CKD, Case based discussion

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May 14, 2017
CKD, Case presentation

- Agenda
- Present cases to discuss specific points in the management of cases with chronic kidney disease (CKD).
- Definition of CKD.
- Case 1, Acute vs chronic kidney disease.
CKD, Case presentation

- Case 2: Treatment of diabetes in a patient with CKD
- Case 3: Use of RAAS blockade in moderately advanced CKD
- Case 4: Diuretic resistance in CKD
- Case 5: What should I eat?
- Case 6: ESRD: Breaking bad news
- When to refer to the nephrologist
CKD, Definition

- 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 (CGA). KDIGO Guidelines, 2012
CKD definition

- Creatinine assay
- Creatinine measurement versus estimating equations.
- Which estimating equation is the best?
  (C7G, MDRD, CKD EPI)
- Proteinuria: which parameters?
CURRENT CHRONIC KIDNEY DISEASE (CKD) NOMENCLATURE USED BY KDIGO

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 (CGA).

<table>
<thead>
<tr>
<th>Persistent albuminuria categories Description and range</th>
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<tbody>
<tr>
<td>A1</td>
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<tr>
<td>Normal to mildly increased</td>
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<tr>
<td>&lt;30 mg/g &lt;3 mg/mmol</td>
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</tbody>
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GFR categories (ml/min/1.73 m²)

<table>
<thead>
<tr>
<th>Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012</th>
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<tbody>
<tr>
<td>G1 Normal or high ≥90</td>
</tr>
<tr>
<td>G3a Mildly to moderately decreased 45-59</td>
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<tr>
<td>G4 Severely decreased 15-29</td>
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</table>

Prognosis of CKD by GFR and albuminuria category

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.
Conceptual model of CKD

- Normal
  - Screening for CKD
  - Risk factors
- Increased risk
  - CKD risk factor reduction, screening for CKD
- Damage
  - Diagnosis and treatment, treat comorbid conditions, slow progression
- ↓ GFR
  - Estimate progression, treat complications, prepare for replacement
- Kidney failure
  - Replacement by dialysis and transplant
- EOL/death

Complications
Figure 2: Symptoms and signs of CKD

**Appearance**
- pallor secondary to anaemia of CKD

**Hypertension**
- common in CKD as either primary or secondary effect

**Shortness of breath**
- may be due to any of: fluid overload, anaemia cardiomyopathy, or occult ischaemic heart disease

**Kidneys**
- kidney shape on imaging may give clues to cause of CKD
- bilaterally small kidneys with thinned cortices suggest intrinsic disease (eg, glomerulonephritis)
- unilateral small kidney may indicate renal arterial disease
- clubbed calyces and cortical scars suggest reflux with chronic infection or ischaemia
- enlarged cystic kidneys suggest cystic kidney disease

**Itch and cramps**
- common in advanced CKD
- cause of itch is incompletely understood but may involve deregulation of immune response and opioid systems
- cramps are typically worse at night, and are likely to be due to neuronal irritation caused by biochemical abnormalities of CKD

**Cognitive changes**
- CKD increases risk of cognitive impairment by 65%
- cognition is affected early in CKD but different skills decline at different rates
- language and attention may be particularly affected

**Gastrointestinal symptoms**
- anorexia, vomiting, and taste disturbance may occur with advanced CKD. Their cause is incompletely understood, and may have a genetic component.
- uraemic odour may occur in advanced CKD, caused by breakdown of urea by saliva

**Change in urine output**
- polyuria where tubular concentrating ability is impaired
- oliguria
- nocturia as a consequence of impaired solute diuresis or oedema
- persistently frothy urine may indicate proteinuria

**Haematuria**
- glomerular bleeding results from immune injury to the glomerular capillary wall. Differentiated from lower tract bleeding by microscopy showing dysmorphic red cells and casts

**Proteinuria**
- tubular damage results in low grade proteinuria typically <2 g, of low molecular weight proteins (eg, beta-2 microglobulin)
- glomerular damage results in loss of selectivity to protein filtration often exacerbated by hyperfiltration. Losses >3.5 g are regarded as nephrotic range

**Peripheral oedema**
- due to renal sodium retention
- exacerbated by reduced oncotic gradient in nephrotic syndrome, because of hypoalbuminaemia
Prevalence of CKD

Figure 1: Burden of kidney disease globally

(A) Proportion of total mortality attributed to kidney disease. (B) Prevalence of chronic kidney disease. Chronic kidney disease was defined variably in different cohort studies; see appendix for specific details.
Mortality due to kidney disease

Antiretroviral therapies also have nephrotoxic effects including crystal deposition, tubular dysfunction, and interstitial nephritis. Hepatitis B and hepatitis C infections each affect 2–4% of the world’s population and are both associated with severe kidney lesions and CKD.

