Session 9: Optimizing the Management of Patients with Chronic Kidney Disease

Learning Objectives

1. Understand the impact of chronic kidney disease (CKD) as a common condition of the adult US population.
2. Apply the latest evidence-based recommendations for diagnosis and management of patients with stages 1-3 CKD.
3. Slow CKD progression by treating risk factors such as hypertension and diabetes.
Session 9: Optimizing the Management of Patients with Chronic Kidney Disease

Faculty

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SESSION 9
1:30–2:45pm
Optimizing the Management of Patients with Chronic Kidney Disease

SPEAKER
Gerald Hladik, MD

Presenter Disclosure Information
The following relationships exist related to this presentation:
► Education Director for MOC, American Society of Nephrology

Off-Label/Investigational Discussion
► In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Learning Objectives
• Understand the impact of chronic kidney disease (CKD) as a common condition in the adult US population
• Apply the latest evidence-based recommendations for diagnosis and management of patients with stages 1 to 3 CKD
• Slow CKD progression by treating risk factors such as hypertension and diabetes

Case: George
• 63-year-old previously healthy white male accountant who had some blood work drawn prior to purchasing life insurance
• Noted to have an eGFR, calculated by the MDRD study equation, of 50 mL/min/1.73m²
• Performed an internet search and is distressed to find that he has a “moderate decrease” in kidney function

What should you do next?

KDOQI 2002: Clinical Practice Guidelines for Chronic Kidney Disease
Defined 2 independent criteria for CKD:
– Decreased GFR for ≥ 3 months
OR
– Markers of kidney damage (structural, functional, or pathological) for ≥ 3 months
– Classified CKD by severity according to GFR

GFR = Glomerular filtration rate
KDOQI Stages of CKD

<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>≥90</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild ↓ GFR</td>
<td>60-89</td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓ GFR</td>
<td>30-59</td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓ GFR</td>
<td>15-29</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
</tr>
</tbody>
</table>

Primary care clinicians provide first line of management for patients with CKD STAGES 1-3 CKD

KDOQI 2002: Clinical Practice Guidelines for Chronic Kidney Disease

- Resulted in reporting of eGFR with creatinine
- Lead to a marked increase in awareness by providers of CKD
- Lead to significant concern by patients and providers due to over identification of CKD 2 and 3 and diagnosis of a non-problem
- Equations use creatinine, age, sex and race and increased age leads to underestimating true GFR

Currently Recommended Prediction Equations to Estimate GFR (eGFR)

- Modification of Diet in Renal Disease (MDRD) study equation (recommended by KDOQI 2002 guidelines)
- CKD Epidemiology Collaboration (CKD-EPI) equation (recommended by KDIGO 2012 guidelines)

Currently, eGFR is routinely reported by > 75% of US clinical laboratories

Caveats

Measurement of creatinine clearance using timed urine collections may improve eGFR in individuals with:

- Significant decreases in muscle mass
  - eg, amputations, malnutrition, muscle wasting, cirrhosis
- Unusual diets
  - eg, vegetarian or creatine supplements
- Pregnancy

Assessment of Prognosis

- How do we better define our patients who are at risk?
- What else tells me they may progress to ESRD or develop other problems?

Testing for Proteinuria

Urine Albumin:Creatinine Ratio (ACR) is preferred:

- Albumin is the principal component of proteinuria in glomerular disease
- ACR has greater sensitivity than PCR in the detection of low levels of proteinuria (often not measured on a urine dipstick but significant none the less)
- Cardiovascular risk in people with CKD begins to increase at low levels of albuminuria (below the sensitivity limits of PCR)

\[
ACR = \frac{Albumin}{creatinine} \\
PCR = \frac{Protein}{creatinine}
\]
**Practical Definition of CKD**

Presence of kidney damage  
OR  
decreased kidney function for ≥ 3 months  
- Albuminuria → Kidney damage  
  (> 30 mg/g ACR)  
- eGFR → Decreased kidney function  
  (<60 mL/min/1.73 m²)  
  
MDRD or CKD-EPI equations


**KDIGO: Updated Clinical Practice Guidelines (2012)**

- CKD should be classified by Cause, GFR category, and Albuminuria category (CGA staging)
- Prediction of prognosis and frequency of monitoring should be guided by GFR and albuminuria categories


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**Over 26 million Americans Have CKD**

- 1 in 10 adults have some level of CKD
- ~700,000 Late Stage CKD patients
- ~400,000 ESRD patients


**ESRD Rates in Patients with DM and HTN is High**

Incident counts & rates of ESRD, by primary diagnosis adjusted for age, gender, race

United States Renal Data System 2013 Annual Data Report (Vol 2) Figure 1.c.

