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Dietary glycemic index, dietary glycemic load, and incidence of heart failure events: a prospective study of middle-aged and elderly women

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Abstract

Objective—Dietary glycemic index (GI) and glycemic load (GL), measures of the propensity of dietary carbohydrate to increase blood glucose, have been associated with risk of coronary heart disease, but their association with incidence of heart failure (HF) is unknown. We therefore assessed whether dietary GI and GL were associated with rates of HF events.

Methods—We conducted a prospective, observational study of 36,019 women 48–83 years old without baseline HF, diabetes, or myocardial infarction who were participants in the Swedish Mammography Cohort, a prospective cohort study. Diet was measured using food-frequency questionnaires. Women were followed from January 1, 1998 through December 31, 2006 for HF hospitalization or death through the Swedish inpatient and cause-of-death registers. Cox proportional hazards models adjusted for age and other risk factors were used to estimate incidence rate ratios (RR) and 95% confidence intervals (CI).

Results—Over 9 years of follow-up, 639 of 36,019 women died of HF ($n = 54$) or were hospitalized for HF for the first time ($n = 585$). We did not find statistically significant associations between dietary GI and HF events (RR comparing highest to lowest quartile = 1.12, 95% CI 0.87–1.45, p for trend = 0.31) or between dietary GL and HF events (RR comparing highest to lowest quartile = 1.30, 95% CI 0.87–1.93, p for trend = 0.16). Results were not significantly different in normal weight and overweight women.

Conclusions—In this population, dietary GI did not appear to be associated with incident HF events. There was a suggestion of an association between dietary GL and HF which did not reach statistical significance.

Keywords

glycemic index; glycemic load; heart failure

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INTRODUCTION

Heart failure (HF), which results from insufficiency in the heart's ability to fill with or eject blood, causes dyspnea, fatigue, and fluid retention [1]. It is the most common cause of hospitalization among people 65 and older in the United States [2]; lifetime risk of HF is approximately 20% [3]. In Europe, an estimated 0.4%-2% of the population have prevalent HF [4]. HF is a major cause of hospitalization in Sweden with 171 first hospitalizations for HF for every 100,000 women in 2000 [5]. Although treatment of HF has improved, mortality among HF patients is high [6].

Dietary glycemic index (GI) and glycemic load (GL), measures of the degree to which carbohydrate from food increases blood glucose [7-9], have been associated coronary heart disease [10-14], stroke [10], and diabetes [10,15,16] in observational studies. However, there is little evidence for an association with coronary heart disease among men [17,18]. In trials, low GI or GL diets had beneficial effects on total cholesterol [19-21], LDL cholesterol [19, 21,22], HDL cholesterol [23-25], triacylglycerol concentration [26,27], plasminogen activator inhibitor 1 [27], insulin resistance [19,26], and inflammation [26,28,29], supporting an association between the glycemic burden of diet and cardiovascular disease. Although the association of dietary GI and GL with HF is not known, some investigators have suggested that a low-carbohydrate, low-GI diet may help prevent HF [30].

We therefore examined the associations of dietary GI and GL with incident HF hospitalization or mortality in a population of middle-aged and elderly Swedish women. Because previous studies have observed stronger association of dietary GI and GL with cardiovascular disease in overweight participants [12,13,31,32], we tested whether the associations varied by body mass index. In a previous study in a Swedish population, we found that dietary GL was associated increased mortality in men with established cardiovascular disease only in the setting of relatively low fiber consumption [33]. We therefore examined whether the associations of dietary GI and GL with HF varied by fiber intake.

POPULATION AND METHODS

Study Population

This study included 36,019 women who participated in the Swedish Mammography Cohort. The recruitment process, characteristics, and study methods of this cohort have been previously described [34]. The Swedish Mammography Cohort includes women born between 1914 and 1948 living in Västmanland and Uppsala counties in central Sweden. The women completed questionnaires with items on demographic, behavioral, and anthropometric factors and consumption of foods and beverages in late 1997. Participants who did not provide or provided incorrect national identification numbers, who reported implausible energy intakes (>3 standard deviations from the natural logarithm-transformed mean), who had a previous diagnosis of cancer (other than nonmelanoma skin cancer) or who left more than half of the food and beverage items blank were excluded ($n = 1,390$). Additionally for these analyses, participants who at baseline had a history of HF, myocardial infarction (MI), or diabetes were excluded ($n = 1,818$). Participants with baseline MI or diabetes were excluded because people who develop these diseases receive dietary counseling and may change both their diet and their reporting of diet. History of HF and MI were determined through linkage to the inpatient register; history of diabetes was assessed using self-report and linkage to the inpatient register. The study was approved by the Regional Ethical Review Board at Karolinska Institute, Stockholm, Sweden. Completion and return of the self-administered questionnaire was taken to imply consent.

