RESULTS

in diabetes risk (unadjusted)

- prevalent in U.S. populations, especially teenagers
- CH cutpoint: top tertile of fasting insulin (9.9 microIU/mL)
- inclusion criterion: all CARDIA participants; exclusion criteria:
  - retrospective analysis of the Coronary Artery Risk Development in Young Adults (CARDIA) study cohort
  - inclusion criterion: all CARDIA participants; exclusion criteria: hypertension, hyperglycemia, hypertriglyceridemia, low HDL-C, pregnancy, not-fasting or diabetes at baseline; does not meet criteria for prediabetes or metabolic syndrome; eludes screening for diabetes risk

Research Question

Does CH early in life increase the risk for future diabetes?

Specific Aim

- estimate the risk of incident diabetes in young adults with CH, relative to those with low fasting insulin.

Experimental Approach

- retrospective analysis of the Coronary Artery Risk Development in Young Adults (CARDIA) study cohort
- inclusion criterion: all CARDIA participants; exclusion criteria: hypertension, hyperglycemia, hypertriglyceridemia, low HDL-C, pregnancy, not-fasting or diabetes at baseline; 3,507 participants, ages 18-30 years at baseline, with 30-year mean follow-up.
- CH cutpoint: top tertile of fasting insulin (9.9 microIU/mL)
- analysis: Cox proportional hazard regression analysis.

Hypothosis:

Compensatory hyperinsulinemia is an independent risk factor for type 2 diabetes.

Target population:

- young adults with CH.

Flow chart:

Compensatory hyperinsulinemia (CH): the pancreatic response to early insulin resistance (IR)

- insulin secretion (pancreas)
- insulin sensitivity (muscle, liver, adipose)
- normal glucose & lipid tolerance

β-cell insulin secretion is intact and adaptive

- effect size: hazard ratio (HR), 95% confidence limits (CI)

- primary outcome: time to incident type 2 diabetes

Hypothosis:

Compensatory hyperinsulinemia is a Hidden Risk Factor for Type 2 Diabetes:

- CH evades conventional screening for diabetes risk
- for obese individuals, CH at baseline
- an independent risk factor for future diabetes among young adults in CARDIA
- for obese individuals, CH at baseline
- doubled the risk for future diabetes
- for non-obese individuals, CH at baseline
- tripled the risk for future diabetes
- CH evades conventional screening for diabetes risk – new strategies are needed to detect this early, hidden condition

Compensatory hyperinsulinemia (CH) & non-obese

- CH & non-obese: 3.3 (2.1, 5.0) <0.0001
- hypertension, >=400/90 or meds

Compensatory hyperinsulinemia (CH) & obese

- CH & obese: 2.6 (2.0, 3.5) <0.0001
- hypertension, >=400/90 or meds

Summary of Cox Models and CH Hazards Ratios

<table>
<thead>
<tr>
<th>Model</th>
<th>Model Number</th>
<th>Number</th>
<th>HR (95% CI)</th>
<th>p-value</th>
<th>Baseline Predictor Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>1</td>
<td>1.0 (0.8, 1.3)</td>
<td>0.6944 (NS)</td>
<td>sex, male</td>
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<tr>
<td>2</td>
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<td>1</td>
<td>1.8 (1.3, 2.5)</td>
<td>0.0022</td>
<td>model 4 with insulin/BMI interaction: CH &amp; obese</td>
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<td>2.6 (2.0, 3.5)</td>
<td>&lt;0.0001</td>
<td>insulin only</td>
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<td>model 4 with insulin/BMI interaction: CH &amp; non-obese</td>
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<tr>
<td>5</td>
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<td>1</td>
<td>1.9 (1.4, 2.7)</td>
<td>&lt;0.0001</td>
<td>model 4 with insulin/BMI interaction: CH &amp; non-obese</td>
</tr>
</tbody>
</table>

SUMMARY & CONCLUSIONS

Compensatory hyperinsulinemia:

- an independent risk factor for future diabetes among young adults in CARDIA
- for obese individuals, CH at baseline tripled the risk for future diabetes
- for non-obese individuals, CH at baseline doubled the risk for future diabetes
- CH evades conventional screening for diabetes risk – new strategies are needed to detect this early, hidden condition