Evaluation of Chronic Kidney Disease in Geriatric Patients

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Objectives

• Review prevalence of chronic kidney disease (CKD) in geriatric population.
• Review methods of assessing renal function and CKD in geriatric patients.
• Review important risk factors for development of CKD and acute kidney injury (AKI) in geriatric patients.
• Review important causes of hospital acquired AKI.
• Management of CKD and AKI in geriatric population.
Definition of CKD

• CKD defined as structural kidney damage for 3 or more months:

  – Elevated serum Creatinine (Cr) levels
  – Measurement of Glomerular filtration rate (GFR) using calculated equations.
  – Proteinuria +/- hematuria.
## Stages of Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Stage of CKD</th>
<th>Description</th>
<th>GFR (ml/min per 1.73 m²)</th>
<th>Detection, Evaluation, and Management</th>
<th>US Prevalence in 2000b (%, n in thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage with normal or increased GFR</td>
<td>&gt;90</td>
<td>Diagnosis and treatment, treatment of comorbid conditions, slowing progression, CVD risk reduction</td>
<td>2.8; 5600</td>
</tr>
<tr>
<td>2</td>
<td>Kidney damage with mild decreased GFR</td>
<td>60 to 89</td>
<td>Estimate progression</td>
<td>2.8; 5700</td>
</tr>
<tr>
<td>3</td>
<td>Moderate decreased GFR</td>
<td>30 to 59</td>
<td>Evaluating and treating complications</td>
<td>3.7; 7400</td>
</tr>
<tr>
<td>4</td>
<td>Severe decreased GFR</td>
<td>15 to 29</td>
<td>Referral to nephrologist and consideration for kidney replacement therapy</td>
<td>0.1; 300</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td>Kidney replacement therapy (if uremia present)</td>
<td>0.2; 300</td>
</tr>
</tbody>
</table>

*Table 1. Stages of CKD with prevalence in the US (NHANES 1999 to 2000) and stage specific recommendations for detection, evaluation and management (NKF-K/DOQI)*

CKD Prevalence in Geriatric Patients

United States Renal Data System (USRDS) 2012 Annual Data Report: Chapter 2 Identification and care of Patients with CKD; Figure 2.2.

CKD Diagnosis in Geriatric Patients by Age, Gender, and Race

Medicare patients age 65 & older & MarketScan patients age 50–64, alive & eligible for all of 2010. CKD claims as well as other diseases identified in 2010.

United States Renal Data System (USRDS) 2012 Annual Data Report: Chapter 1 CKD In General Population; Figure 2.6.  http://www.usrds.org/atlas12.aspx
CKD Categorized by Age & Risk Factors


United States Renal Data System (USRDS) 2012 Annual Data Report: Chapter 1 CKD in General Population; Figure 1.8.  http://www.usrds.org/atlas12.aspx
Risk Factors for CKD

Initiating factors:
- Age
- Gender
- Ethnicity
- Family history of CKD
- Diabetes mellitus
- Metabolic syndrome
- Hyperfiltration state
- High normal urinary albumin excretion
- Dyslipidemia
- Nephrotoxins
- Primary kidney disease
- Urological disorders
- Cardiovascular disease

Traditional progression factors or markers:
- African American ethnicity
- Proteinuria
- Hypertension
- High protein intake
- Obesity
- Anemia
- Dyslipidemia
- Smoking
- Nephrotoxins
- Cardiovascular disease

Emerging progression factors or markers:
- ADMA
- FGF23
- Phosphate
- PTH
- Adrenomedullin
- ANP
- NT-proBNP
- L-FABP
- KIM-1
- NGAL
- ApoA-IV
- Adiponectin
- Genetic polymorphisms

Progression of CKD: GFR decline and ESRD

Kronenberg, F. Nature Reviews Nephrology 5, 677-689
Measurement of Renal Function

• Estimating GFR via equations is clinically better than Cr alone.
  – Serum Cr can only be used to estimate GFR in patients with stable kidney function.

• Challenges with GFR measurement in elderly
  – Serum Cr levels lower due to lower muscle mass
    • Under-recognition of CKD in elderly due to “normal” lab Cr
  – Aging kidney physiology

Dousdampanis P et al. Aging and Disease 2012 3(5); 360-372,
Traynor, J. BMJ. 2006;333(7571):733.
Clinical Importance of Calculating GFR

90 year old male:
Weight: 40 kg
Serum Cr= 1.3 mg/dl

GFR = 35 mL/min

21 year old male:
Weight: 110 kg
Serum Cr= 1.9 mg/dl

GFR = 71 mL/min
Measuring Renal Function

- Creatinine clearance
  - Cockgroft-Gault Equation
  - 24 hour urine measurement

