Chronic Kidney Disease and ADRD

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Renal Medicine Division
March 7, 2023
Genitourinary system
Kidney: Nephron

- Parts of the Nephron
  - Nephron
  - Unfiltered Blood In
  - Filtered Blood In
  - Filtered Blood Out
  - Unfiltered Blood Out
  - Urine Out

- Kidney Cross Section
- One Nephron
  - Glomerulus
  - Tubule
  - Urine Out
GFR Equations

- **Serum creatinine**

- **Cockcroft-Gault Equation**
  - \( \text{CrCl (ml/min)} = (140 - \text{age}) \times \text{lean body wt (kg)} / \text{Cr} \times 72. \)
  - then multiply by 0.85 if women

- **MDRD Equation**
  - \( \text{CrCl (ml/min)} = 175 \times \text{SCr (exp[-1.154])} \times \)
  - \( \text{Age (exp[-0.203])} \times (0.742 \text{ if female}) \times (1.21 \text{ if black}) \)

- **CKD-EPI Equation (elderly more precise)**
  - \( \text{GFR} = 141 \times \min(\text{Scr}/\kappa,1)^{\alpha} \times \max(\text{Scr}/\kappa,1)^{-1.209} \times \)
  - \( 0.993^{\text{Age}} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]} \)
Kidney function

- Estimated GFR (eGFR) reporting at Emory Healthcare uses the CKD-EPI equation and it reports out kidney function for African-Americans vs. Non African-Americans.

- CKD-EPI Equation:
  \[
  GFR = 141 \times \min\left(\frac{\text{Scr}}{\kappa}, 1\right)^\alpha \times \max\left(\frac{\text{Scr}}{\kappa}, 1\right)^{-1.209} \times 0.993^{\text{Age}} \times 1.018 \times \begin{cases}1.159 & \text{if black} \\ 1 & \text{if female} \end{cases}
  \]

<table>
<thead>
<tr>
<th>Creatinine</th>
<th>1.37</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN/Creat Ratio</td>
<td>12</td>
</tr>
<tr>
<td>Estimated GFR, Non African American</td>
<td>* 64</td>
</tr>
<tr>
<td>Estimated GFR, African American</td>
<td>* 74</td>
</tr>
</tbody>
</table>
CKD Definition (KDIGO - 2012)

• Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for 3 months, with implications for health and CKD is classified based on cause, GFR category, and albuminuria category.

Stages of CKD

G category Stages

- GFR
  - G1 >90 ml/min
  - G2 60-89 ml/min
  - G3a 45-59 ml/min
  - G3b 30-44 ml/min
  - G4 15-29 ml/min
  - G5 Kidney Failure, <15 ml/min

A category

- Albuminuria
  - A1 <30 mg/g
  - A2 30-300 mg/g
  - A3 >300 mg/g
Prevalence of CKD

• Prevalence of CKD in the United States: A Sensitivity Analysis Using the National Health and Nutrition Examination Survey (NHANES)
  • 1999-2004
  • 13.07% of adults
  • 26.3 million Americans
  • MDRD Study equation

Prevalence of CKD

<table>
<thead>
<tr>
<th>Persistent albuminuria categories Description and range</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal to mildly increased</td>
<td>55.6</td>
<td>1.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Moderately increased</td>
<td>32.9</td>
<td>2.2</td>
<td>0.3</td>
</tr>
<tr>
<td>Severely increased</td>
<td>3.6</td>
<td>0.8</td>
<td>0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>G1: Normal or high</td>
</tr>
<tr>
<td>G2: Mildly decreased</td>
</tr>
<tr>
<td>G3a: Mildly to moderately decreased</td>
</tr>
<tr>
<td>G3b: Moderately to severely decreased</td>
</tr>
<tr>
<td>G4: Severely decreased</td>
</tr>
<tr>
<td>G5: Kidney failure</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GFR categories (mL/min/1.73m²) Description and range</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1: Normal or high</td>
</tr>
<tr>
<td>G2: Mildly decreased</td>
</tr>
<tr>
<td>G3a: Mildly to moderately decreased</td>
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<tr>
<td>G3b: Moderately to severely decreased</td>
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<tr>
<td>G4: Severely decreased</td>
</tr>
<tr>
<td>G5: Kidney failure</td>
</tr>
</tbody>
</table>
### Stage 5 CKD Incidence Rates per Million Vary by Ethnicity

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Incidence Rate per Million</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Black</td>
<td>*</td>
<td>3.89</td>
</tr>
<tr>
<td>Native American</td>
<td>*</td>
<td>2.74</td>
</tr>
<tr>
<td>Asian</td>
<td>*</td>
<td>1.56</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>†</td>
<td>1</td>
</tr>
<tr>
<td>Hispanic</td>
<td>*</td>
<td>1.45</td>
</tr>
</tbody>
</table>

*P<0.0001, †Reference population.