Genetics and epigenetics

There are many single and polygenic causes of CKD. Some, such as the diseases that result in congenital abnormalities of the kidney and urinary tract, are evident from birth or early childhood, and others typically present later in life, such as autosomal dominant.

Figure 1: Burden of kidney disease globally

(A) Proportion of total mortality attributed to kidney disease. (B) Prevalence of chronic kidney disease. Chronic kidney disease was defined variably in different cohort studies; see appendix for specific details.
AKI vs CKD

- WK, a 35 year old young nulliparous woman was found to have increased creatinine when she was seen by an internist for easy fatigability of a few weeks duration.

- Patient denied any history of body swelling, gross hematuria, hypertension or diabetes. No recent history of volume loss, fever, use of NSAIDs. There was no weight loss. The only medical conditions she was treated for were ‘typhoid / typhus’.

- Labs from the referring doctor: normal urinalysis, and creatinine 2mg/dl.
AKI vs CKD

- On initial evaluation: unremarkable physical findings except for BP of 140/95 mmHg. On further questioning she admitted that high BP had been detected some 3 years back but no treatment was given.

- She also reported that she had been investigated for primary infertility a few years back and was told to be in excellent health. Did not recall if RFT’s were done and did not have any past lab results at home.

- Additional tests: u/a negative, creatinine 1.8mg/dl and ultrasound: chronic kidney disease (parenchymal insult)
AKI vs CKD

❖ Questions are

❖ 1. Is this AKI or CKD?

❖ 2. What tests will help us to distinguish between AKI and CKD?( the best test is evolution through time)
AKI vs CKD

- This is very likely to be CKD but by strict definition one has to wait for 3 months before making the final pronouncement.
- Helpful hints: history (diabetes, HTN, family history), physical exam not helpful.
- Imaging: ultrasound, not very specific. Skeletal X-ray. Lab: anemia, hypocalcemia are perceived to be indicative of chronicity but are not so specific.
- If kidney size is ok and there are no contraindications a kidney biopsy.
- Why make the distinction: avoiding unnecessary aggressive therapy, prognosis, etc.
Type 2 diabetic with CKD

• T.K is a 56 year old gentleman with diabetes, hypertension and CKD( +? AKI) who was referred to me in mid March 2015 for ‘difficult to control BP’.

• Diabetes for 17 years, hypertension for 9 years. ‘Kidney dysfunction’ noted 6 months ago. Creatinine had risen from 1.4mg/dl to 2 and then 2.3 mg/dl.

• Meds: NPH( + regular) Insulin, Amlodipine 10mg/day, Candesartan 16 mg/day, Atenolol 50 mg/day, Simvastatin 20mg/day and Furosemide 40mg/day. Metformin recently discontinued because of ‘kidney dysfunction’.

• Physical exam was notable for obesity( BMI31.2Kg/M2) and hypertension with BP of 190/80 mmHg.

• Lab 2+ proteinurias, Hemoglobin 12.2gm/dl, serial FBS 190-246mg/dl and creatinine 2.0mg/dl. No recent HgbA1C.
Type 2 diabetic with CKD

- Patient was noted to be noncompliant to antihypertensive meds.
- Over a period of 8 weeks BP came down to mean of 150/80 mmHg without any additional meds.
- Creatinine remained elevated, 1.7 to 1.8mg/dl (eGFR~42ml/min/1.73m2BSA). FBS remained elevated.
- Metformin was reintroduced.
Type 2 diabetic with CKD

- Was the decision to discontinue Metformin by the internist appropriate in the face of poor glycemic control?
- Was the decision later, by the nephrologist, to reintroduce Metformin evidence based?
- What other agents can be used safely in a diabetic patient with CKD?
Hypoglycemia risk

- Metformin
- Alpha glucosidase inhibitor
- DPP-IV inhibitors
- Incretin mimetics
- TZD’s
- SGLT-2 inhibitors

- Short-acting SU derivates or SU derivates with inactive metabolites
- Meglitinides

- Drug-drug interactions
- Hepatic failure
- CKD stage 5
- Gastroparesis

- Insulin
- Long-acting SU derivates with active metabolites
Diabetes management in CKD

- Dose adaptations of insulin are not, however, based on kidney function but are guided by glycemic measurements.