Diet Assessment

Self-administered food-frequency items in the questionnaires asked participants to report usual frequency of consumption of 96 foods and beverages over the previous year. For foods such as milk, coffee, cheese, and bread that are commonly eaten in Sweden, participants reported their consumption in servings per day or per week. For other foods there were 8 predefined responses ranging from never to ≥ 3 times/day. Portion sizes for most foods were not specified. In validation studies using weighed diet records, habitual portion sizes were found to vary by age. The total consumption of foods and beverages was calculated by multiplying the frequency of consumption by age-specific portion sizes. Nutrient values were calculated using food composition data from the Swedish National Food Administration [35].

A database of GI and GL values with white bread as the reference food was created based primarily on the international GI and GL tables [36]. Food items and mixed meals with no reported GI value were assigned the value for a comparable food. We calculated average dietary

GI using the formula dietary $GI = \frac{\sum_{foods} F \times C \times GI}{\sum_{foods} F \times C}$ where F represents the frequency of consumption, C represents the available carbohydrate content of an age-specific portion of food, and GI represents the glycemic index of a specific food [7]. Dietary GL was calculated as the product of the dietary GI and carbohydrate intake divided by 100 [7]. Using the residuals method [37], nutrient values and dietary GL were adjusted to 1,700 kcal/d, the mean energy intake from the validation study diet records. The correlation between the food-frequency questionnaire used in this study and two one-week weighed diet records was 0.62 for dietary GI and 0.77 for dietary GL in a population of men from central Sweden [38].

HF Follow-up

Participants were followed through record linkage to the Swedish inpatient and cause-of-death registers. The inpatient register captures more than 99% of inpatient care [39]. Hospitalization for or death from HF was identified by codes 428 (International Classification of Disease-9), I50, or I11.0 (International Classification of Disease-10). Ingelsson and colleagues found that 95% of people with these codes as primary diagnosis in the inpatient register had HF on medical record review using European Society of Cardiology criteria [40]. We included only hospitalizations or deaths with HF listed as the primary diagnosis and only the first HF event recorded in the registers for each individual. Follow-up time accrued from January 1, 1998 until the date of hospitalization or death from HF, the date of death from other causes, or December 31, 2006, whichever was earliest. Incident MI during follow-up was also assessed through the inpatient register.

Statistical Analysis

Because some of the participants were missing data on physical activity (22.1%) or height and weight needed to calculate body mass index (1.6%) we used Markov chain Monte Carlo multiple imputation to simulate 5 complete datasets [41]. All statistical analyses described were performed in each of the datasets separately. The results were averaged, and confidence intervals and p -values were calculated accounting for the uncertainty in the imputed estimates [41].

We calculated means and proportions of baseline covariates. To estimate incidence rate ratios for the association of quartiles of dietary GI and GL with incidence of HF events, we used Cox proportional hazards models which accounted for the effect of age by allowing the baseline rate to vary and adjusted for education (less than high school, high school, university), body mass index (linear term), physical activity (linear term), cigarette smoking (current, past, never), living alone (yes, no), postmenopausal hormone use (yes, no), total energy intake (linear term), alcohol intake (linear term), fiber intake (linear term), sodium intake (linear term),

saturated fat (linear term), polyunsaturated fat (linear term), protein (linear term), carbohydrate (linear term, dietary glycemic index only), family history of MI before 60 years (yes, no), self-reported history of hypertension (yes, no), and self-reported history of high cholesterol (yes, no). We tested for linear trend by entering the median in each quartile as a continuous variable. We examined the associations of dietary GI and GL with HF events in subpopulations defined by body mass index ($< 25 \text{ kg/m}^2$ vs $\geq 25 \text{ kg/m}^2$) and by fiber intake (quartile 1, $< 18.4 \text{ g/d}$, vs quartiles 2-4, $\geq 18.4 \text{ g/d}$) and performed formal tests of interaction by entering the product of an indicator variable and the median value for each quartile into the models. Because there appeared to be violation of the assumption of proportional hazards ($p = 0.03$ for dietary GI, $p = 0.07$ for dietary GL), we examined the associations of dietary GI and GL with HF in the first and second halves of follow-up.

