Fish Intake and Risk of Incident Heart Failure

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OBJECTIVES

Our aim was to investigate the relation between fish consumption and incidence of congestive heart failure (CHF).

BACKGROUND

The incidence and health burden of CHF are rising, particularly in older persons. Although n-3 fatty acids have effects that could favorably influence risk of CHF, the relation between fish intake and CHF incidence is unknown.

METHODS

Among 4,738 adults age ≥65 years and free of CHF at baseline in 1989–90, usual dietary intake was assessed using a food frequency questionnaire. In a participant subsample, consumption of tuna or other broiled or baked fish, but not fried fish, correlated with plasma phospholipid n-3 fatty acids. Incidence of CHF was prospectively adjudicated.

RESULTS

During 12 years' follow-up, 955 participants developed CHF. In multivariate-adjusted analyses, tuna/other fish consumption was inversely associated with incident CHF, with 20% lower risk with intake 1 to 2 times/week (hazard ratio [HR] = 0.80, 95% confidence interval [CI] = 0.64 to 0.99), 31% lower risk with intake 3 to 4 times/week (HR = 0.69, 95% CI = 0.52 to 0.91), and 32% lower risk with intake ≥5 times/week (HR = 0.68, 95% CI = 0.45 to 1.03), compared with intake <1 time/month (p trend = 0.009). In similar analyses, fried fish consumption was positively associated with incident CHF (p trend = 0.01). Dietary long-chain n-3 fatty acid intake was also inversely associated with CHF (p trend = 0.009), with 37% lower risk in the highest quintile of intake (HR = 0.73, 95% CI = 0.57 to 0.94) compared with the lowest.

CONCLUSIONS

Among older adults, consumption of tuna or other broiled or baked fish, but not fried fish, is associated with lower incidence of CHF. Confirmation in additional studies and evaluation of potential mechanisms is warranted. (J Am Coll Cardiol 2005;45:2015–21) © 2005 by the American College of Cardiology Foundation

Congestive heart failure (CHF) is a growing clinical and public health problem. In the U.S., nearly 5 million individuals have CHF, more than 500,000 new cases are diagnosed yearly, and CHF health care costs exceed \$28 billion annually (1). Congestive heart failure is particularly common with advancing age (2) and is the leading cause of hospitalization among adults age ≥65 years (3). Among older adults, CHF incidence is ~2% per year (4) and predicts three to six times higher mortality (5). Identification of measures for preventing CHF, particularly among older individuals, is therefore of considerable clinical and public health importance.

In experimental studies, fish oil favorably affects hemodynamics (6), inflammation (7), vascular responses (8–10), and left ventricular (LV) indices (11–17), each of which could reduce risk of CHF. In cross-sectional analyses (18),

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intake of tuna or other broiled or baked fish is inversely associated with systolic blood pressure, C-reactive protein levels, and carotid intimal medial thickness, whereas fried fish intake is positively associated with systolic blood pressure and carotid intimal medial thickness, all independent risk factors for CHF (4). However, although the relation between fish intake and coronary heart disease risk has been investigated (19), little is known regarding relation of fish intake, or indeed, any dietary factor, with incidence of CHF in humans.

We investigated associations between fish consumption and incidence of CHF in the Cardiovascular Health Study, a population-based cohort study of determinants of cardiovascular disease among adults age ≥65 years. Our hypothesis was that consumption of tuna and other broiled or baked fish, but not fried fish, would be associated with a lower incidence of CHF.

METHODS

Design and population. In 1989 to 1990 and 1992, 5,888 men and women age ≥65 years were randomly selected and enrolled from Medicare eligibility lists in four U.S. communities (20,21). Baseline evaluation included health status, medical history, physical examination, electrocardiography, echocardiography, carotid ultrasonography, pulmonary function testing, and laboratory testing (2,4,5,20–22). We excluded 687 participants enrolled in 1992 (a food frequency questionnaire [FFQ] was not administered in 1992), 105

Abbreviations and Acronyms

CHF = congestive heart failure

CHS = Cardiovascular Health Study

CI = confidence interval DHA = docosahexaenoic acid

EPA = eicosapentaenoic acid

FFQ = food frequency questionnaire

HR = hazard ratio LV = left ventricular

participants with incomplete data on fish consumption, and 358 participants with baseline CHF (22) or abnormal LV ejection fraction (<45%) (5) (final n = 4,738). Each center's institutional review committee approved the study, and all subjects gave informed consent.

