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ORIGINAL CONTRIBUTION

Serum taurine and risk of coronary heart disease: a prospective, nested case–control study

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Abstract
Purpose Taurine (2-aminoethanesulfonic acid), a molecule obtained from diet, is involved in bile acid conjugation, blood pressure regulation, anti-oxidation and anti-inflammation. We performed the first prospective study of taurine and CHD risk.
Methods We conducted a case–control study nested in the New York University Women's Health Study to evaluate the association between circulating taurine levels and risk of coronary heart disease (CHD). Taurine was measured in two yearly pre-diagnostic serum samples of 223 CHD cases and 223 matched controls and averaged for a more reliable measurement of long-term taurine levels.
Results Mean serum taurine was positively related to age and dietary intake of poultry, niacin, vitamin B1, fiber and iron, and negatively related to dietary intake of saturated fat (all p values ≤ 0.05). There was no statistically significant association between serum taurine levels and the risk of CHD in the overall study population. The adjusted ORs for CHD in increasing taurine tertiles were 1.0 (reference), 0.85 (95% CI, 0.51–1.40) and 0.66 (0.39–1.13; p for trend = 0.14). There was a significant inverse association between serum taurine and CHD risk among women with high total serum cholesterol (>250 mg/dL) (adjusted OR = 0.39 (0.19–0.83) for the third versus first tertile; p for trend = 0.02) but not among those with low total serum cholesterol (p for interaction = 0.01). The data suggest a possible inverse association of serum taurine with diabetes and hypertension risk.
Conclusions The findings suggest that high levels of taurine may be protective against CHD among individuals with high serum cholesterol levels.

Keywords Taurine · Serum · Coronary heart disease · NYUWHS · Epidemiology

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Introduction

Coronary heart disease (CHD) is the leading killer of American men and women causing one in five deaths [1]. Large prospective epidemiologic studies have provided evidence that nutritional factors are important modifiable risk factors for CHD. Nutrients such as beta carotene, folate, fiber, and vitamins A, B, and C have been shown to be beneficial to the cardiovascular system [2, 3]. Identification of novel dietary protective factors may improve the understanding, control, and prevention of CHD.

Taurine (2-aminoethanesulfonic acid) is a sulfur-containing molecule obtained mainly through diet in humans,

with miniscule amounts made endogenously. Interest in the health effects of taurine originated from human [4, 5] studies in which intakes of foods rich in sulfur-containing amino acids, such as fish, were inversely associated with the risk of hypertension and cardiovascular disease (CVD). In vitro and animal studies have suggested that taurine is involved in a variety of biological processes, including bile salt conjugation, osmoregulation, blood pressure regulation, and anti-oxidation [6]. Ecological analyses from the WHO Cardiovascular Diseases and Alimentary Comparison (WHO-CARDIAC), a multicenter cross-sectional study, have reported an inverse correlation between group means of urinary excretion of taurine, a surrogate of taurine intake, and mortality rates due to ischemic heart disease (IHD) in both men [7] and women [8]. However, the observed correlations could be the result of ecologic fallacy because factors associated with disease rates at the group level may not be associated with disease at the individual level [9]. In addition, the correlations may be confounded by unmeasured factors related to both taurine intake and IHD at the individual level. Several clinical trials, ecologic studies, and cross-sectional studies have reported that taurine can lower cholesterol [5, 10, 11] and blood pressure [5, 10, 12, 13]. However, these studies were limited in sample size, short in the duration of follow-up, and/or potentially subject to ecologic fallacy [14]. Although taurine has been a popular supplement and ingredient in "energy drinks" in recent years, to date, no prospective epidemiologic studies have evaluated the association between taurine intake and the risk of CHD.

We conducted a prospective case–control study nested in the New York University Women's Health Study (NYUWHS) to evaluate whether a high concentration of serum taurine is protective against CHD risk. We also assessed the distribution and correlates of serum taurine as well as the associations between serum taurine and risk factors for CHD.