- Glipizide undergoes near-complete hepatic biotransformation to inactive metabolites, and its half-life is unaffected by kidney function, making dose adjustments in patients with reduced GFR unnecessary.

- Gliclazide is metabolized in the liver and its renal clearance is low and so may be used in patients with renal failure.

- Glimepiride does not accumulate in patients with reduced GFR, but urinary excretion of its metabolites is reduced. Prolonged hypoglycemia has been reported in patients with reduced GFR.
Diabetes management in CKD

- Metformin is eliminated both rapidly and actively by the kidney. The mean renal clearance in subjects with normal renal function was reported as 510 ml±130 ml/min suggesting tubular secretion following glomerular filtration.

- In view of its renal clearance & its association with lactic acidosis the reluctance to use it in patients with impaired kidney function is understandable. Metformin induced lactic acidosis is rare and the fear is, hence, unwarranted.

- Guidelines are now more relaxed allowing Metformin use down to eGFR of 30ml/min/1.73 m2 BSA.

- Some advocate using Metformin, of course with great care even in patients with ‘severe’ renal failure.

- Metformin must be withdrawn in conditions of pending dehydration, when undergoing contrast media investigations, or in situations with an increased risk for AKI.
Diabetes management in CKD

- DPP4 inhibitors: Lindagliptin, Vildagliptin, Sitagliptin, and Saxagliptin more suited for patients with reduced GFR in that order.

- SGLT2 inhibitors: The rate of urinary glucose excretion is proportional to the GFR (as well as to the blood glucose concentration). So the effect of SGLT2 inhibitors is less in subjects with CKD. In CKD3 with eGFR 45–60 ml/min HgA1c reductions of only 0.3–0.4% are seen, <45 ml/min almost no reduction in HgA1c is seen. Hence there is no indication to use these drugs below eGFR of 45 ml/min.
Impact of diabetes therapies on different outcomes

<table>
<thead>
<tr>
<th>Class</th>
<th>Metformin</th>
<th>Koorpropamide</th>
<th>Acetohexamide</th>
<th>Tolazamide</th>
<th>Tolbutamide</th>
<th>Glibizide</th>
<th>Gliclazide</th>
<th>Glyburide</th>
<th>Glimepiride</th>
<th>Glicludone</th>
<th>Repaglinide</th>
<th>Nateglinide</th>
<th>Acarbose</th>
<th>Miglitol</th>
<th>Sitagliptin</th>
<th>Vildagliptin</th>
<th>Saxagliptin</th>
<th>Linagliptin</th>
<th>Alogliptin</th>
<th>Exenatide</th>
<th>Liraglutide</th>
<th>Lixisenatide</th>
<th>Pramlintide</th>
<th>Dapagliflozin</th>
<th>Canagliflozin</th>
<th>Empagliflozin</th>
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</thead>
<tbody>
<tr>
<td>dose adaptation in advanced CKD</td>
<td>Yes</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
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<td>Avoid</td>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Avoid</td>
<td>Red</td>
<td>Red</td>
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</tbody>
</table>

Note: The table indicates the impact of different diabetes therapies on various outcomes and suggests whether there is a need for dose adaptation in advanced CKD.
# Dose recommendations in CKD

Here is a table outlining dose recommendations for various medications in chronic kidney disease (CKD) stages 1 to 5D.

