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Incident Heart Failure Is Associated with Lower Whole-Grain Intake and Greater High-Fat Dairy and Egg Intake in the Atherosclerosis Risk in Communities (ARIC) Study

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Abstract

Background—Prospective studies evaluating associations between food intake and risk of heart failure (HF) in diverse populations are needed.

Objectives—Relationships between incident HF (death or hospitalization) and intake of seven food categories (whole grains, fruits/vegetables, fish, nuts, high-fat dairy, eggs, red meat) were investigated in an observational cohort of 14,153 African-American and white adults, age 45 to 64 years, sampled from four US communities.

Methods—Between baseline (1987–1989) and Exam 3 (1993–1995), dietary intake was based on responses to a 66-item food frequency questionnaire administered at baseline; thereafter, intake was based on averaged baseline and Exam 3 responses. Hazard ratios (HR [95% CI]) for HF were calculated per 1–daily serving difference in food group intake.

Results—During a mean of 13 years, 1,140 HF hospitalizations were identified. After multivariable adjustment (energy intake, demographics, lifestyle factors, prevalent cardiovascular disease, diabetes, hypertension), HF risk was lower with greater whole-grain intake (0.93 [0.87, 0.99]), but HF risk was higher with greater intake of eggs (1.23 [1.08, 1.41]) and high-fat dairy (1.08 [1.01, 1.16]). These associations remained significant independent of intakes of the five other food categories, which were not associated with HF.

Conclusions—In this large, population-based sample of African-American and white adults, whole-grain intake was associated with lower HF risk, whereas intake of eggs and high-fat dairy were associated with greater HF risk after adjustment for several confounders.

Heart failure (HF) affects approximately 5 million people in the United States, resulting in heavy demands on health care resources (1). Consequently, identifying lifestyle factors that can reduce risk of HF independent of medical intervention is critical. Diet is among the prominent lifestyle factors that influence major HF risk factors: coronary artery disease, obesity, diabetes/insulin resistance, and hypertension. HF represents a subtype of

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cardiovascular disease (CVD) and, therefore, may be underrepresented in studies investigating associations between diet and total CVD only, especially in younger cohorts among whom there is a lower incidence of HF. Furthermore, surprisingly little diet-related research has been specific to heart failure, despite the increasing health care burden of this disease given the aging US population (2).

Although studies suggest that micronutrient supplementation can reduce symptoms and improve quality of life in HF patients (3), a more critical investigation of the temporal relationship between diet and the development of HF is needed, including attention to more tangible dietary factors, ie, foods rather than food components such as micronutrients. Few such studies exist. In the Cardiovascular Health Study, Mozaffarian and colleagues found that consumption of baked or broiled fish, but not fried fish, was inversely associated with incident HF (4). More recently, Djousse and Gaziano found that consumption of cereals, particularly whole-grain cereals, was inversely associated with incident HF (5), whereas egg consumption was positively associated with incident HF (6). Although these observations suggest the value of making practical dietary decisions in terms of HF (increasing whole-grain consumption and minimizing egg consumption), more research is needed in larger, more diverse populations because these previous studies were limited to mainly whites (4–6) or to only men (5,6).

The Atherosclerosis Risk in Communities (ARIC) study provides an opportunity to investigate the relationship between dietary intake and HF in both men and women and in a biracial sample (whites and African Americans). This paper describes the relationship between intake of foods from seven food categories and risk of incident HF in ARIC, a longitudinal cohort study. The working hypothesis was that consumption of foods rich in antioxidants and fiber, such as whole grains and fruits and vegetables, and foods rich in polyunsaturated fatty acids, such as fish and nuts, would be inversely associated with risk of incident HF. In contrast, foods high in saturated fat and cholesterol, such as red meat, eggs, and high-fat dairy foods, were hypothesized to be positively associated with incident HF.

METHODS

The ARIC study is a population-based, observational cohort study including African-American and white men and women, age 45 to 64 years. The baseline exam was conducted in 1987–1989, with follow-up exams completed during 1990–1992 (Exam 2), 1993–95 (Exam 3), and 1996–1998 (Exam 4). Four field centers from the following communities participated in the study: Forsyth County, North Carolina; Jackson, MS; northwest Minneapolis suburbs, Minnesota; Washington County, Maryland (7). All protocols were approved by each field center's institutional review board.