Methods

New York University Women's Health Study (NYUWHS)

Details of the NYUWHS have been described elsewhere [15]. Briefly, a total of 14,274 women, 34–65 years of age, were enrolled between 1985 and 1991 at a breast cancer screening center in New York City. At the time of enrollment, demographic, medical and lifestyle information was collected using a self-administered questionnaire. Active follow-up of the cohort is conducted with questionnaires mailed approximately every 2–4 years. Lost participants are located using the National Change of Address database of the US Postal Service, the Choice Point credit bureau database, internet-based resources, primarily telephone directories and the Social Security Death Index, the National Death Index (NDI), and telephone calls to contacts. The response rate for the last round of follow-up, completed in 2006, was 83% of the original cohort members.

Physical activity at baseline was assessed in two follow-up questionnaires in which participants were directed to report their activity levels during the baseline period. Cases of hypertension and diabetes were identified using self-report information on physician-diagnosis of the condition, and/or medicine use for these conditions collected at baseline and in all follow-up questionnaires.

Dietary information for the year prior to cohort enrollment was collected at baseline using a self-administered food frequency questionnaire (FFQ) of 70 typical American food items. The questionnaire was similar to the validated Block FFQ [16], with minor modifications to the food list. Details of the dietary assessment in the NYUWHS, including its reproducibility, have been described elsewhere [17]. Daily nutrient intakes were calculated using food composition tables elaborated at the National Cancer Institute [16], with minor modifications.

Non-fasting blood was collected at enrollment, centrifuged, and the serum was stored at −80 °C for subsequent analysis. Fifty-one percent of the participants ($n = 7{,}344$) gave blood at more than one visit at yearly intervals. Compared with women who gave blood once, women who donated blood two or more times were older (mean age 53.4 vs. 49.3 years old) and more likely to be of European descent (81% vs. 77%). Distributions of body mass index (BMI), education, smoking status, and multivitamin use were similar in the two groups (data not shown).

The study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the IRB of New York University School of Medicine. Written informed consent was obtained from all subjects at the time of enrollment.

Ascertainment of CHD endpoints

In each follow-up round of the NYUWHS, participants who reported a CHD event were contacted for further information, including authorization to obtain their medical records. CHD cases were ascertained and verified based on medical chart review and NDI. CHD cases included women who had documented non-fatal or fatal MI, fatal CHD, or surgery to remedy restricted blood flow including coronary artery bypass grafting (CABG) and percutaneous transluminal coronary angioplasty (PTCA). Fatal CHD was classified when: (1) fatal MI was the finding at autopsy, or (2) the underlying cause of death from the NDI was CHD (ICD9 codes 410–414 or ICD10 codes I20–I25), provided

that during previous follow-up there was evidence from questionnaires or medical records of pre-existing CHD. Non-fatal MI was confirmed if it met the World Health Organization criteria of symptoms [18] for either diagnostic electrocardiographic changes or elevated levels of cardiac enzymes.

Nested case–control study design and subject selection

In a pilot study [19], we determined that the mean of two yearly measurements would provide an estimate of the long-term taurine serum concentration with temporal reliability similar to that of other biomarkers in epidemiologic studies [20, 21], i.e., an intraclass correlation coefficient of 0.65. We, therefore, selected the first 223 CHD cases (1986–2006) from NYUWHS participants who had donated blood ≥2 times during follow-up visits, and who had no history of CVD at the time of blood donation. For each CHD case, one control was selected at random from the NYUWHS subjects who were alive and free of CVD at the date of the coronary event of the case. Cases and controls were matched on age at baseline (±6 months), menopausal status (pre- and postmenopausal), total number of blood donations (2 or >2), and the dates of both blood donations (±6 months).

Analysis of serum taurine, total cholesterol, and HDL-cholesterol

Laboratory personnel were blinded to the identity and case–control status of study participants. Taurine was determined using a high performance liquid chromatography (HPLC) (Waters, Millford, MA) with pre-column derivitization using o-phthaldialdehyde (Sigma-Aldrich HPLC) and 3-mercaptopropionic acid (Fluka Biochemika) with fluorescence detection. The reagents, sample preparation, and derivitization methods were slightly modified from a previously published protocol [22] as previously described [19]. The coefficient of variation (CV) was 7.3%.

