Dietary Iron as a Risk Factor for Myocardial Infarction

Public Health Considerations for Nova Scotia

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ABSTRACT

Background: Epidemiological and experimental studies have suggested that high levels of dietary iron and hemeiron can lead to myocardial injury. Lean meat, a primary source of iron and hemeiron, is promoted because it is lower in fat and cholesterol. Does lean meat put us at risk for myocardial infarction, and should we reconsider its promotion?

Methods: We analyzed the importance of dietary iron and hemeiron as a risk for myocardial infarction among 2,198 Nova Scotians who participated in a nutrition survey and who were followed for eight years, using logistic regression.

Results: Acute myocardial infarction incidents occurred in 94 (4.3%) participants. We found no increased risk for myocardial infarction associated with high intake of iron and hemeiron.

Conclusions: Based on Nova Scotian data showing no increased risk for myocardial infarction with high intake of iron and hemeiron, there is no need for immediate reconsideration of promotion of lean meat.

La traduction du résumé se trouve à la fin de l'article.

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A large portion of the Western diet consists of meat, and other parts of the world are moving towards a Western diet. Within the Western diet, meat is the primary source of iron. Recommendations for iron intake are 11 mg for 14 to 18 year old males and 8 mg for adult males.¹ For females, recommendations are 15 mg for ages 14 to 18, 18 mg for ages 19 to 50, and 8 mg for those over 50 years.¹ These recommendations can generally be met with a North American diet.

Animal experiments have demonstrated that high amounts of dietary iron can lead to myocardial injury.^{2,3} In 1981, Sullivan proposed that higher incidence of heart disease in men and postmenopausal women was due to higher levels of stored iron.⁴ A Finnish study in 1992 reinforced that serum ferritin was associated with risk of acute myocardial infarction.⁵ It has since been shown that a high intake of iron and cholesterol simultaneously could cause more severe atherosclerotic lesions than high intake of cholesterol alone.⁶ In addition, high iron levels may have a greater impact on risk of myocardial infarction in the presence of diabetes, hypertension, and smoking.⁶ The various epidemiological studies that evaluated serum iron levels and dietary iron, however, have been inconsistent with respect to the risk for myocardial infarction.⁷⁻²⁰ A recent European study suggested that dietary hemeiron is associated with increased incidence of myocardial infarction.²⁰ This finding may have important public health implications because current health promotion activities advocate reducing the consumption of meat rich in fat and cholesterol which implies the promotion of lean meat. Lean meat has a high iron content, of which approximately 40% constitutes hemeiron. The promotion of lean meat may have unforeseen negative health consequences if hemeiron puts consumers at risk for myocardial infarction. Therefore, it is important to confirm the findings of the European study, particularly in settings that differ with respect to dietary habits and lifestyle risk factors. In the present study, we investigate dietary iron and hemeiron in relation to the risk of myocardial infarction in the province of Nova Scotia, using the 1990 Nova Scotia Nutrition Survey and eight years of follow-up on myocardial infarction incidence and mortality.

METHODS

Study population

The study population consisted of participants of the 1990 Nova Scotia Nutrition Survey. A sample of 3,684 non-institutionalized individuals between the ages of 18-74 and stratified by age, sex, and county were identified among registrants of the Nova Scotia Medical Services Insurance.²¹ Among the 2,777 (75%) individuals who were located, 2,198 (79%) individuals agreed to participate and completed the survey.²¹ Nine individuals were excluded from the present study since they had a myocardial infarction incident in the year prior to the interview.

Dietary and risk factor assessment

The Nova Scotia Nutrition Survey was conducted in 1990 and consisted of a face-to-face interview, including a 24-hour dietary recall questionnaire, a modified food frequency questionnaire, and questions on demographics, socioeconomic status, and other risk factors including smoking and diabetes.²¹ Macro and micro-nutrients in these individuals' diets were calculated using the Canadian Dietary Information software program.²¹ Hemeiron was estimated as 40% of the iron in meat, fish, and poultry.^{20,22-24} Body Mass Index (BMI) was calculated by dividing weight in kilograms by the square of height in meters.

