Relationship Between 24-hr Urinary Oxalate and Incident Chronic Kidney Disease Among Patients with and without Underlying Gastrointestinal Disease

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Disclosures

• Marja Puurunen, Caroline Kurtz, Richard Riese and Aoife Brennan are employees of Synlogic Inc.
• Gary Curhan is an employee of OM1, Section editor for UpToDate, and consultant for Allena Pharmaceuticals
• Michael Behling is an employee of OM1
• James McDougall is a consultant to Synlogic Inc.
Background

• Urinary oxalate is potentially toxic to the kidney

• Hyperoxaluria may result from:
  • intake of high oxalate foods
  • enhanced intestinal absorption
  • malabsorptive GI disorders such as: Crohn’s disease, short bowel syndrome, gastric bypass surgery, and chronic pancreatitis.

• Hyperoxaluria has been associated with adverse renal outcomes, including chronic kidney disease (CKD), but larger studies are needed.
Methods

• Longitudinal retrospective observational cohort study in US
• Patients who had completed at least one 24-hr urine collection between 1/2013 and 12/2020 were eligible for inclusion
• Data from a multi-source data cloud containing deterministically linked, de-identified, individual-level healthcare claims and electronic medical records (EMR) was used
• CKD and malabsorption were defined by the presence of relevant ICD 9/10 or CPT codes
• Patients with CKD at baseline were excluded from incident analysis
• Association between categories of urine oxalate (UOx) and incident CKD was modeled using logistic regression
Study Population

- Entry into the study was triggered by available data from at least one 24-hr urine collection
- Total number of adults identified: 764,860

- **Cohort 1**: 447,958 adults with at least 6 months of baseline and 6 months of follow-up data
  - Median follow-up: 37 months (IQR: 20, 56)
  - N=426,896 of Cohort 1 had no evidence of CKD (based on eGFR values and ICD codes) at baseline and were included in the incident analysis

- **Cohort 2**: 12,522 adults (2.8%) who had an underlying malabsorptive condition preceding index urine
# Results: Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1 (Overall)</th>
<th>Cohort 2 (Malabsorptive condition)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=447,958</td>
<td>N=12,522</td>
</tr>
<tr>
<td>Age, yr</td>
<td>55.4</td>
<td>54.3</td>
</tr>
<tr>
<td>Female</td>
<td>49.6%</td>
<td>58.0%</td>
</tr>
<tr>
<td>White race</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30.2</td>
<td>29.9</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>2.3</td>
<td>2.8</td>
</tr>
<tr>
<td>Number of kidney stone events in the baseline period, median (IQR)</td>
<td>2 (0-5)</td>
<td>3 (1-7)</td>
</tr>
<tr>
<td>eGFR, ml/min/1.73 m²</td>
<td>81.3</td>
<td>82.3</td>
</tr>
</tbody>
</table>
## Results: 24-Hr Urine Results

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1 (Overall) N=447,958</th>
<th>Cohort 2 (Malabsorptive condition) N=12,522</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxalate, mg/d</td>
<td>36.1</td>
<td>40.5</td>
</tr>
<tr>
<td>Calcium, mg/d</td>
<td>197</td>
<td>161</td>
</tr>
<tr>
<td>Citrate, mg/d</td>
<td>595</td>
<td>462</td>
</tr>
<tr>
<td>Creatinine, mg/d</td>
<td>1639</td>
<td>1497</td>
</tr>
<tr>
<td>Oxalate &gt;= 40mg/d</td>
<td>31.0%</td>
<td>39.5%</td>
</tr>
<tr>
<td>Oxalate &gt;=45 mg/d</td>
<td>21.0%</td>
<td>30.7%</td>
</tr>
</tbody>
</table>
Baseline Prevalence of CKD is Elevated with Increasing UOx and Underlying Malabsorptive Condition

CKD Prevalence by Baseline UOx Category*

*Analysis based on subpopulation of Cohort 1 with no CKD at baseline (N=426,896)
Risk for Incident CKD Increases with UOx Level and is Heightened with Underlying Malabsorption Condition
Conclusions

• This is the largest population-based study on the relationship of UOx and incident CKD to date
• Prevalence of CKD increased across categories of 24-hr urine oxalate
  • Prevalence of CKD was twice as high in patients with UOx >= 80 mg/d compared with < 20 mg/d
• Among patients without a history of CKD, higher urine oxalate is associated with higher risk of developing incident CKD
  • Risk is substantially higher among those with an underlying malabsorptive condition
• These data strongly support findings from smaller previous studies that higher urine oxalate may contribute to the risk of developing CKD
• Currently no pharmacological therapies targeted at UOx lowering are available. These data highlight an unmet medical need