Total cholesterol and HDL-cholesterol measurements were performed by Pacific Biometrics Incorporated, in Seattle, Washington. Total cholesterol was measured using CDC-standardized enzymatic assay with a Trinder end-point reaction. HDL-cholesterol was measured using dextran sulfate precipitation [23] followed by an enzymatic in-house method similar to that used by the CDC Cholesterol Reference Method Laboratory [24].

Statistical analysis

The distribution of baseline characteristics and established CHD risk factors in CHD cases and controls were compared using conditional logistic regression model, which takes into account the matching factors [25]. The mean of the serum taurine in the two, yearly, samples was the main exposure variable and for simplicity is referred to as serum taurine from here on.

To investigate determinants of serum taurine, linear regression models were used with serum taurine as the dependent variable and participants' characteristics as the independent variables. Pearson partial correlation coefficients (r) were used to quantify the association between serum taurine and consumption of food groups and intakes of macro- and micronutrients, adjusting for variables that may be associated with intakes of taurine and other dietary factors, i.e., age, CHD status, BMI, and total calories. The nutrients of interest were those relevant to CHD risk [2, 26–30]. Nutrient intakes estimated from the FFQ were energy-adjusted using the residual method [31]. Dietary data from participants who reported unreasonable total caloric intake of less than 500 ($n = 9$) or greater than 3,500 calories per day ($n = 10$) were excluded. Serum taurine and dietary intakes were log-transformed to improve the normality of their distributions. The analyses were also conducted in controls only.

To evaluate the association between serum taurine and CHD risk, we estimated odds ratios (ORs) and 95% confidence intervals (CIs) for CHD in relation to tertiles of serum taurine using conditional logistic regression. Cutoff points for tertiles were determined based on the distribution of serum taurine in cases and controls combined. ORs were first adjusted for BMI, smoking status, and serum total cholesterol, which are all major risk factors for CHD. ORs were further adjusted for total calories and potential confounders related to both CHD risk and serum taurine in our data, i.e., energy-adjusted intakes of saturated fat, folate, fiber, and potassium. Tests for linear trend were conducted using an ordered variable for tertile categories of serum taurine.

To examine whether the association between serum taurine and CHD differs by established risk factors for CHD, analyses were stratified by BMI (≤ and > median, i.e., 25 kg/m^2), smoking status (never/ever), and total serum cholesterol (≤ and > median, i.e., 250 mg/dL). Multiplicative interaction was tested using a cross-product term representing the product of a potential effect-modifier and serum taurine.

To assess whether a high concentration of pre-diagnostic serum taurine is protective against subsequent occurrence of hypertension or diabetes, we conducted unconditional logistic regression analyses in cases and controls combined as well as in controls only. Prevalent cases of diabetes or hypertension at baseline were excluded from the respective analyses. All analyses were completed using SAS (version 9.2; SAS Institute Inc, Cary, NC).

Table 1 Baseline characteristics of CHD cases and controls, and geometric mean of average taurine