Statistical analyses were performed using SAS version 9.1 (Cary, NC). A 2-sided p -value < 0.05 was considered statistically significant.

RESULTS

Over 9 years of follow-up, 639 of 36,019 women died of HF ($n = 54$) or were hospitalized for HF for the first time ($n = 585$), corresponding to a rate of 20.5 cases per 10,000 person-years. Women with high dietary GI and GL tended to be older, less likely to take postmenopausal hormones, and less likely to have completed high school or university compared to women with lower dietary GI and GL (Table 1). High dietary GI and GL was associated with lower alcohol and protein intake and higher carbohydrate intake. In addition, dietary GL was positively associated with fiber intake and negatively associated with saturated fat.

Although dietary GI was associated with a higher rate of HF events in age-adjusted models (RR comparing highest to lowest quartile = 1.24, 95% CI 0.99-1.55, p for trend = 0.03), there was no association apparent in multivariable-adjusted models (RR comparing highest to lowest quartile = 1.12, 95% CI 0.87-1.45), p for trend = 0.31 (Table 2). Women in the highest quartile of dietary GL had higher rates of HF events compared to those in the lowest quartile in multivariable-adjusted models, but the association did not reach statistical significance (RR comparing highest to lowest quartile = 1.30, 95% CI 0.87-1.93, p for trend = 0.16).

The association between dietary GI and HF events did not vary by overweight (body mass index $\geq 25 \text{ kg/m}^2$) (RR comparing highest to lowest quartile in overweight individuals = 1.10, 95% CI 0.77-1.58, p for trend = 0.65; RR comparing highest to lowest quartiles in normal weight individuals = 1.11, 95% CI 0.75-1.63, p for trend = 0.38; p for interaction = 0.51). There was a suggestion of a positive association between dietary GL and HF events in overweight individuals that did not reach statistical significance (RR comparing highest to lowest quartile in overweight individuals = 1.47, 95% CI 0.84-2.58, p for trend = 0.13; RR comparing highest to lowest quartile in normal weight individuals = 1.11, 95% CI 0.62-2.00, p for trend = 0.68; p for interaction = 0.55).

We did not observe a statistically significant difference in the association of dietary GI with HF by fiber intake (RR comparing highest to lowest quartile of dietary GI in individuals with low fiber intake = 0.89, 95% CI 0.55-1.43, p for trend = 0.69; RR comparing highest to lowest quartile of dietary GI in individuals with high fiber intake = 1.30, 95% CI 0.95-1.78, p for trend = 0.08; p for interaction = 0.39). Similarly, the difference in the association between dietary GL and HF between those with low and high fiber intake did not reach statistical significance (RR comparing highest to lowest quartile of dietary GL in individuals with low fiber intake = 1.16, 95% CI 0.55-2.44, p for trend = 0.45; RR comparing dietary GL in individuals with high fiber intake = 1.35, 95% CI 0.83-2.19, p for trend = 0.20; p for interaction = 0.32).

High dietary GI appeared to be associated with higher rates of HF events during the first half of follow-up (RR comparing highest to lowest quartiles = 1.33, 95% CI 0.88-2.02, *p* for trend 0.09) and no association in the second half of follow-up (RR comparing highest to lowest quartiles = 1.00, 95% CI 0.72-1.40, *p* for trend = 0.96). Results were similar for the association of dietary GL and HF events (RR comparing highest to lowest quartiles in the first half of follow-up = 1.78, 95% CI 0.94-3.35, *p* for trend = 0.053; RR comparing highest to lowest quartile in the second half of follow-up = 1.06, 95% CI 0.63-1.77, *p* for trend = 0.81).

DISCUSSION

In this population, we did not find associations of dietary GI with HF events in overweight women, normal weight women or in the population as a whole. Rates of HF events were higher in women with high dietary GL, but the association was not statistically significant. The associations did not vary by fiber intake. The results suggested that diets high in GI or GL may be associated with higher rates of HF events in the short-term; however, these unexpected results require independent confirmation.

