Glycated Hemoglobin (HbA1c) and Cognitive Decline: The Atherosclerosis Risk in Communities (ARIC) Study

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Background

• Diabetes is associated with an increased risk of cognitive decline and development of dementia.
• It remains unclear HbA1c is a predictor of cognitive decline independent of diabetes diagnosis.

Objective

• To examine the association between HbA1c and 6-year change in cognitive middle-aged persons with and without diabetes.
• To examine the association of HbA1c with risk of hospitalization with an ICD-9 code for dementia during 14 years of follow-up

Methods

• Study Population: Prospective cohort study of 8,948 participants in the ARIC study.

HbA1c: Measured HbA1c in stored whole blood samples from ARIC Visit 2 (1990-92).

• Digit Symbol Substitution Test (DSST): Test of executive function and processing speed.
• Delayed Word Recall Test (DWRT): Test of verbal learning and recent memory.
• Word Fluency Test (WFT): Test of executive function and expressive language.

Incident Dementia Hospitalization: Continuous surveillance of all hospitalizations; ICD-9 codes: Alzheimer’s disease (331.0), vascular dementia (290.4) or dementia of other etiology (290.0-290.3, 290.9, 294.1, 294.2, 294.8, 294.9, 331.1, 331.2, 331.8, 331.9).

Statistical Analysis:
• Logistic regression models to estimate the adjusted odds ratios for the top quintile of annual cognitive decline for each test.
• Cox regression models to estimate the adjusted hazard ratios for dementia hospitalization.
• Model: sex, education, income, body mass index, smoking, drinking, systolic and diastolic blood pressures, hypertension medication use, and total cholesterol concentration.

Results

Table 1. Adjusted Odds Ratios (95% Confidence Intervals) for Top Quintile of Yearly Cognitive Decline

<table>
<thead>
<tr>
<th>Cognitive Test</th>
<th>Diagnosed Diabetes (Yes Versus No)</th>
<th>No Diabetes</th>
<th>HbA1c&lt;5.7</th>
<th>HbA1c 5.7-6.5</th>
<th>HbA1c 6.5-7.0</th>
<th>P-Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSST</td>
<td>1.42 (1.14, 1.75)</td>
<td>1.60 (1.29, 1.96)</td>
<td>1.00 (reference)</td>
<td>0.94 (0.81, 1.09)</td>
<td>0.94 (0.69, 1.26)</td>
<td>0.566</td>
</tr>
<tr>
<td>DWRT</td>
<td>1.13 (0.91, 1.41)</td>
<td>1.10 (0.89, 1.35)</td>
<td>1.00 (reference)</td>
<td>0.90 (0.77, 1.04)</td>
<td>1.30 (1.00, 1.71)</td>
<td>0.462</td>
</tr>
<tr>
<td>WFT</td>
<td>1.20 (0.96, 1.50)</td>
<td>0.99 (0.73, 1.33)</td>
<td>1.00 (reference)</td>
<td>0.95 (0.82, 1.10)</td>
<td>0.99 (0.73, 1.33)</td>
<td>0.589</td>
</tr>
</tbody>
</table>

Table 2. Adjusted Hazard Ratios (95% Confidence Intervals) for Incident Dementia Hospitalization

<table>
<thead>
<tr>
<th>Cognitive Test</th>
<th>Diagnosed Diabetes (Yes Versus No)</th>
<th>No Diabetes</th>
<th>HbA1c&lt;5.7</th>
<th>HbA1c 5.7-6.5</th>
<th>HbA1c 6.5-7.0</th>
<th>P-Value for Trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSST</td>
<td>2.80 (1.83, 4.30)</td>
<td>2.00 (1.30, 3.02)</td>
<td>1.00 (reference)</td>
<td>0.90 (0.58, 1.41)</td>
<td>1.34 (1.00, 1.81)</td>
<td>0.320</td>
</tr>
<tr>
<td>DWRT</td>
<td>2.00 (1.29, 3.16)</td>
<td>1.10 (0.75, 1.62)</td>
<td>1.00 (reference)</td>
<td>0.90 (0.77, 1.04)</td>
<td>1.08 (0.80, 1.46)</td>
<td>0.971</td>
</tr>
<tr>
<td>WFT</td>
<td>1.20 (0.96, 1.50)</td>
<td>1.00 (reference)</td>
<td>1.00 (reference)</td>
<td>0.95 (0.82, 1.10)</td>
<td>1.22 (0.90, 1.66)</td>
<td>0.011</td>
</tr>
</tbody>
</table>

During a median of 14 years of follow-up, there were 165 cases of incident hospitalization with dementia listed as an ICD-9 code, including 135 in the no diabetes group and 30 in the diagnosed diabetes group.

Discussion

• Hyperglycemia, as measured by HbA1c, did not add predictive power beyond diabetes status for 6-year cognitive decline in this middle-aged population.
• Higher values of HbA1c were independently associated with dementia hospitalization in persons without diabetes, but not in persons with diabetes.
• Additional work is needed to identify the non-glycemic factors by which diabetes may contribute to cognitive decline.