Baseline characteristics	*n* (%) or median (10th and 90th percentiles) Cases ($n = 223$)	*n* (%) or median (10th and 90th percentiles) Controls ($n = 223$)	*p* value	Geometric mean of taurine[a] (nmol/mL) $n = 446$	*p* value
Age at baseline (years)					
<55	64 (28.7)	66 (29.6)	Matched	117.7	<0.01
55–59	62 (27.8)	61 (27.4)		127.8	
≥60	97 (43.5)	96 (43.0)		132.2	
Continuous	58.9 (47.2–64.2)	58.6 (47.1–64.3)			
Menopausal status at enrollment					
Pre-menopausal	45 (20.2)	45 (20.2)	Matched	126.7	0.98
Postmenopausal	178 (79.8)	178 (79.8)		126.6	
Length of sample storage time (years)					
Continuous	22.7 (21.7–23.5)	22.7 (21.7–23.5)	Matched		
Race					
Caucasian	182 (86.6)	178 (84.4)	0.73	126.7	0.75
African–American	17 (8.1)	17 (8.1)		128.2	
Hispanic	5 (2.4)	10 (4.7)		123.8	
Other	6 (2.9)	6 (2.8)		123.7	
Education[b]					
≤High school	85 (41.9)	79 (39.1)	0.37	127.0	0.92
Some college or equivalent	62 (30.5)	45 (22.3)		123.2	
College degree	56 (27.6)	78 (38.6)		127.7	
BMI (kg/m^2)					
≤25	97 (43.5)	126 (56.5)	0.01	127.5	0.51
25.1–30	83 (37.2)	68 (30.5)		126.2	
>30	43 (19.3)	29 (13.0)		124.9	
Continuous	25.8 (21.6–32.3)	24.2 (20.2–30.9)	<0.01		
Physical activity (MET-h/week)					
0	13 (6.0)	7 (3.2)	0.70	140.2	0.60
>0–10	91 (42.2)	101 (46.8)		125.5	
>10–20	42 (19.4)	34 (15.7)		123.8	
>20	70 (32.4)	74 (34.3)		129.0	
Continuous	11.0 (0.6–48.1)	10.3 (0.8–54.8)	0.74		0.52
Smoking status					
Never	87 (40.1)	103 (48.6)	0.34	125.0	0.44
Past	50 (23.0)	32 (15.1)		126.4	
Current	80 (36.9)	77 (36.3)		127.6	
Parental history of heart attack					
Yes	90 (46.2)	74 (39.6)	0.01	125.2	0.25
No	105 (53.9)	113 (60.4)		128.9	
Prevalent hypertension					
Yes	60 (26.9)	32 (14.4)	<0.01	121.7	0.15
No	163 (73.1)	191 (85.6)		128.1	
Serum total cholesterol (mg/dL)					
<200	16 (7.2)	34 (15.2)	<0.01	125.2	0.15
200–239	58 (26.1)	80 (35.9)		124.4	
240–269	62 (27.9)	50 (22.4)		125.0	
≥270	86 (38.7)	59 (26.5)		130.5	
Continuous	257.0 (206.0–312.0)	239.0 (188.0–297.0)	<0.01		0.10

Table 1 continued

Baseline characteristics	*n* (%) or median (10th and 90th percentiles) Cases ($n = 223$)	*n* (%) or median (10th and 90th percentiles) Controls ($n = 223$)	*p* value	Geometric mean of taurine[a] (nmol/mL) $n = 446$	*p* value
Serum HDL-cholesterol (mg/dL)					
<50	30 (13.5)	15 (6.7)	<0.01	123.6	0.70
50–59	130 (58.3)	112 (50.2)		128.5	
≥60	63 (28.3)	96 (43.1)		124.8	
Continuous	52.0 (38.0–73.0)	57.0 (41.0–76.0)	<0.01		
Serum taurine (nmol/mL)					
1st Measurement	127.4 (80.0–180.1)	128.9 (85.6–173.2)	0.33	–	–
2nd Measurement	131.3 (87.0–195.0)	130.7 (89.1–183.1)	0.84		
Average of 1st and 2nd measurement	126.9 (92.5–173.0)	130.1 (93.3–165.7)	0.65		

p values for *n* or the median were obtained from conditional logistic regression excluding those with missing information. Variables with categories were entered as ordered categorical

Average of two yearly measurements was used to calculate the geometric mean

p values for the geometric mean of taurine were obtained from linear regression with taurine as the dependent variable adjusted for age. Variables with categories were entered as ordered categorical

[a] Geometric mean adjusted for age (except for age variable)

[b] Data were missing on education for 21 cases and 21 controls; on race for, respectively, 13 and 12 subjects; on physical activity for 7 and 7 subjects; on parental history of CVD for 28 and 36 subjects; on smoking status at baseline for 6 and 11 subjects; and on total serum cholesterol for 1 case (this was an outlier)

