Chronic Kidney Disease -an Overview

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Objectives

- Review basic renal functions
- Define various stages of CKD
- Classify various stages of CKD
- Discuss evaluation & management of complications of CKD
- Describe renal replacement options

Glomerular Filtration

20-25 % of C.O i.e. 1-1.2L / min goes to kidneys

Filters only 10% =125 ml/min. GFR= Volume of filtrate formed /minute

Tubules reabsorb 99% so 1ml /min or 60ml /hr or 60 X 24 = 1440ml (1.5-2L) urine is excreted / day

GFR=125X60X24=180L / day. Plasma is 3L & it is filtered 180L/3L=60 times /day

Cross section of a Glomerulus

KDOQI CKD EVALUATION, CLASSIFICATION AND STRATIFICATION (2002)

- Defined 2 independent criteria for CKD:
  - Glomerular filtration rate (GFR) <60 ml/min per 1.73 m² for 3 months
  - Presence of kidney damage (structural, functional, or pathological abnormality, e.g., albuminuria) for ≥3 months
- Classified CKD by severity according to GFR
- Provided a common language for kidney disease that would:
  - Facilitate new research
  - Provide clinicians with a stage-specific clinical action plan
  - Inlcude a framework for developing a public health approach towards renalin
**KDIGO 2012 Update**

- CKD is defined as
  - Abnormalities of Kidney structure or function present for more than 3 months with implications for health

- Either of the following present > 3 months
  - Markers of kidney damage (one or more)
  - GFR < 60 ml/minute/1.73 m²

**CKD Criteria**

GFR < 60 ml/min/1.73 m²

- GFR is the best index of renal function in health & disease
- Normal GFR in an adult is 125 ml/min/1.73 m²
- GFR < 15 ml/min/1.73 m² is defined as kidney failure
- GFR can be detected by current estimating equations based on serum creatinine or cystatin-c (estimated GFR) but not by just serum creatinine or cystatin-c values alone
- Decreased GFR can be confirmed by measured GFR

**Creatinine alone cannot detect CKD Stage**

<table>
<thead>
<tr>
<th>Patient Profile</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
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<tbody>
<tr>
<td>SCr (mg/dl)</td>
<td>1.2</td>
<td>1.2</td>
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<tr>
<td>Gender</td>
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<tr>
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<td>60 years</td>
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<td>Caucasian</td>
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<tr>
<td>Weight</td>
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<td>100 lb</td>
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<td>Risk Factors</td>
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<td>Diabetic</td>
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<tr>
<td>GFR (ml/min/1.73 m²)</td>
<td>92²</td>
<td>48³</td>
<td>60³</td>
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<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No CKD</th>
<th>Stage 3 CKD</th>
<th>Stage 3 CKD</th>
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<tbody>
<tr>
<td>Identifying CKD Stages</td>
<td></td>
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</tbody>
</table>

**MDRD Equation**

\[
\text{Estimated GFR} (\text{ml/min/1.73m}²) = \frac{186 \times (\text{Scr}^{1.154} \times (\text{Age}^{0.203} \times \text{0.742 for women} \times 0.909 if African American})}{(1 + 0.209 \times \text{[(BMI-18.5)]})}
\]

For explanation, see text and references 17,18.

**Markers of Kidney Damage**

- Albuminuria: Albumin to Creatinine ratio ≥ 30 mg/G
- Urine sediment abnormalities
- Electrolyte & other abnormalities due to tubular disorders
- Pathological abnormalities detected by histology
- Structural abnormalities detected by imaging
- History of Kidney transplant

**GFR Categories for CKD Staging**

<table>
<thead>
<tr>
<th>GFR Category</th>
<th>GFR (ml/min/1.73 m²)</th>
<th>Terms</th>
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<tr>
<td>G1</td>
<td>≥ 90</td>
<td>Normal or high</td>
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<tr>
<td>G2</td>
<td>60-89</td>
<td>Mildly decreased*</td>
</tr>
<tr>
<td>G3a</td>
<td>45-59</td>
<td>Mildly to moderately decreased</td>
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<tr>
<td>G3b</td>
<td>30-44</td>
<td>Moderately to severely decreased</td>
</tr>
<tr>
<td>G4</td>
<td>15-29</td>
<td>Severely decreased</td>
</tr>
<tr>
<td>G5</td>
<td>&lt; 15</td>
<td>Kidney failure</td>
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</table>

