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PANCREAS, BILIARY TRACT, AND LIVER

High Dietary Glycemic Load Increases the Risk of Non–Gallstone-Related Acute Pancreatitis: A Prospective Cohort Study

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BACKGROUND & AIMS: **Obesity and type 2 diabetes—diseases linked to glucose intolerance and insulin resistance—have been positively associated with the risk of acute pancreatitis. However, it is unclear whether consumption of foods that increase postprandial glycemia and insulinemia have similar associations. We examined the association between dietary glycemic load and risk of non–gallstone-related acute pancreatitis.**

METHODS: **We performed a prospective study of 44,791 men and 36,309 women (aged 45–84 years), without a history of acute pancreatitis, from the Cohort of Swedish Men and the Swedish Mammography Cohort. Glycemic loads were calculated from food frequency questionnaire data collected in 1997, and participants were followed for the development of non–gallstone-related acute pancreatitis through 2010 via linkage to the Swedish National Patient Register. Hazard ratios (HRs) were estimated using Cox proportional hazard models.**

RESULTS: **During a total follow-up of 967,568 person-years, there were 364 cases of incident non–gallstone-related acute pancreatitis (236 in men and 128 in women). Incidence rates, standardized for age and sex, were 49 cases per 100,000 person-years in the highest quartile of glycemic load and 33 cases per 100,000 person-years in the lowest. The multivariate-adjusted HR of non–gallstone-related acute pancreatitis was 1.60 (95% confidence interval [CI], 1.17–2.18) for the highest compared with the lowest quartile. Every 50-unit increase in glycemic load per day (~3 servings of white bread) had an HR of 1.38 in men (95% CI, 1.11–1.72) and women (95% CI, 1.02–1.86).**

CONCLUSIONS: **Based on a large, prospective cohort study, diets with high glycemic load are associated with an increased risk of non–gallstone-related acute pancreatitis.**

Keywords: Pancreas; Inflammation; Carbohydrate; Sweden.

Observational studies have shown an increased risk of acute pancreatitis among people with type 2 diabetes[1–3] and obesity,[3–5] that is, diseases linked to glucose intolerance and insulin resistance. Hyperinsulinemia and hyperglycemia have been reported to have several physiological effects that might be of importance in the pathogenesis of acute pancreatitis, including increased levels of inflammation and oxidative stress as well as increased triglyceride levels (reviewed in Solanki et al[6]).

Dietary carbohydrates influence postprandial glycemia and insulinemia.[7] Glycemic responses vary, however, by physical form, chemical structure, particle size, and fiber content of carbohydrate-containing foods. To quantify the glycemic response to a fixed amount of carbohydrates in various foods, the glycemic index was introduced as a measure of carbohydrate quality. Glycemic load (ie, the product of a specific food's glycemic index and its carbohydrate content) is a related measure that combines quality and quantity of carbohydrates.[8] In humans, stepwise increases in dietary glycemic load have been shown to predict stepwise elevations in

Abbreviations used in this paper: BMI, body mass index; CI, confidence interval; COSM, Cohort of Swedish Men; FFQ, food frequency questionnaire; HR, hazard ratio; *ICD*, *International Classification of Diseases*; SMC, Swedish Mammography Cohort; SNPR, Swedish National Patient Register.

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postprandial glycemia and insulinemia.[9] It is, therefore, plausible that diets with high glycemic load may increase the risk of acute pancreatitis; but the association has never been studied.

To test this hypothesis, we examined the association between dietary glycemic load and risk of non–gallstone-related acute pancreatitis in 2 prospective cohorts of men and women. In addition, to differentiate between the qualitative and the quantitative aspect of glycemic load, we examined the associations with glycemic index and carbohydrate intake.