<table>
<thead>
<tr>
<th>Medication</th>
<th>CKD-1</th>
<th>CKD-2</th>
<th>CKD-3</th>
<th>CKD-4</th>
<th>CKD-5SND</th>
<th>CKD-5D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>No adjustments</td>
<td>150-850 mg/day*</td>
<td>500 mg/day**</td>
<td>Consider carefully/Awaiting further data</td>
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<td></td>
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<tr>
<td>Chlorpropamide</td>
<td>No adjustments</td>
<td>100-125 mg/day</td>
<td>To be avoided</td>
<td></td>
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<tr>
<td>Acetohexamide</td>
<td>To be avoided</td>
<td></td>
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<tr>
<td>Tolazamide</td>
<td>To be avoided</td>
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<tr>
<td>Tolbutamide</td>
<td>250mg, 1-3 times/day</td>
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<tr>
<td>Glipizide</td>
<td>No adjustments</td>
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<tr>
<td>Gliclazide</td>
<td>Start at low doses and dose titration every 1-4 weeks</td>
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<tr>
<td>Glyburide</td>
<td>To be avoided</td>
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<tr>
<td>Glimepiride</td>
<td>Reduce dosage to 1 mg/day</td>
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<tr>
<td>Gliquidone</td>
<td>No adjustments</td>
<td></td>
<td></td>
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<tr>
<td>Repaglinide</td>
<td>No adjustments</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Nateglinide</td>
<td>Limited experience available</td>
<td></td>
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<td></td>
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<tr>
<td>Acarbose</td>
<td>No adjustments</td>
<td></td>
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<tr>
<td>Migliitol</td>
<td>Limited experience available</td>
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<tr>
<td>Pioglitazone</td>
<td>No adjustments</td>
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<tr>
<td>Sitagliptin</td>
<td>No adjustments</td>
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<tr>
<td>Vildaglaptin</td>
<td>Reduce to 50 mg/day</td>
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<tr>
<td>Saxagliptin</td>
<td>No adjustments</td>
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<tr>
<td>Linagliptin</td>
<td>Reduce to 25 mg/day</td>
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<tr>
<td>Alogliptin</td>
<td>No adjustments</td>
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<tr>
<td>Exenatide</td>
<td>Reduce dose to 5 mg/once to twice daily</td>
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<tr>
<td>Liraglutide</td>
<td>Limited experience available</td>
<td></td>
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<tr>
<td>Linagliptide</td>
<td>Careful use if GFR 80-50 mL/min</td>
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<tr>
<td>Pramlintide</td>
<td>Limited experience available</td>
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<tr>
<td>Dapagliflozin</td>
<td>Limited experience available</td>
<td></td>
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<tr>
<td>Canagliflozin</td>
<td>Reduced efficacy</td>
<td></td>
<td></td>
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<tr>
<td>Empagliflozin</td>
<td>Careful monitoring</td>
<td></td>
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<td></td>
<td>To be avoided</td>
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</table>
Diabetes management in CKD

- Was the decision to discontinue Metformin by the internist appropriate in the face of poor glycemic control? **MAYBE**

- Was the decision later, by the nephrologist, to reintroduce Metformin evidence based? **YES**

- What other agents can be used safely in a diabetic patient with CKD?
RAAS Blockers in CKD

Case 3: DY, a 46 year old employee of BGI from Kombolcha has had proteinuric CKD(? Chronic GN) for the last 12 years. He has received steroids over the years with variable results. Has been on ACE-Is in the past but were discontinued when he was admitted for pneumonia with complications.

Usual BP 130-140/80-90 mmHg with most clinic measurements ~140/90 mmHg. He is on Amlodipine 10 mg/day.

Most recent lab results: urinalysis +2 albumin, 24 hour urine protein 780mg, creatinine 1.9mg/dl (eGFR 41ml/minute).
RAAS Blockers in CKD

- Enalapril 5mg/day was started. Repeat creatinine 2 weeks later was 2.3mg/dl.
- How should we proceed? Continue with Enalapril or hold it?
- What do the guidelines say about treatment of high BP in CKD?
- KDIGO 2012, 3.2: We suggest that non-diabetic adults with CKD ND and urine albumin excretion >300mg per 24 hours (or equivalent*) whose office BP is consistently >130mmHg systolic or >80mmHg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <130 mm Hg systolic and <80 mm Hg diastolic. (2C)
- 3.5 We recommend that an ARB or ACE-I be used in non-diabetic adults with CKD ND and urine albumin excretion >300 mg per 24 hours (or equivalent*) in whom treatment with BP-lowering drugs is indicated. (1B)
RAAS Blockers in CKD

❖ So, the decision to start an ACE-I, Enalapril, was according to recommendations in guidelines.

❖ Should we be worried about the rise in creatinine? 1.9 to 2.3mg/dl (21%)??????

❖ Is there a cutoff point beyond which it is inadvisable to use RAAS Blockers?

Study aimed to assess the efficacy and safety of Benazepril in patients without diabetes who had advanced renal insufficiency.

