Predictive Value of 1-Hour Glucose Elevations during Oral Glucose Tolerance Testing for Cystic Fibrosis-Related Diabetes

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Introduction

• Outcomes for cystic fibrosis (CF) have improved in recent years, illustrated by an increased median predicted survival.
• With increased longevity, the prevalence of cystic fibrosis-related diabetes (CFRD) and diabetes-related complications are expected to increase.
• Current CFRD screening cut-offs are based on the oral glucose tolerance test (OGTT) 2-hour glucose (2hG) in people with CF (PwCF) and are the same for other types of diabetes.
• Elevations in 1-hour glucose (1hG) have been described to represent early glucose intolerance, but studies on the predictive value of 1hG are limited.

Methods

• Single CF center, retrospective study
• Data collected via chart review from patients seen between 2/2010 - 6/2019
• Inclusion Criteria:
  - absence of CFRD at first OGTT,
  - at least one OGTT between 2/2010 and 6/2019, and
  - a baseline OGTT in this time frame that included the 1hG
• Data collected:
  - Age, sex, CF genotype
  - Hemoglobin A1c and OGTT results
  - Body mass index (BMI) %tile
  - Pulmonary function testing (PFT)
• Statistical Analysis – 2 cohorts:
  - Group 1 cross-sectional cohort with all participants
    - Mixed effect models: whether baseline glucose predicts trajectories of BMI %tile and PFTs
  - Group 2 longitudinal cohort with participants with ≥2 OGTTs
    - Kaplan Meier: likelihood of progression to CFRD
    - Cox proportional hazard models: whether baseline glucose predicts time to development of CFRD

Results

Table 1. Demographics and baseline variables

<table>
<thead>
<tr>
<th></th>
<th>Cross-sectional Cohort</th>
<th>Longitudinal Cohort</th>
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<tbody>
<tr>
<td></td>
<td>n=243</td>
<td>n=177</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>120 (49%)</td>
<td>94 (53%)</td>
</tr>
<tr>
<td>Race, Caucasian, n (%)</td>
<td>194 (80%)</td>
<td>142 (80%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>12.7 ± 3.0</td>
<td>12.4 ± 2.6</td>
</tr>
<tr>
<td>Fasting OGTT (mg/dL)</td>
<td>89 ± 8</td>
<td>89 ± 8</td>
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<tr>
<td>1-hour glucose (mg/dL)</td>
<td>163 ± 45</td>
<td>162 ± 45</td>
</tr>
<tr>
<td>2-hour glucose (mg/dL)</td>
<td>117 ± 33</td>
<td>116 ± 33</td>
</tr>
<tr>
<td>BMI %tile</td>
<td>18.8 ± 3.0</td>
<td>19.0 ± 3.1</td>
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<tr>
<td>HbA1c (%)</td>
<td>5.5 ± 0.4</td>
<td>5.5 ± 0.4</td>
</tr>
<tr>
<td>Genotype, n (%)</td>
<td>213 (88%)</td>
<td>159 (90%)</td>
</tr>
<tr>
<td>2 Minimal function mutations</td>
<td>91.6 ± 16.9</td>
<td>90.7 ± 15.7</td>
</tr>
<tr>
<td>ppFEV1</td>
<td>99.1 ± 15.0</td>
<td>98.3 ± 13.7</td>
</tr>
<tr>
<td>ppFVC</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.1</td>
</tr>
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Note: Data presented as n (%) or mean±SD as indicated.

Abbreviations: BMI body mass index, CFTR cystic fibrosis transmembrane conductance regulator, F/U follow-up, OGTT oral glucose tolerance test, ppFEV1 percent predicted forced expiratory volume in the first second, ppFVC percent predicted forced vital capacity

Figure 1: Kaplan–Meier survival curves comparing baseline glucose and the likelihood of developing diabetes between (a) patients with elevated 1 hG (≥140 mg/dL) with normal glucose tolerance (2 hG < 140 mg/dL) to low 1 hG (<140 mg/dL) with normal glucose tolerance, (b) patients with elevated 1 hG (≥140 mg/dL) including those with impaired glucose tolerance (2 hG ≥140 mg/dL) to low 1 hG (<140 mg/dL) including those with impaired glucose tolerance, and (c) patients with elevated 2 hG (≥140 mg/dL) to low 2 hG (<140 mg/dL), regardless of 1 hG concentrations.

Discussion

• Findings highlight the unique strengths of 1hG and 2hG for clinical decision-making:
  - 1hG appears to be useful for predicting future CFRD risk and identifying individuals at high vs. low risk for developing diabetes, and
  - 2hG better predicted clinical declines.
• Despite the clinical value of the OGTT, annual CFRD screening remains a significant challenge for many patients and CF centers.
  - A less frequent screening approach supported by our findings, would be to use the 1 hG to identify individuals at low risk for CFRD who might benefit from reduced screening frequency (for example, every 3-5 years instead of annually).
• Our data were examined prior to the widespread adoption of the latest triple combination CFTR modulator:
  - Long-term impacts of modulator therapy on CFRD progression are unknown.
  - Prospective, multicenter studies in this new era are needed.

References

• Cystic Fibrosis Foundation, Cystic Fibrosis Foundation Patient Registry, Bethesda, Maryland, 2021.

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