**Mortality Rates Increase as CKD Stage Increase**

Adjusted mortality rates per 1000 Medicare patient years

United States Renal Data System 2013 Annual Data Report. Adapted from Table 3.c (Vol 1).

**KDOQI Guideline 1**

Adverse outcomes can often be prevented or delayed through early detection and treatment

### KDOQI: Risk Factors for CKD

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Definition</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptibility factors</td>
<td>Increased susceptibility to chronic kidney damage</td>
<td>• Age &gt; 70; obesity (BMI &gt; 30)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• FH of CKD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Decreased kidney mass</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• U.S. racial or ethnic minority status</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Low income or education</td>
</tr>
<tr>
<td>Initiation factors</td>
<td>Directly initiate kidney damage</td>
<td>• Diabetes, high blood pressure, cardiovascular disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Autoimmune diseases, systemic or urinary tract infection, GN, multiple myeloma, h/o AKI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Urinary stones, lower urinary tract obstruction</td>
</tr>
</tbody>
</table>


### Role of Primary Care Physician in CKD

1. Early detection: Assess risk in all patients
2. Screen at risk patients with eGFR and ACR (controversial)
3. For all patients, modify risk factors for CKD when possible
   a. Diabetes
   b. Hypertension
   c. Cardiovascular disease

### The SCreening for Occult Renal Disease (SCORED) Survey

**Total Score**

- ≥ 4 points
  - 1 in 5 chance of having CKD. Have a blood test done at next visit
- 0-3 points
  - Probably don’t have CKD, but take survey at least yearly


### After Risk Assessment and Screening, What’s Next?

4. Establish the stage and cause
5. Treat reversible causes
6. Determine the rate of progression:
   a. Defined as a decline in GFR category accompanied by ≥ 25% drop in eGFR from baseline (with annual measurements)
   b. Rapid progression defined as sustained decline in eGFR of more than 5 mL/min/1.73 m²/yr

### 7. Manage Patients with CKD Stages 1,2,3

- Prevent or slow progression
- Manage comorbidities
- Avoid nephrotoxins and adjust drug doses for level of eGFR
- Administer appropriate vaccinations
- Comanage complications of CKD
- Spare non-dominant arm from venipuncture and PICC lines
- All patients with CKD Stages 1,2,3 should be managed by primary care physicians

### 8. Referral to Nephrologist If:

- Red blood cell casts, dysmorphic hematuria, excessive proteinuria (ACR ≥ 300 mg/g) regardless of CKD stage
- Inability to determine cause or suspected primary renal disorder
- Rapid progression
- Refractory hypertension (not at goal on ≥ 3 meds)
- eGFR < 30 mL/min/1.73 m² (Stage 4)
Roles of the Primary Care Clinician and the Nephrologist

MANAGE RISKS
- Diabetes
- Hypertension
- CVD
- Obesity

Primary Care Physician Management
- Stage 1, 2, 3

Nephrologist Management
- Co-management (Stage 3)
- Stages 4, 5

COMANAGE COMPLICATIONS
- PCP/Nephrologist

Screening Patients at Increased Risk for CKD

All Patients with Increased Risk
- Measurement of blood pressure
- Estimation of GFR
- Albumin to creatinine
- Examination of the urine dipstick for red blood cells, white blood cells and if indicated, urine sediment examination for casts

Once CKD is identified or if Risk Factors
- Ultrasound imaging (e.g. BPH)
- Serum electrolytes, calcium, phosphorus, especially if > CKD stage 3b

Diabetic Kidney Disease

Variability in Clinical Course

Increased or Normal GFR (Normoalbuminuria)
- Time
- Diabetes onset
- ~5 years
- ~10 years
- ~15-20 years

Decreased GFR

Overt Nephropathy

Diabetic Kidney Disease

Microalbuminuria

Overt Nephropathy

Increased or Normal GFR (Normoalbuminuria)

Eighth Annualized Percentage
(Number of Patients)

Other glomerular -15.5% [N=51]
Focal and segmental glomerulosclerosis -13.3% [N=34]
Obstructive uropathy -4.6% [N=109]
Autosomal recessive polycystic kidney disease -4.4% [N=18]
Reflux nephropathy -3.8% [N=82]
Aplastic/hypoplastic/dysplastic kidneys -3.3% [N=96]
Other nonglomerular -2.5% [N=119]

Factors in CKD Progression

Risk Factors for CKD Progression

- Higher levels of proteinuria
- BP above target
- Poor glycemic control
- Smoking
- Recurrent kidney injury
- Metabolic acidosis
- Obesity
- Dyslipidemia
- H/O CV disease
- Nephrotoxic agents, eg NSAIDs, over the counter agents, radiographic materials