Classification of CKD

- CKD is classified
  - Cause
  - GFR category (G1, G2, G3A & G3B, G4, G5)
  - Albuminuria category (A1, A2, A3)

- This is known as “CGA staging”

- This is revised from previous KDOQI CKD guidelines which was only based on GFR level

Need for 24 hr Cr clearance

- Extreme age and body size
- Severe malnutrition or obesity
- Disease of skeletal muscle
- Paraplegia or quadriplegia
- Vegetarian diet
- Rapidly changing kidney function
- Dosing significantly toxic drugs except by kidney

Prevalence of CKD in NHANES 1988-2012

Progression of CKD

Loss of nephrons \(\rightarrow\) compensatory hyper filtration \(\rightarrow\) glomerular HTN \(\rightarrow\) further loss of nephrons.

Complications of CKD

All cause adjusted mortality rate per 1000 pt. years (Age >66) for CKD: 2001 -2013

Adapted from USRDS 2010 data report

USRDS Data Source
**CV Disease in Patients With CKD 2013**

![Graph showing CV Disease in Patients With CKD 2013](USRDS Data Source: Medicare patients)

**Evaluation of Patient in CKD Clinic**
- Diagnose CKD and assess the stage
- Manage Proteinuria
- Control HTN, DM & Hyperlipidemia
- Manage Anemia & Mineral Bone Disorder (MBD)
- Manage Fluid, Acid-base & Electrolytes
- Nutrition & CKD education
- Appropriate medications & dosing
- Preparation for RRT

**CKD patients receiving care from a Nephrologist 12 months before the start of Dialysis, 2013**

![Map showing CKD patients receiving care](Data Source: ESRD Medical Evidence CMS 2728 form)

**Labs in CKD clinic**
- U/A & Random Urine Protein & Creatinine ratio
- CBC with diff
- Renal Panel
- 25(OH)Vit.D, intact PTH
- Iron (Total Iron, TIBC, Ferritin, Iron saturation)
- Uric Acid
- HbA1C, lipid profile

**Vitamin D Metabolism.**

![Diagram of Vitamin D Metabolism](Thacher TD, Clarke BL Mayo Clin Proc. 2011;86:50-60)

**PTH-Regulation in Normal Kidney.**

![Diagram of PTH-Regulation](Cunningham J et al. CJASN 2011;6:913-921)
Case: An Office Patient

What is your plan?

A. Reduce the dose of Lisinopril to half and add another BP agent if needed
B. Stop Metformin
C. Consider taking off Omeprazole
D. Advise not to take OTC NSAIDS & repeat renal function in 3 months.

Metformin in Kidney Disease

Metformin is not directly nephrotoxic but can cause serious lactic acidosis in the setting of kidney and liver disease
Not recommended if e-GFR < 30.
Do not start for patients with e-GFR of 30-45
If patient is already on with e-GFR < 45 consider the risk vs benefit
Hold Metformin 48 hours pre and post IV contrast for imaging if GFR < 60.

Case: An Office Patient

60 YO W over weight male with HTN, DM, GERD came to see you for routine f/u. His vitals & physical exam is normal. He is stable and on same dose of Lisinopril 40 mg q.d, Omeprazole 40 mg q.d and Metformin 500 mg BID for last 3 years but he takes OTC Ibuprofen 200 mg once or twice a month. His lab work showed that his creatinine was 1.1 (2 years ago), 1.3 last year and now 1.4. UA is negative except A:C is 200mg/mg

Recommended Ca, P & PTH level in CKD

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>GFR Range (ml/min/1.73 m^2)</th>
<th>Phosphorus (mg/dL)</th>
<th>Calcium (Corrected) (mg/dL)</th>
<th>Ca × P</th>
<th>Intact PTH (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>30-65</td>
<td>2.7-4.6</td>
<td>8.4-10.2</td>
<td>30-70</td>
<td></td>
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<tr>
<td>4</td>
<td>15-29</td>
<td>2.7-4.6</td>
<td>8.4-10.2</td>
<td>70-110</td>
<td></td>
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<tr>
<td>5</td>
<td>&lt;15, dialysis</td>
<td>3.5-5.5</td>
<td>8.4-8.5</td>
<td>&lt;50</td>
<td>150-500</td>
</tr>
</tbody>
</table>

