CHRONIC KIDNEY DISEASE
Diagnosis, Treatment, & Prevention

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Women’s Home & Overseas Missionary Society
A.M.E. Zion Church
Outline

- Chronic Kidney Disease
  - Definitions
  - Epidemiology
- Screening for CKD
- Treating Complications of Advanced CKD
  - Hypertension
  - Control of volume
  - Alterations in bone metabolism
  - Anemia
  - Nutrition
  - Hyperkalemia
- Suggested K-DOQI action plan based on disease severity
- When to refer and why
- Slowing Progression of CKD
- Evidence supporting antihypertensive use
- Cardiovascular Risk Modification
- Getting the word out
What is Chronic Kidney Disease?
Defining CKD

- Kidney damage for ≥ 3 months as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either:
  - Pathological abnormalities; or
  - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging testing

- Glomerular Filtration Rate (GFR) < 60 ml/min/1.73 m² for ≥ 3 months, with or without structural kidney damage

19,000,000

- Chronic Kidney Disease: 372,000
- Dialysis: 80,000
Stages of CKD

Proposed NKF-K/DOQI Guidelines. NKF Clinical Nephrology Meetings 2001; Orlando, Fla.

CKD Continuum

1. Kidney Damage
2. Mild GFR ↓
3. Moderate GFR ↓
4. Severe GFR ↓
5. Kidney Failure
6. ESRD

GFR (mL/min/1.73 m²)

90 80 70 60 50 40 30 20 <15

Proposed NKF-K/DOQI Guidelines. NKF Clinical Nephrology Meetings 2001; Orlando, Fla.
# Prevalence of CKD

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>GFR (mL/min/1.73 m²)</th>
<th>Prevalence in US Pop.*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney damage</td>
<td>&gt; 90**</td>
<td>10,259</td>
</tr>
<tr>
<td>2</td>
<td>Mild GFR ↓</td>
<td>60 – 89**</td>
<td>5,300 – 7,100</td>
</tr>
<tr>
<td>3</td>
<td>Moderate GFR ↓</td>
<td>30 – 59***</td>
<td>7,553</td>
</tr>
<tr>
<td>4</td>
<td>Severe GFR ↓</td>
<td>15 – 29</td>
<td>363</td>
</tr>
<tr>
<td>5</td>
<td>Kidney failure</td>
<td>&lt; 15 or dialysis</td>
<td>300</td>
</tr>
</tbody>
</table>

*Population of 177 million adults age over 20

** with presence of proteinuria or hematuria +/- structural changes

*** do not need proteinuria or hematuria, just GFR <60
Further, African Americans develop ESRD at a younger age 55.8 vs 62.2 yo

Although only 12.6% of the US population, African Americans constitute 50% of the ESRD population

USRDS 2007 Annual Report AJKD 51, Suppl 1, Jan 2008
Familial Influences

- Inherited Nephropathies
- Family history is a strong risk factor for diabetic nephropathy
- In all ethnic groups studied to date diabetic siblings of pts with ESRD 2/2 DM were at markedly increased risk of developing ESRD.
- Particularly common in African Americans with an increased incidence rate of 4-25 fold greater than Caucasians

AJKD 2008, 51 (1), 29-37
Etiology of Chronic Kidney Disease

- Diabetes: 43%
- HTN: 25%
- GN: 12%
- Other: 20%

USRDS 2001
Identifying patients at risk: National Kidney Foundation Recommendations (KDOQI)

- Individuals at increased risk for CKD should be tested at the time of health evaluations to determine if they have CKD. This should include patients with:
  - DM
  - HTN
  - Autoimmune diseases
  - Chronic systemic infections
  - Recovery from acute renal failure
  - Age > 60yrs
  - Family history of kidney disease
  - Exposure to drugs or procedures associated with an acute decline in kidney function
  - Kidney donors and transplant recipients

*(AJKD, 39, 2002, pS214)*
Relationship of Serum Creatinine to GFR

SERUM CREATININE (mg/dl) VS. GFR

Serum Creatinine

Iothalamate GFR
Physiologic Changes in Chronic Kidney Disease

- Increased single nephron GFR
- Afferent arteriolar vasodilation
- Intraglomerular hypertension
- Loss of glomerular permselectivity
- Inability to appropriately dilute or concentrate the urine in the face of volume challenge
Anatomic and Histologic Features Due to Glomerular Hypertension