Dietary assessment. A picture-sort FFQ was administered at baseline to assess usual dietary intake of tuna fish, other fish (broiled or baked), and fried fish or fish sandwiches (fried fish burgers) (18,23). For each type, participants reported their usual intake during the past year, with response categories ranging from ≤ 4 times a year to ≥ 5 times/week. For most nutrients, the midpoint of each category was used to sum intakes of different items. On the basis of detailed assessments of fish consumption performed in a separate cohort (24) (D. Siscovick, personal communication, October 18, 2004), the median fish intakes for the two highest response categories were calculated to be slightly less than the category midpoint; this had no effect on the relative ranking of participants' fish intakes or the estimates of relative risk among participants, but likely better estimated the absolute fish intake for each participant. We have shown that as a biomarker of fish oil content, plasma phospholipid levels of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) correlate with intake of tuna fish (Spearman correlation [r] = 0.35, p < 0.01), other fish (r = 0.59, p < 0.001), and combined tuna/other fish (r = 0.59, p < 0.001), and combined tuna/other fish (r = 0.59), and combined tuna/other fish (r = 0.59), and combined tuna/other fish (r = 0.59). = 0.55, p < 0.001), but not fried fish (r = 0.04, p = 0.78) (19). Dietary EPA + DHA was calculated from FFQ responses using estimates for each fish serving (3 to 5 oz) (25), including shellfish, and U.S. commercial landings data (26); this estimate correlated with plasma phospholipid EPA + DHA levels (r = 0.52, p < 0.001, n = 65).

Ascertainment of CHF. Potential cases of CHF were identified from annual examinations, six-month phone contacts, and hospitalization discharge summaries. Incident cases were centrally adjudicated using interviews, outpatient records, discharge summaries, history and examination data, and review of relevant diagnostic tests and consultations (4,27). Confirmation of a diagnosis of CHF required each of the following: 1) CHF symptoms (shortness of breath, fatigue, orthopnea, paroxysmal nocturnal dyspnea) and signs (edema, rales, tachycardia, gallop rhythm, displaced apical impulse) or clinical findings (such as on echocardiography, contrast ventriculography, or chest radiography); 2) diagnosis of CHF by a treating physician; and 3) medical therapy

for CHF (diuretics and either digitalis or a vasodilator [nitroglycerin, hydralazine, angiotensin-converting enzyme inhibitor]).

Analysis. Kaplan-Meier methods were used to evaluate CHF-free survival. Risk was estimated using Cox proportional hazards (time at risk until first event, death, or latest follow-up through June 30, 2001), with covariates based on clinical interest, associations with incident CHF (4), or associations with exposures/outcomes in the present analysis. The final model included age; gender; race; enrollment site; education; diabetes; body mass index; prevalent coronary heart disease; prevalent stroke/transient ischemic attack; and intakes of tuna/other fish, fried fish, and total calories. A second model was further adjusted for other behavioral and lifestyle factors including smoking; leisuretime physical activity; and intakes of saturated fat, fruits, vegetables, and alcohol. We also evaluated for potential mediation or confounding by levels of systolic blood pressure, diastolic blood pressure, baseline LV systolic function, low-density lipoprotein, high-density lipoprotein, triglycerides, and C-reactive protein. For parsimony in model construction, we excluded from the final models other covariates that did not materially alter relations between fish consumption and CHF risk, including annual income; treated hypertension; exercise intensity; forced expiratory volume in 1 s; carotid intimal medial thickness; atrial fibrillation; M-mode echocardiography-estimated LV mass; use of aspirin, beta-blockers, lipid-lowering medication, fish oil, and estrogen; serum fasting glucose, insulin, creatinine, and fibrinogen; and estimated intakes of total fat, carbohydrates, protein, linolenic acid, fiber, beef/pork, wine, thiamine, and vitamin C. Missing covariate values (typically <1%) were imputed using age, race, gender, diabetes, and prevalent cardiovascular disease; analyses using population medians or excluding missing data were not appreciably different. Tests for trend were evaluated with intake categories entered as ordinal variables. Potential effect modification was assessed using stratified analyses and likelihoodratio testing (exposure times covariate term). Analyses were performed using Stata 8.0 (D.M.) (Stata Corp., College Station, Texas), with two-tailed alpha = 0.05.

RESULTS

Mean participant age was 73 years at baseline. Median fried fish and tuna/other fish consumption were 0.5 and 1.0 servings/week, respectively. Tuna/other fish consumption was associated with younger age, female gender, higher education, and generally a more favorable cardiovascular risk profile, although higher intake was also associated with greater body mass index and higher low-density lipoprotein cholesterol (Table 1). Tuna/other fish consumption was positively associated with intakes of fruits, vegetables, alcohol, and total energy and inversely associated with saturated fat intake. Fried fish consumption was associated with male gender, non-white race, lower education, a generally less

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