Welcome to today’s webinar:

“The New Role of STAT Creatinine Testing”
Presenter: Brad S. Karon MD, PhD

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The New Role of STAT Creatinine Testing

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Learning objectives

• Describe benefits and limitations of estimated glomerular filtration rate (eGFR) as a screening tool for chronic kidney disease (CKD)

• Compare recommendations regarding the use of eGFR for CKD screening and prevention of contrast-induced nephropathy

• List factors to consider before instituting whole blood creatinine/eGFR for prevention of contrast-induced nephropathy
Outline

• **Kidney function**
  - Renal physiology
  - CKD as public health problem
  - Creatinine and eGFR measurement

• **Guidelines and recommendations for eGFR**
  - K/DOQI recommendations
  - NKDEP recommendations

• **Contrast-induced nephropathy (CIN)**
  - Definition of problem
  - Radiology/cardiology recommendations
  - Controversies

• **Data on whole blood creatinine for CIN**

• **Conclusions**
Kidney function

- Filter blood
- Remove toxins/drugs
- Maintain water balance
- Acid-base balance
- Electrolyte balance
- Filter unit = nephron
Renal function = ability to filter blood
- 50-75% decrease in filtering capacity before problem
- 85-90% decrease in filtering need for dialysis
Kidney function

• Measuring renal function
  - (micro) albuminuria/proteinuria
  - Measure glomerular filtration rate (GFR)
    ◦ Blood filtered per unit time
    ◦ Find inert substance (creatinine, iothalamate, lohexal, Inulin)
    ◦ Measure concentration in blood and urine
    ◦ Calculate GFR
  - Estimate glomerular filtration rate (GFR)
    ◦ Based on serum creatinine alone
    ◦ Based on eGFR calculated from serum creatinine
Kidney function

• What causes kidney disease?
  - Diabetes
  - High blood pressure
  - Glomerular disease (autoimmune, infectious)
  - Inherited and congenital kidney disease
  - Poisons, trauma, medications

• Types of kidney disease
  - Acute kidney disease
  - Chronic kidney disease
  - End stage renal disease
Chronic kidney disease (CKD)
- Affects ~ 19 million people in US
- Associated with diabetes and hypertension
- Loss of renal function over years
- Early detection can delay progression to ESRD
  - Control blood pressure
  - Dietary modification
  - Control blood glucose
Kidney function

How does the health system identify CKD early?

- Serum creatinine measurement
  - Serum creatinine goes up with renal failure

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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<tbody>
<tr>
<td></td>
<td>Blood levels rise when ~50% function lost</td>
</tr>
<tr>
<td>Commonly</td>
<td>Other factors (muscle mass, age, gender, race, illness, diet) affect serum creatinine</td>
</tr>
<tr>
<td>measured analyte</td>
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Kidney function

How does the health system identify CKD early?

• **Bottom Line**: Difficulty identifying CKD with serum creatinine alone

• **Estimated glomerular filtration rate (eGFR)**
  - Formula relating serum creatinine to measured GFR
  - Different formulas developed and tested over time
Guidelines for eGFR

• Goal is facile approach to recognizing CKD
  - Public health effort (access, commutable, cost)

• Many different creatinine assays exist
  - Standardization good but not great

• Several different formulas for eGFR exist

• Different creatinine values x different formulas = chaos

• Need for standardized approach for eGFR
**Guidelines for eGFR**

- **K/DOQI guidelines**
  - Kidney Disease Outcomes Quality Initiative
  - National Kidney Foundation
  - CKD = kidney damage or decreased GFR for 3 or more months
  - Clinical laboratories should report an eGFR using a prediction equation, in addition to serum creatinine
  - Physicians should estimate GFR from prediction equations using serum creatinine and all or some of the following: age, sex, race and body size
## Guidelines for eGFR

### Stages of CKD:
Normal GFR = 120-130 in young adults
Decreases with age

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (ml/min/1.73m²)</th>
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<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>
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K/DOQI Clinical Practice Guidelines on Chronic Kidney Disease
National Kidney Disease Education Program

- Use Modification of Diet in Renal Disease (MDRD) formula to report eGFR on patients > 18 yo
- Use creatinine reported to 2 digits (0.95 mg/dL) to calculate eGFR
• Lab Standardization an issue
  • Bias and interference will affect eGFR values in normal and near-normal range