422 patients were enrolled in the RCT. After an eight-week run-in period, 104 patients with serum creatinine levels of 1.5 to 3.0 mg per deciliter (group 1) received 20 mg of benazepril per day, whereas 224 patients with serum creatinine levels of 3.1 to 5.0 mg per deciliter (group 2) were randomly assigned to receive 20 mg of benazepril per day (112 patients) or placebo (112 patients) and then followed for a mean of 3.4 years. All patients received conventional antihypertensive therapy. The primary outcome was the composite of a doubling of the serum creatinine level, end-stage renal disease, or death. Secondary end points included changes in the level of proteinuria and the rate of progression of renal disease.

**RESULTS:** Of 102 patients in group 1, 22 (22 percent) reached the primary end point, as compared with 44 of 108 patients given benazepril in group 2 (41 percent) and 65 of 107 patients given placebo in group 2 (60 percent). As compared with placebo, benazepril was associated with a 43 percent reduction in the risk of the primary end point in group 2 (P=0.005). This benefit did not appear to be attributable to blood-pressure control. Benazepril therapy was associated with a 52 percent reduction in the level of proteinuria and a reduction of 23 percent in the rate of decline in renal function. The overall incidence of major adverse events in the benazepril and placebo subgroups of group 2 was similar.

**CONCLUSIONS:** Benazepril conferred substantial renal benefits in patients without diabetes who had advanced renal insufficiency.
Benazepril in advanced CKD

NEJM, 2008, 354(2):131

**Figure 2.** Kaplan–Meier Estimates of the Percentage of Patients Not Reaching the Primary Composite End Point of a Doubling of the Serum Creatinine Level, End-Stage Renal Disease, or Death.

Group 1 had a serum creatinine level of 1.5 to 3.0 mg per deciliter, and group 2 had a serum creatinine level of 3.1 to 5.0 mg per deciliter at baseline.
Diuretic resistance in CKD

- H.K is a 20 year old young lady (a nursing student) who presented with body swelling of 10 months duration. She claimed to have gained a lot of weight recently.

- Physical exam was notable for BP of 150/100 mmHg, gross edema of the legs, and ascites.

- Urinalysis 4+ proteinuria on repeated tests, urine sediment unremarkable, creatinine 1.0 mg/dl. 24 hour urine protein 11.2 grams. Tested negative for ANA, HIV, Hep BsAg and Hepatitis C antibodies.
Diuretic resistance in CKD

- She was on Furosemide 40 mg bid and did not respond to escalation of the dose to 80 mg bid and then 120 mg bid.
- Enalapril 5 mg/day was given and soon escalated to 10mg twice daily.
- Edema started decreasing only after adding Hydrochlorothiazide 25 mg bid.
Diuretic resistance in CKD

- **COMMON CAUSES OF DIURETIC RESISTANCE**
  - Incorrect diagnosis (eg, venous or lymphatic edema)
  - Nonadherence to recommended sodium and/or fluid restriction
  - Drug not reaching the kidney (Nonadherence, Dose too low or too infrequent OR Poor absorption)
  - Reduced diuretic secretion (Tubular uptake of diuretic impaired by uremic toxins, Decreased kidney blood flow, Decreased functional kidney mass)
  - Insufficient kidney response to drug (Low glomerular filtration rate, Decreased effective intravascular volume despite elevated total ECF volume, Activation of the RAAS, Nephron adaptation, Use of NSAIDs)
Both pharmacokinetic and pharmacodynamic effects may contribute to diuretic resistance and may arise at any level of the drug absorption and delivery process (Table 2). For example, nephrotic syndrome may cause mucosal edema of the intestine, thereby limiting the absorption of oral diuretics. This may also play a role in patients with heart failure or liver cirrhosis, although in these conditions, decreased intestinal perfusion and reduced intestinal motility are more likely to limit absorption. Even in the absence of these factors, there is a remarkable difference in bioavailability between the different types of loop diuretics. For example, the bioavailability of furosemide (40%-60%) is much lower compared to bumetanide (80%) or torsemide (91%). When an adequate plasma concentration of the diuretic is achieved, it must be secreted adequately into the tubule lumen. This process is frequently compromised in edematous disorders. In nephrotic syndrome, hypoalbuminemia may reduce the delivery of diuretic to the kidney tubule because loop diuretics are highly protein bound. Experimental animal models of nephrotic syndrome suggested that urinary albumin could also bind furosemide after it had been secreted. However, a study of patients with nephrotic syndrome in which loop diuretics were combined with the displacing agent sulfinpyrazone was unable to confirm this mechanism. The effects of adding salt-poor human albumin to intravenous loop diuretics are modest and vary per study. Because it may also have an adverse effect, it is recommended to reserve this treatment for patients with refractory anasarca with respiratory compromise or tissue damage.