- Glomerular hypertrophy
- Focal segmental glomerulosclerosis with hyalinosis
- Interstitial fibrosis
- Vascular sclerosis
- Epithelial foot process fusion
Pathogenesis of Secondary Glomerulosclerosis

Primary Insult

↓

Nephron Mass

Glomerular Sclerosis and Hyalinosis

Glomerular Volume and Glomerular Hypertension

Epithelial Cell Density and Foot Process Fusion

↓

Proteinuria
Hypertension in CKD
Recommendations for Anti-hypertensives in Patients with Chronic Kidney Disease

- Treatment is indicated at any stage of the disease
- Use drugs that lower glomerular capillary pressure (ACE inhibitors, ARB, verapamil and diltiazem)
- Goal is to keep the blood pressure < 130/80 mmHg (< 120 SBP in DM)
Effects of Various Anti-hypertensives on Glomerular Capillary Pressure

Afferent Arteriole

ACE-I

Vasoconstrict
Vasodilate

Dihydropyridines
Nifedipine
Felodipine
Amlodipine

Pressure

Vasodilate

ARB
Verapamil
Diltiazem

Efferent Arteriole
A Hierarchy of Agents

ACE-I
ARB
β-Blockers
Thiazide Diuretics
Vasodilators
α-Blockers
Central Agents
CCB’s

More Preferred
Less Preferred
Hyperparathyroid Related Bone Disease

- Renal Mass
- Acidosis
- Impaired Absorption
- 1-alpha-hydroxylase
- 25(OH)D$_3$
- 1,25(OH)$_2$D$_3$
- Osteitis Fibrosa Cystica
- PTH

Ca$^{2+}$, Pi

+ Acidosis
- Impaired Absorption
+ 1-alpha-hydroxylase
+ 25(OH)D$_3$
- 1,25(OH)$_2$D$_3$
Use of Phosphate binders

- Given with meals, timing essential
- Aluminum based medicines; (Basaljel, Amphogel)
- Calcium Based
  - Calcium Carbonate/Magnesium Carbonate (Magnebind)
  - Calcium Carbonate (Tums, Calcichew, Calcimix)
  - Calcium Acetate (Phoslo)
Use of Phosphate binders

- The use of calcium based binders is now falling out of favor because of the recognition of accelerated vascular calcification proposed to be associated with them (Disputed by the manufacturers of same)
  - Sevelamer hydrochloride (“Renagel”), cationic polymer, binds phosphate thru’ ion exchange, can promote/worsen metabolic acidosis
  - New product Sevelamer carbonate (“Renvela”) does not lead to acidosis
  - Lanthanum carbonate (“Fosrenol”), long term effects unknown
  - VERY EXPENSIVE (Sevelamer 800mg tab $1.93 each, dose varies 3-9 tabs a day, $173-521 each month, Fosrenol 1000mg tab $4.87 each, dose 3 tabs daily, $438 each month)
Several Vitamin D sterols are now available to replace naturally occurring 1,25 Vitamin - D$_3$, levels of which fall with declining renal mass.

- Rocaltrol (Calcitriol, oral)
- Doxercalciferol (Hectoral, D$_2$ prohormone, available in oral and parenteral forms)
- Paracalcitrol (Zemplar), oral and parenteral forms available
Complications of Long Term Calcium and Phosphorus imbalance

- Tertiary hyperparathyroidism
- Renal osteodystrophy
  - Demineralization
  - Bone pain
  - Fractures
- Systemic toxicity
  - Cutaneous - Calciphylaxis
  - Cardiovascular, accelerated vascular calcification
  - Nervous
**Calciphylaxis** Calciphylaxis of the leg in a patient with end-stage renal disease. Ischemic necrosis has led to both violaceous lesions and black, leathery eschar-like lesions.
**Calciphylaxis**  Low and high power view of characteristic arterial calcifications in the absence of vasculitic change from a patient with calciphylaxis.
Anemia of Chronic Kidney Disease

- Develops when the GFR decreases to < 30-35 ml/min
  - decreasing production of erythropoietin 2/2 reduced renal mass
  - Uremic inhibition of bone marrow
  - Decreased RBC life-span
  - PTH induced marrow fibrosis
  - Iron deficiency
  - Aluminum related bone disease

- Normochromic, normocytic
Nutrition

- Balancing the impact of decreased protein intake on the rate of progression of renal disease, against hypoalbuminemia and malnutrition

- Can we restrict protein intake sufficiently, without leading to malnutrition, especially important in patients with eGFR < 25 ml/min
## Hyperkalemia