• Recommended one of two MDRD equations
  • One for assays calibrated to isotope dilution mass spectrometry (IDMS) reference method
  • One for conventional calibration
MDRD Study Equation (conventional)

$$186 \times Cr^{-1.154} \times Age^{-0.203}(x0.742 \text{ if female})(x \ 0.192 \text{ if African Amer.})$$

MDRD Study Equation (IDMS-traceable)

$$175 \times Cr^{-1.154} \times Age^{-0.203}(x0.742 \text{ if female})(x \ 0.192 \text{ if African Amer.})$$
• Limitations to eGFR calculated thru MDRD
  - Equation validated mainly in patients with CKD
    ◦ Less accurate in normal renal function
  - Equation validated for ages 18-70
    ◦ Do not use in children, caution with > 70
  - Inter-lab differences in assays and imprecision affect estimation in near-normal range
    ◦ Report eGFR over 60 mL/min/1.73 m² as “> 60”
NKDEP Laboratory working group recommendations

• Primary reasons for recommending MDRD eGFR:
  - The MDRD equation is superior to other methods of approximating GFR
  - The MDRD equation does not require weight or height variables
NKDEP Laboratory working group recommendations

- Populations for whom MDRD eGFR may be inaccurate or has not been well validated:
  - Elderly (> 70 years)
  - Pregnant patients
  - Extremes of body size, muscle mass or nutritional status
  - Sick hospitalized patients
  - Patients with near-normal kidney function

- Labs may want to limit patients for whom eGFR is reported due to these limitations
In my lab/practice today we...

1. Report no eGFR values
2. Report eGFR on outpatients only
3. Report eGFR on patients 18-70 only
4. Report eGFR on all patients
5. Report eGFR on some other selected patient group
Contrast-induced nephropathy (CIN)

- Radiographic contrast media used for CT and angiography can be toxic to kidney
- CIN = increase in baseline creatinine within 48 hr of contrast (25%, 0.25-0.5 mg/dL)
- 3rd leading cause of hospital-acquired renal failure
Patients at risk of CIN

- CKD
- Diabetes
- Shock/hypotension (volume depletion)
- Advanced age (> 75 yo)
- Advanced congestive heart failure
CIN

• Recognizing risk can prevent CIN
  - Hydration
  - Change contrast agents
  - Reduce contrast dose or volume
  - Sodium bicarbonate?

• Focus on recognizing CKD before contrast
• Recommendations for CIN prevention
  - Society for Cardiovascular Angiography and Interventions
  - Routine use of eGFR recommended to identify patients at risk of CIN (MDRD)
  - eGFR > 60 mL/min/1.73 m² low risk
  - eGFR < 60 mL/min/1.73 m² high risk
    ◦ Consider one of several risk reduction strategies
CIN

• Recommendations for CIN prevention
  - Canadian Association of Radiologists
  - eGFR > 60 mL/min/17.3 m² very low risk
  - eGFR 30-60 mL/min/1.73 m² low to moderate risk
  - eGFR < 30 mL/min/1.73 m² high risk
  - Screen at-risk patients with creatinine/eGFR
Controversies and conflicts

• Age > 75 higher risk for CIN

• eGFR in patients > 70 not well established
  - Radiology guidelines use eGFR for all patients
  - Many labs report eGFR for patients 18-70 only
### Case for and against use of eGFR for patients > 70

**Pros**
- eGFR simple screening tool for radiologists

**Cons**
- eGFR lacks sensitivity in older patients
- eGFR lacks specificity in older patients
- Benefit vs. harm of changing contrast dose/regimen
Controversies and conflicts

- Use of whole blood (POC) creatinine
  - Real-time CIN screening of great benefit
  - Even lab creatinine performance of concern, don’t report eGFR over 60
  - Whole blood creatinine methods greater imprecision, more interferences
  - How accurate are whole blood methods in discriminating eGFR < 60 mL/min/1.73 m²?
Controversies and conflicts

• Reporting whole blood and serum/plasma results
  - Will results both go in permanent medical record?
  - Will physicians understand discrepancies 1 wk, 1 mo later?
  - What level of concordance is required between whole blood and serum/plasma?
Controversies and conflicts

- Will lab report eGFR on all patients?
  - If eGFR reported only 18-70, then creatinine must be used > 70
  - Both concordance in eGFR and correlation in creatinine necessary
  - Determines how institution must evaluate whole blood creatinine
1. Use WB creatinine to report eGFR for radiology for all patients with stat need
2. Use WB creatinine to report eGFR for radiology patients 18-70
3. Report only WB creatinine for radiology patients
4. Do not perform WB creatinine for radiology
Whole blood creatinine/eGFR