Results

Serum samples were stored for an average of 22.7 years. At the time of baseline blood donation, the median age of the study participants was 58, and CHD events occurred at an average age of 70 years. Compared with controls, cases had a significantly higher BMI, and were more likely to have a parental history of heart attack, to be hypertensive, and to have a higher total serum cholesterol as well as a lower serum HDL-cholesterol at baseline (*p* values <0.05) (Table 1). There were no differences between CHD cases and controls by race, level of education, physical activity, or smoking status. The median of serum taurine was similar in cases and controls (126.9 nmol/mL and 130.1 nmol/mL, respectively, $p = 0.65$). The geometric mean of taurine differed significantly by age at baseline ($p < 0.01$) (Table 1). There were no significant associations between all other baseline characteristics and serum taurine, with *p* values ranging from 0.15 to 0.98.

Serum taurine was significantly negatively associated with dietary intake of saturated fat ($r = -0.10$) and positively related to dietary intakes of niacin ($r = 0.11$), vitamin B1 ($r = 0.11$), iron ($r = 0.10$), and fiber ($r = 0.10$) (Table 2). Of the food groups, consumption of poultry was significantly positively associated with serum taurine ($r = 0.14$). There was no apparent correlation between serum taurine and other dietary factors. These correlations were similar among the controls (data not shown).

Overall, there was no statistically significant association between the risk of CHD and serum taurine levels (Table 3). The adjusted ORs for CHD associated with increasing tertiles of serum taurine were 1.0 (reference), 0.85 (95% CI, 0.51–1.40), and 0.66 (0.39–1.13), respectively, (*p* for trend = 0.14), adjusting for BMI, smoking, and total cholesterol.

The association between serum taurine and CHD risk did not differ appreciably according to baseline BMI (*p* for interaction = 0.27) (Table 3). Although the inverse association was stronger among never smokers (*p* for trend = 0.09) than among ever smokers (*p* for trend = 0.77), there was no statistical evidence of interaction on the multiplicative scale (*p* for interaction = 0.25). Among women with high total serum cholesterol (>250 mg/dL), those in the highest two tertiles of serum taurine were less likely to develop CHD than those in the lowest tertile (OR = 0.31 (0.15–0.67 and 0.39 (0.19–0.83) for second and third tertile, respectively). There was no association between serum taurine and CHD risk in women with low cholesterol level (*p* for interaction = 0.01). Further adjustment for total calories and energy-adjusted intakes of saturated fat, folate,

Table 2 Pearson partial correlation coefficient of log (average taurine) and log dietary variables

Dietary variables	Pearson partial correlation coefficient[a]	*p* value
Macronutrients[b]		
Total calories (kcal/day)	−0.02	0.68
Saturated fat (g/day)	−0.10	0.04
Carbohydrates (g/day)	0.06	0.20
Total fat (g/day)	−0.06	0.24
Cholesterol (mg/day)	−0.04	0.42
Protein (g/day)	0.02	0.69
Micronutrients[b]		
Niacin (mg/day)	0.11	0.03
Vitamin B1 (mg/day)	0.11	0.03
Fiber (g/day)	0.10	0.05
Iron (mg/day)	0.10	0.05
Folate (μg/day)	0.09	0.06
Potassium (mg/day)	0.08	0.12
Vitamin E (mg/day)	0.05	0.27
Phosphorus (mg/day)	0.06	0.24
Oleic acid (g/day)	−0.05	0.31
Linoleic acid (g/day)	0.04	0.40
Vitamin B2 (mg/day)	0.04	0.42
Vitamin C (mg/day)	0.03	0.48
Vitamin A (IU/day)	0.03	0.49
Carotene (μg/day)	0.01	0.86
Retinol (μg/day)	<−0.01	0.92
Sodium (mg/day)	<−0.01	0.95
Calcium (mg/day)	−0.01	0.93
Food groups (g/day)		
Poultry	0.14	<0.01
Shellfish and mollusks (oysters, clams, shrimp)	−0.11	0.06
Fruit	0.06	0.24
Vegetables	0.05	0.34
Meat	−0.03	0.51
Fish	0.01	0.86

[a] All partial Pearson correlations were adjusted for CHD case/control status, age, BMI and log(total calories) except for the correlation with "total calories" which was not adjusted for log(total calories). Participants with caloric intake <500 and >3,500 were excluded

[b] All macro- and micronutrients were log-transformed and energy-adjusted using the residual method

fiber, and potassium did not materially change the effect estimates for main effect and interaction analyses (data not shown).