Health outcomes

All Nova Scotia administrative health records from 1989 onwards are stored at the Population Health Research Unit of Dalhousie University.²⁵ Incidence of non-fatal and fatal acute myocardial infarction (ICD-9 code 410) was obtained by linking participants with these administrative databases, including hospital discharge records, physician visits, and vital statistics. Information up to the end of the 1998 calendar year was included in the analyses. The linkage procedure also revealed out-of-province migration of 206 participants, and their information was included until the date of migration.

Data analysis

We adjusted for the intake of iron and hemeiron for the total energy intake (iron/hemeiron intake per 1000 Kcal).^{26,27}

TABLE I

Demographic and Dietary Characteristics of the 2,189 Nova Scotia Nutrition Survey Participants and Odds Ratios for Myocardial Infarction*

		Total† (N=2189)	MI‡ (N=94)	non-MI§ (N=2095)	Odds Ratio	95% CI
Age (mean in years)		49	63	48	2.32	1.88-2.85
Gender	Females	1136 (51.9)	38 (40.4)	1098 (52.4)	0.63	0.41-0.97
	Males	1053 (48.1)	56 (59.6)	997 (47.6)	1	—
Smokers		673 (30.7)	29 (30.9)	644 (30.7)	1.40	0.88-2.23
BMI	Low < 20	108 (4.9)	3 (3.2)	105 (5.0)	0.80	0.24-2.71
	Medium 20-27	1082 (49.4)	39 (41.5)	1043 (49.8)	1	—
	High ≥ 27	999 (45.6)	52 (55.3)	947 (45.2)	1.32	0.85-2.23
Household income	< \$20,000	587 (26.8)	43 (45.7)	544 (26.0)	1	—
	\$20,000-\$40,000	733 (33.5)	27 (28.7)	706 (33.7)	0.85	0.50-1.43
	> \$40,000	558 (25.5)	10 (10.6)	548 (26.2)	0.55	0.26-1.16
No response		311 (14.2)	14 (14.9)	297 (14.2)	0.86	0.45-1.62
Education	< High school	961 (43.9)	66 (70.2)	895 (42.7)	1	—
	High school/vocational	624 (28.5)	18 (19.1)	606 (28.9)	0.71	0.41-1.23
	Some college/university	604 (27.6)	10 (10.6)	594 (28.4)	0.38	0.19-0.75
Energy intake (mean in Kcal)		1967	1709	1980	0.73	0.53-1.00
Iron intake (mean in mg)		6.95	7.13	6.94		
	Low tertile¶	4.59	4.59	4.59	1	—
	Medium tertile	6.43	6.59	6.42	0.77	0.46-1.30
	High tertile	9.82	10.16	9.81	0.67	0.40-1.15
Hemeiron intake (mean in mg)		0.65	0.60	0.65		
	Low tertile¶	0.15	0.16	0.15	1	—
	Medium tertile	0.47	0.49	0.47	0.81	0.49 - 1.34
	High tertile	1.33	1.40	1.32	0.69	0.41-1.18

* Odds ratios (OR) are adjusted for age and gender, except OR for age (only adjusted for gender) and OR for gender (only adjusted for age)

† The total study sample

‡ Participants with a myocardial infarction during the follow-up period

§ Participants without a myocardial infarction during the follow-up period

|| Reference category

¶ Iron and hemeiron intake tertiles are energy-adjusted

CI = confidence interval: estimates are considered statistically significant if the 95% CI are not embracing 1

This adjustment was suggested by Willet et al. on the basis of a higher correlation between subsequent nutrition surveys when adjusted for caloric intake.²⁸ We divided study participants into tertiles based on energy-adjusted intake of iron and hemeiron. The lowest intake group was used as the reference group. Age was considered as a continuous covariate and divided by 10 to quantify the impact of 10-year age increments. Similarly, energy intake was considered as a continuous covariate and the impact of 1000 Kcal increments was examined. We applied logistic regressions with myocardial infarction (nonfatal and fatal combined) as the dependent variable. In initial analyses, we adjusted for age and gender. In subsequent analyses, we further adjusted for established confounders including smoking, BMI, diabetes, income, total fat, saturated fat, and cholesterol. Sample weights are generally applied in the analysis of surveys with stratified sampling. For longitudinal analysis of survey data with follow-up, Korn and Graubard recommend adjusting

for the variables used in defining the sample weights (age, gender, and county) and not incorporating sample weights.²⁹ We applied these recommendations in all analyses. However, since county did not substantially affect any of our estimates of interest, we excluded this covariate from our analyses.³⁰