- GFR measurements
  - Calculated formulas (MDRD and CKD-EPI)
  - Serum Cystatin C

- Use of 24 hour urine Cr clearance helpful in certain cases:
  - Very high or low muscle mass
  - Muscle wasting syndromes
  - Patients who have amputated extremities
  - Obese or very thin patients
  - CKD 4 patients about to start dialysis

Dousdampanis P et al. Aging and Disease 2012 3(5); 360-372.
Traynor, J. BMJ. 2006;333(7571):733.
Relationship Serum Creatinine and GFR

Simon J et al. Cleveland Clinic Journal of Medicine March 2011 vol. 78 3 189-195
# Measurement of Renal Function

<table>
<thead>
<tr>
<th>Equation</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Kidney Disease Epidemiology Collaboration</td>
<td>Age, sex, race, serum creatinine level</td>
</tr>
<tr>
<td>Cockcroft-Gault</td>
<td>Age, weight, sex, serum creatinine level</td>
</tr>
<tr>
<td>Modification of Diet in Renal Disease</td>
<td>Age; sex; race; and serum urea, nitrogen, albumin, and creatinine levels</td>
</tr>
</tbody>
</table>
CKD Equations and Elderly

- Cockcroft-Gault Formula (CGF)
  - Calculates creatinine clearance
  - Requires body weight (kg)
    - Over estimates GFR in obese patients
    - Under estimates GFR in elderly patients >65

- Modification of Diet in Renal Disease (MDRD)
  - Measures GFR - does not use body weight.
  - Tends to over diagnose CKD

- CKD-Epi Equation
  - Newer & better equation for GFR.
  - Researched in more diverse patient population +/- CKD.
  - Provides more accurate estimate of GFR among individuals with normal or mild reduced GFR.

Dousdampanis P et al. Aging and Disease 2012 3(5); 360-372.
Cystatin C

• A low molecular weight protein
  – Produced by all nucleated cells & filtered at the glomerulus.
  – Rate of production relatively constant

• Appears more sensitive in identifying mild reductions in kidney function than Cr.
  – Less dependent on muscle mass, weight.
  – More dependent on age, sex, smoking and acute inflammatory conditions.

• Cons:
  – costly and less readily available in labs.

• Cystatin C & serum Cr combination more accurate for the assessment of GFR.

• Current guidelines still recommend estimating GFR with Cr based CKD-EPI or MDRD.

Key Risk Factors for CKD in Geriatric

- Age related renal physiology changes
- Hypertension
- Diabetes Mellitus
- Cardiovascular Disease
- Acute Kidney Injury (AKI)
- Medication
- Benign Prostatic Hypertrophy (BPH)
Renal Physiology Changes in Elderly

• Reduced renal mass (30-50% sclerosis)
  – Diminished functioning glomeruli
• Advance arteriosclerosis and tubular atrophy of blood vessels.
  – Nephrosclerosis 58% for age 60-69,
  – Greater than 70% by age 70+
• Decreased ability to regulate sodium and water
  – Maladaptive renin-aldosterone axis
  – More prone dehydration esp in acute illnesses
• Impaired potassium secretion and sodium reabsorption
  – Result of tubular atrophy and interstitial scarring.

Hypertension

- The prevalence of hypertension in Elderly population >60 years old is 60-80%.
- HTN is present in 80% of CKD patients.
  - Arteriosclerosis & physiology changes due to aging.
  - Systolic HTN strong independent predictor CKD progression and CHF.
- Increased activity of the renin-angiotensin system.
  - Albuminuria as indicator endothelial dysfunction.
- Increased autonomic dysregulation leads to increased orthostatic hypotension.
- Elevated risk of cardiovascular disease with CKD and HTN.

Hypertension and CKD Cycle

Disordered mineral metabolism
  Metabolic acidosis
Systemic inflammation
Electrolyte disturbances
Anemia

Autonomic dysregulation
  Sodium retention
Nephrosclerosis
Endothelial dysfunction
Lost arterial compliance
Hyperuricemia

Diminished GFR

Vascular resistance
  Left ventricular hypertrophy
Arterial occlusion
Ventricular remodeling

Cardiovascular disease

Elevated blood pressure

Figure 1 | Joint contribution of CKD and hypertension to cardiac risk. CKD, chronic kidney disease; GFR, glomerular filtration rate.

Figure. 2014 Hypertension Guideline Management Algorithm

Adult aged ≥18 years with hypertension

Implement lifestyle interventions (continue throughout management).

Set blood pressure goal and initiate blood pressure lowering medication based on age, diabetes, and chronic kidney disease (CKD).