NOTE that nearly all are modifiable

Prevent or Manage Comorbidities

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Action/Outcome</th>
</tr>
</thead>
</table>
| Educate and assist with therapeutic lifestyle changes | - Stop Smoking  
- Exercise  
- Healthy diet  
- Attain or maintain ideal body weight |
| Control diabetes                     | - Hb A1C < 7%                                       |
| Manage hyperlipidemia                | - Statin therapy per KDIGO guidelines               |
| Treat hypertension                   | - Treat to BP goal                                  |


Treatment of Hypertension in Patients with CKD: JNC 8 Recommendations

Ages > 18 to < 70 years
- Antihypertensive therapy to lower BP when SBP ≥ 140 mm Hg or DBP ≥ 90.

Ages > 70 years
- Individualize antihypertensive therapy
  - Initial treatment for most patients should include an ACEI or ARB to improve kidney outcomes if proteinuria

ACEI = angiotensin-converting enzyme inhibitor  
ARB = angiotensin receptor blocker


Algorithm for Cholesterol Lowering Treatment in Persons with Nondialysis CKD

Nondialysis CKD Stage 1-5
- AASK study
  - ACEI or ARB for initial therapy (higher likelihood of progression)

Nondialysis CKD Stage 1-5, aged < 50 Y
- ALLHAT trial
  - Calcium channel blocker, thiazide type diuretic, ACEI or ARB


Recommended Frequency of Monitoring by GFR and Albuminuria

Guide to Frequency of Monitoring (number of times per year) by GFR and Albumin Category

Guide to Monitoring by GFR and Albumin Category

Referral Recommendations by GFR and Albumin Category


Figure 17, p. 63.

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Guide to Monitoring by GFR and Albumin Category

Guide to Frequency of Monitoring (number of times per year) by GFR and Albumin Category

Reprinted with permission.
Important CKD Management Considerations

√ Avoid nephrotoxins if possible
  – Nonsteroidal antiinflammatory drugs
  – Radiocontrast materials
  – Oral phosphate containing bowel preparations
  – Aminoglycosides

√ Administer vaccines
  – Influenza vaccine annually
  – Hepatitis B vaccine for patients at high risk of progression or who have eGFR < 30 mL/min/1.73 m²
    • Requires higher dose (40 mcg rather than 20 mcg; schedule depends on formulation)

Manage Complications of CKD: Anemia and Metabolic Bone Disease

− Anemia: 20% of patients with stages 1,2,3 CKD have anemia
− Metabolic bone disease:
  − 20 to 25% of patients with stage 3 CKD will have elevated PTH
  − 10% will have decreased 25(OH) vitamin D deficiency

Consider co-management with a nephrologist if these conditions are suspected

Medication Management in Patients with CKD

✓ Adjust the dosage of renally excreted drugs for GFR: www.bnf.org
✓ Temporarily d/c nephrotoxic drugs during significant intercurrent illness (eg, ACEI, ARBs, diuretics, NSAIDs; metformin, lithium, digoxin)
✓ Avoid herbal remedies
✓ Use metformin with caution in diabetics with eGFR 30-45 mL/min/1.73m². Avoid altogether with eGFR < 30 mL/min/1.73m²
✓ Do not order gadolinium studies when the eGFR is <30 mL/min/1.73m²
✓ Monitor GFR, electrolytes, and drug levels in patients taking lithium, calcineurin inhibitor immunosuppressants (eg, cyclosporine), and other nephrotoxic agents

Important CKD Management Considerations

√ Vaccines (cont)

Pneumococcal Immunization
ACIP recommends immunization with both pneumococcal conjugate vaccine (PCV13) and pneumococcal polysaccharide vaccine (PPSV23) for adults with chronic renal failure or nephrotic syndrome
  − If no previous PCV13 or PPSV23: single dose PCV13, then single dose PPSV23 ≥ 8 weeks later
  − If previous PPSV23: Single dose PCV13 ≥ 1 year after PPSV23

Recommended PPSV23 revaccination: ≥ 5 years after first PPSV23
  − If both doses given before age 65, revaccinate with 1 more PPSV23 dose after age 65

http://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html

United States Renal Data System Annual Data Report 2013. Figure 2.5, (Vol 1).
2011
42% of all patients with ESRD – and 95% of Hispanics with ESRD – had not previously seen a nephrologist at the onset of renal replacement therapy.