Methods

Participants

Data were derived from 2 population-based cohorts in central Sweden: the Swedish Mammography Cohort (SMC) and the Cohort of Swedish Men (COSM).[10] The SMC was established between 1987 and 1990 when 74% of all female residents in Uppsala and Västmanland counties (aged 40–75 years) completed a dietary questionnaire. In the fall of 1997, an expanded questionnaire on diet, lifestyle, and medical history was sent to all surviving participants; 70% responded. The COSM was started simultaneously in 1997 when 49% of all male residents in Västmanland and Örebro counties (aged 45–79 years) completed an identical questionnaire to the expanded SMC questionnaire. Eligible for the present study were 48,850 men and 39,227 women who completed the 1997 questionnaire.

Ethical approval was acquired from the Regional Ethical Board at Karolinska Institutet (Stockholm, Sweden), and return of the completed questionnaire was considered to imply informed consent.

Dietary Assessment

A 96-item food frequency questionnaire (FFQ) was used to assess diet in 1997. The consumption of each food during the past year was reported with 8 predefined answers: from "never" to "$\geq$3 times per day". For foods commonly consumed (eg, milk and bread), there were open-ended questions. The total score of glycemic load was calculated by multiplying the carbohydrate content of each food (in age- and sex-specific portion sizes [grams per serving]) by its glycemic index, multiplying that product by the frequency of consumption (servings per day), and then summing the values from all foods. Values for the carbohydrate content were obtained from the Swedish Food Administration Database,[11] and values for the glycemic index were acquired from international tables using white bread as the reference food.[12] Each unit of glycemic load represents the equivalent of 1 g of carbohydrate from white bread. The overall score of glycemic index was calculated by dividing the total score of glycemic load by the total carbohydrate intake.

The FFQ-based estimates of total glycemic load, overall glycemic index, and total carbohydrate intake have been validated by comparing them with two 1-week diet records; the correlation was 0.77 for glycemic load, 0.62 for glycemic index, and 0.76 for carbohydrates.[13]

The estimates of dietary covariates were calculated from the FFQ. Nutrients and glycemic load were energy-adjusted using the residual method.[14]

Assessment of Nondietary Covariates

Information on education, smoking, body mass index (BMI), waist circumference, and physical activity was obtained from the questionnaire. History of diabetes, hyperlipidemia, and autoimmune disease (ie, celiac disease and inflammatory bowel disease) was acquired via linkage to the Swedish National Diabetes Register and the Swedish National Patient Register (SNPR). Additional information on diabetes and hyperlipidemia was obtained from the questionnaire.

Case Ascertainment

Via the participants' personal identity numbers, we identified all diagnoses of acute pancreatitis (code of 577.0 in the *International Classification of Diseases, Ninth Revision* [*ICD*-9] and K85 in *ICD-10*) via linkage to the SNPR. An episode of non–gallstone-related acute pancreatitis that occurred between January 1, 1998, and December 31, 2010, was classified as a case. This was defined by (1) an *ICD-10* code of K85.0, K85.2–3, or K85.8–9 and (2) absence of cholelithiasis (*ICD-10* code, K80) and gallbladder surgery (*NOMESCO Classification of Surgical Procedures* code, JKA20-21, JKE00, JKE02, JKE12, JKE18, or JKB30) within 90 days after the index episode. Information on other exocrine pancreatic diseases (code of 577.1-2 in *ICD-9* and K86-87 in *ICD-10*), cancer, and death was obtained from the SNPR, the Swedish National Cancer Registry, and the Swedish National Cause of Death Register, respectively.

The SNPR covers nearly all hospital discharges in Sweden[15] and was recently validated for a recorded diagnosis of acute pancreatitis.[16] In total, 530 medical records were reviewed, of which 98% (83% with strict criteria) were correct.

Our cohort was representative for Sweden regarding incidence of acute pancreatitis in 1998–2003. For example, the incidence rate per 100,000 men (aged 60–69 years) was 69 cases in our cohort and 66 cases in Sweden.[17] Corresponding values among women were 49 and 52 cases, respectively.

Statistical Analysis

Of eligible participants (48,850 men and 39,227 women) at baseline (January 1, 1998), we excluded 540 with an incorrect personal identity number, 5135 with a history of cancer (except for nonmelanoma skin cancer)