After providing informed consent, 15,792 participants were enrolled (8,710 women and 7,082 men). The current analysis excludes racial groups with limited representation (n=48), African Americans from the Minnesota and Maryland field centers (n=55, due to small numbers), and those who provided insufficient dietary data or reported extreme energy intakes (<600 kcal or >4,200 kcal per day for men or <500 kcal or >3,600 kcal per day for women) (n=364). To focus on incident HF, participants with prevalent HF at baseline were also excluded from these analyses (n=751). Prevalent HF was defined as current use of medications for heart failure at the baseline exam (n=83) or evidence of manifest heart failure, stage 3, according to the Gothenburg criteria (n=700) (8,9). These analyses included 14,153 participants.

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Incident HF

Incident HF cases were identified through review of county death certificates and local hospital discharge lists and defined according to the International Classification of Diseases Codes (ICD-9 or ICD-10). Incident HF was defined as first HF hospitalization (428, ICD-9) or any death where the death certificate included an HF code (428, ICD-9 and I50, ICD-10). Nonhospitalized, nonfatal HF was not captured. During a mean of 13.3 years of follow-up through 2003, 1,140 cases of incident HF were identified in this sample (639 men, 501 women; 360 African Americans, 780 whites). The HF incidence rate was 6 per 1,000 person-years; 3% of cases were deaths related to HF.

Diet Assessment

At baseline (1987–1989) and Exam 3 (1993–1995), participants completed an interviewer-administered, 66-item semiquantitative food frequency questionnaire (FFQ), modified (10) from the 61-item FFQ designed and validated by Willett and colleagues (11). Participants responded with the frequency they consumed specific foods and beverages according to nine predefined frequency categories, ranging from never or less than one time per month to six or more times per day (standard portion sizes were given as a reference for intake estimation: pictures and food models were shown to the participants by the interviewer). The brand name of the breakfast cereal most commonly consumed (open-ended response) and use of salt in cooking and at the table (two questions) were also ascertained. Nutrient intakes were derived from the FFQ responses using the Harvard Nutrient Database.

Food Groups

Relationships between HF and food groups previously shown to be significantly associated with HF (4,5) or total CVD (12–18) were assessed: whole grains (oatmeal or grits, whole-grain cold cereal, whole-grain/dark bread), eggs (boiled, poached, fried, scrambled, omelets, egg salad, quiche, not including egg substitutes), fruits and vegetables (fruits and fruit juices; tomatoes; potatoes; cruciferous, carotenoid, green leafy, legumes, other vegetables), fish (seafood, dark-meat fish, tuna, other fish), and nuts (nuts, peanut butter). HF risk was also evaluated in relation to intake of high-fat dairy (whole milk, other cheese, ice cream) and red meat (hamburger, meat in sandwiches or mixed dishes, hot dogs, sausage/salami, bacon, liver) because these foods contribute substantially to saturated fat intake.

Data Analysis

Baseline characteristics of the study sample were determined with analysis of variance, stratified by incident HF status. Cox proportional hazards regression was used to determine hazard ratios (hereafter, referred to as relative risks [RR]) for incident HF according to dietary intake [per 1 standard deviation difference in dietary pattern score or per 1 daily serving difference in food group intake]). Between baseline and the third ARIC exam, dietary intake was based on responses from the baseline FFQ; thereafter, intake was based on the mean of baseline and Exam 3 responses.

Two main models were used to evaluate the relationship between dietary intake and incident HF. Model 1 adjusted for energy intake (kcal/day). Model 2 adjusted for energy intake, plus demographics (age; sex; race group; study center; education level [up to and including grade school, high school without diploma, high school graduate, vocational school, college graduate, graduate school/professional school]; lifestyle factors including smoking status [current, former, never smoker], smoking intensity [cigarettes/year], physical activity level [sport and exercise activity and nonsport activity during leisure from Baecke questionnaire (19)], and alcohol consumption status [current, former, never]; and baseline history of disease (prevalent

CVD [coronary heart disease and stroke], diabetes, and hypertension [systolic/diastolic blood pressure ≥140/90 or use of medications to treat hypertension].