Primary Diagnosis For Patients Who Start Dialysis

- Diabetes: 50.1%
- Hypertension: 27%
- Glomerulonephritis: 13%
- Other: 10%

United States Renal Data System. Annual data report 1984-2010

No of Patients
95% CI

R² = 99.8%
CKD Risk Factors

- Diabetes
- Hypertension
- Coronary artery disease
- Obesity
- Genetics/family history
- Older age
- Chronic illnesses (HIV, Lupus)
- Nephrotoxic medications (like NSAIDS, some chemotherapy)
Predictors for Progression

- Level of GFR (kidney function at baseline)
- Albuminuria (protein in urine)
- Hypertension
- Race and male gender
- Advanced age
- Obesity and smoking
- Poor glycemic control (diabetes)
- Ongoing nephrotoxic medication use (NSAID pain meds, certain antibiotics or chemo)
- Hyperlipidemia and cardiovascular disease

CKD Treatment Recommendations

• The 2012 KDIGO guidelines on the evaluation and management of BP in CKD recommended:
  • a goal BP ≤130/80 mm Hg for patients with CKD (with or without diabetes) and micro- or macroalbuminuria (protein in urine).
  • and a goal of ≤140/90 mm Hg for those without albuminuria.
• Some recommendations of <130/80 for everyone.
• The guideline also recommended using ACEi or ARB in diabetic patients and patients with protein in urine.
  • Examples: Lisinopril (ACEi) and losartan (ARB)
• SGLT2 inhibitors (Farxiga and Jardiance)
In this report of two randomized trials, patients with type 2 diabetes at risk for cardiovascular disease received the sodium–glucose cotransporter 2 inhibitor canagliflozin or placebo and were followed for 188 weeks.

Hypothesis: Canagliflozin reduced the risk of cardiovascular events.
Rates of Hospitalization for Heart Failure, Death from Any Cause, and Kidney Outcomes in the Integrated CANVAS Program.

### Prevalence of CKD complications by GFR category

<table>
<thead>
<tr>
<th></th>
<th>&gt;90%</th>
<th>60-89%</th>
<th>45-59%</th>
<th>30-44%</th>
<th>&lt;30%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anemia</strong></td>
<td>4%</td>
<td>4.7%</td>
<td>12.3%</td>
<td>22.7%</td>
<td>51.5%</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>18.3</td>
<td>41</td>
<td>71.8</td>
<td>78.3</td>
<td>82.1</td>
</tr>
<tr>
<td><strong>Vitamin D Deficiency</strong></td>
<td>14.1</td>
<td>9.1</td>
<td>10.7</td>
<td>10.7</td>
<td>27.2</td>
</tr>
<tr>
<td><strong>Acidosis</strong></td>
<td>11.2</td>
<td>8.4</td>
<td>9.4</td>
<td>18.1</td>
<td>31.5</td>
</tr>
<tr>
<td><strong>High phos</strong></td>
<td>7.2</td>
<td>7.4</td>
<td>9.2</td>
<td>9.3</td>
<td>23</td>
</tr>
<tr>
<td><strong>High PTH</strong></td>
<td>5.5</td>
<td>9.4</td>
<td>23</td>
<td>44</td>
<td>72.5</td>
</tr>
</tbody>
</table>

Cardiovascular Disease

• Dyslipidemia
  • Screen all patients with Chronic Kidney Disease (CKD)

• Rationale:
  • High prevalence of cardiovascular disease
  • Possible contribution to progression of CKD

• LDL goal < 100 mg/dL
  • Treatment of TG important if >500 mg/dL
  • *Controversial KDIGO Guidelines 2013 on Lipid Management – released 2014*
    • Not to follow LDL but put all with CKD on statins and lifestyle modification for TG levels
Initiation of Dialysis

*End-stage Kidney Disease*

*Kidney Failure*

• Indications:
  • GFR approximately 10 mL/min/1.73m²
    • A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis. BA Cooper et al. N Engl J Med 2010; 363:609-619
  • **Malnutrition (low albumin, weight loss)**
  • **AEIOU**
    • Acidosis, Electrolyte problems, Intoxication, Overload (fluid), and Uremia (BUN)

