Aging Kidney and Fluid Balance

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Disclosures

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• Conflicts of interest: None
Significance

- Aging kidney is not synonymous with chronic kidney disease (CKD)

- CKD is common in adults aged > 65

- Alterations in Kidney Fluid Balance and Urine Production are predominant factors in development of urinary incontinence in older adults
Topic Outline

• Aging Kidney
  – Fluid Balance
  – Urine Production

• CKD
  – Management
  – Complications

NIDDK website
Aging Kidney

• Creatinine Clearance (CrCl) can decline by 0.75ml/min/year in older adults without kidney disease or other comorbidities.

• Not all older adults experience this decline in CrCl.

• Independent of CrCl, kidney physiology changes with aging.
Water and Sodium

• **Excess Water loss**
  – Maximum urine osmolality declines with age
  – Kidney tubule response to Antidiuretic hormone (ADH) is muted
  – Risk of Dehydration

• **“Sodium Wasting”**
  – Independent of Volume status
  – Impaired response by Loops of Henle
  – Caused by a decline in Aldosterone levels
**Regulation of Urine Formation**

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Effect of Aging on Secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renin-Angiotensin-Aldosterone</td>
<td>Decreased</td>
</tr>
<tr>
<td>Atrial Natriuretic Hormone (ANH)</td>
<td>Increased</td>
</tr>
<tr>
<td>Antidiuretic Hormone (ADH)</td>
<td>Decreased*</td>
</tr>
</tbody>
</table>

*Decreased Nocturnal Secretion

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**ANH** → **Renin Angiotensin Aldosterone** → **Sodium and Water Excretion**

↓ **ADH** → **Urine Flow At Night**
Circadian Rhythm of ADH secretion typically yields lower urine production at night; however, this changes with older age.

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Old</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day</td>
<td>Night</td>
</tr>
<tr>
<td>Urine Volume (ml/h)</td>
<td>75</td>
<td>35</td>
</tr>
<tr>
<td>Urine Osmolality (mosm/kg)</td>
<td>700</td>
<td>830</td>
</tr>
<tr>
<td>Plasma AVP (pg/ml)</td>
<td>1.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Plasma ANH (pg/ml)</td>
<td>19</td>
<td>17</td>
</tr>
</tbody>
</table>

Day

Night

50

70

510

450

1.9

1.3

40

55
Nocturnal Polyuria

- 7pm-7am urine volume is more than half of total 24-hr volume.
- Predisposing factors:
  - Aging
  - CKD
  - Edema when recumbent
  - Osmotic diuresis
- Yields increased urinary frequency
Desmopressin Therapy

- AVP analog to reduce urine production, especially at night
  - Effective in small trials
- Evidence seen in Alzheimer's disease and other older adults with nocturnal polyuria
- Caution: Older adults with CHF, COPD
- May not be effective in those with CKD
CKD Management

- CKD = GFR <60ml/min/1.73m² and/or kidney damage

Routine Monitoring involves:
- Hypertension/Volume Overload
- Anemia
- Secondary Hyperparathyroidism
- Metabolic Acidosis

Only **volume status** management has the potential to affect urinary incontinence.
Diuretics

- Small study shows urgency incontinence in CKD patients is associated with high odds of diuretic avoidance
  - OR 5.9, (95% CI 1.5-22.8) (adjusted for age, sex, diuretic type)

Fig. 1 Self-reported avoidance of diuretics by urinary incontinence type and status
Vitamin D Deficiency

• Secondary hyperparathyroidism can develop in Stage 3 CKD (eGFR <60)
  – 25(OH)D and 1, 25(OH)D fall
  – Proteinuria worsens 25(OH)D deficiency

• 25(OH)D insufficiency (20 to <30 ng/ml) is associated with increased odds for urinary incontinence in community-dwelling older adults.

Vaughn CP Eur J Clin Nutr 2016 PMC5014687
Albuminuria and low eGFR individually increase risk of Cognitive Impairment.

Kurella-Tamura AJKD 2008 PMC2593146
Kurella-Tamura AJKD 2011 PMC3199339
## Knowledge Gaps

<table>
<thead>
<tr>
<th>Content Area</th>
<th>Knowledge Gap</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid Balance</td>
<td>Do some conditions accelerate these aging processes in the kidney? (e.g., acute kidney injury, peripheral vascular disease)</td>
</tr>
<tr>
<td>Urine Production</td>
<td>Feasibility of targeted therapy to reverse hormonal changes (e.g., DDAVP) in older adults with CKD</td>
</tr>
<tr>
<td>CKD Management</td>
<td>Dose-response of diuretics to UI</td>
</tr>
<tr>
<td>CKD Complications</td>
<td>Whether Vitamin D therapy influences UI</td>
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</table>
Research Opportunities

• Cohort studies in CKD do not typically assess for voiding problems
  – Chronic Renal Insufficiency Cohort (CRIC) Study has an emphasis on older adults (2013-2015)

Ideas for future research approaches:
• Use adherence to diuretics as an outcome in clinical trials
• Use Urinary Incontinence for prognostication of survival in older adults with advanced CKD
Summary

• The kidneys play significant role in the pathophysiology of urinary incontinence.

• The aging kidney and CKD complications should be considered in development of new therapies for urinary incontinence.