In food group analyses, an additional model was used that mutually adjusted intakes of whole grains, high-fat dairy, fruits/vegetables, fish, nuts, eggs, and red/processed meat (Model 3).

To determine whether the relationship between dietary intake and HF differed depending on baseline body mass index (BMI), prevalent CVD, and prevalent diabetes, a cross product term (eg, eggs×CVD) was added to the variables listed in Model 2.

All statistical analyses were done with SAS version 9.1 (SAS Institute, Inc, Cary, NC).

RESULTS

Sample Characteristics

Demographic and lifestyle characteristics of participants who remained without HF, compared with those in whom HF developed, are shown in Table 1. Participants in whom HF developed over the course of follow-up were older, more frequently African American, less frequently female, less educated, less physically active, and more frequently current smokers but less frequently current drinkers ($P \leq 0.02$ for all). Both baseline BMI and waist circumference were greater in those in whom HF developed. Greater levels of other traditional CVD risk factors, diabetes, coronary heart disease (CHD), and stroke were also more common in those in whom HF developed later ($P < 0.001$ for all).

Dietary Intake

After adjustment for total energy intake, consumption of refined grains, high-fat dairy, and red or processed meat were significantly greater, and whole-grain intake significantly less, in those with incident HF vs those remaining disease-free ($P < 0.05$ for all).

Risk of Incident HF according to Food Group Intake

In energy-adjusted models, greater intakes of eggs, high-fat dairy, and red or processed meat were associated with a higher risk of HF, whereas greater whole-grain intake was associated with a lower risk of HF (Model 1, Table 2). After multivariable adjustment (Model 2, Table 2), estimates were slightly attenuated but remained significant, with greater intake of eggs (RR per 1 serving/day=1.23 [1.08, 1.41]) and high-fat dairy foods (RR per 1 serving/day=1.08 [1.01, 1.16]) associated with greater risk of HF, and greater whole-grain intake associated with a slightly lower risk of HF (RR per 1 serving/day=0.93 [0.87, 0.99]). These risk associations were similar and remained significant after adjusting for other food groups (RR per 1 serving/day of eggs=1.23 [1.07 to 1.42]); high-fat dairy=1.09 [1.01, 1.17]; whole grains=0.92 [0.86, 0.98] (Model 3), sodium intake (RR per 1 serving/day of eggs=1.23 [1.07 to 1.41]); high-fat dairy=1.08 [1.01, 1.16]; whole grains=0.91 [0.85, 0.98]), or baseline BMI (a potential pathway intermediate) (RR per 1 serving/day of eggs=1.23 [1.07 to 1.42]); high-fat dairy=1.09 [1.01, 1.17]; whole grains=0.92 [0.86, 0.98]). Furthermore, adjustment for follow-up BMI and incident CVD, diabetes, and hypertension (modeled as time-varying covariates) had only slight effects on risk estimates (RR per 1 serving/day of eggs=1.25 [1.01 to 1.56]; high-fat dairy=1.08 [0.97, 1.20]; whole grains=0.90 [0.82, 0.98]). Other studied food groups—fruits and vegetables, fish, nuts, and red meat—were not significantly associated with HF risk after multivariable adjustment (Table 2).

Because knowledge of HF risk factors or other early symptoms may influence dietary intake, an additional sensitivity test that excluded participants with CVD, diabetes, or hypertension at baseline was conducted. In the considerably smaller group of subject without these conditions (n=8,594), hazard ratios were similar, but confidence intervals were wide (RR per 1 serving/day of eggs=1.26 [0.99, 1.59]; high-fat diary=1.05 [0.92, 1.20]; whole grains=0.84 [0.74, 0.95]).

Interactions

There were no significant interactions between dietary intake variables and BMI, sex, race, or baseline disease status (CVD, diabetes, or hypertension) (data not shown).

