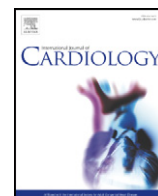




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Letter to the Editor

Are higher serum IgE concentrations associated with adult cardiovascular disease?

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The burden of cardiovascular disease (CVD) is high and likely to increase in future decades as a result of demographic and epidemiological transitions in populations. In the United States, CVD is responsible for 17% of national health expenditures. As the population ages, these costs are expected to continue to increase substantially [1]. Continuous identification of novel risk and protective contributors will play an important role in preventing and delaying the disease and therefore saving costs at all levels and prolonging life expectancy. Previous research studies have suggested that IgE-mediated events may play a role in the pathogenesis of CVD, involving platelet activation and arterial spasm [3]. In this context, it was aimed to determine the relationships between serum total and allergen-specific immunoglobulin E (IgE) and risk of CVD in a national population-based setting.

As described elsewhere [2], United States National Health and Nutrition Examination Surveys is a national, population-based, multi-year, cross-sectional study. Information on demographics, lifestyle factors, and medical conditions including self-reported CVD with ever coronary heart disease, stroke, heart failure, heart attack, and angina was obtained by household interview using questionnaires. Written informed consent was obtained for all subjects. In the 2005–2006 cohort, participants aged 1 year and older were tested for serum total IgE concentrations and people aged 6 and above were tested for additional allergen-specific IgE concentrations using the Pharmacia Diagnostics ImmunoCAP 1000

System (Kalamazoo, Michigan). A detailed description of the laboratory method can be found at NHANES 2005–2006 web page (http://www.cdc.gov/nchs/data/nhanes/nhanes_05_06/al_ige_d.pdf). Since people aged 20 and over were asked in relation to cardiovascular disease conditions, participants aged 20 and above were eligible to be included in the current analysis.

Effects of serum total (cutoff: 170 kU/L) and 19 allergen-specific (cutoff: 0.35 kU/L) IgE concentrations on risk of CVD were examined by *t*-test, generalized linear model, and logistic regression model, with $P < 0.05$ considered statistically significant. Total CVD was counted as having any of subtypes (binary: categorical variable) and was summed by all subtypes as number of CVD events (continuous variable). Covariates included age, sex, ethnicity, education (cutoff: high school), body mass index, high blood pressure (≥ 140 mm Hg for systolic blood pressure and ≥ 90 mm Hg for diastolic blood pressure), active smoking (cotinine as a proxy), serum insulin, serum LDL-cholesterol, and alcohol consumption (≥ 12 drinks in a year). Final models were also weighted. Statistical software STATA version 12.0 (STATA, College Station, Texas, USA) was used to perform all the analyses. Since this study is secondary data analysis by extracting data from the NHANES website, no further ethics approval is required.

Table 1 presents the characteristics of included participants ($N = 4979$). Table 2 shows the effects of serum total IgE concentrations on the risk of CVD by subtypes. Apparently, people with any CVD type had higher levels of serum total IgE concentrations. In the multi-level regression modeling after full adjustments and being weighted, people with higher serum total IgE concentrations were likely to have coronary heart disease (OR 2.02, 95%CI 1.001–4.08, $P = 0.05$). Moreover, among all allergen-specific IgE concentrations, only serum shrimp IgE antibody was significantly associated with coronary heart disease (OR 2.96, 95%CI 1.06–8.28, $P = 0.04$). However, serum shrimp antibody was not significantly associated with other CVD subtypes (Table 3). Although number of CVD events seemed to be related to higher serum shrimp IgE antibody, it did not reach significance.

In the present study, the effects of serum total and seafood-specific IgE concentrations on risk of CVD subtypes and number of events were firstly examined in a national and population-based setting. It was observed that serum total IgE concentrations and serum shrimp IgE antibody were significantly associated with an increased risk of coronary heart disease. The current finding is similar to a previous population-based study showing an association between serum IgE concentrations and CVD [3].

How serum IgE concentrations may play a role in the pathway to CVD is not completely known until today. Literature in this field is scarce. IgE-mediated events may be in the pathogenesis of CVD,

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Table 1
Characteristics of adult participants (aged 20 and above).

N = 4979	n (%) or mean (SD)
Sex	
Male	2387 (47.9%)
Female	2592 (52.1%)
Age	47.5 (18.2)
Serum total IgE concentrations (kU/L)	163.7 (479.2)
High IgE (≥ 170 kU/L)	1389 (27.9%)
Serum seafood-specific IgE antibody (kU/L)	0.5 (3.1%)
Positive antibody response (≥ 0.35 kU/L)	320 (7.2%)
Education < high school	1394 (28.1%)
High blood pressure (mm Hg)	1730 (34.8%)
Systolic blood pressure	123.4 (19.4)
Diastolic blood pressure	69.1 (13.1)
Active smoker	1715 (34.4%)
Cotinine (ng/mL)	58.3 (125.2)
Body mass index	28.8 (6.7%)
Cardiovascular disease	
Stroke	193 (3.9%)
Heart failure	180 (3.6%)
Coronary heart disease	200 (4.1%)
Heart attack	215 (4.3%)
Angina	154 (3.1%)
Any of above	560 (11.3%)
Number of cardiovascular disease (CVD)	
No known CVD	4392 (89.2%)
1 CVD	304 (6.2%)
2 CVD	135 (2.7%)
3 CVD	60 (1.2%)
4 CVD	23 (0.5%)
5 CVD	8 (0.2%)

involving platelet activation and arterial spasm [3]. Moreover, IgE-mediated release of histamine or other mast cell products may produce coronary spasms that were previously observed in humans in vitro [4]. Other pathway included strict dietary avoidance of food-specific protein to reduce CVD events [5]. On the other hand, the mechanism through reaction of anaphylaxis has received attention and seafood allergy can lead to this life-threatening reaction [6].