General population (no diabetes or CKD)  
Diabetes or CKD present

Age ≥60 years  
Blood pressure goal SBP <150 mm Hg DBP <90 mm Hg  
Initiate thiazide-type diuretic or ACEI or ARB or CCB, alone or in combination.

Age <60 years  
Blood pressure goal SBP <140 mm Hg DBP <90 mm Hg  
Initiate thiazide-type diuretic or CCB, alone or in combination.

All ages Diabetes present  
No CKD

All ages  
CKD present with or without diabetes

Blood pressure goal SBP <140 mm Hg DBP <90 mm Hg

Nonblack  
Black

Select a drug treatment titration strategy
A. Maximize first medication before adding second or
B. Add second medication before reaching maximum dose of first medication or
C. Start with 2 medication classes separately or as fixed-dose combination.

Important Side Effects of HTN Medications

• Thiazide Diuretics
  – Traditionally the mainstay of HTN treatment
  – Side effect:
    • Volume depletion and dehydration
    • Electrolyte abnormalities (K and Mg)
    • AKI secondary to reduced renal blood flow

• ACE-Inhibitors / Angiotensin II Receptor Blockers
  – AKI in the setting of volume depletion
  – Hyperkalemia
  – Caution in bilateral renal artery stenosis

• Combination Therapy
  – ACE-I or ARB with Aldosterone antagonist
    • Severe hyperkalemia
    • In cases of dehydration or hypovolemia, may lead to profound AKI.
  – Diuretic with ACE-I or ARB combination

Diabetic Nephropathy

• Risk factors
  – Genetic susceptibility
  – Poor glycemic control (HgA1C)
  – HTN
  – Race (African Americans, Hispanics, Pima Indians)
  – Age
  – Obesity
  – Smoking

• Diabetic retinopathy typically precedes nephropathy

• Albuminuria is also independently linked with poor cardiovascular outcomes.
  – Likely due to advanced endothelial dysfunction

Albuminuria and CKD

- Normal albumin excretion < 30 mg/day
- Microalbuminuria 30 and 300 mg/day
- Macroalbuminuria is above 300 mg/day

CKD and Diabetes Guidelines

- Yearly screening for micro-albuminuria with random P/Cr urine ratio.
- A reduction in albuminuria to less than 500mg/day.
  - ACE-I or ARB, but not both.
- Reduction of BP less than 130/80 (NKF)
  - JNC 8 recommends SBP< 140/90
- If appropriate, use of both thiazide diuretic with ACE-I or ARB medication.

Clinical Findings Less Suggestive of Diabetic Nephropathy

• Absence of albuminuria with stage 3-5 CKD
• Absence of retinopathy with CKD
• Active urinary casts
• Newly diagnosed DM less than 5 years
• Rapid worsening proteinuria
• Make sure to evaluate other CKD risk factors
  – HIV, lupus + autoimmune dz, vasculitis, hepatitis, myeloma, etc.
Important CKD Case Example

HTN

DM

Amyloidosis
Cardiovascular disease and CKD

• CVD is highly prevalent in CKD population.

• Associated with progression of CKD.

• CKD patients with CVD suffer higher morbidity and mortality rates.

• Complex pathophysiology CKD <-> CVD

Acute Myocardial Infarction Incidence by CKD Status

Medicare pts. age 66 & older; first AMI event in 2007 or 2010.
USRDS 2012 Annual Data Report: Cardiovascular disease and CKD
Probability of Death Following Acute Myocardial Infarction in CKD

USRDS 2012 Annual Data Report: Cardiovascular disease and CKD
Coronary artery disease

Traditional risk factors
- Advanced age
- Hypertension
- Diabetes mellitus
- Dyslipidaemia
- Tobacco use
- Family history
- Male sex

Chronic kidney disease

Novel risk factors
- Albuminuria
- Disordered bone and mineral metabolism
- Anaemia
- Vascular stiffness
- Prothrombotic milieu
- Oxidative stress
- Protein–energy wasting
Cardio-Renal-Anemia Complexity

- Hypoxia
- Vasodilation
- Volume overload
- Tachycardia
- Increased cardiac output

LVH → CHF

- Chronic Inflammation
- ↓Erythropoiesis
- Perturbed iron metabolism

Anemia → Renin-angiotensin-aldosterone activation → Renal ischemia

CKD

- Peritubular cell death
- Dysregulated EPO production and release

Age and Hospital Acquired AKI

Outcomes AKI Medicare Age 65 +

AKI and CKD: A Complex Relationship

Risk Factors for Hospital AKI

• Age related decrease in GFR
• Co-existing illness (HTN, DM, CVD, Infection)
• Hypotension / Hypovolemic
• Medication related nephrotoxicity
  – ACE-I / ARB
  – Diuretics
  – NSAIDs
  – Antibiotics
• Contrast induced nephropathy
• Peri-operative factors

Avoiding Iatrogenic Hypotension in Geriatric Population

• Appropriate adjustments in anti-hypertensive medication
  – Recognize when to hold ACE-I or ARB
  – Diuretics dose adjustment
  – Post operative state

• Relative hypotension
  – Abrupt drop in systolic pressure 15-20mmHg.