In CKD, the secretion of diuretics may be inhibited by retained organic anions, uric acid, or acidosis. Because our patient had both nephrotic syndrome and CKD, both mechanisms may have contributed to diuretic resistance. In heart failure or liver cirrhosis, the primary mechanism limiting diuretic secretion is usually vasoconstriction of kidney blood vessels due to reduced cardiac output or splanchnic vasodilation, respectively. In patients with heart failure, the dose-response curve for loop diuretics (fractional sodium excretion vs plasma furosemide concentration) exhibits both a rightward and a downward shift (secretory defect and decreased maximal response). In contrast, CKD causes only a rightward shift in the dose-response curve.

**Figure 2.** Schematic of a nephron shows sites of action of diuretics along the various segments. Abbreviations: CNT, connecting tubule; DCT, distal convoluted tubule; G, glomerulus.

**Table 2.** Pharmacokinetics of Loop Diuretics

<table>
<thead>
<tr>
<th></th>
<th>Healthy Kidney Disease</th>
<th>Liver Disease</th>
<th>Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Furosemide</em></td>
<td>50 (range, 10-100)</td>
<td>1.5-2</td>
<td>2.8</td>
</tr>
<tr>
<td>Bioavailability, %</td>
<td></td>
<td></td>
<td>2.5</td>
</tr>
<tr>
<td>Oral Dose Absorbed</td>
<td></td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>Elimination Half-Life, h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.6-2</td>
<td>2.3</td>
<td>1.3</td>
</tr>
<tr>
<td><em>Bumetanide</em></td>
<td>80-100</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Bioavailability, %</td>
<td></td>
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<tr>
<td>Oral Dose Absorbed</td>
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<tr>
<td>Elimination Half-Life, h</td>
<td></td>
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<tr>
<td></td>
<td>3-4</td>
<td>4-5</td>
<td>8</td>
</tr>
<tr>
<td><em>Torsemide</em></td>
<td>80-100</td>
<td>3-4</td>
<td>6</td>
</tr>
<tr>
<td>Bioavailability, %</td>
<td></td>
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<tr>
<td>Oral Dose Absorbed</td>
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<td>Elimination Half-Life, h</td>
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<tr>
<td></td>
<td>8-10</td>
<td>6</td>
<td>6-8</td>
</tr>
</tbody>
</table>

Data from Shankar and Brater. 7 Am J Kidney Dis. 2017;69(1):136-142 Hoorn and Ellison
First, the possibility of non-adherence or the use of nonsteroidal anti-inflammatory drugs should be ruled out (Box 1). In addition, dietary counseling may be indicated to help institute a low-sodium diet. If the patient remains resistant to diuretics, the potential pharmacokinetic causes of diuretic resistance should be addressed by increasing the dose of oral diuretic or by admitting patients for intravenous loop diuretic treatment (as in our case). The type of loop diuretic that is prescribed for oral administration may be relevant, as illustrated by an open-label randomized trial showing fewer readmissions for heart failure with torsemide than with furosemide.
Doctor, what should I eat?

- M.S is a 60-year-old woman with ADPKD diagnosed about 20 years ago. She has a strong family history, with 2 sisters and a daughter also diagnosed. Recently, she was diagnosed with Type 2 diabetes, not on any anti-diabetic medication yet. She is on Amlodipine 5 mg/day for hypertension.

- BP now <140/90 on most instances. Normal urinalysis, creatinine 1.6 mg/dl.

- Was advised to take a low salt, low protein diet and to take large volumes of water.

- The patient is really confused about what to eat and what not to as she has received conflicting recommendations from different professionals.
Doctor, what should I eat?

- The KDOQI guidelines recommend that dietary sodium intake should be restricted to ≤2.4 g daily (corresponding to ≤6 g daily salt intake, or 100 mmol daily urinary sodium excretion). Similarly, the KDIGO guidelines also recommend lowering sodium intake to <2 g daily, unless contraindicated (level of evidence 1C).

