WHAT TO DO IN SOMEONE WITH DIABETIC KIDNEY DISEASE BEFORE REFERRING TO A NEPHROLOGIST

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CONFLICT OF INTEREST

• National Clinical Trial Principal Investigator Studies - (direct funding to University of Chicago) Bayer, Janssen, AbbVie
• Consultant: Merck, Vascular Dynamics, Reylpso
• Editor, Am J Nephrol; Nephrology, Editor-in-Chief, UpToDate; Nephrology and Hypertension Section Editor
• Assoc. Ed, Diabetes Care, Hypertension Research, Nephrology Dialysis and Transplant.

A large integrated health system including 1,120,295 patients with serum creatinine measured between 1996-2000 and median follow-up of 2.84 years.


LOWER EGFR IS ASSOCIATED WITH CARDIOVASCULAR EVENTS AND DEATH

Risk of coronary events in people with CKD compared with diabetes: A population-level cohort study.


NEW CONCEPTS ABOUT DIABETIC KIDNEY DISEASE

• Microalbuminuria (MAU) is NOT synonymous with presence of kidney disease
• Treatment with an ACE inhibitor or ARB is not indicated in normotensive people with diabetes even if MAU is present.
• If >300 mg/day albuminuria ACEi or ARB must be part of BP lowering plan and goal BP should be <130/80 mmHg

DeBoer I et al. Diabetes Care 2017; 40:1273–1284; Clinical Practice Guidelines 2018

Molitch M and Bakris GL Diabetes Care 2014
STUDIES WITH PRIMARY RENAL ENDPOINTS THAT SHOW DIFFERENCES IN OUTCOME:

Diabetes
• Captopril Trial, N Engl J Med, 1993
• Harradouche et al B Med, 1994
• Bakris et al Kidney Int, 1996
• Bakris et al Hypertension, 1997
• CREDEDE (pending)

* Signifies GFR measured using iothalamate or iohexol

Relationship Between Achieved BP and Decline in Kidney Function from Primary Renal Endpoint Trials

Composite Ranking for Relative Risks by glomerular filtration rate (GFR) and Albuminuria (Kidney Disease: Improving Global Outcomes (KDIGO) 2009

Composite ranking for relative risks by GFR and albuminuria (KDIGO 2009)

Referral to Nephrology by CKD Stage

Indications for referral to specialist kidney care services for people with CKD

Late nephrology referral before the onset of chronic kidney failure remains common.
U.S. data from 2011 reveal 42.1% of new dialysis starts had no prior nephrology care.*
A 42-year-old African American man with diabetic nephropathy and hypertension has a stable eGFR of 25 mL/min/1.73m². Observational Studies of Early versus Late Nephrology Referral have demonstrated which of the following?

A. Reduced 1-year Mortality  
B. Increase in Mean Hospital Days  
C. No change in serum albumin at the initiation of dialysis or kidney transplantation  
D. Decrease in hematocrit at the initiation of dialysis or kidney transplantation  
E. Delayed referral for kidney transplantation

Observational Studies of Early vs. Late Nephrology Consultation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early referral mean (SD)</th>
<th>Late referral mean (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall mortality %</td>
<td>11.0</td>
<td>22.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fever incidence %</td>
<td>17.4</td>
<td>25.1</td>
<td>1.037</td>
</tr>
<tr>
<td>Hospital length of stay (days)</td>
<td>10.0 (3.2)</td>
<td>20.1 (4.8)</td>
<td>0.007</td>
</tr>
<tr>
<td>Serum albumin at HFT start (g/dl)</td>
<td>3.4 (0.3)</td>
<td>3.4 (0.3)</td>
<td>1.007</td>
</tr>
<tr>
<td>Hematocrit at HFT start</td>
<td>32.0 (4.8)</td>
<td>29.7 (10.3)</td>
<td>0.853</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication errors</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity (nephrologic or other)</td>
<td></td>
</tr>
<tr>
<td>Improper dosing</td>
<td></td>
</tr>
<tr>
<td>Inadequate monitoring</td>
<td></td>
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<tr>
<td>Electrolytes</td>
<td></td>
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<tr>
<td>Hyperkalemia</td>
<td></td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td></td>
</tr>
<tr>
<td>Hypermagnesemia</td>
<td></td>
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<tr>
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<td></td>
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<td>Miscellaneous</td>
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</tr>
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<td>Multidrug-resistant infections</td>
<td></td>
</tr>
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<td>Vessel preservation/dialysis access</td>
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</tr>
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CKD Patient Safety Issues

- Medication errors
  - Toxicity (nephrologic or other)
  - Improper dosing
  - Inadequate monitoring
- Electrolytes
  - Hyperkalemia
  - Hypoglycemia
  - Hypermagnesemia
  - Hyperphosphatemia
- Miscellaneous
  - Multidrug-resistant infections
  - Vessel preservation/dialysis access
- Diagnostic tests
  - Iodinated contrast media: AKI
  - Gadolinium-based contrast: NSF
  - Sodium Phosphate bowel preparations: AKI, CKD
- CVD
  - Missed diagnosis
  - Improper management
  - Fluid management
  - Hypotension
  - AKI
  - CHF exacerbation

Impact of ACE Inhibition on Blood Pressure and GFR: Acute vs. Chronic Effects

**Notes:** *P<0.05 compared to baseline

Impact of ACE Inhibition on Blood Pressure and GFR: Acute vs. Chronic Effects

**Notes:** *P<0.05 compared to baseline

Change in GFR from Baseline in AASK
Main Clinical Composite Outcome: Declining GFR Event, ESRD, or Death

<table>
<thead>
<tr>
<th>Event</th>
<th>Metoprolol vs. Amlodipine: RR= 22%, p=0.042</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ramipril vs. Metoprolol: RR= 38%, p=0.004</td>
</tr>
<tr>
<td>Follow-up Month</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>RR = Risk Reduction, Adjusting for Baseline Covariates</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ramipril vs. Metoprolol: RR = 22%, p = 0.042</td>
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Decline in Kidney Function Over Time in Total Cohort.

