CARDIOVASCULAR MEDICINE

Carbohydrates, dietary glycaemic load and glycaemic index, and risk of acute myocardial infarction

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Objectives: To assess the relation between selected carbohydrate foods, dietary glycaemic load and glycaemic index, and the risk of non-fatal acute myocardial infarction in a population with a high intake of refined carbohydrates.

Design and setting: Hospital based case–control study conducted in Milan, Italy, between 1995 and 1999.

Patients: 433 non-diabetic subjects with a first episode of non-fatal acute myocardial infarction, and 448 controls admitted to hospital for a wide spectrum of acute conditions unrelated to known or potential risk factors for acute myocardial infarction.

Methods: Information was collected by interviewer administered questionnaires. Multivariate odds ratios (OR) and 95% confidence intervals (CI) were obtained by multiple logistic regression models.

Results: Compared with patients in the lowest tertile of intake, the multivariate OR for those in the highest tertile was 1.00 for bread, 1.27 for pasta and rice, 1.38 for soups, 0.78 for potatoes, 0.97 for desserts, and 1.00 for sugar. The OR for the highest tertile of score was 1.08 for glycaemic load and 1.38 for glycaemic index. None of the estimates was significant. A significant association with acute myocardial infarction risk was found for glycaemic index in patients aged ⩾ 60 years (OR 1.81, 95% CI 1.07 to 3.07 for the highest tertile of score compared with the lowest) and in those with a body mass index ⩾ 25 kg/m^2 (OR 2.02, 95% CI 1.21 to 3.34).

Conclusions: In this Italian population high glycaemic load and glycaemic index were not strongly associated with acute myocardial infarction risk, but slightly increased odds ratios were observed for glycaemic index in elderly people and in association with overweight.

The potential role of carbohydrates on the risk of coronary heart disease is still unclear and several mechanisms may be involved.[1] A high carbohydrate intake can raise serum concentrations of very low density lipoproteins and triglycerides and decrease those of high density lipoproteins, thus favouring a lipid profile at higher risk for coronary heart disease.[2 3] However, carbohydrate foods contain several nutrients that may reduce risk factors for coronary heart disease such as fibre, linoleic acid, vitamin E, phyto-oestrogens, and several phenolic acids with antioxidant properties. Dietary carbohydrates consumed in the form of whole grains have been shown to be protective against ischaemic heart disease.[4–6] Two prospective studies—the Puerto Rico Heart Health Program[7] and the Honolulu Heart Program[8]—found a weak inverse association of carbohydrate intake with coronary heart disease risk, which disappeared after adjustment for total energy intake. Most epidemiological studies considering the relation between cereal fibre and coronary heart disease have reported that it is protective.[1]

Another way of exploring the role of carbohydrates on coronary heart disease risk is through the glycaemic response that follows their ingestion.[4 9] Carbohydrate foods can produce different glycaemic responses depending on their chemical structure, particle size, amount and type of dietary fibre, fats, proteins, antinutrients, and food processing.[10] The glycaemic response can be quantified by the glycaemic index, which is a measure of the rate of carbohydrate absorption from the gastrointestinal tract and the postprandial blood glucose response.[11 12] Foods with a low glycaemic index, such as legumes and whole grains, reduce the rate of glucose absorption, resulting in lower postprandial rises in blood glucose and insulin compared with high glycaemic index foods (for example, white bread).[13] High insulin concentrations are risk factors for insulin resistance, type 2 diabetes,[9 14] and increased coronary heart disease.[9 15] Diets with a high glycaemic index and glycaemic load (the product of the average daily glycaemic index and total carbohydrate intake—that is, a measure of quality and amount of carbohydrates consumed) have been shown to increase the risk of type 2 diabetes[9 16 17] and coronary heart disease.[4 9]

There is very little epidemiological evidence on the relation between glycaemic index, glycaemic load, and the risk of coronary heart disease. The Nurses' Health Study, based on 761 incident cases, found that dietary glycaemic load was associated with risk for the disease, particularly among women with the highest body mass index, and that carbohydrate foods with the highest glycaemic index increased the risk of coronary heart disease.[4] However, the Zutphen Elderly Study, based on 94 non-diabetic men with incident coronary heart disease, found no relation between the disease and a high glycaemic index diet.[18]

To provide further information on the relation of carbohydrate foods, glycaemic load and glycaemic index, and the risk of acute myocardial infarction, we have analysed the results of a case–control study conducted in Italy, where carbohydrate consumption is high and contains foods with both high glycaemic index (white bread) and intermediate glycaemic index (pasta al dente).

