RESEARCH LETTERS

One-Hour Glucose, Mortality, and Risk of Diabetes: A 44-Year Prospective Study in Men

Two-hour postload glucose measurement is currently recommended for early detection of diabetes. The less time-consuming 1-hour postload glucose measurement (1-hour glucose) has been reported to predict cardiovascular mortality and Medicare expenditure and to be associated with carotid intima-media thickness. Recently, 1-hour glucose has also aroused interest in the prediction of diabetes both in United States and Finnish cohorts and in the assessment of risk for chronic kidney disease. However, the status of 1-hour glucose as a risk-predicting tool is still far from established. Because blood 1-hour glucose was used to assess cardiovascular risk in early midlife in the Helsinki Businessmen Study during the 1960s, we had a unique opportunity to evaluate how this relatively simple test in conjunction with body mass index (BMI) would predict mortality and development of diabetes over 44 years of follow-up.

Methods. This study was approved by the Ethics Committee of the Helsinki University Hospital Department of Medicine. The characteristics of this cohort of mainly business executives, born between 1919 and 1934, have been described previously. Baseline examinations between 1964 and 1973 included measurements of blood 1-hour glucose level, BMI (calculated as weight in kilograms divided by height in meters squared; normal weight <25, overweight 25-29, and obese ≥30), and cardiovascular risk factors. Follow-up of the cohort for this report is through December 2007. Mortality and causes of deaths were ascertained from national registers and development of diabetes from mailed questionnaire surveys performed between the years 1985 and 2007 and from the national drug reimbursement register. Because results were similar when self-reported cases were added to the register-verified cases of diabetes, all cases were used in the analyses to increase statistical power. Statistical analyses were performed with NCSS 2004 (NCSS, Kaysville, Utah). Statistical significance was defined as a 2-sided P value lower than .05.

Results. A total of 2756 healthy men with 1-hour glucose and without diagnosed diabetes or cardiovascular disease at baseline were included in the analyses, giving a median follow-up time of 37 years (interquartile range [IQR], 29-40 years; maximum 44 years) and 91,066 person-years. Median age at baseline was 42 years (IQR, 39-46 years), median age of survivors by 2007 was 79 years (IQR, 76-83 years). Median blood 1-hour glucose and BMI were 108 mg/dL (to convert glucose to millimoles per liter, multiply by 0.0555) (IQR, 88.2-133 mg/dL), and 25.7 (IQR, 24.1-27.5), respectively. At baseline, BMI (P < .001), systolic and diastolic blood pressure (P < .001), and cholesterol level (P = .002) increased significantly with increasing 1-hour glucose quartiles, while there was no significant difference in ever smokers between quartiles (P = .30).

During follow-up, a total of 1287 men (46.7%) died, 509 men died of cardiovascular disease, and 357 men (13.0%) developed diabetes (68 cases were from questionnaire data only). There was a strong and graded relationship between 1-hour glucose quartiles and both total and cardiovascular mortality (P < .001) and development of diabetes (P < .001) during follow-up. One-hour glucose was not related to noncardiovascular mortality in this cohort. Both BMI and 1-hour glucose (both available for 2709 men [1263 deaths and 355 incident cases of diabetes]) in the same model independently predicted diabetes risk (P < .001). The impact of their combinations on total mortality and diabetes risk during follow-up are given in the Table. Especially, the combination of blood 1-hour glucose level higher than 144 mg/dL (plasma value, >161 mg/dL: the cut point used in the study by Manco et al) and BMI of 30 or higher was associated with a 10.1-fold increase of diabetes risk independently of cardiovascular risk factors (Table). Only 3.2% (86 of 2705) of the cohort belonged to this subgroup of the highest risk (BMI ≥30 and 1-hour glucose level >161 mg/dL); 84.2% of all incident diabetes (299 of 355) occurred among those who were either overweight (BMI ≥25, 48.2% of cases), had 1-hour glucose level higher than 161 mg/dL (26.8% of cases), or both (9.3% of cases) at baseline. Finally, 43.9% and 81.6% of patients in the lowest and highest baseline risk subgroup, respectively (P < .001), had either died or developed diabetes during follow-up.