DISCUSSION

After 13.3 years of follow-up in this cohort of approximately 14,000 white and African-American men and women, greater intake of eggs and of high-fat dairy foods were both associated with greater risk of incident HF, whereas greater intake of whole-grain foods was associated with lower risk of incident HF. These associations were independent of demographic characteristics, lifestyle factors, prevalent CVD, diabetes, hypertension, and other food groups.

Consistent with the findings of the present investigation, whole-grain intake has been associated with lower risk of overt CVD (15) and hypertension (20), improvements in glycemic control (21,22), and lower levels of inflammatory biomarkers (23), all factors related to HF risk (24–26). Also consistent with the data presented here are the results of a recent report from the Physicians’ Health Study, which showed that greater cereal intake—particularly whole-grain cereal—was associated with a significantly lower risk of HF (5). However, that study, like the current study, relied on a relatively simple FFQ to quantify intake (5), and the previous study did not evaluate the association between HF risk and total whole-grain intake.

The Physicians’ Health Study also reported a positive association between egg consumption and HF risk (6), which was corroborated in the current analysis. Furthermore, the risk estimates presented here were of similar magnitude to those observed in the Physician’s Health Study: ie, if analyses were modeled in categories similar to those used in the previous study, risk of HF was approximately 30% in individuals who regularly consumed eggs (at least daily) vs those who did not consume eggs or who consumed eggs less than once per week. Although the association was independent of the intake of other foods, egg consumption may simply be a marker for a larger dietary pattern that, in total, influences HF risk. Given the long history of debate regarding egg consumption and CVD in general (27), it is important that these observations be disentangled in studies of varying design to determine whether to recommend omitting eggs from the diet.

A positive association between high-fat dairy intake and HF risk also existed in the ARIC cohort. The positive association between CVD risk and intake of saturated fat, which is found in high-fat dairy foods, is fairly well established (28). Although few studies have reported specifically on associations between intake of high-fat dairy foods and CVD, existing studies suggest the fat content of dairy foods (high-fat vs low-fat) is important. Low-fat dairy generally shows more favorable associations with CVD and risk factors than high-fat dairy, suggesting that the fat component of high-fat dairy foods may be partly responsible for these associations.

The hypothesis that fish consumption would be related to lower risk of incident HF was not supported by the ARIC data, but the contrasting effects of fried vs baked or broiled fish may partly explain the absence of association in this cohort. Mozaffarian and colleagues (4) observed a 20% to 30% lower incidence of HF in those who consumed baked/broiled fish at least weekly vs those who consumed baked/broiled fish less than once per month. In contrast, fried fish was associated with greater HF risk. Unfortunately, unlike the Mozaffarian study, the current study was unable to differentiate fried fish from fish prepared in other ways. Given the frequency of total fried food consumption in the ARIC study (approximately 70%

consumed fried food weekly and approximately 17% consumed fried food daily), it seems likely that a large proportion of the fish consumed was fried.

In the current study, neither consumption of fruits and vegetables nor consumption of low-fat dairy was associated with HF risk, despite prior evidence suggesting these food groups would be inversely associated with risk (12–14,29–31). At the time dietary intake was assessed in this study, foods low in fat and cholesterol, such as fruits and vegetables and low-fat dairy, were recommended for health maintenance and for specific CVD conditions (32–34). Thus, it is possible that awareness of these diet-disease relationships among those at greater risk for HF may have prevented us from detecting true associations. That is, intake reflective of lifelong habits (which may be most relevant to the development of HF), may not have been accurately measured. However, this limitation is not unique to the ARIC study but is a well-known limitation of any analysis relying on a proxy measure of food intake.

There are limitations to this study. First, because the ARIC study relied on hospital discharge records and death certificates to ascertain cases of HF, outpatient HF was not included (therefore, less severe cases were likely not included) (35). Although this compromises sensitivity and generalizability, it results in high specificity of the HF definition. It is also likely that subjects with less-severe HF in early years of follow-up were eventually hospitalized by the end of the 13.3 years of follow-up.