METHODS

The data were derived from a case–control study of non-fatal acute myocardial infarction conducted in the greater Milan, Italy, between 1995 and 1999.[19] Cases were 507 patients (378 men, 129 women; median age 61 years, range 25–79 years) with a first episode of non-fatal acute myocardial infarction, defined according to the World Health Organization criteria,[20] admitted to a network of teaching and general hospitals in the

Table 1 Odds ratios* and corresponding 95% confidence intervals according to energy adjusted intake of carbohydrate foods among 433 non-diabetic cases of acute myocardial infarction and 448 controls, Milan, Italy, 1995 to 1999

	Tertile of intake†			
Servings/week	I‡	II	III	χ^2 trend (p value)
Bread				
Cases/controls	139/150	154/149	140/149	
Upper limit§	15.3	22.2		
OR (95% CI)	1	1.19 (0.83 to 1.71)	1.00 (0.70 to 1.45)	0.00 (0.99)
Whole grain bread				
Cases/controls	406/410	27/38		
OR	1	0.77 (0.44 to 1.37)		
Pasta and rice				
Cases/controls	129/149	130/151	174/148	
Upper limit§	4.5	6.3		
OR (95% CI)	1	0.97 (0.67 to 1.40)	1.27 (0.88 to 1.84)	1.70 (0.19)
Soups				
Cases/controls	148/150	113/149	172/149	
Upper limit§	1.7	3.5		
OR (95% CI)	1	0.86 (0.59 to 1.25)	1.38 (0.95 to 2.00)	2.94 (0.09)
Potatoes				
Cases/controls	156/150	160/149	117/149	
Upper limit§	1.1	2.0		
OR (95% CI)	1	1.11 (0.78 to 1.59)	0.78 (0.54 to 1.12)	1.63 (0.20)
Desserts				
Cases/controls	164/149	132/150	137/149	
Upper limit§	2.8	7.8		
OR (95% CI)	1	0.85 (0.59 to 1.23)	0.97 (0.67 to 1.40)	0.04 (0.84)
Sugars				
Cases/controls	143/150	122/149	168/149	
Upper limit§	19.6	30.5		
OR (95% CI)	1	0.79 (0.54 to 1.14)	1.00 (0.70 to 1.44)	0.00 (0.99)

*Estimates from unconditional logistic regression models, including terms for sex, age, education, body mass index, physical activity, tobacco, alcohol, cholesterol, hypertension, hyperlipidaemia, and family history of ischaemic heart disease.
†Tertiles based on the distribution of controls. For whole grain the categories were only consumers *v* non-consumers, given the low prevalence of use.
‡Reference category.
§Servings per week.
CI, confidence interval; OR, odds ratio.

area. Controls were 478 patients (297 men, 181 women; median age 59 years, range 25–79 years) from the same geographical area, admitted to the same hospitals for a wide spectrum of acute conditions unrelated to known risk factors for acute myocardial infarction. Among controls, 34% had trauma, 30% non-traumatic orthopaedic disorders, 14% acute surgical conditions, and 22% miscellaneous other illnesses. Fewer than 5% of cases and controls approached refused to participate. Cases and controls reporting a diagnosis of diabetes were excluded, thus leaving 448 cases and 433 controls in the present analysis.

Interviews were conducted in hospital using a structured questionnaire, including information on sociodemographic factors, anthropometric variables, smoking, alcohol, and coffee consumption, and other lifestyle habits, a problem oriented medical history, physical activity, and a history of acute myocardial infarction in relatives. Cholesterol concentrations were obtained from clinical records.

Information on diet was based on a food frequency questionnaire, tested for reproducibility[21 22] and validity,[23] which included questions on 78 foods or food groups and 15 questions aimed at assessing patterns of fat intake and meal frequency. Energy and nutrient intakes were computed using an Italian food composition database.[24]

We expressed glycaemic index as a percentage of the glycaemic response elicited by white bread.[25] For each subject we calculated the average daily glycaemic index by summing the products of the carbohydrate content per serving in grams for each food or recipe, by the average number of servings per week and by its glycaemic index, all divided by the total amount of available weekly carbohydrate intake.[26] A score for the daily average glycaemic load was computed as the average daily glycaemic index, but without dividing by the total amount of available carbohydrate. We assigned glycaemic index values to 50 foods or recipes present in the questionnaire, as 28 of them—mainly meat, cheese, and fish based foods—contained only negligible amounts of carbohydrate.[27] Glycaemic index values were derived primarily from international tables[25] and from Italian sources for a few local recipes.[28] Particular attention was paid to Italian cooking habits (for example, pasta "al dente") which may influence the rate of carbohydrate absorption. Food items for which a glycaemic index was not determined were assigned the glycaemic index of the nearest comparable food (for example, tangerines were assigned the glycaemic index of oranges).