RESULTS

During the eight years following the survey, 94 (4.3%) individuals had an acute myocardial infarction incident, of which 17 were fatal. Table I presents demographic and dietary characteristics of participants with and without myocardial infarctions. The study participants had a mean iron intake of 6.95 mg per 1000 Kcal and a mean hemeiron intake of 0.65 mg per 1000 Kcal (Table I). Adjusting for age and gender differences, individuals in the highest iron intake tertile had 0.67 times the risk of an acute myocardial infarction compared to those in the lowest iron intake tertile (95% CI of 0.40 to 1.15). Individuals

TABLE II

Odds Ratios for Myocardial Infarction by Iron and Hemeiron Intake Tertiles of the 2,189 Nova Scotia Nutrition Survey Participants*

	N(%) [‡]	Odds Ratio	95% CI
Iron intake [†]			
Low tertile	30 (4.1)	1§	–
Medium tertile	33 (4.5)	0.71	0.41-1.22
High tertile	31 (4.2)	0.59	0.34 - 1.05
Hemeiron intake [†]			
Low tertile	38 (5.2)	1§	–
Medium tertile	31 (4.2)	0.80	0.48-1.33
High tertile	25 (3.4)	0.65	0.37-1.14

* Odds ratios are adjusted for age, gender, smoking, Body Mass Index, diabetes, income, dietary lipids, saturated fat, and cholesterol

[†] Iron and hemeiron intake tertiles are energy-adjusted

[‡] Number (percentage) of individuals with a myocardial infarction during follow-up

[§] Reference category

CI = confidence interval: estimates are considered statistically significant if the 95% CI are not embracing 1

in the highest hemeiron intake tertile had 0.69 times the risk of an acute myocardial infarction compared to those in the lowest hemeiron intake tertile (95% CI of 0.41 to 1.17). In other words, the risk for myocardial infarction is less among individuals with high iron or high hemeiron intake, although these differences are not statistically significant. Statistically significant differences were obtained with respect to age and gender: each 10-year increment in age more than doubled the risk of myocardial infarction, while females had 0.63 times the risk of males. In addition, individuals with diabetes and limited education had a higher risk of myocardial infarction. Smokers and individuals with low income and high BMI also had a greater risk of myocardial infarction, but the associations were not statistically significant (Table I).

Table II presents the risk for myocardial infarction associated with iron/hemeiron intake when simultaneously adjusted for the following confounders: age, gender, smoking, BMI, diabetes, income, dietary lipids, saturated fat, and cholesterol. The risk of myocardial infarction for individuals in higher iron and hemeiron intake tertiles was less than that of individuals in the lowest intake tertiles, but these associations were not statistically significant.

All the above results were almost identical when the analyses were further adjusted for the length of follow-up as a means to control for the 206 participants who moved out of province (results not shown).

DISCUSSION

We found no increased risk for myocardial infarction among individuals with high

iron or high hemeiron intake. Rather, individuals with higher iron and hemeiron intake seemed to be at lower risk for myocardial infarction, but these associations were not statistically significant.

Diet is cultural, and there are major differences between countries and regions. Therefore, it is important to investigate dietary patterns and risks locally. Intake of iron and hemeiron in the Nova Scotia population appeared to be lower than in the European study²⁰ that reported an increased risk of myocardial infarction with increased hemeiron intake. The higher risk in the European study may be attributable to high hemeiron intake and high risk of nonfatal myocardial infarctions in their highest tertile, since there were no substantial risk differences between their lowest and medium tertiles. With lower hemeiron intake among the Nova Scotia population, our study participants would primarily fall in the lower and middle tertiles of the European sample, with only very few in their highest tertile. We speculate that this may be the reason that the two studies have different results. With respect to the risk associated with iron, our results are consistent with those of a previous Canadian study among participants of a nutrition survey conducted between 1970 and 1972,¹⁶ and with two other North American studies among older populations.^{8,9}

