Prediction of End-Stage Renal Disease in Children with Chronic Kidney Disease and Obstructive Uropathy

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Background

• CKD in children: rare, but significant health complications from progressive loss of function.

• Kidney Failure Risk Equation (KFRE) developed to aid clinical decisions in adults.¹

• KFRE accurately estimated short-term risk of end-stage renal disease (ESRD) in children with CKD of different etiologies.²

• Unknown if accurate in children with CKD due to obstructive uropathy (OU)

¹ Tangri et al. 2012. JAMA
² Winnicki et al. 2018. JAMA Pediatr
Objectives

1. Determine accuracy of the KFRE to predict the risk of ESRD in children with OU.

2. Evaluate usefulness of KFRE scores as a decision aid to identify patients likely to progress to ESRD in the OU cohort.
Methods: Study Design and Population

• Retrospective cohort study of children with OU in the CKiD study.

• CKiD: longitudinal, observational cohort of children with mild-to-moderate CKD, recruited from 48 North American Pediatric Nephrology Centers.³

• N=891 in the overall CKiD cohort (baseline visits in 2005-2013)

• Participants undergo yearly follow-up visits/examinations: renal function, CVD, growth, cognition and behavior.

Methods: Exposure and Outcome Measures

• Outcome: Progression to ESRD (long-term dialysis or transplant) within 5 years.

• Analysis: Calculated 5-year ESRD risk for each patient using baseline data for age, sex, eGFR, and urine albumin/Cr and the published KFRE parameters.\(^4\)

• Estimated model discrimination, calibration, sensitivity, specificity and predictive values.

• Previously, KFRE discriminated the 1-, and 5-year risks of ESRD in overall CKiD cohort, with C statistics of 0.90 and 0.81.\(^2\)

\(^2\) Winnicki et al. 2018. JAMA Pediatr
\(^4\) Tangri et al. 2016. JAMA
Results: Baseline Characteristics and Outcomes

- N=118 (Primary diagnosis: OU; eGFR<60)
- 84.8% male; median age: 10 years (IQR: 6-14)
- Median eGFR: 42 mL/min/1.73m² (IQR: 32-53)
- Median follow-up time: 4.5 years (IQR: 2.7-7.2)
- 23 patients (19.5%) developed ESRD within 5 years (1 patient within 2 years).
Results: Model Discrimination & Calibration for the 5-year risk of ESRD

- C statistic (95% CI):
  - 0.75 (0.68-0.82)
## Results: Sensitivity and Specificity of the KFRE Predicted Risk Threshold

<table>
<thead>
<tr>
<th>Predicted Risk Threshold</th>
<th>ESRD by 5 y (n=23)</th>
<th>No ESRD by 5 y (n=95)</th>
<th>Sensitivity/TPR, % (95% CI)</th>
<th>Specificity/TNR, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9%</td>
<td>At/above 23</td>
<td>43</td>
<td>100 (85.0-100)</td>
<td>54.7 (44.2-65.0)</td>
<td>34.9</td>
<td>100 (93.2-100)</td>
</tr>
<tr>
<td></td>
<td>Below 0</td>
<td>52</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>20%</td>
<td>At/above 19</td>
<td>32</td>
<td>82.6 (61.2-95.1)</td>
<td>66.3 (55.9-75.7)</td>
<td>37.2</td>
<td>94.0 (85.4-98.4)</td>
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<tr>
<td></td>
<td>Below 4</td>
<td>63</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>30%</td>
<td>At/above 19</td>
<td>24</td>
<td><strong>82.6 (61.2-95.1)</strong></td>
<td><strong>74.7 (64.8-83.1)</strong></td>
<td><strong>44.2</strong></td>
<td><strong>94.7 (86.9-98.5)</strong></td>
</tr>
<tr>
<td></td>
<td>Below 4</td>
<td>71</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40%</td>
<td>At/above 15</td>
<td>21</td>
<td>65.2 (42.7-83.6)</td>
<td>77.9 (68.2-85.8)</td>
<td>41.7</td>
<td>90.2 (81.7-95.7)</td>
</tr>
<tr>
<td></td>
<td>Below 8</td>
<td>74</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50%</td>
<td>At/above 9</td>
<td>18</td>
<td>39.1 (19.7-61.5)</td>
<td>81.1 (71.7-88.4)</td>
<td>33.3</td>
<td>84.6 (75.5-91.3)</td>
</tr>
<tr>
<td></td>
<td>Below 14</td>
<td>77</td>
<td></td>
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</tbody>
</table>

TPR, true positive rate; TNR, true negative rate; PPV, positive predictive value; NPV, negative predictive value
Conclusions

• KFRE provided moderate discrimination and accuracy for predicting the 5-year risk of ESRD among children with CKD due to OU.

• A predicted risk threshold of 30% provided 82.6% sensitivity and 74.7% specificity in identifying patients who progressed to ESRD.

• Research is ongoing to identify novel markers of progression that may further improve predictive accuracy of ESRD risk.