Data analysis

Odds ratios (OR) of acute myocardial infarction, and the corresponding 95% confidence intervals (CI), for subsequent tertiles of food intake, glycaemic load, and glycaemic index were derived using unconditional multiple logistic regression models,[29] including terms for age, sex, education, body mass index, cholesterol, tobacco smoking, alcohol drinking, physical activity, hyperlipidaemia, diabetes, hypertension, and a family history of ischaemic heart disease in first degree relatives. Adjustment for energy was made using the residual

Table 2 Odds ratios* and corresponding 95% confidence intervals according to energy adjusted glycaemic index and glycaemic load among 433 non-diabetic cases of acute myocardial infarction and 448 controls, Milan, Italy, 1995 to 1999

	Tertile of score†			χ^2 trend (p value)
	I‡	II	III	
Glycaemic index				
Cases/controls	124/150	148/148	161/150	
Upper limit§	72.8	76.8		
OR (95% CI)	1	1.35 (0.93 to 1.98)	1.38 (0.95 to 2.00)	2.70 (0.10)
Glycaemic load				
Cases/controls	144/150	133/148	156/150	
Upper limit§	204.8	237.8		
OR (95% CI)	1	0.99 (0.68 to 1.46)	1.08 (0.73 to 1.60)	0.16 (0.69)

*Estimates from unconditional logistic regression models, including terms for sex, age, education, body mass index, physical activity, tobacco, alcohol, cholesterol, hypertension, hyperlipidaemia, and family history of ischaemic heart disease.
†Tertiles based on the distribution of controls.
‡Reference category.
§Unit per day.
CI, confidence interval; OR, odds ratio.

method.[30] Tests for trend were based on the likelihood ratio test between the models with and without a linear term for each variable of interest.

RESULTS

Table 1 gives the distribution of cases and controls and the corresponding OR according to intake of selected carbohydrate-rich foods. Compared with the lowest tertile of consumption, the OR of acute myocardial infarction for the highest was 1.00 for bread, 1.27 for pasta and rice, 1.38 for soups, 0.78 for potatoes, 0.97 for desserts, and 1.00 for sugar. Compared with non-consumers, subjects eating whole grain bread had an OR of 0.77. Neither these estimates nor their corresponding trends in risk were significant.

The relation of glycaemic index and glycaemic load with acute myocardial infarction risk is shown in table 2. The OR in the highest tertile compared to the lowest was 1.38 for glycaemic index and 1.08 for glycaemic load. None of the estimates was significant.

Table 3 shows the relation of glycaemic index and glycaemic load with acute myocardial infarction risk in strata of sex, age at diagnosis, and body mass index. A significant association was found for glycaemic index in patients aged ⩾ 60 years (OR 1.81, 95% CI 1.07 to 3.07 for the highest tertile of score compared with the lowest) and in those with a body mass index ⩾ 25 kg/m^2 (OR 2.02, 95% CI 1.21 to 3.34). No different pattern of risk between men and women was found.

DISCUSSION

In this study there was no consistent relation between consumption of various carbohydrate foods and risk of acute myocardial infarction. Carbohydrate intake in the Italian population is peculiar, as Italy shows the highest consumption of carbohydrates from refined cereals among affluent countries[31]—that is, up to more than 300 g/day in the highest quintile of consumption. The main sources of carbohydrates in the Italian population are white bread and its substitutes (such as crackers, grissini, and melba toasts) and various types of pasta or rice dishes, accounting altogether for almost 40% of the total carbohydrate intake.[32] Consumption of sugar and cakes is relatively low in Italy[32] and was not associated with risk for acute myocardial infarction in this study. We found no significant association of myocardial infarction risk with whole grain food consumption, although a tendency for a decreased odds ratio emerged. An inverse association between whole grain intake and risk of ischaemic heart disease has been reported in the Iowa Women's Health Study cohort, which was attributed to the phytochemicals, fibre, and antioxidants contained in such foods.[5] However, in this Italian population only 6.2% of cases and 8.5% of controls consumed whole grains and in relatively low amounts, potentially explaining the lack of a significant protection in this study.

