CLINICAL RESEARCH STUDY

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Total Antioxidant Capacity of Diet and Risk of Heart Failure: A Population-based Prospective Cohort of Women

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ABSTRACT

BACKGROUND: Few studies have investigated the association between individual antioxidants and risk of heart failure. No previous study has investigated the role of all antioxidants present in diet in relation to heart failure. The aim of this study was to assess the association between total antioxidant capacity of diet, which reflects all of the antioxidant compounds in food and the interactions between them, and the incidence of heart failure among middle-aged and elderly women.

METHODS: In September 1997, 33,713 women (aged 49-83 years) from the Swedish Mammography Cohort completed a food-frequency questionnaire. Estimates of dietary total antioxidant capacity were based on the Oxygen Radical Absorbance Capacity assay measurements of foods. Women were followed for incident heart failure (hospitalization or mortality of heart failure as the primary cause) through December 2009 using administrative health registries. Cox proportional hazard models were used to calculate relative risks and 95% confidence intervals.

RESULTS: During 11.3 years of follow-up (394,059 person-years), we identified 894 incident cases of heart failure. Total antioxidant capacity of diet was inversely associated with heart failure (the multivariable-adjusted relative risk in the highest quintile compared with the lowest was 0.58 [95% confidence interval, 0.47-0.72; P for trend $< .001$]). The crude incidence rate was 18/10,000 person-years in the highest quintile versus 34/10,000 person-years in the lowest quintile.

CONCLUSIONS: The total antioxidant capacity of diet, an estimate reflecting all antioxidants in diet, was associated with lower risk of heart failure. These results indicate that a healthful diet high in antioxidants may help prevent heart failure.

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KEYWORDS: Antioxidants; Diet; Epidemiology; Heart failure

Heart failure has many causes, including structural and functional cardiac abnormalities, elevated blood pressure, diabetes mellitus, and ischemic heart disease.[1] Recent research has suggested that oxidative stress also may increase the risk of heart failure.[2-4] High concentrations of reactive oxygen and nitrogen species may promote cardiovascular disease through oxidation of lipids, damage to the endothelium, and decrease in the bioavailability of the vasodilator nitric oxide.[5-8]

There are limited studies on whether antioxidants may help prevent heart failure. One recent study observed that plasma vitamin C, an antioxidant that reflects fruit and vegetable consumption, was inversely associated with heart failure.[9] Consistency with the Dietary Approaches to Stop Hypertension dietary pattern, which includes a high intake of fruits, vegetables, and whole grains, was associated with a lower risk of heart failure events.[10] Trials of antioxidant supplementation have not shown benefits for cardiovascular disease and, in some cases, have even demonstrated harm.[11-14]

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However, these trials provided high doses of single or 2 to 3 antioxidants separated from the context of other food components.

No previous study has investigated the overall effect of antioxidants present in diet on heart failure. The total antioxidant capacity reflects all of the antioxidant compounds present in food and the interactions between those compounds.[15] The total antioxidant capacity of diet has been inversely associated with cardiovascular diseases, such as myocardial infarction[16] and stroke.[16,17]

We examined the association between the total antioxidant capacity of diet estimated as the sum of the total antioxidant capacity contributed by foods and beverages[15] and incidence of heart failure (including both hospitalization and mortality due to heart failure as the primary cause) in a prospective population-based study of middle-aged and elderly Swedish women.

CLINICAL SIGNIFICANCE

- This is the first study aiming to investigate the association between all antioxidants present in the diet and heart failure.
- Total antioxidant capacity aims to give an estimate of all present antioxidants and the synergistic effects between them.
- A diet high in total antioxidant capacity, based on fruits, vegetables, coffee, and whole grains, was associated with a lower rate of heart failure among 33,713 middle-aged and elderly women.

MATERIALS AND METHODS

Study Population

The Swedish Mammography Cohort was established between 1987 and 1990 among women residing in Uppsala and Västmanland counties in central Sweden. All women born in 1914 to 1948 received a mailed questionnaire concerning diet, educational level, weight and height, and reproductive factors; 74% completed the questionnaire. To expand exposure data, a new questionnaire was sent in 1997 to all 56,030 eligible cohort members. The 1997 questionnaire included questions not only on diet but also on vitamin supplement use; cigarette smoking; alcohol consumption; physical activity; weight; height; diagnosis of hypertension, hypercholesterolemia, or diabetes (complemented with information from diabetes registers); and family history of myocardial infarction. Because more information on risk factors for heart failure was collected on the second questionnaire, which was completed by 38,984 women (70%), the 1997 questionnaire served as the baseline in the present study. The study complies with the Declaration of Helsinki and was approved by the Regional Ethical Review Board at Karolinska Institutet, Stockholm, Sweden. Completion and return of the self-administered questionnaire were taken to imply consent.

We excluded women with a diagnosis of cancer (except nonmelanoma skin cancer), myocardial infarction, angina pectoris, stroke, and congestive heart failure (identified through the Swedish Hospital Discharge Registry and the Swedish Cancer Registry) before the baseline in 1997 (n = 4873). These women were excluded because the diagnoses may affect dietary intake and development of heart failure. We also excluded 442 women reporting extreme total energy intake (>3 standard deviations from the mean value for $\log_e$-transformed energy). The remaining cohort of 33,713 women was followed from September 15, 1997, to December 31, 2009.

Food-frequency Questionnaire-based Total Antioxidant Capacity Estimates

Women completed a 96-item food-frequency questionnaire that asked how often, on average, they had consumed each type of food or beverage during the last year. There were 8 predefined response categories, ranging from "never/seldom" to "3 or more times per day." Open-ended questions were used for foods and beverages commonly consumed (eg, bread, coffee, and tea). The calculation of total antioxidant capacity estimates has been described in detail,[15] and the methods are briefly summarized in this article. We constructed total antioxidant capacity estimates by using a database of the foods in the United States analyzed with the Oxygen Radical Absorbance Capacity (ORAC) assay.[18,19] This assay measures the inhibition of peroxyl radical–induced oxidation by the test sample and is expressed as μmol Trolox equivalent (TE)/100 g; Trolox is a potent antioxidant derived from vitamin E.[19] The total antioxidant capacity of diet was calculated by multiplying the average frequency of consumption of each food by ORAC content (μmol TE/100 g) of age-specific portion sizes. Overall, in the 96-item food-frequency questionnaire there were 31 items (17 fruit and vegetable items) with ORAC values. Total antioxidant capacity of diet was adjusted for total energy intake with the residual method.[20] Because antioxidants in coffee and tea have been shown to be poorly absorbed, we took into account absorption (6% for coffee and 4% for tea)[21] when calculating total antioxidant capacity of diet. The Pearson correlation coefficient between total antioxidant capacity of diet (taking into account absorption) and plasma ORAC was 0.31.[22]

Identification of Cases and Follow-up of the Cohort

Incident cases of heart failure hospitalization (n = 769) and heart failure mortality (n = 125) (International Statistical Classification of Disease, 10th Revision code I21 as the primary diagnosis) between September 1997 (baseline) and December 2009 were ascertained through linkage via the national registration number to Swedish Hospital Discharge Registry and the Cause of Death Registry, which are considered to be nearly complete. Previous studies found that