- Restriction of dietary sodium intake decreases both blood pressure and proteinuria, while augmenting the antiproteinuric effects of ACE inhibitors and nondihydropyridine calcium channel antagonists. Restriction of sodium intake is, therefore, the cornerstone of hypertension management in patients with CKD.
Doctor, what should I eat?

- Low protein diet including VLPD (supplemented by ketoanalogues & essential amino acids).
- Fruits and vegetables beneficial by reducing net endogenous acid production (NEAP).
- Plant-based diets and diets rich in fruits and vegetables exhibit beneficial metabolic effects in patients with non-diabetic CKD and seem to be safe, although these data were obtained from small studies.
Doctor, What should I eat?

- More than three servings per week of fruits and more than five servings per week of vegetables should be suggested for patients with diabetic nephropathy receiving RAAS inhibitors, to improve their metabolic profile and potentially slow the progression of CKD progression.

- Jain, N. & Reilly, R. F. Nat. Rev. Nephrol. 10, 712–724 (2014); Effects of dietary interventions on incidence and progression of CKD
Figure 2. Decline in kidney function between first and last assessment over 5.7 years (n = 2148). eGFR, estimated GFR.
CKD, What should I eat?

The kidneys play a key role in regulating fluid balance, which is guided by tight homeostatic control of plasma osmolality. Whereas increased plasma osmolality stimulates the release of arginine vasopressin, causing the kidney to retain water and decrease urine production, decreased plasma osmolality inhibits the excretion of vasopressin, causing the kidney to increase urine output (30,31). In addition to regulating fluid balance, the kidneys filter waste from the blood and require a minimum obligatory urine volume to remove the solute load (31,32). Kidneys may function more efficiently in the presence of an abundant supply of water (33). Higher fluid intake increases the clearance of sodium, urea, and osmoles (4,28,34), and high fluid intake is the most effective therapeutic measure to prevent kidney stones (6,7,35). If the kidneys are made to economize on water and produce more concentrated urine to maintain plasma osmolality, they may incur greater metabolic demand, as demonstrated in studies of rats (23,32,36,37).

Osmolar excretion and urine volume are affected by gender and race. Some argue that the greater food consumption among men compared with women, and their consequent higher daily osmolar loads and higher arginine vasopressin, might contribute to their increased susceptibility to kidney disease and salt-sensitive hypertension. Similarly, black individuals excrete similar...

### Adjusted risk for mild to moderate renal decline†

<table>
<thead>
<tr>
<th>24-hr urine volume</th>
<th>OR* [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 L</td>
<td>1.33 [1.01, 1.75]</td>
</tr>
<tr>
<td>1-1.9 L (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>2-2.9 L</td>
<td>0.84 [0.67, 1.05]</td>
</tr>
<tr>
<td>≥3 L</td>
<td>0.66 [0.46, 0.94]</td>
</tr>
</tbody>
</table>

### Adjusted risk for rapid renal decline ‡

<table>
<thead>
<tr>
<th>24-hr urine volume</th>
<th>OR* [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 L</td>
<td>1.32 [0.83, 2.09]</td>
</tr>
<tr>
<td>1-1.9 L (reference)</td>
<td>1.0 (reference)</td>
</tr>
<tr>
<td>2.2-9 L</td>
<td>1.01 [0.70, 1.44]</td>
</tr>
<tr>
<td>≥3 L</td>
<td>0.46 [0.23, 0.92]</td>
</tr>
</tbody>
</table>

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*Multinomial logistic regression adjusted for age, sex, baseline eGFR, dipstick protein ≥ 1g/L, medication use for hypertension (including diuretics), diabetes and cardiovascular disease.

†Mild to moderate renal decline: eGFR decline from baseline between 1% and 4.9%.

‡Rapid renal decline: eGFR decline from baseline ≥5%.
Doctor, What should I eat?

- Increased water intake is, therefore, a promising therapy in patients with ADPKD but its efficacy, in terms of reducing hard clinical outcomes, including progression to ESRD remains to be proven.

- Increasing fluid intake to achieve a daily urine volume $>3$ l is inexpensive and well tolerated in most patients with CKD, except those with stages 4–5, for whom safety and tolerability data are not available.

