CKD Update – What's new in the guidelines?

CSHP Annual Spring Update
April 17, 2013

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BRITISH COLUMBIA RENAL AGENCY

No disclosures

Objectives - By the end of the presentation the learner will be able to:

- understand the most recent CKD definition and classification and the rationale behind the reclassification
- understand the significance of albuminuria in CKD and the implications of having albuminuria
- review the recommended management of common CKD complication (anemia, mineral metabolism, acidosis)
- review the current recommendations for treating cholesterol and hypertension in CKD

Consider the following patients

- 86 year old woman
  - GFR 30 mL/min
  - Urine ACR 1.0 mg/mmol
  - Normal Ca, P, bicarb, albumin

- 72 year old man
  - GFR 30 mL/min
  - Urine ACR 70 mg/mmol
  - Normal Ca, P, bicarb, albumin

- 48 year old man
  - GFR 30 mL/min
  - Urine ACR 450 mg/mmol
  - Normal Ca, bicarb, albumin, PO4 1.7

CKD definition/classification update

KDOQI/KDIGO Classification of CKD 2002

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR</th>
<th>Qualifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage, N or ↑GFR</td>
<td>≥90</td>
<td>Kidney damage for &gt;3 months</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage, mild ↓GFR</td>
<td>60-89</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Moderate ↓GFR</td>
<td>30-59</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Severe ↓GFR</td>
<td>15-29</td>
<td>GFR &lt; 60 mL/min for &gt;3 months or kidney damage</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15 (or dialysis)</td>
<td></td>
</tr>
</tbody>
</table>

Criteria for CKD

Markers of kidney damage (one or more)
- Albuminuria (ACR ≥ 3 mg/mmol)
- Urine sediment abnormalities
- Electrolyte and other abnormalities due to tubular disorders
- Pathological abnormalities detected by histology or inferred
- Structural abnormalities detected by imaging
- Kidney transplantation

The last decade has promoted discussions, other perspectives and areas of confusion...

- Over diagnosis
  - Prevalence too high
  - Age and CKD a function of eGFR
- Terminology
  - Disease or risk factor?
  - Lack of cause
- Questionable estimating equations
  - Imprecise and biased
  - Not validated in all populations
- Proteinuria measurements

KDIGO 2012 CPG for Evaluation and Management of Chronic Kidney Disease*

- Serves to update the 2002 KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification
- Follows a decade of focused research and clinical practice in CKD

Definition of CKD

CKD is defined as:
- Abnormalities of kidney structure or function (GFR < 60 ml/min/1.73 m²)
- Present for >3 months, with implications for health

How does the definition compare with 2002 KDOQI?
- Definition remains intact but includes "with implications for health"
  - Reflects notion that a variety of abnormalities of kidney structure or function may exist, but not all have implications for health of individuals, and therefore need to be contextualized.

Age and eGFR

True or False?

eGFR measurements can be used as a reliable estimate of kidney function in elderly patients

False
Caveats and practical interpretations of eGFR

- Age caveats
  - Age >75 — accuracy questionable and may underestimate true kidney function. Values 45-60 mL/min may be normal variation in the absence of other conditions
  - Age >85 — equation very problematic and risk of progression much less.
  - Caution persists with medications, dye, and risk of AKI with severe illness

Considering age — a way to contextualize

- 77 year old man with eGFR 45-48 mL/min on 2 repeated occasions over a 4 month period
  - urine ACR normal or minimally elevated
  - other lab parameters (hemoglobin, calcium, phosphate, potassium) are normal
  - This person is unlikely to have significant CKD and is at low risk for progression and should not be referred.

New classification of CKD

- It is recommended that CKD be classified by:
  - Cause
  - GFR category
  - Albuminuria category
  - This is collectively referred to as “CGA Staging”
  - Previous documents have failed to explicitly emphasize these important dimensions in both classification and prognostication

CGA Staging – Cause

- Causes of systemic diseases or conditions affecting the kidney
- Examples of primary kidney disease or conditions affecting the kidney

CGA Staging – GFR category

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Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

*Relative to young adult level

In the absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Assign GFR categories

CGA Staging - Albuminuria

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*Note that there are many different ways in which to classify CKD. This method of separating systemic diseases and primary kidney diseases is only one, proposed by the KDIGO Work Group, to aid in conceptual approach.

