Chronic Kidney Disease for the non-nephrologist

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Outline

- Why should you care about CKD?
- How to recognize CKD
- Basic management of kidney disease
- When to refer
- How to slow disease progression
Outline

* Why should you care about CKD?
* How to recognize CKD
* Management of kidney disease
* When to refer
* How to slow disease progression
Kidney dysfunction is associated with worse outcomes. Go et al. NEJM. 2004.
High mortality rates are associated with both kidney dysfunction and albuminuria.

Outline

Why should you care about CKD?

How to recognize CKD

Management of kidney disease

When to refer

How to slow disease progression
Serum creatinine estimates renal function on a logarithmic scale.
Pitfalls with Creatinine

- Serum creatinine is a function of muscle production and renal excretion.
- Serum creatinine is not a reliable measure of kidney function among:
  - Age > 70
  - Children
  - Liver disease
  - Amputation
  - Individuals with extremes of muscle mass
Estimated GFR is a better measure than serum creatinine

Formulas for Estimating GFR in Adults*

Abbreviated MDRD study equation

\[
\text{GFR (mL per minute per 1.73 m}^2) = 186 \times (S_{\text{Cr}})^{-1.154} \times (\text{age})^{-0.203} \\
\times (0.742, \text{ if female}) \times (1.210, \text{ if black})
\]

Cockcroft-Gault equation

\[
C_{\text{Cr}} (\text{mL per minute}) = \frac{(140 - \text{age}) \times \text{weight}}{72 \times S_{\text{Cr}}} \times (0.85, \text{ if female})
\]

Normal is roughly 110-120 ml/min/1.73m²
The “tea and toast” Paradox

- 40 yo AA gentleman
  - serum creatinine = 2.0 mg/dL
  - MDRD estimated GFR 48 ml/min

- 70 yo Caucasian woman
  - serum creatinine = 2.0 mg/dL
  - MDRD estimated GFR 25 ml/min
Taking body surface area into account...

- 40 yo AA gentleman, 90kg
  - serum Cr = 2.0 mg/dL; eGFR = 48 ml/min
  - true GFR = 55ml/min

- 70 yo Caucasian woman, 55kg
  - serum Cr = 2.0 mg/dL; eGFR = 25 ml/min
  - true GFR = 18 ml/min
# National Kidney Foundation Stages

## TABLE 2

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR (mL per minute per 1.73 m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥90</td>
</tr>
<tr>
<td>2</td>
<td>60 to 89</td>
</tr>
<tr>
<td>3</td>
<td>30 to 59</td>
</tr>
<tr>
<td>4</td>
<td>15 to 29</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15 or dialysis</td>
</tr>
</tbody>
</table>

*GFR = glomerular filtration rate.*

*Information from reference 1.*
Interim Summary

* Chronic kidney disease is important to recognize.
* CKD is easily recognizable.
  * eGFR
  * NKF staging system is helpful to assess lifetime risk of adverse events
  * Don’t forget albuminuria
Outline

Why should you care about CKD?

How to recognize CKD

Management of kidney disease

Determining etiology

When to refer

How to slow disease progression
Case #1: Mr. S

ID: 55 yo AA gentleman with HTN x 3 years

Exam: 150/90, 70, 98% RA, BMI = 32
    Obese, JVP 10cm, 2/6 SM at RUSB, trace edema

Meds:
    Metoprolol 50mg bid
    HCTZ 25mg daily

Labs:
    Hgb: 12.5, K: 4.1, Bun/Cr: 35/1.8
    eGFR = 40

What’s your approach to his kidney dysfunction?
Framework for evaluation of abnormal eGFR

Elevated Creatinine (or low eGFR)

“Post-renal” obstruction

“Intrinsic”

“Pre-renal” Low volume
Intrinsic Renal Disease — 4 Compartments

1. Vasculature
2. Interstitium
3. Tubules
4. Glomerulus
Evaluation of proteinuria is key

Intrinsic Renal Disease

- Glomerular
  - Diabetes
  - Myeloma/Amyloid
- Tubular
  - prolonged low flow
  - Rhabdomyolysis
  - Sepsis

Vascular

- Hypertension

Interstitial

- Drugs/NSAIDS
- Herbs

Minimal Protein

500mg - 1g/day Protein

≥ 3.5g/Day Protein

< 1.5g/Day Protein

Normal amount of proteinuria: <30mg/day
DM and HTN are the most common causes of CKD