- Dietary intervention is inexpensive but may not be easy to implement in the long term (adherence) or without adverse effects (malnutrition, hyponatremia)
You have ESRD

- Case 5: A 58 year old lady who presented with nausea of a few weeks duration. Mother of 2, last delivery 28 years ago. Hypertension for 10 years that was self managed, no diabetes. No history to suggest any chronic disease.

- Hgb 8 gm/dl, creatinine on repeated measurements 5-6mg/dl. Ultrasound: smallish and echogenic kidneys.

- Diagnosis: ESRD.

- Should you break ‘the bad news’ to the patient or pass the buck to another specialist?

- If you decide to break the bad news how should you do it?
You have ESRD

- Breaking bad news is a complex skill as, in addition to the verbal component, it also requires the ability to recognise and respond to the patient's emotions, dealing with the stress that the bad news creates and yet still being able to involve the patient in any decisions and maintaining hope where there may be little.
SPIKES is a six-step protocol which has been shown to improve the confidence of clinicians who use it when breaking bad news to cancer patients:

- Setting up the interview.
- Assessing the patient's Perception.
- Obtaining the patient's invitation, as shunning information is a valid psychological coping mechanism.
- Giving Knowledge and information to the patient.
- Addressing the patient's emotions with empathetic response.
- Having a strategy and summarising.
Referral to nephrologist

- KDIGO CKD Guidelines 2012

- 5.1.1: We recommend referral to specialist kidney care services for people with CKD in the following circumstances (1B):
  - AKI or abrupt sustained fall in GFR;
  - GFR <30 ml/min/1.73 m² (GFR categories G4-G5)*;
  - A consistent finding of significant albuminuria (ACR >300 mg/g [>30 mg/mmol] or AER >300 mg/24 hours, approximately equivalent to PCR >500 mg/g [>50 mg/mmol] or PER >500 mg/24 hours);
  - Progression of CKD (change in CKD category with 25% decline in eGFR from baseline or decline in GFR>5 ml/min/year);
Referral to nephrologist

5.1.1  - urinary red cell casts, RBC >20 per high power field sustained and not readily explained;
    - CKD and hypertension refractory to treatment with 4 or more antihypertensive agents;
      - persistent abnormalities of serum potassium;
      - recurrent or extensive nephrolithiasis;
      - hereditary kidney disease.

5.1.2: We recommend timely referral for planning renal replacement therapy (RRT) in people with progressive CKD in whom the risk of kidney failure within 1 year is 10–20% or higher, as determined by validated risk prediction tools. (1B)
Referral decision making by GFR & albuminuria

<table>
<thead>
<tr>
<th>Persistent albuminuria categories</th>
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<tbody>
<tr>
<td>Description and range</td>
</tr>
<tr>
<td>A1</td>
</tr>
<tr>
<td>Normal to mildly increased</td>
</tr>
<tr>
<td>A2</td>
</tr>
<tr>
<td>Moderately increased</td>
</tr>
<tr>
<td>A3</td>
</tr>
<tr>
<td>Severely increased</td>
</tr>
</tbody>
</table>

- <30 mg/g
- <3 mg/mmol
- 30–300 mg/g
- 3–30 mg/mmol
- >300 mg/g
- >30 mg/mmol

<table>
<thead>
<tr>
<th>GFR categories (ml/min/1.73 m²)</th>
<th>Description and range</th>
<th>A1</th>
<th>A2</th>
<th>A3</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>Normal or high</td>
<td>≥90</td>
<td>Monitor</td>
<td>Refer*</td>
</tr>
<tr>
<td>G2</td>
<td>Mildly decreased</td>
<td>60–89</td>
<td>Monitor</td>
<td>Refer*</td>
</tr>
<tr>
<td>G3a</td>
<td>Mildly to moderately decreased</td>
<td>45–59</td>
<td>Monitor</td>
<td>Monitor</td>
</tr>
<tr>
<td>G3b</td>
<td>Moderately to severely decreased</td>
<td>30–44</td>
<td>Monitor</td>
<td>Monitor</td>
</tr>
<tr>
<td>G4</td>
<td>Severely decreased</td>
<td>15–29</td>
<td>Refer*</td>
<td>Refer*</td>
</tr>
<tr>
<td>G5</td>
<td>Kidney failure</td>
<td>&lt;15</td>
<td>Refer</td>
<td>Refer</td>
</tr>
</tbody>
</table>
THANK YOU