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Association of CKD & PPI

- 10,482 patients without CKD from ARIC study
- PPI use ↑ from < 5% to >25% from 1996-99 to 2011
- ↑ rate of CKD in PPI compared to non users A risk ↑ 3.3% (number needed to harm =30)
- Finding was replicated in another cohort in Geisinger Health system & H2 blocker was not related to CKD

Xie et al : (JASN.27: 3153–3163, 2016)
- 5 year F/U of VA database and compared PPI (170,000) & H2 blockers (20,000) users
- Increased risk of both CKD and AKI with PPI

Case: CKD Patient With Pain

36 YO patient with Type-II DM, HTN & Obesity is in the ER with severe Right renal colic. Physical exam: BP 150/80, HR 110, R 20, AF rest of the exam is unremarkable except Rt. CVA tenderness.
Labs: WBC 14,000, Creatinine 3.8 (base 3.5), BUN 55, CO2 19, UA 1.015, Protein -300, WBC 20, RBC TNC. CT abdomen without contrast shows Rt UPJ 8mm stone.

CKD Patient with Pain

Which of the following is a safe approach for initial management of this patient?

A. IV hydration and IV Ketorolac
B. IV hydration and IV Morphine
C. IV hydration and IV Meperidine
D. IV hydration and IV Hydromorphone

Morphine in Low Kidney Function

Morphine is heptatically metabolized to morphine-3-glucoronide (55%), morphine-6-glucuronide (10%) and normorphine (4%) & excreted by kidney with 10% of the parent drug. These active metabolites accumulate with repetitive dosing in CKD & increase the risk for respiratory depression and adverse CNS effects

Meperidine in CKD

Normeperidine, a major metabolite of meperidine, has 50% of the potency of meperidine as an analgesic but 2-3 times more potent as a neuro excitatory agent(seizure) and mostly cleared by kidneys. Meperidine and normeperidine toxicities are not reversed by naloxone

Which one of the following best relates to the use of acetaminophen in CKD stage 4 - 5?

A. Acetaminophen use accelerates decline in GFR in 20% of patients.
B. Acetaminophen use leads to an increased risk for diuretic resistant hypertension.
C. Acetaminophen is the preferred first-line nonnarcotic analgesic.
D. Acetaminophen dosing requires adjustment for level of eGFR.
**Analgesics in CKD**

**Avoid**
- Morphine
- Codeine
- Meperidine
- NSAIDS

**Safe**
- Acetaminophen
- Steroids
- Hydromorphone
- Fentanyl
- Oxycodone
- Methadone

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**ESRD & Kidney Failure**

**Definition of End-stage Renal Disease:**
ESRD is an administrative term for the condition for which payment is made by the Medicare ESRD Program. ESRD indicates the chronic low level of GFR at which the signs & symptoms of kidney failure needs initiation of RRT. ESRD includes patients treated by chronic dialysis or transplantation, irrespective of the level of GFR.

**Definition of Kidney Failure:**
1) Level of GFR <15 mL/min/1.73 m², accompanied by signs and symptoms of uremia
Or
2) Need for initiation of RRT (dialysis or transplant) for complications of low GFR (irrespective of level), which would otherwise increase the risk of mortality and morbidity.

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**Cause of ESRD**

- Diabetes 45%
- Hypertension 28%
- Cystic Disease 3%
- Glomerulonephritis 7%
- Other 17%

**Preparation for Dialysis**

- Pts should have permanent access at the initiation of dialysis.
- In CKD-4/5 avoid I/V stick on the side of future access, avoid subclavian line & PICC line
- AVF should be placed 6 month & AVG 3-4 weeks before initiating HD
- PD cath should be placed at least 3-4 wks before starting PD

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**Initiation of Dialysis**

**Preparation:** CKD- 4 should receive education on kidney failure & treatment options i.e. kidney transplant, Dialysis modalities or conservative treatment

Estimation: of GFR(equation or 24 hr Cr & urea clear.) guides decision not the serum Creatinine

Timing of therapy: CKD-5 Nephrologists should evaluate the benefits, risks & disadvantages of beginning RRT.