Lastly, we evaluated the associations of serum taurine with the risk of hypertension and diabetes, excluding prevalent cases at baseline. Serum taurine was significantly lower among women who developed hypertension (123.0 nmol/mL) compared with those who did not (130.2 nmol/mL, $p = 0.04$). In logistic regression models, serum taurine was inversely associated with the risk of hypertension, although the association was not statistically significant (Table 4). Among controls, the association between serum taurine and hypertension risk was significant, with a 45–60% reduction in the risk of hypertension for women in the highest two tertiles of serum taurine compared with those in the first tertile (OR = 0.65 (0.29–1.46) and 0.40 (0.17–0.97) for second and third tertile, respectively, (p for trend = 0.04)). Serum taurine was lower among women who developed diabetes (118.5 nmol/mL) compared with those who did not (127.5 nmol/ml, $p = 0.07$). There was also a non-significant inverse association between serum taurine and risk of diabetes (Table 4). The analysis regarding diabetes risk was not conducted in controls only due to the limited numbers of diabetes cases.

Discussion

To the best of our knowledge, this is the first prospective study to examine the relationship between serum taurine and CHD risk. Overall, there was no statistically significant association between the risk of CHD and serum taurine levels (p for trend = 0.14). We found a significant inverse association between serum taurine and CHD risk among women with higher serum total cholesterol, which was not observed in women with lower serum total cholesterol.

Although we measured serum taurine in two yearly serum samples to reduce the potential misclassification of taurine levels, it remains possible that taurine has a small effect on CHD risk that could not be detected in the present study, given the sample size of the study. In addition, it is possible that the beneficial effects of taurine on CHD risk may be exerted at a much higher level of taurine intake. In clinical trials of taurine and blood pressure [10, 11, 13], taurine was given at 3–6 g/day, much higher than the typical daily intake of 40–400 mg/day [32, 33].

Our data suggest that cholesterol level may modify the effect of taurine on CHD risk. Taurine may be protective against CHD risk in the presence of adverse effects associated with high cholesterol level. There is evidence linking hypercholesterolemia with increased generation of reactive oxygen species, leading to high levels of circulating oxidized LDL [34] and pro-inflammatory cytokines [35], and numerous cellular and animal studies have demonstrated that taurine has antioxidant and anti-inflammatory properties. Taurine supplementation has been shown to significantly attenuate oxidized LDL-induced cell injury in Sprague–Dawley rats [36]. In spontaneously hyperlipidemic mice, taurine supplementation significantly