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Evaluation of Albuminuria

• Understand settings that may affect interpretation of measurements of albuminuria and order confirmatory tests as indicated

• Confirm reagent strip positive albuminuria and proteinuria by quantitative laboratory measurement and express as a ratio to creatinine wherever possible

• Confirm ACR ≥3 mg/mmol on a random untimed urine with a subsequent early morning sample of urine

• If a more accurate estimate of albuminuria or total proteinuria is required, measure albumin excretion rate or total protein excretion rate in a timed urine sample

CGA Staging - Examples

<table>
<thead>
<tr>
<th>Cause</th>
<th>GFR Category</th>
<th>Albuminuria Category</th>
<th>Criterion for CKD</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic kidney disease</td>
<td>G5</td>
<td>A3</td>
<td>↓ GFR, Albuminuria</td>
<td>Common in low clearance clinic</td>
</tr>
<tr>
<td>Polycystic kidney disease</td>
<td>G2</td>
<td>A1</td>
<td>Imaging abnormality</td>
<td>Most common single genetic mutation</td>
</tr>
<tr>
<td>Hypertensive kidney disease</td>
<td>G4</td>
<td>A2</td>
<td>↓ GFR and albuminuria</td>
<td>Long-standing hypertension, refer (severely ↓ GFR)</td>
</tr>
<tr>
<td>Vesicoureteric reflex</td>
<td>G1</td>
<td>A1</td>
<td>Imaging abnormality</td>
<td>Common in children</td>
</tr>
<tr>
<td>CKD presumed due to DM &amp; HT</td>
<td>G3a</td>
<td>A2</td>
<td>↓ GFR and albuminuria</td>
<td>Very common, may not require referral</td>
</tr>
<tr>
<td>CKD cause unknown</td>
<td>G3b</td>
<td>A1</td>
<td>↓ GFR</td>
<td>Common, may not require referral</td>
</tr>
</tbody>
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Evaluating progression and significance of proteinuria

True or False?

A patient with a GFR of 45 mL/min and an ACR of 1.0 mg/mmol (normal) has a similar risk of adverse events (cardiovascular and renal) as a patient with a GFR of 70 mL/min and an ACR of 15 mg/mmol

True

What are the outcomes/implications of having proteinuria?

Prognostic significance of abnormal ACR

• Albuminuria was linearly related to events along its entire distribution (it may be even more informative than eGFR)

• An ACR >3 is not normal and is associated with a higher risk of CKD, AKI, cardiovascular mortality, all cause mortality, even if GFR normal

• These effects are independent of GFR and independent of traditional cardiac risk factors

Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis

www.thelancet.com Vol 375, June 12, 2010
Prognosis of CKD by GFR and Albuminuria Categories

Predicting Prognosis of CKD

- In predicting risk outcomes, identify:
  - Cause of CKD
  - GFR category
  - Albuminuria category
  - Other risk factors and co-morbid conditions
- Use estimated risk of concurrent complications and future outcomes to guide decisions for testing and treatment for CKD complications

Kidney Failure Risk Equation

- Provides the 2 and 5 year probability of kidney failure in CKD 3 and 4 patients

Summary of Relative Risks Predicting Prognosis of CKD

- Cause of CKD
- GFR category
- Albuminuria category
- Other risk factors and co-morbid conditions
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Kidney Failure Risk Equation

- Provides the 2 and 5 year probability of kidney failure in CKD 3 and 4 patients
Translating to clinical practice

Management of CKD complications – anemia, mineral metabolism, acidosis

Complications By GFR Category

<table>
<thead>
<tr>
<th>Complication</th>
<th>GFR category (mL/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;90</td>
</tr>
<tr>
<td>Anaemia</td>
<td>4.0%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>18.3%</td>
</tr>
<tr>
<td>↓25(OH) Vit D</td>
<td>14.1%</td>
</tr>
<tr>
<td>Acidosis</td>
<td>11.2%</td>
</tr>
<tr>
<td>↑phosphate</td>
<td>7.2%</td>
</tr>
<tr>
<td>↓albumin</td>
<td>1.0%</td>
</tr>
<tr>
<td>↑PTH</td>
<td>5.5%</td>
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Data from Inker et al JASN 2011;22(12):2322-31

Treatment of CKD related anemia

- No absolute rules of what “is in proportion/out of proportion” to level of kidney function, look at trends, however unusual to have Hb < 100 if eGFR > 45 mL/min
- Measure iron sat, aim for 0.25 at least, may require IV iron to get there – start with ferrous fumarate 300mg po qhs -> up to 900mg po qhs
- Consider referring for ESA’s in patients with Hb below 90 -100, target is 100-115 (esp to avoid transfusion if potential transplant candidate in future)
- Caveats if risk of stroke, if HTN, or if current or past malignancy

Treatment of CKD related metabolic bone disease

- The more we learn the less we know!
- Recommendations to:
  - measure Ca²⁺, PO₄, PTH at least once if GFR <45 to determine baseline
  - not do BMD if GFR <45
  - not use bisphosphonates if GFR <30
  - Targets for treatment
    - normal Ca²⁺ and PO₄
    - optimal PTH unknown
  - Recommendations not to routinely use vit D: vit D analogs to suppress PTH in patients with CKD not on dialysis in the absence of suspected deficiency