Comment. Our exceptionally long follow-up demonstrates the very high diabetes and mortality risk associated with elevated 1-hour glucose level measured in early midlife. The risk was independent of traditional cardiovascular risk factors, cholesterol level, blood pressure, and smoking, and it was accentuated when combined with BMI. Our results suggest that diabetes risk could be assessed with a less time and resource-consuming method. Closer examination of high-risk individuals who survive to old age without diabetes and low-risk men who develop diabetes would give further information about pathways to diabetes. The obvious need is to compare 1-hour glucose with fasting and 2-hour postload glucose levels as well as hemoglobin A1c in a similar setting and in various populations. Because 1-hour glu-
Table. Multivariable-Adjusted Hazard Ratios (With 95% Confidence Intervals) of Total Mortality and Diabetes Over 44 Years

<table>
<thead>
<tr>
<th>Variable</th>
<th>1-h Glucose ≤161 mg/dL and BMI ≤25 (n=920; 367 Deaths and 56 Incident Cases of Diabetes)</th>
<th>1-h Glucose ≤161 mg/dL and BMI ≥25 (n=1313; 627 Deaths and 171 Incident Cases of Diabetes)</th>
<th>1-h Glucose &gt;161 mg/dL and BMI &lt;30 (n=390; 213 Deaths and 95 Incident Cases of Diabetes)</th>
<th>1-h Glucose &gt;161 mg/dL and BMI ≥30 (n=86; 56 Deaths and 33 Incident Cases of Diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Deaths</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model A</td>
<td>1 [Reference]</td>
<td>1.23 (1.08-1.40)</td>
<td>.002</td>
<td>1.33 (1.13-1.58)</td>
</tr>
<tr>
<td>Model B</td>
<td>1 [Reference]</td>
<td>1.23 (1.08-1.40)</td>
<td>.002</td>
<td>1.33 (1.12-1.57)</td>
</tr>
<tr>
<td>Model C</td>
<td>1 [Reference]</td>
<td>1.14 (1.00-1.29)</td>
<td>.06</td>
<td>1.19 (1.00-1.41)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model A</td>
<td>1 [Reference]</td>
<td>2.37 (1.75-3.20)</td>
<td>&lt;.001</td>
<td>5.06 (3.8-7.05)</td>
</tr>
<tr>
<td>Model B</td>
<td>1 [Reference]</td>
<td>2.36 (1.7-3.19)</td>
<td>&lt;.001</td>
<td>5.03 (3.61-7.02)</td>
</tr>
<tr>
<td>Model C</td>
<td>1 [Reference]</td>
<td>2.27 (1.67-3.08)</td>
<td>&lt;.001</td>
<td>4.71 (3.36-6.60)</td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
SI conversion factor: To convert glucose to millimoles per liter, multiply by 0.0555.

* Hazard ratio was calculated using the Cox proportional hazards model.
† Cut point used by Manco et al.
‡ Model A adjusted for age.
§ Model B adjusted for age and smoking.
∥ Model C adjusted for age, smoking, systolic blood pressure, and total cholesterol level.

Financial Disclosure: Although not directly related to this epidemiological study, some of the authors have had various cooperation with companies also marketing antidiabetic products. Dr T. E. Strandberg has had consultancies and/or received speaker honoraria for Abbott, AstraZeneca, Boehringer, Leiras, Merck, Novartis, and Pfizer; developed educational presentations for Leiras and Novartis; has stock (small amount) in Orion Pharma; and received meeting expenses from Bayer, Leiras, and Merck. Dr Strandberg has developed educational presentations for Leiras and Novartis and owns stock (small amount) in Orion Pharma. Dr Pitkalä has received speaker honoraria from Janssen, Leiras, Lundbeck, Novartis, and Pfizer. Dr Tilvis has received speaker honoraria from Novartis and Pfizer and meeting expenses from Boehringer.

Funding/Support: The study was supported by the Johnson Foundation (Dr T. E. Strandberg), the University Central Hospital of Oulu, and the University Central Hospital of Helsinki.

Role of the Sponsors: The funding sources had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

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Carpal tunnel syndrome (CTS) is a common cause of upper-extremity disability. Moderate to severe CTS often requires carpal tunnel release (CTR) surgery. A few studies have estimated the incidence of CTS, showing large differences between countries. Intercountry variations in incidence of surgery may reflect differences in CTS incidence and/or in use of surgical treatment. It is unknown whether such differences are age or sex related. In the present study, we estimate the incidence of physician-diagnosed CTS and surgery in the general population in southern Sweden and compare it with corresponding incidence in a US general population.