- KDOQI –Clinical practice guideline 2006

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**Initiation of Dialysis**

Optimum timing of dialysis prevents complications. But Dialysis has significant effect on the quality of life. As GFR ↓ we must weigh risks & benefits

Decision is complex for older and fragile pts. Consider if the benefits outweigh the risks and psychosocial toll of treatment. Some social & psychological factors may lead to earlier start & in some to later start.

The initiation of dialysis remains a decision informed by clinical art, as well as by science and the constraints of regulation and reimbursement.

- KDOQI –Clinical practice guideline 2006
11/6/2016

Medicare ESRD Expenses 2003-2013

Data Source: USRDS ESRD Database, Reference Table K.2. Abbreviations: ESRD, end-stage renal disease.

Renal Patient in ER

83 yo white female with mental status change, gradual decline of health, nausea and poor intake. She has pruritus & insomnia. She maintains good urine output.

PMH: HTN, OA.

Home Meds: ASA 81 mg, Amlodipine 5mg and Multivitamins.

P/E Vitals: 105/70, 105, 18, AF. Rest of the exam. unremarkable except confusion.

Abnormal Labs: Hb 7.8, BUN 38, Cr 3.5 (was 2.6, 14 months ago), K 5.1, CO2 18, Ca 6.8, Alb 3, PO4 5.3. U/A unremarkable. Renal US: Rt-7.8 & Lt-7.9cm. No hydro.

Renal Patient in ER

How do you manage this patient?

A. Admit and hydrate with IVF mixed with NaHCO3 & consult Renal
B. Admit & consult Renal for initiation of dialysis
C. Admit and hydrate with NS & consult Renal
D. Admit & order CT of the head & consult Renal and Neurology

Uremic Syndrome

Symptoms & signs that result from toxic effects of ↑ levels of nitrogenous wastes in the blood.

Symptoms:
Nausea (Vomiting in morning), fatigue & weakness, pruritus, insomnia, altered mental status

Signs:
Sallow coloration of skin, NH3 or urinose breath, pericardial rub, wrist or foot drop, tremor, asterexis, myoclonus, seizure, prolonged bleeding time.

Relationship between uremic syndrome and eGFR

Uremic syndrome commonly develops when the eGFR falls below 10 mL/min/1.73 m². Certain individuals, especially those with co-morbidities, appear to be especially susceptible and may require earlier initiation of chronic dialysis (e.g., when the eGFR falls to 15 mL/min/1.73 m²)

Peritoneal Dialysis

Probability of survival for HD patients. USRDS 2010

Causes of Death for Hemodialysis Patients Ages 45 to 64 Years by Diabetes Status (2004–2006)

ESKD & Dialysis Has High Mortality
Life Expectancy of Dialysis and Transplant patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Dialysis Male</th>
<th>Dialysis Female</th>
<th>Transplant Male</th>
<th>Transplant Female</th>
<th>General U.S. population, 2012 Male</th>
<th>General U.S. population, 2012 Female</th>
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<tr>
<td>0-14</td>
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Waiting Transplant Candidates and Living & Deceased Donor Recipients

Number of Transplants

Data Source: Reference Tables E8, E8(2), and E8(3). Counts of transplants are for all dialysis patients (volume 2, ESRD).

Number of Kidney Transplants, 1996-2013

Data Source: Reference Tables E8, E8(2), and E8(3). Counts of transplants are for all dialysis patients (volume 2, ESRD).

Nephrogenic Systemic Fibrosis

A rare disease in AKI and severe CKD(4/5) due to exposure of gadolinium-based contrast agent(GBCA). Risk goes up with higher & repeated doses

The condition is painful & debilitating

NSF causes thickening of skin, joints and fibrosis of all organs of the body

Clinical Features of NSF or NFD

- History of MRI or MRA with GBCA
- Pain, burning/itching skin, red/dark areas of skin, edema firm texture of skin
- Raised yellow discoloration on sclera
- Joint stiffness, restricted limb motion
- Joint pain and muscle weakness
- Limitation of motion within weeks to months

Nephrogenic Systemic Fibrosis

UpToDate, Inc
How to Minimize Risk of NSF?

Consider risk vs. benefit of GBCA-MRI
Avoid GBCA in AKI- particularly in HRS, Peri-op liver Tx
Avoid in CKD-4/5 & ESRD patients
Risk in CKD-2/3 is unknown but thought to be extremely low
Removal of GBCA with HD after exposure

Thank You For Your Attention