Diets with a high consumption of refined carbohydrates (high glycaemic index foods) tend to raise blood glucose and insulin concentrations to a greater extent than slowly

Table 3 Odds ratios* and 95% confidence intervals of acute myocardial infarction according to glycaemic index and glycaemic load in strata of selected covariates, Milan, Italy, 1995 to 1999

	Glycaemic index			Glycaemic load		
	II tertile	III tertile	χ^2, trend	II tertile	III tertile	χ^2, trend
Sex						
Men	1.24 (0.78 to 1.96)	1.29 (0.82 to 2.06)	1.12 (p=0.29)	0.74 (0.45 to 1.21)	0.85 (0.52 to 1.38)	0.33 (p=0.57)
Women	1.41 (0.68 to 2.92)	1.48 (0.73 to 3.02)	1.16 (p=0.28)	1.58 (0.76 to 3.27)	1.73 (0.81 to 3.69)	1.98 (p=0.16)
Age at diagnosis (years)						
<60	1.09 (0.62 to 1.92)	1.07 (0.61 to 1.88)	0.05 (p=0.82)	0.89 (0.49 to 1.60)	0.89 (0.50 to 1.59)	0.15 (p=0.70)
⩾60	1.72 (1.01 to 2.94)	1.81 (1.07 to 3.07)	4.70 (p=0.03)	1.07 (0.62 to 1.82)	1.29 (0.75 to 2.25)	0.84 (p=0.36)
Body mass index (kg/m^2)						
<25	1.91 (1.00 to 3.65)	0.80 (0.43 to 1.49)	0.79 (p=0.37)	0.85 (0.45 to 1.61)	0.69 (0.37 to 1.31)	1.29 (p=0.26)
⩾25	1.21 (0.75 to 1.98)	2.02 (1.21 to 3.34)	7.52 (p=0.006)	1.09 (0.65 to 1.84)	1.42 (0.84 to 2.39)	1.76 (p=0.18)

*Estimates from unconditional logistic regression models, including terms for sex, age, education, body mass index, physical activity, tobacco, alcohol, cholesterol, hypertension, hyperlipidaemia, and family history of ischaemic heart disease. The reference category was the lowest tertile.

absorbed carbohydrates (low glycaemic index foods), such as legumes and whole grains,[33 34] and have been directly associated with risk of coronary heart disease,[4 9] type 2 diabetes,[9 16 17] and obesity.[9 35] Our data do not support the hypothesis of a strong effect of glycaemic index and glycaemic load on the risk of acute myocardial infarction, although a moderately increased odds ratio associated with high glycaemic index foods was found in selected categories of subjects, such as people over 60 years of age and in people with a body mass index > 25 kg/m^2. This latter result can be related to impaired insulin resistance in elderly overweight subjects and is in agreement with the results of the Nurses' Health Study, which found a doubled risk of coronary heart disease with a high glycaemic load in women with a body mass index of $\geqslant 23$ kg/m^2, but not in those with lower body mass index.[4] No differences by sex were found in our study for the relation of glycaemic index and glycaemic load to risk of acute myocardial infarction. In this analysis we excluded subjects with diabetes. However, if the glycaemic load is related to type 2 diabetes, as several investigators have suggested,[16 17] then there may still be a link between glycaemic load and coronary heart disease, albeit indirect.

With regard to potential sources of bias, in this study cases and controls were interviewed in the same hospitals and came from the same geographical area; participation was almost complete; and patients admitted for chronic conditions or diseases related to known or potential risk factors for acute myocardial infarction or modification of diet were excluded from the comparison group. The potential confounding of covariates associated with acute myocardial infarction risk in this study,[36 37] including energy intake, was allowed for in the analysis. The food frequency questionnaire was satisfactorily valid and reproducible[21–23] and there is no reason to assume different recall of intake of bread, pasta, and other carbohydrates on the basis of the disease status, because the possibility of a relation between these foods and acute myocardial infarction was unknown to most subjects.

