Optimizing the Management of Patients with Chronic Kidney Disease

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Session 8: 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.

Faculty

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Dr Wish is certified by the American Board of Internal Medicine, holds subspecialty certification in nephrology, and is a fellow of the American College of Physicians. He is past officer of the Renal Physicians Association and past president of End-Stage Renal Disease (ESRD) Networks 9 and 10 and the National Forum of ESRD Networks. He served on the board of trustees of the American Association of Kidney Patients and was the recipient of their 2005 Visionary Award. He has been a member of many expert panels sponsored by Medicare to develop quality measures for the ESRD program.

Dr Wish has given numerous national and international presentations on clinical standards and quality initiatives in the field of nephrology and has published more than 80 original articles in peer-reviewed medical journals. His major research interests include anemia management and the impact of quality improvement programs on outcomes in patients with chronic kidney disease.

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Optimizing the Management of Patients with Chronic Kidney Disease

SPEAKER
Jay B. Wish, MD, FACP

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

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
- Led to a marked increase in awareness by providers of CKD
- Led to significant concern by patients and providers due to over identification of CKD 2 and 3 and diagnosis of a non-problem
- Both 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)
  - http://www.qxmd.com/calculate-online/nephrology/ckd-epi-egfr

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

Testing for Proteinuria

Urine 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 = Albumin to creatinine ratio
PCR = Protein to creatinine ratio

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
CKD Progression Across Diagnosis Categories of Primary Renal Disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Annualized Percentage (Number of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other glomerular</td>
<td>-15.5% [N=51]</td>
</tr>
<tr>
<td>Focal and segmental glomerulosclerosis</td>
<td>-13.3% [N=34]</td>
</tr>
<tr>
<td>Obstructive uropathy</td>
<td>-4.6% [N=109]</td>
</tr>
<tr>
<td>Autosomal recessive polycystic kidney disease</td>
<td>-4.4% [N=18]</td>
</tr>
<tr>
<td>Reflux nephropathy</td>
<td>-3.8% [N=82]</td>
</tr>
<tr>
<td>Aplastic/hypoplastic/dysplastic kidneys</td>
<td>-3.3% [N=96]</td>
</tr>
<tr>
<td>Other nonglomerular</td>
<td>-2.5% [N=119]</td>
</tr>
</tbody>
</table>


KDOQI: 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


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

Mortality Rates Increase as CKD Stage Increase

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); FH of CKD; Decreased kidney mass; U.S. racial or ethnic minority status; Low income or education</td>
</tr>
<tr>
<td>Initiation factors</td>
<td>Directly initiate kidney damage</td>
<td>Diabetes, high blood pressure, cardiovascular disease; Autoimmune diseases, systemic or urinary tract infection, GN, multiple myeloma, h/o AKI; 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
3. For all patients, modify risk factors for CKD when possible
   a. Diabetes
   b. Hypertension
   c. Cardiovascular disease

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

4. Establish the **stage** and **cause**
5. Treat **reversible causes**
6. Determine **disease progression**:
   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
- Co-manage complications of CKD

- Patients with CKD Stages 1,2,3 can be managed by primary care physicians

**8. Referral to Nephrologist If:**

- Red blood cell casts, > 20 RBC/HPF, 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

COMANAGE COMPLICATIONS
- PCP/Nephrologist Co-management
- Stage 3 (if specific indications)

MANAGE ESRD
- Nephrologist Management
- Stages 4, 5

**Screening Patients at Increased Risk for CKD**

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

Selected Patients, Depending on Risk Factors
- Ultrasound imaging
- Serum electrolytes
- Urinary concentration or dilution (specific gravity or osmolality)
- Urinary acidification (pH)
### 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
- Nephrotic agents, eg NSAIDs, over the counter agents, radiocontrast 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 > 140mm 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


### Treatment of Hypertension in Black Patients with CKD: JNC 8 Recommendations

**CKD with proteinuria**

- ACEI or ARB for initial therapy (higher likelihood of progression) (AASK study)

**CKD without proteinuria**

- Calcium channel blocker, thiazide type diuretic, ACEI or ARB (ALLHAT trial)


### Algorithm for Cholesterol Lowering Treatment in Persons with Nondialysis CKD

1. Statin Regimen
2. Nondialysis CKD Stage 1-5 aged >50Y
3. Nondialysis CKD Stage 1-5, aged <50 y
4. Known Vascular Disease
5. Diabetes
6. 10-y Coronary Risk >10%