Second, although the ARIC study used a fairly short FFQ to quantify dietary intake, the questionnaire has been validated (11) and criterion validity with respect to cardiovascular outcomes in the ARIC cohort has been demonstrated (13).

Third, some questions assessing intake of grains included a combination of whole- and refined-grain foods (eg, rice included white rice, brown rice, and wild rice) (13). However, this type of measurement error would likely attenuate risk estimates, suggesting estimates of HF risk associated with whole-grain intake may actually be greater than presented here.

Fourth, although confounding was carefully assessed and several variables known to confound diet–CVD associations were included in the multivariable model, the possibility of residual confounding cannot be excluded. Because these data were based on HF hospitalizations and death only, it is equally possible that dietary changes may have occurred secondary to HF symptoms, resulting in attenuated risk estimates. However, sensitivity analyses excluding participants with prevalent conditions known to influence HF risk largely addressed this possibility. Although there was less power in the smaller subset, whole-grain and egg intake remained associated with HF risk. Furthermore, when CVD, diabetes, and BMI were modeled as time-varying covariates (status updated throughout follow-up), again, there was no substantial attenuation in risk estimates.

Lastly, these data indicate only association. Randomized interventions are necessary to demonstrate causality and begin to better understand potential mechanisms.

CONCLUSIONS

Greater intake of eggs or high-fat dairy foods and lower intake of whole grains were each associated with an increase in the risk of HF in this large biracial cohort. Overall, these data are consistent with traditional diet–CVD hypotheses and support recent findings suggesting greater whole-grain intake reduces HF risk (5) and greater egg intake increases HF risk (6). Although risk estimates were modest (7% lower risk per one-serving increase in whole-grain intake; 8% greater risk per one-serving increase in high-fat dairy intake; 23% greater risk per one-serving increase in egg intake), the totality of literature in this area suggests it would be prudent to recommend that those at high risk of HF increase their intake of whole grains and reduce intake of high-fat dairy foods and eggs, along with following other healthful dietary practices recommended by the American Heart Association (36).

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Table 1

Baseline characteristics of 15,143 men and women from the Atherosclerosis Risk in Communities Study according to incidence of heart failure status[a]

	Incident Heart Failure		
Demographic and lifestyle factors	**No (n=13,013)**	**Yes (n=1,140)**	***P* value**
	←*mean±standard error*→		
Age (y)	53.9±0.05	57.0±0.2	<0.001
Race (% African American)	24.2±0.4	31.2±1.3	<0.001
Sex (% female)	55.5±0.4	43.7±1.5	<0.001
High school degree (%)	79.0±0.4	60.7±1.3	<0.001
Exercise activity level (% in quintile 5)	20.9±0.4	17.8±1.2	0.017
Nonsport leisure activity (% in quintile 5)	18.8±0.3	14.6±1.1	0.001
Smoking status (% current)	24.3±0.4	37.0±1.3	<0.001
Drinking status (% current)	58.2±0.4	47.2±1.5	<0.001
Body mass index[b]	27.3±0.05	29.4±0.2	<0.001
Other CVD[c] risk factors			
LDL-C[d] (mg/dL)	137.2±0.4	142.7±1.2	<0.001
HDL-C[e] (mg/dL)	52.3±0.2	46.3±0.5	<0.001
Triglycerides (mg/dL)[a]	110.6 (109.7, 111.6)	135.3 (131.3, 139.5)	<0.001
Fasting glucose (mg/dL)	104.5±0.3	128.8±1.0	<0.001
Systolic blood pressure (mm Hg)	120.1±0.2	130.2±0.6	<0.001
Diastolic blood pressure (mm Hg)	73.4±0.1	75.9±0.3	<0.001
Hypertension (%)	30.3±0.4	54.9±1.4	<0.001
Type 2 diabetes (%)	8.4±0.3	28.6±0.9	<0.001
Prevalent CVD			
Coronary heart disease (%)	3.1±0.2	15.5±0.6	<0.001
Stroke (%)	1.4±0.1	3.3±0.4	<0.001
Nutrient intake			
Total energy intake (kcal)	1,624±5	1,664±18	0.039
Total energy intake (kJ/d)	6,799±21	6,967±75	0.039
Protein (% of energy)	17.8±0.04	18.1±0.1	0.094
Carbohydrate (% of energy)	48.9±0.08	48.2±0.3	0.029
Total fat (% of energy)	32.9±0.06	33.2±0.2	0.086
Saturated fat (% of energy)	12.0±0.03	12.2±0.09	0.065
Trans fat (% of energy)	1.6±0.01	1.5±0.02	0.001
Monounsaturated fat (% of energy)	12.6±0.03	12.8±0.09	0.12
Polyunsaturated fat (% of energy)	5.0±0.01	5.0±0.04	0.64
Cholesterol (mg)	249.4±0.9	267.8±2.9	<0.001
Dietary fiber (g)	17.2±0.1	17.1±0.2	0.73
Sodium (mg)	1472±3	1,499±10	0.01
Foods consumption (servings/d)[f]			
Whole grains	1.3±0.01	1.1±0.04	<0.001
Fruits and vegetables	4.0±0.02	4.1±0.06	0.18
High-fat dairy	0.82±0.01	0.87±0.02	0.049