• Preparation:
  • KDIGO – **nephrologist** – eGFR <30 for all, before if >300 mg/day proteinuria, uncontrolled bp, significant hematuria, AKI, and fast progression (>5 ml/min/year).
  • Dialysis preparation if initiation within 1 year.
  • Choice of modality and dialysis access placement
Hemodialysis
**Risk Factors**

**Dementia**
- Genetics
  - Family history
- Hypertension
- Diabetes
- Smoking
- High cholesterol
- Older age
- Coronary artery disease
- Stroke (cerebrovascular disease)
- Obesity
- Physical inactivity
- Chronic illnesses (HIV, Lupus)
- CKD
- Medications

**CKD**
- Diabetes
- Hypertension
- Coronary artery disease
- Obesity
- Genetics/family history
- Older age
- Chronic illnesses (HIV, Lupus)
- Nephrotoxic medications
APOL1 risk variants increase the risk of many different types of kidney disease in blacks

David J. Friedman, and Martin R. Pollak
CJASN doi:10.2215/CJN.15161219
Cognitive impairment in dialysis patients. A comprehensive battery of neurocognitive tests was administered in the first hour of hemodialysis to 314 patients.

Association between Blood Pressure variability and incidence of dementia in CKD patients
Prevalence and correlates of cognitive impairment in the frequent hemodialysis network (FHN) trials
-Modified Mini-Mental State Exam score <80
Stroke and dialysis in the stroke belt

Strokes are generally more common in the southern United States. States with O/E adjusted odds ratios significantly >1 for new ischemic stroke, after successive adjustments. (A) Adjusted for age. (B) Adjusted for age and sex. (C) Adjusted for age, sex, and race. (D) Full multivariable adjustment.

Stroke and the “Stroke Belt” in Dialysis: Contribution of Patient Characteristics to Ischemic Stroke Rate and Its Geographic Variation

Wetmore, James B.; Ellerbeck, Edward F.; Mahnken, Jonathan D.; Phadnis, Milind A.; Rigler, Sally K.; Spertus, John A.; Zhou, Xinhua; Mukhopadhyay, Purna; Shireman, Theresa I.


doi: 10.1681/ASN.2012111077
# Association between cholinesterase inhibitors and kidney function decline in patients with Alzheimer’s dementia.

## Population
- **11,898 patients with an incident Alzheimer’s dementia diagnosis**
- **Jan 2007 – Dec 2018**
- **Observational study in health system’s data: SCREAM and Swedish dementia Registry.**

## Exposure
- **Start treatment with cholinesterase inhibitors within three months from diagnosis (n=6,803) vs non-start (n=5,095)**
- **Median 3.0 years follow-up**

## Findings

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Adjusted Hazard ratio (95% CI) of use vs non-use</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD progression Composite of &gt;30% decline or kidney replacement therapy or kidney related death</td>
<td>0.82 (0.71-0.96)</td>
</tr>
<tr>
<td>Kidney replacement therapy or kidney related death</td>
<td>0.68 (0.51-0.89)</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.79 (0.72-0.86)</td>
</tr>
</tbody>
</table>

## CONCLUSION:
In patients with Alzheimer’s dementia undergoing routine care, use of cholinesterase inhibitors (vs no-use) was associated with lower risk of CKD progression, lending indirect support to the role of cholinergic anti-inflammatory pathway activation on preservation of kidney function.

**Xu H et al, 2022**
Summary

• Risk factors of CKD
  • Diabetes, Hypertension, Coronary artery disease, Obesity, Genetics/family history, Older age, Chronic illnesses (HIV, Lupus), and nephrotoxic medications (like NSAIDS, some chemotherapy)

• Common causes
  • Diabetes #1, Hypertension #2, Glomerulonephritis #3

• Treatment of CKD
  • Treat underlying causes (i.e diabetes/hypertension)
  • ACEi (i.e lisinopril or enalapril) and ARBs (i.e losartan or valsartan)
  • SGLT2i (i.e Jardiance and Farxiga)

• CKD and ADRD
  • Similar risk factors
  • CKD risk factor for ADRD
  • High prevalence of cognitive impairment and dementia/ADRD in CKD/ESRD (dialysis)
  • Causes of ADRD in CKD/ESRD – blood pressure, uremia (toxins), stroke
Thank you!

KIDNEY HEALTH FOR ALL

PREPARING FOR THE UNEXPECTED, SUPPORTING THE VULNERABLE!

World Kidney Day

9 MARCH 2023

#worldkidneyday #kidneyhealthforall
www.worldkidneyday.org

World Kidney Day is a joint ISN Initiative

Emory University School of Medicine
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Emory Dialysis

Emory Healthcare