Although we are not aware of previous studies of the association between diets high in carbohydrates with a propensity to increase blood glucose and HF, dietary GI and GL were associated with coronary heart disease events in several studies of women [11,13,31]. However, no association was evident in studies of men [17,18], including a population of Swedish men where dietary GI and GL were assessed with the food-frequency questionnaire used in the present study. The differing results in men and women may be due to differences in the lipid responses to carbohydrate intake or differences in the strength of triacylglycerol concentration, which increases with high GI or GL diets, as a risk factor for cardiovascular disease [42,43]. In a meta-analysis which combined the prospective studies in men and women, there was a significant association with coronary heart disease [14]. However, data on a possible interaction between sex and dietary GI or GL in populations including both men and women is limited.

The women studied had high intake of fiber compared to the amounts consumed in some of the other populations where the association of dietary GI and GL with coronary heart disease has been examined. We previously reported that dietary GL was associated with higher mortality in men with existing cardiovascular disease only in the setting of relatively low fiber intake [44]. However, in this population, the association of dietary GI and GL with HF was stronger in women with higher fiber intake, though the difference did not reach statistical significance.

Feeding trials have not been long enough to determine the effect of GI or GL on cardiovascular disease events, but a number of trials have demonstrated metabolic effects of diets with low GI or GL that would be expected to result in lower rates of HF [19-29]. Although HF shares risk factors with other cardiovascular diseases, the relative importance of blood pressure is higher for HF [6]. The OMNI Heart Study demonstrated that diets higher in monounsaturated fat or protein resulted in lower blood pressure than diets higher in carbohydrate [45], but dietary GI and GL have not been shown to have major effects on blood pressure [24,28].

There are several important limitations of this study. Although the accuracy of the diagnosis of HF in the Swedish registers was shown to be high [40], only cases of HF that resulted in hospitalization or death were recorded. In addition, the registers do not contain information on HF etiology or subtype. Our assessment of medical history was based on self-report, which is inherently less reliable than clinical measurement. Dietary GI and GL were measured using food-frequency questionnaires. Correlations between the food-frequency questionnaire and weight diet records were 0.62 for dietary GI and 0.77 for dietary GL in a population of Swedish men from the same region [38]. Using questionnaires to assess diet resulted in some exposure

misclassification. If the misclassification of diet was unrelated to HF incidence, the results would likely be biased towards the null. However, this assumption was not verifiable with available data. We cannot rule out residual or unmeasured confounding that could mask an association of dietary GI and GL with incidence of HF.

CONCLUSION

In conclusion, we did not find an association between diets with high GI and HF events in this population of middle-aged and elderly Swedish women or in subpopulations defined by body mass index or fiber intake. There was a suggestion of an association between dietary GL and HF which did not reach statistical significance.

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Abbreviations

CI	confidence interval
GI	glycemic index
GL	glycemic load
HF	heart failure
MI	myocardial infarction
RR	rate ratio

