

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Average Measured GFR by Age in People Without CKD

**Kidney function and eGFR decline with age**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean eGFR (mL/min/1.73 m²)</th>
</tr>
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<tbody>
<tr>
<td>20–29</td>
<td>116</td>
</tr>
<tr>
<td>30–39</td>
<td>107</td>
</tr>
<tr>
<td>40–49</td>
<td>99</td>
</tr>
<tr>
<td>50–59</td>
<td>93</td>
</tr>
<tr>
<td>60–69</td>
<td>85</td>
</tr>
<tr>
<td>70+</td>
<td>75</td>
</tr>
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</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

<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
- Autoimmune disease
- Reduced renal mass (solitary kidney)
- DM
- Obstruction
- Nephrotoxin exposure
- FH of CKD
- Prior AKI
- Certain ethnicities

eGFR

- microalbuminuria or proteinuria

If eGFR is abnormal and +proteinuria proceed to heat map

If eGFR is normal and no microalbuminuria, repeat kidney check tests in 1-2 years (annually for DM and HTN)
When to refer to nephrology?

- AKI 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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**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

- Avoid gadolinium (MRI) for eGFR <30

- No Dual RAAS blockade (JNC 8)

- 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
10 commandments of CKD management by primary care providers

- 10. Thou shalt evaluate and treat cardiovascular risk and comorbidities
- 9. Thou shalt treat BP to target ranges
- 8. Thou shalt use mathematical formulas to estimate eGFR
- 7. Thou shalt screen for microalbuminuria/proteinuria in high risk patients
- 6. Thou shalt pay attention to patient safety issues related to CKD stages 3 onward, including radiocontrast for diagnostic imaging.
- 5. Thou shalt dose medications appropriately
- 4. Thou shalt monitor progression according to the "heat map"
- 3. Thou shalt embrace ACE inhibitors (until the bitter end unless otherwise contraindicated)
- 2. Thou shalt avoid NSAIDs
- 1. Thou shalt make appropriate nephrology referrals

CKD in the Clinic
A joint venture between nephrology and primary care

Thank you!
Conditions of ↑ CKD Risk

- Diabetes
- Hypertension
- Cardiovascular Disease
- Age > 60 years
- Ethnic / Racial Minority
- Obesity
- Family History of CKD
- AKI History

CKD G Stage

- eGFR < 60 ml/min/1.73 m²
  - 45 – 59 = 3a
  - 30 – 44 = 3b
  - 15 – 29 = 4
  - < 15 = 5

A Stage

- ACR > 30 mg/g
  - < 30 = normal or mild ↑
  - 30-299 = moderately ↑
  - > 300 = severely ↑

Patient Safety

- eGFR < 60 = Patient Safety Risk
  - Drug dosing consider eGFR
    - Reduce risk of AKI volume depletion
    - Avoid contrast or minimize dose
    - Consider isotonic saline infusion before, during and after procedure
    - Withhold metformin, RAAS blockers and diuretics

- eGFR 45 – < 60
  - Avoid prolonged NSAIDs
  - Continue metformin use

- eGFR 30 – < 45
  - Avoid prolonged NSAIDs
  - Use metformin with close monitoring at 50% dose

- eGFR < 30
  - Avoid any NSAIDs
  - Avoid bisphosphonates
  - Avoid metformin
  - Avoid PICC lines, use single and double lumen central catheters instead
  - Monitor PT INR closely given increased risk of warfarin anticoagulation bleeding

CKD Progression + Complications

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

- DM - Target HbA1c ~7%

- CKD Complications Testing
  - Anemia – CKD 3+ Evaluation if Hb < 13.0 for men and < 12.0 for women. Treat iron deficiency first. Refer to nephrology for ESA to treat Hb < 10 g/dl (Target 9-11.5)
  - Ancestry – Bicarbonate goal > 22-26, use sodium bicarbonate 850 mg thrice daily
  - CVD-MBD – CKD 3b+ calcium, phosphate, 25-OH vit D, and IPHT. Supplement vitamin D deficiency. If hyperphosphatemia or significant IPHT elevation refer to nephrology

- Vaccination for influenza + pneumococcus

- Nephrology Referral
  - eGFR < 30 or ACR > 300 mg/g
  - 25% decrease in eGFR (AKI or progressive CKD may be difficult to distinguish)
  - 2nd hyperparathyroidism
  - Persistent hyperkalemia /metabolic acidosis
  - Recurrent kidney stones
  - Unexplained hematuria
  - Hereditary or unknown cause of CKD

CKD and CVD

- CKD = ↑CVD risk
- Consider lipid lowering therapy
  - All > 50 years
  - 18-50 years at high CVD risk
    - (VLD LDL, DM, VLD ischemic CVA, 10 yr risk of MI > 10%)
- ASA for secondary prevention unless bleeding risk outweighs benefits

* Confirmed for 3 or more months
A 5-step plan for CKD evaluation and referral

1. **Know** the criteria for CKD
   - Abnormalities of kidney structure or function, present for > 3 months, with implications for health
   - Either of the following must be present for > 3 months:
     - Markers of kidney damage (one or more)
     - GFR < 60 mL/min/1.73m²

2. **Recognize** risk factors. CKD risk factors include, but are not limited to the following:
   - Diabetes
   - Hypertension
   - Family history of kidney disease
   - Age 60 or older (GFR declines normally with age)
   - Race/U.S. ethnic minority status - African Americans, Hispanics, Asians/Pacific Islanders, and American Indians
   - Frequent NSAID use
   - History of acute kidney injury

3. **Screen** for CKD with two simple tests
   - Spot urine for albumin-to-creatinine ratio (ACR) to detect albuminuria
   - Serum creatinine to estimate glomerular filtration rate (GFR)

4. **Classify** CKD to guide testing and treatment
   - Assign GFR category
   - Assign albuminuria category
   - Determine prognosis of CKD based on GFR and albuminuria category (see chart below)

5. **Implement** a clinical action plan based on patient’s CKD classification
   - Consider comanagement with a nephrologist if the clinical action plan cannot be carried out
   - Refer to a nephrologist when GFR < 30 mL/min/1.73 m² or ACR > 300 mg/g
**Classification of CKD Based on GFR and Albuminuria Categories: “Heat Map”**

CKD is classified based on:
- **Cause (C)**
- **GFR (G)**
- **Albuminuria (A)**

<table>
<thead>
<tr>
<th>GFR categories (ml/min/1.73 m²)</th>
<th>Description and range</th>
<th>A1: Normal or high</th>
<th>A2: Moderately increased</th>
<th>A3: Severely increased</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
<td>≥90</td>
<td>1 if CKD</td>
<td>Monitor 1</td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased</td>
<td>60-89</td>
<td>1 if CKD</td>
<td>Monitor 1</td>
</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased</td>
<td>45-50</td>
<td>Monitor 2</td>
<td>Monitor 2</td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>30-44</td>
<td>Monitor 2</td>
<td>Monitor 3</td>
</tr>
<tr>
<td>G3</td>
<td>Severely decreased</td>
<td>15-29</td>
<td>Refer* 3</td>
<td>Refer* 3</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td>Refer 4+</td>
<td>Refer 4+</td>
</tr>
</tbody>
</table>

**Colors:** Represents the risk for progression, morbidity and mortality by color from best to worst. **Green:** low risk (if no other markers of kidney disease, no CKD); **Yellow:** moderately increased risk; **Orange:** high risk; **Red:** very high risk.

**Numbers:** Represent a recommendation for the number of times per year the patient should be monitored.

**Refer:** Indicates that nephrology referral and services are recommended.

*Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referral.*