Early Referral to a Nephrologist
- KDIGO: Recommends early referral to a nephrologist
  - At least 1 year before start of renal replacement therapy
- Protocolized multidisciplinary nephrology care improves outcomes
  - CKD education
  - Nutritional counseling; vascular access coordination; transplant options
  - Ethical, psychological and social care
  - Discussions re modality of choice for dialysis vs preemptive kidney transplant

Patients with Stage 5 CKD: Early Referral Improves Outcomes

<table>
<thead>
<tr>
<th>Control of risk factors for CKD progression, adverse outcomes</th>
<th>Late referral to nephrology (all patients were receiving primary care)</th>
<th>Early referral to nephrology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure control (to recommended goal)</td>
<td>39%</td>
<td>69%</td>
</tr>
<tr>
<td>HbA1c &lt;7%</td>
<td>44%</td>
<td>82%</td>
</tr>
<tr>
<td>ACEI/ARB use (for proteinuria &gt;1 g/day)</td>
<td>36%</td>
<td>96%</td>
</tr>
<tr>
<td>Anemia treatment (to recommended goal)</td>
<td>9%</td>
<td>52%</td>
</tr>
<tr>
<td>Nutritional Status Management</td>
<td>65%</td>
<td>81%</td>
</tr>
</tbody>
</table>


Early Versus Late Referral in Patients with ESRD at Renal Replacement Therapy Start

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early Referral Mean (SD)</th>
<th>Late Referral Mean (SD)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall mortality, %</td>
<td>11 (3)</td>
<td>23 (4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1-year mortality, day</td>
<td>13 (4)</td>
<td>29 (5)</td>
<td>0.028</td>
</tr>
<tr>
<td>Hospital length of stay, days</td>
<td>13.5 (2.2)</td>
<td>25.3 (3.8)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Serum albumin at RRT start, g/dl [g/l]</td>
<td>3.62 (0.05) [36.2 (0.5)]</td>
<td>3.40 (0.03) [34.0 (0.3)]</td>
<td>0.0001</td>
</tr>
<tr>
<td>Hematocrit at RRT start, %</td>
<td>30.54 (0.18)</td>
<td>29.71 (0.10)</td>
<td>0.013</td>
</tr>
</tbody>
</table>


Controversies: To Screen or Not to Screen for CKD?

<table>
<thead>
<tr>
<th>Guideline</th>
<th>No Risk Factors</th>
<th>Risk Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>KDOQI</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>KDIGO</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>USPSTF</td>
<td>Data Inconclusive</td>
<td>YES</td>
</tr>
<tr>
<td>ACP (2013)</td>
<td>NO</td>
<td>Data Inconclusive</td>
</tr>
<tr>
<td>ASN</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

USPSTF = US Preventive Services Task Force
ACP = American College of Physicians
ASN = American Society of Nephrology


Controversies: To Test or Not to Test for Albuminuria?

- ACP Guidelines for CKD Stages 1 to 3:
  Recommendation 2: Patients with or without diabetes taking an ACEI or ARB should not be tested for proteinuria
  Rationale: Results would not change treatment. No data that says that benefits outweigh possible harms (eg, more testing; increased costs)

Controversies: Should Patients with CKD Stages 1 to 3 be Routinely Monitored?

- **ACP Guidelines for Stages 1 to 3 CKD:** There may be no net benefit of routinely monitoring patients with stages 1 to 3 CKD. (Inconclusive evidence, not a recommendation)

  **Rationale:** There is a lack of evidence that modifying treatment when progression occurs improves patient outcomes.


Back to George

63-year-old white male

eGFR (MDRD) = 50 mL/min/1.73 m²

**What should you do next?**

- Measure ACR
- Since the MDRD study equation underestimates GFR in many patients, particularly the elderly, recalculate the eGFR using CKD EPI
- Use the KDIGO grid to determine prognosis by GFR and albuminuria

George (cont)

- If ACR is < 30 mg/g and eGFR is between 60 to 89 mL/min/1.73 m², his CGA category would be G2A1. His risk for progressive CKD is low
- If his ACR < 30 mg/g and eGFR remains between 45 to 59 mL/min/1.73 m², his category is G3aA1, with a moderately increased risk for progressive CKD
- In both cases, modify risk factors for cardiovascular disease and progression and follow up annually with eGFR and ACR

Summary

- Diabetes, hypertension, and cardiovascular disease are significant risk factors for CKD
- Roles for the PCP
  - Screen at risk patients for CKD
  - Monitor for progression
  - Manage risk factors contributing to progression
  - Manage comorbid conditions such as hypertension, CAD, and diabetes
- Cardiovascular disease is the most common cause of morbidity and mortality in patients with CKD

Summary (cont)

- Have a low threshold for referring Stage 3 CKD to a nephrologist for comanagement
- All patients with CKD stage 4 should be referred to a nephrologist
- Early referral prior to renal replacement therapy improves outcomes in patients with ESRD

Questions

?