Table 1

Baseline characteristics ^a by quartile of dietary glycemic index and load

	Quartile dietary glycemic index				Quartile dietary glycemic load			
	1	2	3	4	1	2	3	4
Age (y)	60.1 (8.8)	60.5 (8.8)	61.8 (9.2)	63.9 (9.4)	59.8 (8.8)	60.8 (8.9)	62.0 (9.1)	63.6 (9.3)
Physical activity (MET hr/d)	42.3 (4.7)	42.4 (4.7)	42.6 (4.7)	42.5 (5.0)	42.0 (4.7)	42.4 (4.7)	42.6 (4.8)	42.8 (4.9)
Body mass index (kg/m ²)	25.0 (3.9)	24.9 (3.8)	25.0 (3.9)	25.0 (4.1)	24.8 (4.0)	24.9 (3.8)	24.9 (3.8)	25.2 (4.0)
Cigarette smoking (%)								
Never	47.6	53.7	56.9	56.8	43.3	52.9	57.6	61.2
Past	27.5	24.5	21.7	18.5	26.0	24.1	22.2	19.9
Current	24.9	21.8	21.5	24.7	30.8	23.0	20.2	18.9
Living alone (%)	25.8	21.7	21.9	26.5	25.0	22.4	22.6	22.6
Post menopausal hormone therapy (%)	54.5	53.3	51.0	47.5	52.5	52.4	51.9	49.6
Education (%)								
Less than high school	64.1	68.8	75.9	85.1	66.2	71.1	75.7	81.0
High school	9.5	9.1	7.5	5.8	9.6	8.5	7.5	6.4
University	26.3	22.1	16.6	9.2	24.2	20.4	16.8	12.6
Family history of MI before 60 (%)	17.6	16.9	17.0	16.7	17.4	16.4	17.3	17.1
Hypertension (%)	18.3	19.0	20.7	21.8	16.9	19.4	20.7	22.8
High cholesterol (%)	7.1	8.2	7.9	8.4	5.8	7.1	8.5	10.2
Energy intake (kcal/d)	1,723 (540)	1,733 (494)	1,766 (514)	1,751 (541)	1,767 (571)	1,726 (503)	1,729 (486)	1,752 (527)
Alcohol (g/d)	5.6 (6.4)	4.7 (5.3)	3.8 (4.6)	2.7 (3.9)	6.1 (6.8)	4.6 (5.1)	3.6 (4.2)	2.5 (3.5)
Sodium (mg/d) ^b	2,568 (444)	2,552 (364)	2,526 (358)	2,456 (365)	2,633 (452)	2,563 (352)	2,509 (334)	2,397 (360)
Fiber (g/d) ^b	22.4 (6.0)	22.7 (5.1)	22.1 (5.1)	21.1 (5.6)	19.1 (4.5)	21.6 (4.5)	23.1 (4.9)	24.5 (6.3)
Saturated fat (g/d) ^b	27.4 (6.6)	26.9 (5.9)	27.3 (6.1)	27.6 (6.6)	32.8 (6.0)	28.4 (4.7)	25.9 (4.5)	22.1 (4.7)
Polyunsaturated fat (g/d) ^b	7.9 (2.1)	8.1 (1.8)	8.1 (1.8)	8.0 (1.8)	8.4 (2.3)	8.2 (1.8)	8.0 (1.7)	7.4 (1.6)
Carbohydrate (g/d) ^b	203 (26)	210 (24)	212 (25)	218 (28)	181 (17.1)	204 (11)	218 (11)	241 (17)
Protein (g/d) ^b	76.7 (12.2)	71.7 (10.1)	68.9 (9.7)	64.6 (9.8)	78.4 (12.6)	72.2 (9.2)	68.6 (8.3)	62.7 (8.7)
Dietary glycemic index	68.7 (3.0)	73.3 (0.9)	76.1 (0.9)	80.5 (2.3)	71.1 (4.8)	73.8 (3.7)	75.5 (3.6)	78.1 (3.9)
Dietary glycemic load ^b	140 (20)	154 (18)	162 (19)	175 (23)	128 (12)	150 (4)	165 (4)	188 (15)

^a Mean (standard deviation) or percent
^b Adjusted for energy using the residuals method

Table 2

Dietary glycemic index, dietary glycemic load and incidence of heart failure hospitalization or mortality

	Quartile				P trend
	1	2	3	4	
<i>Dietary glycemic index</i>					
Median intake	69.5	73.3	76.1	79.9	
Cases	117	120	172	230	
Person-years	78,447	78,504	77,960	76,573	
Model 1 RR (95% CI) ^a	1 (reference)	1.01 (0.78-1.30)	1.17 (0.92-1.48)	1.24 (0.99-1.55)	0.03
Model 2 RR (95% CI) ^b	1 (reference)	1.01 (0.78-1.31)	1.14 (0.89-1.47)	1.12 (0.87-1.45)	0.31
<i>Dietary glycemic load</i>					
Median intake	131	150	164	184	
Cases	130	135	166	208	
Person-years	78,313	78,242	77,871	77,058	
Model 1 RR (95% CI) ^a	1 (reference)	0.94 (0.74-1.19)	1.00 (0.79-1.26)	1.02 (0.82-1.28)	0.68
Model 2 RR (95% CI) ^b	1 (reference)	1.05 (0.80-1.38)	1.19 (0.87-1.62)	1.30 (0.87-1.93)	0.16

^aCox proportional hazards model. Baseline rate allowed to vary by age.^bModel 1 additionally adjusted for education (less than high school, high school, university), body mass index (linear term), physical activity (linear term), cigarette smoking (current, past, never), living alone (yes, no), postmenopausal hormone use (yes, no), total energy intake (linear term), alcohol intake (linear term), fiber intake (linear term), sodium intake (linear term), polyunsaturated fat (linear term), protein (linear term), carbohydrate (linear term), dietary glycemic index only), family history of myocardial infarction before 60 years (yes, no), self-reported history of hypertension (yes, no), and self-reported history of high cholesterol (yes, no)