<table>
<thead>
<tr>
<th>Cause</th>
<th>Percent of Cases†</th>
</tr>
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<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>44.9</td>
</tr>
<tr>
<td>Type 1</td>
<td>3.9</td>
</tr>
<tr>
<td>Type 2</td>
<td>41.0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>27.2</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>8.2</td>
</tr>
<tr>
<td>Chronic interstitial nephritis or obstruction</td>
<td>3.6</td>
</tr>
<tr>
<td>Hereditary or cystic disease</td>
<td>3.1</td>
</tr>
<tr>
<td>Secondary glomerulonephritis or vasculitis</td>
<td>2.1</td>
</tr>
<tr>
<td>Neoplasms or plasma-cell dyscrasias</td>
<td>2.1</td>
</tr>
<tr>
<td>Miscellaneous conditions‡</td>
<td>4.6</td>
</tr>
<tr>
<td>Uncertain or unrecorded cause</td>
<td>5.2</td>
</tr>
</tbody>
</table>
How to evaluate proteinuria?

1. Urinalysis
2. Spot urine protein and creatinine
   - The urine protein/creatinine ratio is roughly equal to grams of protein/day.
   - Albumin is approximately 2/3 of urinary protein.
Evaluate Hematuria

<table>
<thead>
<tr>
<th>Two causes:</th>
<th>Hematuria + &gt;1 gram proteinuria/day suggests glomerular disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>* Glomerular/renal (rare)</td>
<td>* Refer to urology for persistent isolated hematuria</td>
</tr>
<tr>
<td>* Urological (common)</td>
<td></td>
</tr>
</tbody>
</table>


Case #1: Mr. S

First visit: 55 yo gentleman with HTN

Labs:
  Hg: 12, K: 4.1, Bun/Cr: 35/1.7

Framework: Is this pre-renal, intrinsic, or post-renal?

- no lower urinary tract type symptoms (frequency, dribbling, nocturia)
- hydrating well, no recent infections
- no history of congestive heart failure, liver disease
Case #1: Mr. S

Additional Studies:
Spot Uprot/cr ratio: 2.5 → losing 2.5g protein/day
U/A: 1+ occult blood, 2-5 RBCs, 3+ protein, no casts

Ddx: Glomerular Damage
DM
Multiple Myeloma, Amyloid
Vasculitis
Early Nephrotic Syndrome:
IgA, FSGS, Membranous, MPGN

What do you do??
1. Refer to Nephrology with e-referral
2. Order some additional labs and studies
Case #1: Mr. S

• What you should order:
  - HbA1C, fasting glucose level
  - SPEP/UPEP
  - ANA, C3/C4
  - Viral Hepatitis serologies
  - HIV

• Other important studies:
  - Fasting lipid panel
  - Renal Ultrasound
Case #1: Mr. S: Management

- Has an appt with me 3-4 weeks later with labs
  - SPEP is positive → I confirm with biopsy
  - Dx: Multiple Myeloma w/ myeloma kidney
Hypertensive Nephrosclerosis

- Hypertension is both a cause and a consequence of kidney disease.
- It is a vascular disease, classically non-proteinuric.
- Typical age of onset is 30 – 50 years.
- It is more common in African-Americans.
- Mean rate of loss of GFR is 2 ml/min/year.
- Decline of more than 5 ml/min/year or presence of >1g of proteinuria should prompt referral.
Case #2: Ms. W

ID: 45 yo woman with HTN, CAD, DM x 4 yrs

Exam: 125/92, 62, 70kg
1+ edema to the mid-shins

Meds:
- Benazepril 10mg daily
- Lasix 20mg BID
- Glipizide 5mg BID
- ASA 81mg daily
- Metoprolol 75mg BID

Labs 5/10:
- Hg 11.5, K 4.5, Bun/Cr: 40/1.4 → eGFR = 65, stage 2
- U/A: 1.015, 2+ proteinuria, no blood, no casts
- U prot/Cr = 1.6g/day
Case #2: Ms. W