Table 3 Association between mean taurine and CHD overall and stratified

	Taurine tertile 1 (35.75–115.00 nmol/mL)	Taurine tertile 2 (115.01–141.71 nmol/mL)	Taurine tertile 3 (141.72–300.31 nmol/mL)	*p* for trend	*p* for interaction
Overall					
Case/control	81/74	73/74	69/75		
Model 1 OR[a] (95% CI)	1.00	0.90 (0.57–1.43)	0.82 (0.50–1.34)	0.42	
Model 2 OR[b] (95% CI)	1.00	0.85 (0.51–1.40)	0.66 (0.39–1.13)	0.14	
BMI < 25					
Case/control	38/45	30/38	29/43		
Model 1 OR[a] (95% CI)	1.00	0.88 (0.45–1.73)	0.77 (0.40–1.48)	0.43	
Model 2 OR[b] (95% CI)	1.00	0.81 (0.40–1.62)	0.64 (0.32–1.28)	0.21	
BMI ≥ 25					0.27
Case/control	43/29	43/36	40/32		
Model 1 OR[a] (95% CI)	1.00	0.84 (0.44–1.60)	0.82 (0.42–1.59)	0.55	
Model 2 OR[b] (95% CI)	1.00	0.81 (0.41–1.58)	0.83 (0.42–1.63)	0.59	
Never smoking					
Case/control	35/34	32/35	20/34		
Model 1 OR[a] (95% CI)	1.00	0.84 (0.42–1.66)	0.54 (0.26–1.13)	0.11	
Model 2 OR[b] (95% CI)	1.00	0.76 (0.38–1.54)	0.51 (0.24–1.09)	0.09	
Ever smoking					0.25
Case/control	45/37	39/35	46/37		
Model 1 OR[a] (95% CI)	1.00	0.93 (0.49–1.77)	1.04 (0.56–1.94)	0.89	
Model 2 OR[b] (95% CI)	1.00	0.83 (0.42–1.74)	0.90 (0.47–1.74)	0.77	
Total cholesterol <250 (mg/dL)					
Case/control	35/56	36/36	29/39		
Model 1 OR[a] (95% CI)	1.00	1.63 (0.86–3.06)	1.19 (0.63–2.27)	0.52	
Model 2 OR[b] (95% CI)	1.00	1.69 (0.89–3.24)	1.19 (0.62–2.30)	0.52	
Total cholesterol ≥250 (mg/dL)					0.01
Case/control	46/18	37/38	40/36		
Model 1 OR[a] (95% CI)	1.00	0.38 (0.18–0.78)	0.45 (0.22–0.93)	0.05	
Model 2 OR[b] (95% CI)	1.00	0.31 (0.15–0.67)	0.39 (0.19–0.83)	0.02	

[a] ORs were calculated using unadjusted logistic regression conditional on the matching factors including age, menopausal status, number and dates of blood donations

[b] ORs were calculated using logistic regression conditional on matching factors with additional adjustment for BMI, smoking, and log (total cholesterol) (except for variable stratified by in stratified analyses)

decreased levels of lipid oxidation and suppressed the development of atherosclerotic lesions [37]. The evidence suggests that taurine may interact with excessive oxidation and inflammation caused by increased cholesterol concentrations, thus reducing the associated CHD risk. Future epidemiologic studies are needed to confirm our findings.

Our study is also the first epidemiologic study to assess the distribution and correlates of serum taurine. Consistent with studies about taurine contents in foods [38–40], we found a significantly positive association between dietary intake of poultry and serum taurine. However, intake of shellfish and mollusks, the foods with the highest concentration of taurine [38–40], was not significantly correlated with serum taurine level. This is most likely the result of infrequent intake of shellfish and mollusks in our study population, with an average intake of only 14 g/week (0.49 oz/week). Our data indicate that poultry intake, with an average consumption of 161 g/week (5.68 oz/week), was the major source of taurine in our study population. The literature indicates that serum and urinary taurine levels are largely determined by dietary taurine intakes, rather than an individual's ethnic or genetic background [5, 41]. However, the content of taurine differs appreciably by type of seafood and cut of meat [14]. Since most of the FFQs, including the one used in our study, do not specify the cut of meat consumed, the association between FFQ-measured dietary food intake and taurine serum level could differ in different populations because of the cuts of meat

Table 4 Association between taurine and incident hypertension and incident diabetes, overall and in controls

	Taurine tertile 1 (35.75–115.00 nmol/mL)	Taurine tertile 2 (115.01–141.71 nmol/mL)	Taurine tertile 3 (141.72–300.31 nmol/mL)	*p* value
Hypertension[a]				
N (yes/no)	45/77	36/77	32/87	
Model 1 OR[b] (95% CI)	1.00	0.78 (0.45–1.35)	0.63 (0.37–1.09)	0.10
Model 2 OR[c] (95% CI)	1.00	0.79 (0.45–1.39)	0.60 (0.34–1.05)	0.07
Diabetes[a]				
N (yes/no)	20/126	10/129	12/129	
Model 1 OR[b] (95% CI)	1.00	0.47 (0.21–1.06)	0.57 (0.26–1.21)	0.13
Model 2 OR[c] (95% CI)	1.00	0.37 (0.16–0.89)	0.50 (0.22–1.11)	0.07
In controls only				
Hypertension[a]				
N CHD controls (yes/no)	14/43	13/49	7/53	
Model 1 OR[b] (95% CI)	1.00	0.69 (0.31–1.53)	0.40 (0.17–0.96)	0.04
Model 2 OR[c] (95% CI)	1.00	0.65 (0.29–1.46)	0.40 (0.17–0.97)	0.04

p value for trend based on taurine tertiles

[a] Prevalent cases of hypertension and diabetes were excluded from the respective analyses