	Incident Heart Failure		
Demographic and lifestyle factors	**No (n=13,013)**	**Yes (n=1,140)**	***P* value**
Eggs	0.29±0.003	0.36±0.01	<0.001
Red meats or processed meats	1.0±0.01	1.1±0.02	<0.001
Fish	0.32±0.003	0.32±0.01	0.50
Nuts	0.37±0.005	0.36±0.02	0.57

[a] Values are mean±standard error, with the exception of triglyceride concentrations, which were analyzed as natural logs and transformed to the geometric scale for presentation (mean and 95% confidence intervals are presented).

[b] Body mass index calculated as kg/m^2.

[c] CVD=cardiovascular disease.

[d] LDL-C=low-density lipoprotein cholesterol.

[e] HDL-C=high-density lipoprotein cholesterol.

[f] With the exception energy intake, nutrients and food groups are adjusted for total energy intake (kcal/d).

Table 2

Relative risks for heart failure risk according to food group intakes (servings/day) in 15,143 men and women from the Atherosclerosis Risk in Communities Study

	Relative risk (95% confidence interval)[a]
Whole grains	
Model 1: energy-adjusted[b]	0.85 (0.80, 0.90)*
Model 2: energy, demographic, lifestyle, and prevalent disease-adjusted[c]	0.93 (0.87, 0.99)*
Fruits and vegetables	
Model 1	1.01 (0.98, 1.04)
Model 2	1.02 (0.99, 1.05)
High-fat dairy	
Model 1	1.14 (1.06, 1.22)*
Model 2	1.08 (1.01, 1.16)*
Eggs	
Model 1	1.56 (1.40, 1.73)*
Model 2	1.23 (1.08, 1.41)*
Red meat or processed meat	
Model 1	1.27 (1.18, 1.37)*
Model 2	1.07 (0.97, 1.17)
Fish	
Model 1	0.99 (0.82, 1.19)
Model 2	0.99 (0.81, 1.22)
Nuts	
Model 1	0.96 (0.85, 1.09)
Model 2	1.09 (0.97, 1.23)

[a]Values are relative risks (95% confidence interval) representing expected change in risk of heart failure per 1-serving/d difference in food group consumption.

[b]Model 1: Relative risk (95% confidence interval) adjusted for energy intake (kcal/d).

[c]Model 2: Relative risk (95% confidence interval) adjusted for energy intake, plus demographics: age, sex, race/center (whites in Minnesota, whites in Maryland, African Americans and whites in North Carolina, African Americans in Mississippi), education level (up to and including grade school, high school without diploma, high school graduate, vocational school, college graduate, graduate school/professional school) lifestyle factors: physical activity level (sport and exercise activity and nonsport activity during leisure), smoking (status and cigarette years), and drinking status (current, former, never), and prevalent disease status: cardiovascular disease, diabetes, and hypertension (present/absent).

*$P<0.05$.