Methods. The Skåne Health Care Register (SHCR) is a comprehensive inpatient–outpatient register for Skåne County in southern Sweden (1.2 million inhabitants, one-eighth of Sweden’s population). The SHCR covers all public health care providers (primary to tertiary) but not private physicians, accounting for 30% of patient visits. We retrieved SHCR data on all county residents who received a physician-made CTS diagnosis during 6 years (2003-2008). Persons with a first-time CTS diagnosis during the last 3 years (2006-2008) were considered incident cases. To account for cases exclusively diagnosed and managed by private physicians, incidence estimates were adjusted by reducing the at-risk population by 20% (level chosen because approximately one-third of patients cared for by private physicians are treated for the same condition by SHCR-covered physicians).

Incidence of surgery was based on residents of Skåne County’s northeastern district (170,000 inhabitants) at the district’s only orthopedic department (Hassleholm-Kristianstad), where virtually all CTR procedures are performed. All surgeon-registered procedures are verified against an anesthesia register. We calculated the incidence of CTR surgery over 10 years (1999-2008) and of CTS in same population (2003-2008).

We calculated overall incidence assuming that adults are the at-risk population, with each person counted once. Differences between sexes were explored using Poisson regression.

We compared the incidence of physician-diagnosed CTS and CTR surgery in southern Sweden with the incidence of medically diagnosed CTS and CTR surgery in Olmsted County, Minnesota (2001-2005). The US estimates, based onwe new cases identified through a medical records linkage system, were age-adjusted to the 2000 US standard population. For this comparison, we standardized our incidence to the same standard.

Results. During 6 years (2003-2008), physician-diagnosed CTS was recorded at 80,309 consultations (primary diagnosis, 94%) in 14,264 individuals (primary diagnosis, 88%). The annual incidence (95% confidence interval [CI]) was 428 (416-440) in women and 182 (174-190) per 100,000 adults, peaking among women aged 45 to 54 years. The female to male incidence ratio (95% CI) was 2.4 (2.3-2.5) in those aged 45 to 54 years; 1.9 (1.8-2.0) in those aged 55 to 64 years, and 1.5 (1.4-1.7) in those 65 years or older.

In the northeastern district, 1,489 women and 554 men had CTR surgery (1999-2008); the annual incidence (95% CI) was 220 (209-231) in women and 85 (78-92) in men per 100,000 adults. The female to male incidence ratio (95% CI) was 2.6 (2.5-2.7) in those younger than 65 years and 1.4 (1.3-1.5) in those 65 years or older. Surgery was used in 33% in those younger than 35 years, 50% in those aged 35 to 74 years, and 60% in those 75 years or older. During the 10 years, 393 women (26%) had a subsequent contralateral CTR procedure (70% within 1 year) and 44 (3%), a repeated CTR procedure, and 143 men (26%) had a contralateral CTR procedure (75% within 1 year) and 16 (2.9%), a repeated CTR procedure. The US-standardized annual incidence of CTS per 100,000 persons (all ages) among women was 324 in Sweden compared with 542 in US and among men 125 compared with 303. The incidence was higher in the United States than in Sweden in all age groups (Figure, A). Among women, the US-standardized annual incidence of CTR surgery per 100,000 persons (all ages) was 166 in Sweden compared with 171 in the United States, and among men, 38 in Sweden compared with 96 in the United States. In those 20 years or older, the incidence (95% CI) was 227 (215-239) vs 243 (224-264) among Swedish vs US women and 83 (76-91) vs 128 (114-145) among Swedish vs US men. The incidence among women younger than 50 years was higher in Sweden, but among women 50 years or older, incidence was higher in the United States; among men younger than 50 years, incidence was similar, but in the United States, in those 50 years or older, incidence was double that in Sweden (Figure, B).

Comment. Physician-diagnosed CTS was common in the general population, and almost half were treated surgically, more frequently elderly patients. The incidence of CTS was substantially higher in the United States than in Sweden, and surgical incidence was substantially higher among US men. Factors behind these differences are unknown. The US-standardized incidence of CTS in the Netherlands was similarly lower than in the United States. The annual incidence of surgery in Sweden and the United States is considerably higher than in the United Kingdom in 2000 (59 per 100,000 women and 27 per 100,000 men). Intercountry variations may reflect true differences in CTS incidence and/or factors influencing the extent individuals with CTS seek health care and receive diagnosis. Research has shown higher prevalence of CTS with overweight or obesity and in certain occupational groups or activities; thus, differences in obesity and in occupational characteristics...