10/10:
Exam: 130/75
Hgb 11.3, K 4.7, Bun/Cr 45/1.5 → eGFR is 60 ml/min/1.73m²

U/S: bilateral echogenic kidneys approx 12cm, no hydronephrosis

Repeat U/A: 1.010, 2+ protein, no blood, no casts

New Labs:
SPEP/UPEP negative
ANA negative
C3/C4 normal
Hepatitis serologies negative
HIV negative
Dx: Diabetic Nephropathy

Your goals:
- BP control < 130/80
- Glycemic control, A1C < 7.5
- Lipid management
- Encourage lifestyle changes

If she continues on her merry way, you refer back to nephrology when her eGFR between 50-60 ml/min/1.73m²
Case #2: Ms. W

10/10:
- Exam: 160/90
- Hgb 11.3, K 4.7, Bun/Cr: 60/3.0 → eGFR is 20

U/S: bilateral echogenic kidneys approx 10cm, no hydronephrosis

Repeat U/A: 1.010, 2+ protein, no blood, hyaline casts

New Labs:
- SPEP/UPEP negative
- ANA negative
- C3/C4 normal
- Hepatitis serologies negative
- HIV negative
Case #2: Ms. W

Page the renal fellow on call; the rapid decline in eGFR, much higher BP, and presence of casts are very concerning.

We overbook her in renal clinic few days later...

Umicro: 2+ proteinuria, no blood, waxy + hyaline casts
stat Labs: Cr of 3.1, eGFR = 19

She undergoes a renal biopsy 1 week later...
Dx: FSGS + underlying diabetic changes
Diabetic Nephropathy

* Leading cause of ESRD in the United States.
* Diabetic nephropathy uniformly has proteinuria.
  * Albuminuria develops before loss of GFR.
  * Microalbuminuria develops after 5-10yrs of DM1
  * ESRD occurs 5-15yrs after development of proteinuria.
* Patients often have concomitant retinopathy
* “Untreated” dz = loss of 8-10ml/min/year
* “Aggressively treated” dz = loss of 4-5ml/min/year
* Rapid loss of GFR, absence of proteinuria, or presence of casts should prompt further work-up.
Summary: when to refer

- Underlying cause of CKD is not clear
- Rapid progression of kidney disease
- Significant proteinuria in absence of DM
- Persistent post-partum proteinuria
- Consider consult at stage III CKD
- Definitely consult at stage IV

Bottom Line: Whenever you aren’t comfortable! We are here to help.
What to Do Before Consultation

- E-referral with consult question
- Urinalysis
- Spot urine protein / creatinine ratio (or albumin)
- Serum chemistries
- CBC
- If U/A has ++ protein or blood:
  - SPEP/UPEP, ANA, C3, C4
  - HIV, Viral Hepatitis serologies
- Renal Ultrasound (normal size is 10cm)
  - Large: DM (initially), Amyloid, HIV-associated, PCKD
  - Small: HTN, Tubulo-interstitial disease
  - Asymmetric: Renovascular, Congenital atresia
Outline

- Why should you care about CKD?
- How to recognize CKD
- Management of kidney disease
  - When to refer
  - How to slow disease progression
Individuals who are referred to nephrology earlier demonstrate slower CKD progression.

Martinez-Ramirez et al. AJKD. 2005
How to slow disease progression

- Stop NSAIDS, herbal teas, Tenofovir

- Aggressive BP control:
  - Target BP < 130/80 in pts with proteinuria
  - < 140/90 in absence of proteinuria
  - Preferred agents in CKD:
    - start with ACE or ARB
    - A diuretic is second line (Loop if eGFR < 45)

- Aggressive proteinuria control:
  - Goal < 500mg/day
  - Dual RAAS blockade?
Additional Interventions in Diabetic patients

- Glycemic control (A1C < 7.5)
- Yearly Uprotein/creatinine ratio
- Lifestyle modifications: stop tobacco, daily exercise, salt restriction
- ASA 81mg daily in patients > 40yrs with CKD
- Lipid lowering
Summary Points

- CKD is a huge risk factor for mortality and CV risk
- eGFR is better than creatinine to identify patients with CKD
  - Remember body surface area
- Quantify proteinuria as part of initial evaluation of CKD
- Refer when:
  - You are uncomfortable
  - Patients don’t fit the norm
  - Presence of casts
- Aggressively treat blood pressure and proteinuria
We are here to help. Don’t hesitate to call, refer, page, email, etc...

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