Previous studies also indicated that serum IgE levels were elevated significantly in patients with cerebral infarction and myocardial infarction [7,8]. However, it was not able to identify people with these two subtypes in this study sample, nor subtypes of stroke (ischemic or hemorrhagic). In the current analysis, the significant associations between serum IgE and coronary heart disease were not significant until being fully adjusted and weighted in the regression modeling. Low-density lipoprotein cholesterol was inversely associated with serum IgE concentrations and could increase the association between serum IgE and CVD. Moreover, weights that are adjusted attempt to account for non-response from observational studies. In the current study sample, the missing value on coronary heart disease is the highest among all CVD subtypes. This may partly explain why the association became significant after the survey weighting [9].

In conclusion, the current study has found the associations of serum total IgE concentrations and serum shrimp IgE antibody and coronary heart disease, although the causality cannot be established in the current cross-sectional study design. Future studies with very large study sample or longitudinal perspective are strongly suggested in confirming or refuting the observation to balance the weak associations in the present study.

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Table 2
Associations of serum total and seafood-specific IgE concentrations and cardiovascular disease.

a) Total IgE			
t-Test	Mean (SD) kU/L	Mean (SD) kU/L	P value
	Yes	No	
Stroke	228.7 (761.8)	161.3 (464.5)	0.07
Heart failure	229.9 (588.4)	161.3 (475.5)	0.08
Coronary heart disease	229.5 (561.4)	160.7 (476.4)	0.06
Heart attack	240.9 (553.6)	160.1 (475.7)	0.02
Angina	202.4 (445.2)	162.4 (480.8)	0.33
Any of above	203.3 (575.2)	158.6 (465.6)	0.05
	Odds ratio	95% CI	P value
<i>Crude model</i>			
Stroke	1.90	0.79–1.49	0.59
Heart failure	1.21	0.88–1.67	0.24
Coronary heart disease	1.27	0.94–1.71	0.13
Heart attack	1.27	0.95–1.70	0.11
Angina	1.01	0.70–1.44	0.97
Any of above	1.09	0.90–1.32	0.38
Number of CVD events	0.03 ^a	–0.004–0.07	0.08
<i>Adjusted model</i>			
Stroke	1.24	0.67–2.29	0.50
Heart failure	0.94	0.46–1.89	0.86
Coronary heart disease	1.36	0.72–2.57	0.35
Heart attack	0.98	0.53–1.83	0.95
Angina	0.87	0.42–1.82	0.72
Any of above	1.05	0.69–1.58	0.83
Number of CVD events	0.01 ^a	–0.05–0.07	0.71
<i>Weighted model</i>			
Stroke	1.17	0.58–2.34	0.64
Heart failure	0.70	0.33–1.48	0.32
Coronary heart disease	2.02	1.001–4.08	0.05
Heart attack	1.04	0.54–2.00	0.90
Angina	0.75	0.32–1.77	0.49
Any of above	1.24	0.78–1.97	0.34
Number of CVD events	0.02 ^a	–0.03–0.08	0.35
b) Seafood-specific IgE antibody			
<i>Crude model</i>			
Stroke	0.99	0.43–2.26	0.97
Heart failure	1.45	0.82–2.56	0.18
Coronary heart disease	1.54	0.92–2.59	0.09
Heart attack	1.50	0.81–2.76	0.18
Angina	1.73	0.71–4.17	0.21
Any of above	1.16	0.80–1.66	0.41
Number of CVD events	0.07 ^a	–0.01–0.14	0.10
<i>Adjusted model</i>			
Stroke	1.55	0.64–3.73	0.33
Heart failure	1.66	0.67–4.11	0.27
Coronary heart disease	1.51	0.58–3.88	0.40
Heart attack	1.19	0.50–2.84	0.70
Angina	1.16	0.42–3.17	0.78
Any of above	1.24	0.68–2.24	0.48
Number of CVD events	0.04 ^a	–0.04–0.13	0.33
<i>Weighted model</i>			
Stroke	1.57	0.45–5.51	0.45
Heart failure	1.70	0.87–3.31	0.11
Coronary heart disease	2.96	1.06–8.28	0.04
Heart attack	1.84	0.66–5.14	0.23
Angina	2.08	0.46–9.45	0.32
Any of above	1.68	0.88–3.22	0.11
Number of CVD events	0.13 ^a	–0.01–0.27	0.08

Note: Adjusted model: adjusting for age, sex, ethnicity, education, body mass index, high blood pressure, serum insulin, LDL-cholesterol, active smoking, and alcohol consumption; weighted model: additionally adjusting for survey weighting. Significant associations were highlighted in bold.

^a Values are presented in beta.

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