- Goal: whole blood creatinine for rapid decision-making re: contrast
- Based on eGFR and/or creatinine
- Acceptance criteria for use:
  - 95% concordance on eGFR (18-70)
  - 95% creatinine results within 0.2 mg/dL of lab
- Design study to determine whether any available whole blood creatinine methods were acceptable
Whole blood creatinine/eGFR

• Study design

• 266 patients presenting for CT, stat creatinine if no value in last 30 d and:
  - Age > 70
  - Hx renal disease/CKD/renal transplant
  - Diabetes
  - Pending creatinine value in lab

• 3 whole blood methods compared to reference
  - Roche Cobas Integra 400 (enzymatic, IDMS)
  - NIST SRM 967 used to verify reference method
• **Study population**
  - Patient age: 68 ± 14 years (range 22-92)
  - 103 females, 163 males
  - 264 non African-American patients, 2 A-A patients

• **eGFR calculated by MDRD formula**
  - Including ethnicity, age and gender
  - Appropriate formula (IDMS or conventional) used
  - One method analyzed concordance with and without offset
Whole blood creatinine/eGFR

Mean bias -0.05  0.09 mg/dL
95% results -0.23 to 0.13 mg/dL
Whole blood creatinine/eGFR

Mean bias 0.13 0.08 mg/dL
95% results -0.03 to 0.29 mg/dL
Whole blood creatinine/eGFR

Mean bias -0.23 0.18 mg/dL
95% results -0.59 to 0.13 mg/dL
## Whole blood creatinine/eGFR

### Concordance among patients 18-70

<table>
<thead>
<tr>
<th></th>
<th>Radiometer</th>
<th>Method C offset</th>
<th>Method B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plasma eGFR &lt; 60</strong>&lt;br&gt;(n=21)</td>
<td>18/21 (86%)</td>
<td>14/21 (67%)</td>
<td>21/21 (100%)</td>
</tr>
<tr>
<td><strong>Plasma eGFR ≥ 60</strong>&lt;br&gt;(n=96)</td>
<td>96/96 (100%)</td>
<td>88/96 (92%)</td>
<td>86/96 (90%)</td>
</tr>
<tr>
<td><strong>Overall concordance</strong></td>
<td>114/117 (97%)</td>
<td>102/117 (87%)</td>
<td>107/117 (91%)</td>
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Only Radiometer met criteria for eGFR concordance (95%) and creatinine correlation (within 0.2 mg/dL)
Whole blood creatinine/eGFR

• What about patients “missed” with Radiometer?
  - 13/68 patients with plasma eGFR < 60 called “normal” by Radiometer WB eGFR
  - All 13 had plasma eGFR > 45 mL/min/1.73 m²
  - All 13 had plasma creatinine ≤ 1.5 mg/dL
  - Likely low risk group for CIN
    ◦ Elderly patients with near-normal creatinine
    ◦ Demonstrates limitation of eGFR in elderly
Options for providing stat risk assessment

- Report only eGFR, do not include in medical record if concordance with lab not great
  - Con: radiologists will want documentation of value used to make medical decision

- Report only creatinine, avoid problem of eGFR limitations in elderly
  - Con: guidelines written with respect to eGFR
Whole blood creatinine/eGFR

• Options for providing stat risk assessment

  - Report eGFR and creatinine for all patients
    ◦ Pro: allows both values to be used
    ◦ Con: eGFR not well validated in elderly
  - Report eGFR/creatinine < 70, creatinine > 70
    ◦ Pro: don’t need to worry about eGFR in elderly
    ◦ Con: radiology has to find guidelines for creatinine
Whole blood creatinine/eGFR

• Options for providing stat risk assessment

- Reporting format/intended use will determine concordance and correlation requirements
- Each practice should determine requirements (concordance and/or correlation) for performing whole blood creatinine
- Consider concordance for all assays
- Consider correlation unless only eGFR will be reported or used clinically
Conclusions

• eGFR is recommended for CKD screening
  - Has limitations relating to age, illness, pregnancy, near-normal renal function in elderly

• CIN serious but can be prevented
  - System needed to identify at-risk patients
  - Whole blood POC creatinine may play a role

• Considerations in choosing WB creatinine
  - Concordance of eGFR between WB and lab
  - Correlation between WB and lab
  - Reporting schemes
Acknowledgements

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Thank you for attending today’s session.

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