Baseline demographics and clinical characteristics

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FACTORS THAT SHOULD PROMPT NEPHROLOGY CONSULT OTHER THAN GFR OR ALBUMINURIA LEVELS

- Persistence elevations in serum potassium i.e., levels >5.2 mEq/L on low potassium diet

SUMMARY OF CREATININE ELEVATIONS

- The current KDIGO guidelines state that a rise of up to 30% in serum creatinine is acceptable in the presence of RAS blocker therapy, if stable and not associated with hyperkalemia.
- Increases in serum creatinine of up to 30% should NOT result in stopping of therapy as it is beneficial in clinical trials
- Use of RAS blocking therapy to improve CKD outcomes is only demonstrated in eGFR values down to 30 ml/min. Below that no evidence of benefit.
CKD: chronic kidney disease.

K⁺ Quiz

Dairy Products

<table>
<thead>
<tr>
<th>Food</th>
<th>Per Serving</th>
<th>mEq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheddar cheese</td>
<td>1 oz.</td>
<td>1.1</td>
</tr>
<tr>
<td>Cottage cheese</td>
<td>1/2 cup</td>
<td>2.4</td>
</tr>
<tr>
<td>Ice cream, hard</td>
<td>1/2 cup</td>
<td>3.2</td>
</tr>
<tr>
<td>Milk, low fat</td>
<td>1 cup</td>
<td>10.6</td>
</tr>
<tr>
<td>Yoghurt, plain, low fat</td>
<td>1 cup</td>
<td>13.6</td>
</tr>
</tbody>
</table>

Fresh Fruits

<table>
<thead>
<tr>
<th>Fruit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blueberry</td>
</tr>
<tr>
<td>Watermelon</td>
</tr>
<tr>
<td>Cantaloupe</td>
</tr>
</tbody>
</table>
**AMETHYST-DN: Study Design**

The effect of treatment with Vetassa for up to 52 weeks was evaluated in an open-label study of 354 hyperkalemic patients with CKD and type 2 diabetes mellitus on RAAS inhibitor therapy.

**AMETHYST-DN (Phase 2 One-Year Study):\nMean (95% CI) Serum Potassium over Time**

<table>
<thead>
<tr>
<th>Time (Month)</th>
<th>Serum Potassium (mEq/L)</th>
<th>Baseline Group</th>
<th>Vetassa Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Baseline (0.3-0.5 mEq/L)</td>
<td>Vetassa (0.3-0.5 mEq/L)</td>
<td></td>
</tr>
<tr>
<td>52</td>
<td>Baseline (0.3-0.5 mEq/L)</td>
<td>Vetassa (0.3-0.5 mEq/L)</td>
<td></td>
</tr>
</tbody>
</table>

**Baseline Demographic Characteristics**

- **Screening**
  - Mean age: 53.8 years
  - Male: 52.2%
  - Female: 47.8%
  - ≥75 years (%): 8.9%

- **Randomization**
  - Mean age: 53.8 years
  - Male: 52.2%
  - Female: 47.8%
  - ≥75 years (%): 8.9%

- **Efficacy**
  - Mean age: 53.8 years
  - Male: 52.2%
  - Female: 47.8%
  - ≥75 years (%): 8.9%

- **Safety**
  - Mean age: 53.8 years
  - Male: 52.2%
  - Female: 47.8%
  - ≥75 years (%): 8.9%

**Indications for referral to specialist kidney care services for people with CKD**

- Acute kidney injury or abrupt sustained fall in GFR (GFR <30 mL/min/1.73 m²) (GFR categories G4-G5)
- Persistent albuminuria (ACR >300 mg/g)
- Progression of CKD
- Uinary red cell casts, RBC more than 20 per HPF sustained and not readily explained
- Hypertension refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease

**Foods That Are High in Potassium**

<table>
<thead>
<tr>
<th>Foods</th>
<th>Potassium (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avocado</td>
<td>850</td>
</tr>
<tr>
<td>Spinach</td>
<td>824</td>
</tr>
<tr>
<td>Raisins</td>
<td>800</td>
</tr>
<tr>
<td>Broccoli</td>
<td>150</td>
</tr>
<tr>
<td>Corn</td>
<td>130</td>
</tr>
</tbody>
</table>

**Other Foods**

- Blue cheese produce
- Chocolate
- Malt, all types (1 cup)
- Molasses (1 Tbsp)
- Nutritional supplements
- Nuts and seeds (1 cup)
- Peanut butter (1/4 cup)
- Salt substitutes (1/4 cup)
- Salt-free broth
Additional Reading?

- To learn more about the entire guideline statements:
  
  - [http://www.ajkd.org/article/S0272-6386(14)00491-0/fulltext](http://www.ajkd.org/article/S0272-6386(14)00491-0/fulltext)