### Recommended Frequency of Monitoring by GFR and Albuminuria

<table>
<thead>
<tr>
<th>Persistent albuminuria categories description and stages</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal to mildly increased (mg/dL)</td>
<td>0-3</td>
<td>3-9</td>
<td>&gt;9</td>
</tr>
<tr>
<td>Moderately increased (mg/dL)</td>
<td>3-9</td>
<td>9-30</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Severely increased (mg/dL)</td>
<td>9-30</td>
<td>30-90</td>
<td>&gt;90</td>
</tr>
</tbody>
</table>

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

- Normal or High
- Mildly decreased
- Moderately decreased
- Severely decreased
- Kidney failure

2012 Guidelines for the Evaluation and Management of CKD. www.kidigo.org/home/guidelines. Figure 17, p. 63.
Referral Recommendations by GFR and Albuminuria

Guide to Monitoring by GFR and Albumin Category

<table>
<thead>
<tr>
<th>GFR Category</th>
<th>Description</th>
<th>Prevalence of Anemia (%)</th>
<th>Prevalence of Hypertension (%)</th>
<th>Prevalence of 25(OH) Vitamin D Deficiency (%)</th>
<th>Prevalence of Acidosis (%)</th>
<th>Prevalence of Hyperparathyroidism (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90</td>
<td>Normal or high</td>
<td>4.0</td>
<td>18.3</td>
<td>14.1</td>
<td>11.2</td>
<td>5.5</td>
</tr>
<tr>
<td>60-89</td>
<td>Moderately decreased</td>
<td>4.7</td>
<td>41.0</td>
<td>9.1</td>
<td>8.4</td>
<td>9.4</td>
</tr>
<tr>
<td>45-59</td>
<td>Moderately to severely decreased</td>
<td>10.7</td>
<td>71.8</td>
<td>10.7</td>
<td>9.4</td>
<td>23.0</td>
</tr>
<tr>
<td>30-44</td>
<td>Severely decreased</td>
<td>27.2</td>
<td>78.3</td>
<td>18.1</td>
<td>9.4</td>
<td>44.0</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Kidney Failure</td>
<td>51.5</td>
<td>82.1</td>
<td>31.5</td>
<td>27.2</td>
<td>72.5</td>
</tr>
</tbody>
</table>


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

Prevalence of CKD Complications by GFR Category Derived from CKD Cohorts

<table>
<thead>
<tr>
<th>Complication</th>
<th>GFR Category (mL/min/1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>&gt;90</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4.0%</td>
</tr>
<tr>
<td>25(OH) Vit D deficiency</td>
<td>18.3%</td>
</tr>
<tr>
<td>Acidosis</td>
<td>11.2%</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
<td>7.2%</td>
</tr>
<tr>
<td>Hyperparathyroidism</td>
<td>5.5%</td>
</tr>
</tbody>
</table>


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

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 discontinue nephrotoxic drugs during significant intercurrent illness (eg, ACEI, ARBs, diuretics, NSAIDs, metformin, lithium, digoxin)

✓ Do not use herbal remedies

✓ Use metformin with caution in diabetics with eGFR < 30 mL/min/1.73m². Avoid altogether with eGFR < 30 mL/min/1.73m

✓ Monitor GFR, electrolytes, and drug levels in patients taking lithium, calcineurin inhibitor immunosuppressants (eg, cyclosporine), and other nephrotoxic agents

So, how are we doing?

Many Patients at Risk for CKD are Not Being Fully Screened

<table>
<thead>
<tr>
<th>Patient Demographic</th>
<th>Chance of having a serum creatinine drawn</th>
<th>Chance of having a urine albumin test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with DM</td>
<td>87%</td>
<td>36%</td>
</tr>
<tr>
<td>Patients with HBP</td>
<td>88%</td>
<td>5%</td>
</tr>
<tr>
<td>Patients with DM &amp; HBP</td>
<td>93%</td>
<td>37%</td>
</tr>
</tbody>
</table>

[United States Renal Data System Annual Data Report 2013. Figure 2.5, (Vol 1).]

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, %</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>


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

[United States Renal Data System Annual Data Report 2013 (Vol 2). Table 1.f.]
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>

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
- Important roles of the PCP are to screen at risk patients for CKD and in CKD stages 1 to 3, to monitor for progression, manage risk factors contributing to progression, and manage comorbid conditions such as hypertension and diabetes
- Cardiovascular disease is the most common cause of morbidity and mortality in patients with CKD
Summary (cont)

- PCPs should have a low threshold for referring patients with Stage 3 CKD to a nephrologist for comanagement if unable to manage comorbid conditions to goal or if complications are suspected.
- All patients with CKD stage 4 should be referred to a nephrologist.
- Early referral to a nephrologist prior to initiating renal replacement therapy results in improved outcomes in patients with ESRD.

Questions?