Glycaemic index estimates have some limitations, as some of them derive from small samples and their variability is unclear.[25 26 38] Statistics on the average glycaemic index and glycaemic load in the Italian population are not available; however, intake of bread and pasta were similar in our controls and in the general population.[32 39] Another limitation of this study is its relatively small sample size, which is inadequate to investigate moderate associations in subgroups or interactions. However, these data are of considerable interest given the paucity of available information on glycaemic index, glycaemic load, and coronary heart disease risk, and the originality of the population studied in terms of carbohydrate amount and carbohydrate composition of diet.[32]

Conclusions

Although no overall relation with glycaemic index or glycaemic load and acute myocardial infarction risk was found in this Italian population, there was a positive association between glycaemic index and acute myocardial infarction in subgroups most likely to have insulin resistance—the older and more overweight subjects. More studies in these high risk subgroups are needed to confirm these observations and to identify foods or classes of foods with specific effects.

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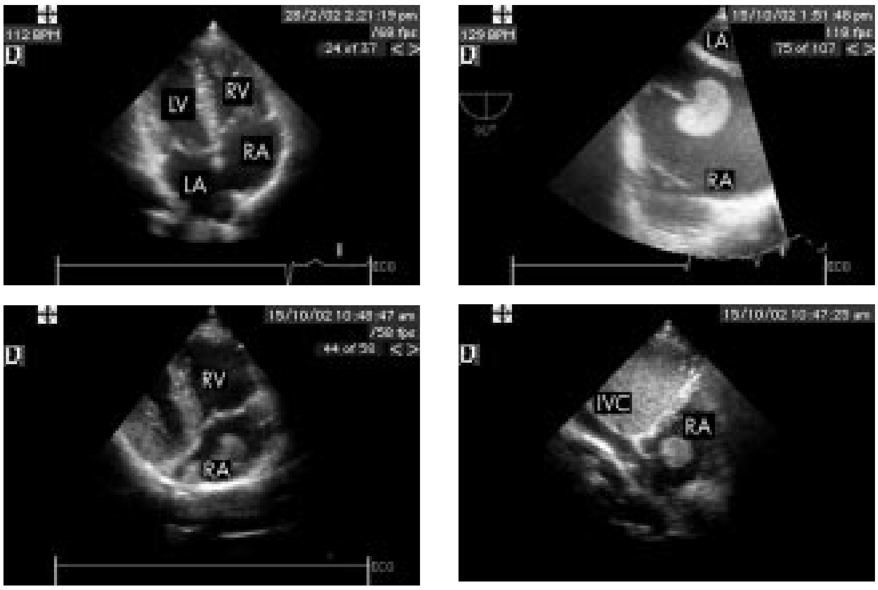
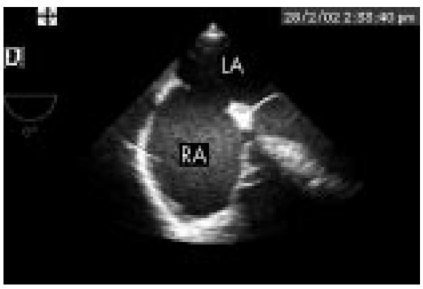
IMAGES IN CARDIOLOGY

Right atrial thrombus following closure of an atrial septal defect

A 20 year old male patient was operated on for atrial septal defect (ASD) at our hospital. No complications were evident one month postoperatively, and clinical and echocardiographic findings were normal. However, six months later transthoracic echocardiography showed a large, highly mobile 2.4×2.3 cm right atrial mass (middle panel, centre column), although no mass was seen in the cardiac chamber at the preoperative transthoracic echocardiogram (upper panel, centre column) in apical four chamber view. Transoesophageal echocardiography revealed a large, mobile, mushroom shaped mass attached by a long thin stalk to the right atrial free wall near the entrance of the inferior vena cava (upper panel, right column) eight months postoperatively. The mass in the right atrium was not detected by transoesophageal echocardiography preoperatively (lower panel, centre column). The similar characteristics of the mass were also determined by subcostal two dimensional echocardiogram (middle panel, right column). Because of concern about the risk of thromboembolism, open heart surgery was performed. The mass was completely removed (lower panel, right column). Histologic studies showed that the mass was composed entirely of thrombotic material with focal regions of calcification. Laboratory data, venous ultrasonography, and pulmonary ventilation perfusion scintigraphy of the patient were normal.

Thrombus formation in the right atrium may occur as a result of endocardial damage following closure of an ASD. To our knowledge, this is the first documented case of a right atrial thrombus following closure of an ASD.





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