Patient Risk Factors Drug Nephrotoxicity

- Age > 60
- Female
- Pre-existing CKD
- Decreased total body water and weight
- Failure to recognize compromised GFR in Geriatric population
  - Overdosing antibiotics
- Hypoalbuminemia
  - Increases free drug level

CKD and Medication Dose Adjustment

• All Antibiotics
  – Especially gentamicin, vancomycin, amphotericin.
  – Anti viral meds (acyclovir, valacyclovir...etc)
• Gout Medication
  – Colchicine and allopurinol
• Hypoglycemic medication
  – Avoid Metformin if GFR<45 and contraindicated <30
• Chemotherapeutics
  – Especially cisplatin and carboplatin
• Bisphosphonates (GFR<40 caution)
  – FSGS reported
• Digoxin

Patient Risk Factors for Contrast Nephropathy

- Age > 75
- Hypotension / volume depletion
- Diabetes
- Decompensated CHF
- Contrast-media volume and osmolality
- Pre-existing CKD
- Concurrent nephrotoxic medication

Kidney Intern 2012; S(2): 69-88
Obstructive Uropathy and CKD

• Nephrolithiasis
• BPH and bladder outlet syndrome
• Neurogenic bladder
  – Diabetes
  – Stroke
  – Trauma patients
• Urological Cancer
Medication Induced Urinary Retention

- Antiparkinson medication
- Anticholinergic medications
- Antipsychotics and anti-depressant
- Sympathomimetics (Sudafed)
- Antihistamines
- Narcotics / Morphine

Management of CKD

• Delaying or halting the progression of CKD
  – Control HTN
  – Control DM
  – Optimize cardiovascular treatment strategies

• Treating the pathologic manifestations of CKD

• Timely planning for long-term renal replacement therapy.
Systemic effects of uremia.
Comprehensive CKD Management

• **HTN**
  – Salt intake <2gm a day
  – Goal SBP < 140/90

• **Proteinuria**
  – Initiate ACE-I or angiotensin receptor blocker
  – Goal SBP<130/80
  – Monitor carefully in advanced CKD 4 patients (risk hyperkalemia)

• **Cardiovascular complication**
  – Volume overload (administer loop diuretic)
  – CVD risk modification
    • Statin if GFR <60 regardless of CVD risk factors.

• **Anemia**
  – CKD (non-HD) Hg target 10-11.5 g/dl
  – Avoid Hg>13

Comprehensive CKD Management

• Hyperparathyroidism
  – Evaluate PTH, phos, and vitamin D 25-OH
  – PTH level goal
    • 35 to 70 pg/mL in CKD 3
    • 70 to 110 pg/mL in CKD 4

• Metabolic acidosis
  – Aim to keep serum bicarbonate level 23-29 meq/L
  – Sodium bicarbonate or sodium citrate

• Dietary modification
  – Lower protein intake 0.8g/kg/day for CKD4
  – Low potassium intake with advanced CKD

Timing of Dialysis in Elderly with CKD

- Conflicting evidence on positive outcomes with early initiation of dialysis on survival.
- Initiating Dialysis Early and Late (IDEAL) Trial
  - GFR 10-14 vs GFR 5-7 ml/min/1.73m²
  - No difference in clinical outcomes
- 1 year mortality after dialysis initiation
  - Age 70-74 (20%); Age 75-79 (31%)
  - Age 80-89 (46%); Age 90+ 46%
- Family and personal patient preferences.

Treit K et al. Sem in Dialysis; 26(6); Nov 2013 p682.
Conservative Non-Dialytic Therapy

• Monitor Potassium closely
  – Kayexalate
  – Discontinuation of ACE-I
• Avoid iatrogenic hypotension
• Lean and lower protein diet (0.8 g/kg)
• Treat anemia and metabolic acidosis
• Low potassium diet education (<2000 mg day)
• Management of volume disorder (CHF)
  – Loop diuretics
Conclusion

• Recognize limitations of serum Cr in evaluating CKD in geriatric patients.
• MDRD and CKD-EPI are best estimation formulas for GFR
• Recognize important changes in renal physiology for elderly patients
• Complex relationship between CVD and CKD
• DM and HTN are most common co-morbid conditions associated with CKD.
• AKI important risk factor for developing CKD + progression
• Focus on comprehensive CKD management goals