The Nova Scotia Nutrition Survey was conducted during spring and fall in order to account for seasonal variations in diet. The survey was also designed to obtain representative samples from different age groups, sex, and geographical regions of the province.²¹ The study is further

strengthened by the high response rate and the high follow-up rate that was established through linkages with administrative health information. In addition to demonstrating the absence of a risk for myocardial infarction associated with high dietary iron and hemeiron intake, the study confirms the higher risk of myocardial infarction for those with diabetes, limited income and education, smoking and high BMI for this study population. A limitation in this respect is our inability to adjust for other risk factors including physical activity, chronic diseases other than diabetes, family history of cardiovascular disease, and occurrence of a cardiovascular disease incident prior to 1989.

Individuals with a high caloric intake are more likely to have a larger amount of iron and other nutrients in their diet. According to Willett et al., individuals may under- or overestimate their food consumption, and thus, nutrient intakes may be more appropriately estimated as a proportion rather than an absolute amount.²⁸ As pointed out by Hampl et al., consumption of nutrients is partially dependent on total energy intake, and the density of the nutrient in the diet is more relevant than the actual gross intake.²⁶ An energy-adjusted analysis may also be more appropriate in terms of public health policy, as it is easier for an individual to change food items rather than to change their appetite. Nevertheless, analyses of absolute iron or hemeiron intake (not shown) revealed risk estimates for myocardial infarction similar to those presented here.

In Canada and most industrialized countries, cardiovascular disease is the leading cause of death for both men and women. In 1997, cardiovascular disease accounted for 37% of all deaths, with 38% of the deaths in women and 36% of the deaths in men.³¹ In Canada in 1993, the direct costs of CVD were estimated to be \$7.27 billion while the indirect costs were estimated at \$12.37 billion.³² In Nova Scotia in 1997, 1,589 individuals died from ischemic heart disease, 806 of these from acute myocardial infarction.³¹ The health of Nova Scotians is among the poorest of all provinces and parallels poor lifestyle and socioeconomic factors.³³⁻³⁵ Clearly, the potential health and monetary benefits associated with national and provincial public health interventions are tremendous.

This study is the first study in Canada to investigate the importance of both dietary iron and hemeiron for the risk of myocardial infarction. We found no increased risk associated with dietary iron and hemeiron intake, and thus there is no need for immediate action towards changing the current public health message promoting the consumption of lean meat, which is rich in iron and hemeiron. The current public health message should be reconsidered if the net benefits gained from reducing the dietary iron and hemeiron intake outweigh the risks associated with iron deficiency and with greater intake of meat high in fat and cholesterol. Since our findings are based on the lifestyle and diet of Nova Scotians, which is potentially different from that of other provincial residents, there is a need to repeat and confirm our findings in other parts of the country.

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RÉSUMÉ

Contexte : Des études épidémiologiques et expérimentales ont suggéré que de hauts niveaux de fer diététique peuvent mener à un accident du myocarde. La viande maigre, une source importante de fer diététique, est favorisée, grâce à un niveau de graisse et de cholestérol relativement bas. Cela nous met-il en danger d'avoir un infarctus du myocarde et devrions-nous reconsidérer la promotion de la viande maigre?

Méthode : Nous avons examiné la relation entre le fer diététique ou érythrocytaire et le risque d'un infarctus aigu du myocarde parmi 2 198 participants d'une enquête alimentaire à la Nouvelle-Écosse.

Résultats : Parmi ces individus, il y a eu 94 incidents d'infarctus aigus du myocarde pendant une période de huit ans. Ayant ajusté pour les variables confondantes, nous n'avons trouvé aucune augmentation du risque d'un infarctus aigu associée avec une ration alimentaire élevée en fer diététique et érythrocytaire.

Conclusions : Étant donné le style de vie et les habitudes alimentaires des Néo-Écossais, il n'y a pas lieu de reconsidérer la promotion de la viande maigre.