Treatment of acidosis in CKD

51 surprising uses for baking soda
Bicarbonate Supplementation Slows Progression of CKD and Improves Nutritional Status

Irene de Brito-Aubrun, Mike Vargason, Martin J. Fizel, and Mohammed N. Yaqoob

GFR decline:
- bicarb group 1.88 mL/min/year
- control group 5.93 mL/min/year

*Explanation of the graph*

Management of cardiovascular complications – hypertension and cholesterol treatment

- People with CKD and bicarbonate < 22 mmol/L should be treated with oral bicarbonate supplementation to maintain serum bicarbonate in the normal range, unless contraindicated


The Patient with early stage CKD is 5 to 10 times more likely to die from a cardiovascular event than progress to ESRD


Treatment of acidosis in CKD

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SHARP – Major atherosclerotic events reduced with fixed dose therapy in CKD

![Graph showing risk ratio and log rank for SHARP study](image)

Risk ratio 0.83 (0.74-0.94)
Log rank 2P=0.0021

Baigent C, Lancet June 2011

Treatment of cholesterol in CKD

- Recommendations are to treat those at high risk for atherosclerotic disease with lipid-lowering therapies, regardless of LDL levels, in those 50 years of age and older

Treatment of blood pressure in CKD

- Individualize BP targets and agents according to age, other co-morbidities and tolerance to treatment
- Inquire about postural dizziness and check for postural hypotension regularly
- Treat to <140/90 in patients with ACR <3 mmol/L
- Treat to <130/80 in patients with ACR >3 mmol/L

How should you treat this patient?

Mr. Smith is a 70 yr old man with dyslipidemia and PVD. His BP is 130/80, eGFR 70mL/min. He is on ASA and statin therapy. An ACR is done and is 21-25 mg/mmol (normal <3) on 3 occasions. His U/A is normal.

You should:

(a) Continue to optimize his other CV risk factors, counsel to avoid precipitants of AKI (no NSAIDS) and follow ACR and renal function q 6-12 mo

(b) Do the above plus start ACE-I or ARB as his ACR is significantly elevated

(c) Do (a) and (b) and refer to nephrology as ACR is significantly elevated

When to treat with an ACE or ARB?

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<td>DM, no HTN</td>
<td>No</td>
<td>Yes</td>
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<td>Yes</td>
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</tbody>
</table>

Antiproteinuric effect is enhanced by a low Na⁺ diet or a diuretic

Recommendations for referral and nephrology team management
Early Intervention = Longer Survival Rates
(as measured by CKD registration)

Survival advantage Clinic + Nephrologist vs Nephrologist alone

Despite exponential growth of CKD, dialysis growth remains relatively constant

Referral and models of care

Early vs. Late Referral – consequences and benefits

Key Messages

- Referral to specialist kidney care services is recommended if:
  - GFR <30 ml/min +/- ACR ≥100 mg/mmol
    *If this is a stable isolated finding, formal referral may not be necessary and advice from a specialist service may be all that is required to facilitate best patient care.
  - Other referral circumstances to consider:
    - AKI or abrupt sustained fall in GFR or Progression of CKD
    - CKD and hypertension refractory to treatment
    - Persistent abnormalities of serum potassium or Recurrent or extensive nephrolithiasis or Hereditary kidney disease
    - People with progressive CKD in whom the risk of kidney failure within 1 year is 10-20% or higher, should be referred for planning renal replacement therapy. The actual amount of time required at a minimum is at least 1 year to ensure appropriate education, understanding and referrals to other practitioners (e.g., vascular surgeons, transplant teams, etc.)
General Guide to Referral Decisions by GFR and Albuminuria Categories

<table>
<thead>
<tr>
<th>Stage</th>
<th>GFR (ml/min)</th>
<th>Albuminuria</th>
<th>Referral</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>≥60</td>
<td>&lt;30 mg/24h</td>
<td>Monitor</td>
</tr>
<tr>
<td>1B</td>
<td>45-59</td>
<td>30-300 mg/24h</td>
<td>Monitor</td>
</tr>
<tr>
<td>1C</td>
<td>30-44</td>
<td>300-3000 mg/24h</td>
<td>Refer</td>
</tr>
<tr>
<td>2A</td>
<td>15-29</td>
<td>≥3000 mg/24h</td>
<td>Refer</td>
</tr>
<tr>
<td>2B</td>
<td>&lt;15</td>
<td>≥3000 mg/24h</td>
<td>Refer</td>
</tr>
</tbody>
</table>

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

Summary

- Remember the CGA staging for CKD and the reason it has been proposed
- Classify CKD by Cause, GFR category, Albuminuria category
- Remember the importance of albuminuria
- Prediction of prognosis and frequency of monitoring should be guided by GFR and albuminuria categories
- GFR 30-60 ml/min and minimal proteinuria have a lower risk of progression and can usually be managed in the primary care/non nephrology setting

Questions?