[b] ORs were calculated using unconditional logistic regression adjustment for age

[c] ORs were calculated using unconditional logistic regression adjusted for age, BMI, case/control status and smoking (no case/control adjustment in controls only analysis)

consumed. The potential beneficial effect of taurine on CHD risk among women with high cholesterol found in the study, if confirmed, may reinforce the role of poultry as part of healthy diet for preventing CHD.

Serum taurine's negative association with saturated fat and positive associations with niacin, vitamin B1, iron, and fiber may be an indirect result of an overall healthy diet pattern that is associated with high levels of taurine and these nutrients. Women who consumed more chicken, which contains high levels of niacin, iron, and taurine, may have also consumed more vegetables, which are associated with high levels of iron and fiber, and more whole grains, which contain more vitamin B1 and fiber. Importantly, the main effect of taurine on CHD risk and the interaction between taurine and cholesterol did not change after controlling for nutritional factors.

The data also suggest that taurine may be associated with hypertension and diabetes. In ecologic studies, Mizushima et al. [5] found a negative association between urinary taurine excretion and hypertension prevalence comparing two different Japanese populations, and Liu et al. [12] showed a negative correlation between urinary taurine excretion and blood pressure in ethnic Chinese groups. A small clinical trial reported that taurine supplementation decreased blood pressure in 19 borderline hypertensive volunteers [13]. The results of the present study extend the findings of the previous studies because taurine and hypertension status were measured at the individual level and participants were healthy at baseline. The evidence of taurine's effect on diabetes is limited. A study of taurine supplementation showed a reduction in glucose levels measured in plasma and urine [42]. Future large studies are needed to evaluate the potential beneficial effects of taurine on hypertension, and possibly diabetes.

The present study has several strengths. The prospective nature of the study design with participants free of CVD at the time of blood donation minimized the likelihood that serum taurine was influenced by disease or a change in diet due to disease. The study involved a long-term follow-up, average of 23 years, allowing us to study long-term effects of taurine. The standardization of sample collection, storage, and handling procedures [43] are also strengths of this study because measurements made from biological samples can be highly dependent on these factors. Because the study enrollment and blood donation occurred between 1985 and 1991, about a decade before the "energy drink" became popular in the United States, it is certain that the main source of taurine measured in the samples of the NYUWHS participants derived from food, not from enhanced drinks or over the counter supplements. Importantly, the use of repeated samples improved the reliability of the measurement of taurine, and consequently the validity of the findings.

It should be noted that our study population included over 80% Caucasian women, and therefore, the generalizability of results to men and other races should be considered with caution. However, there is no evidence that the biological actions of taurine would differ by sex or race. In addition, our results cannot be generalized to indicate health effects of energy drinks, which should be investigated

separately, as these drinks often contain not only very high amounts of taurine but also a multitude of other ingredients such as caffeine and ginseng that may influence CHD risk. Although our ascertainment of hypertension status was based on self-reported data, the validity of self-reported hypertension status has previously been shown to have >80% sensitivity and specificity in other epidemiologic studies [44, 45]. Lastly, we cannot exclude the role of chance, unmeasured confounders, or biases in our findings, especially those relating to subgroup analyses.

In conclusion, we found no significant association between serum taurine and CHD risk overall, although the results are suggestive of an inverse association, especially among individuals with high serum cholesterol levels. The findings also suggest a possible inverse association between serum taurine and the risk of hypertension and diabetes.

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Conflict of interest The authors declare that they have no conflict of interest.

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