### High Potassium foods

<table>
<thead>
<tr>
<th>Fruits</th>
<th>Vegetables</th>
<th>Other foods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apricot</td>
<td>Artichoke</td>
<td>Bran/bran products</td>
</tr>
<tr>
<td>Avocado</td>
<td>Asparagus</td>
<td>Coffee, Tea</td>
</tr>
<tr>
<td><strong>Banana</strong></td>
<td>Beans</td>
<td>Chocolate</td>
</tr>
<tr>
<td><strong>Cantaloupe, Honeydew</strong></td>
<td>Brussel sprouts</td>
<td>Coconut, Granola</td>
</tr>
<tr>
<td>Dates, Figs, dried fruits</td>
<td>Lentils, legumes</td>
<td>Molasses</td>
</tr>
<tr>
<td>Mango, Papaya</td>
<td>Limas, Peas, Okra</td>
<td>Milk, Ice cream</td>
</tr>
<tr>
<td><strong>Orange, Nectarine</strong></td>
<td>Parsnips, Rutabaga</td>
<td>Nuts/seeds</td>
</tr>
<tr>
<td>Peaches, Prunes</td>
<td>Potatoes</td>
<td>Snuff/chewing tobacco</td>
</tr>
<tr>
<td>Raisins, Persimmons</td>
<td>Tomatoes</td>
<td>Salt subs/Lite salt</td>
</tr>
<tr>
<td>Juices of these fruits</td>
<td>Winter squash</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Salt free veg. juice</td>
<td></td>
</tr>
</tbody>
</table>
# Hyperkalemia

## Low Potassium foods

<table>
<thead>
<tr>
<th>Fruits</th>
<th>Vegetables</th>
<th>Starches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apples/applesauce</td>
<td>Broccoli</td>
<td>Rice</td>
</tr>
<tr>
<td>Blackberries</td>
<td>Beans, green/wax</td>
<td>Noodles</td>
</tr>
<tr>
<td>Blueberries/Cranberries</td>
<td>Beets/carrots/corn</td>
<td>Bread/bread products</td>
</tr>
<tr>
<td>Cherries/grapes/gooseberries</td>
<td>Cabbage/cauliflower</td>
<td>Cereals</td>
</tr>
<tr>
<td>Fruit cocktail</td>
<td>Cucumber, lettuce</td>
<td>Cakes, cookies</td>
</tr>
<tr>
<td>Pears, canned/pineapple</td>
<td>Eggplant/onions</td>
<td>Pies (not chocolate or high K fruit)</td>
</tr>
<tr>
<td>Plums/raspberries/Strawberries</td>
<td>Summer squash</td>
<td></td>
</tr>
<tr>
<td>Mandarin oranges/Tangerines</td>
<td>Mushrooms, raw</td>
<td></td>
</tr>
<tr>
<td>Rhubarb, Watermelon</td>
<td>Parsley, radish, turnip</td>
<td></td>
</tr>
<tr>
<td>Juices of these fruits</td>
<td>Greens (collards, kale turnip, mustard)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peas, green</td>
<td></td>
</tr>
</tbody>
</table>
Cardiovascular Risk

- Individuals with CKD are at increased risk for CVD, they should be considered in the “highest risk group for evaluation and management” according to NKF recommendations.

- Remember, there are an estimated 7.5 million people in the US with stage 3 CKD and 363,000 at Stage 4 CKD but only 372,000 on dialysis with only a further 80,000 having received a kidney transplant.

- If we consider the patients at Stages 3 and 4, they have a higher risk of death than progressing to need for dialysis !!!!
Goals of Early Referral

- Patient education, soon Medicare reimbursement for CKD education
  - Choice of modality: HD vs PD vs Transplant
  - Planning of vascular access if HD is the chosen intervention and catheter placement if PD
  - Planning of timing of transplantation work-up
- Institution of interventions to slow progression of renal disease
In Summary:
Important Early Conservative Therapies

- ACE Inhibitor, Angiotensin II Receptor Antagonist, and Beta Blocker Therapy, to control HTN
- Adequate volume control with diuretics
- Early Treatment of hyperphosphatemia with Phosphate binders
- Early Treatment with Active Vitamin D
- Early Treatment with Erythropoietin/Darbepoetin (PROCRIT/ARANESP)
- Early Treatment with Iron Products
- Aggressive control of glucose levels in Diabetics