Short Communication

Association of urinary cadmium and myocardial infarction

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Abstract

We conducted a cross-sectional analysis of individuals 45–79 years old in the National Health and Nutrition Examination Survey III (1988–1994) (NHANES III). Myocardial infarction was determined by electrocardiogram (ECG). Our sample included 4912 participants, which when weighted represented 52,234,055 Americans. We performed adjusted logistic regressions with the Framingham risk score, pack-years of smoking, race-ethnicity, and family history of heart attack, and diabetes as covariates. Urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine had an odds ratio of 1.86 (95% CI 1.26–2.75) compared to urinary cadmium $< 0.43\,\mu g/g$ creatinine. This result supports the hypothesis that cadmium is associated with coronary heart disease. When logistic regressions were done by gender, women, but not men, showed a significant association of urinary cadmium with myocardial infarction. Women with urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine had an odds ratio of 1.80 (95% CI 1.06–3.04) compared to urinary cadmium $< 0.43\,\mu g/g$ creatinine. When the analysis was restricted to never smokers ($N = 2187$) urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine had an odds ratio of 1.85 (95% CI 1.10–3.14) compared to urinary cadmium $< 0.43\,\mu g/g$ creatinine.

1. Introduction

It is likely that chronic high exposure to cadmium is related to cardiovascular disease, but additional human studies are needed to confirm this association (Houston, 2007). Exposure to cadmium has been associated with cardiovascular disease in some studies (Carroll, 1966; Ponteva et al., 1979; Adamska-Dyniewska et al., 1982; Tang et al., 2003; Afridi et al., 2006), but not in others (Staessen et al., 1991, 1996). Both blood cadmium (Navas-Acien et al., 2004) and urinary cadmium (Navas-Acien et al., 2005) have been associated with peripheral arterial disease in the 1999–2000 National Health and Nutrition Examination Survey (NHANES 1999–2000). Tobacco smoking and diet are the main sources of exposure to cadmium. Cadmium-related health effects are thought to be more common among women than among men (Vahter et al., 2007). Consumption of rice heavily contaminated with cadmium has caused itai-itai disease almost exclusively in elderly Japanese women (Ogawa et al., 2004). Itai-itai disease is a combination of kidney damage, osteomalacia, and osteoporosis, often with multiple bone fractures. Gender differences may due to higher body burden of cadmium among women or due to differences in sensitivity to toxic effects (Vahter et al., 2007).

2. Methods

We conducted a cross-sectional analysis of individuals 45–79 years old in the National Health and Nutrition Examination Survey III (1988–1994) (NHANES III) evaluating the association of urinary cadmium with myocardial infarction. Myocardial infarction was determined by electrocardiogram (ECG) using the Cardiac Infarction Injury Score (CIIS; Rautaharju et al., 1981). CIIS $\geqslant 15$ has a sensitivity of 85% and specificity of 95% (i.e. 5% false positives). Persons having CIIS < 15 who indicated a doctor had told them they had a heart attack or congestive heart failure were excluded from our analyses. There were 451 cases of myocardial infarction in our sample of 4912 participants. Urinary cadmium was measured by atomic absorption spectrometry using a modification of the procedure described by Pruszkowska et al. (1983). Urinary cadmium was expressed per gram of creatinine and analyzed as tertiles of the sample. Tertile 1 was $< 0.43\,\mu g/g$ creatinine, tertile 2 was 0.43–0.87 $\mu g/g$ creatinine, and tertile 3 was $\geqslant 0.88\,\mu g/g$ creatinine.

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We performed adjusted logistic regressions using SUDAAN (SUDAAN Statistical Software Center, Research Triangle Park, NC). We used two sets of covariates and analyzed the entire sample, men alone and women alone. Model 1 was adjusted for age, gender, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, hypertension medications, smoking status, pack-years of smoking, race-ethnicity, family history of heart attack, and diabetes. Model 2 was adjusted for the Framingham risk score (NCEP Expert Panel, 2001), pack-years of smoking, race-ethnicity, family history of heart attack, and diabetes. Smoking status was defined as never, former, and current smoker. Former and current smokers had smoked at least 100 cigarettes during their entire life. Pack-years of smoking were calculated using answers to 12 tobacco questions and included assessment of current number of cigarettes smoked, maximum number of cigarettes smoked, and periods during which a current smoker did not smoke. Race-ethnicity was categorized as non-Hispanic White, non-Hispanic Black, Hispanic, and other. A participant was considered to have a family history of heart attack if one of his parents had a heart attack before the age of 50. Diabetes status was determined by self-report.

The Framingham risk score includes age, total cholesterol, smoking status (yes versus no), high-density lipoprotein cholesterol, systolic blood pressure, and treatment for hypertension. The participants were classified based on their total points into 10-year risk percentages ranging from 1% to 30%. The Framingham risk score models an interaction between total cholesterol and age, and an interaction between current smoking and age, and therefore differs from the sum of the individual risk factors.

We also conducted an additional logistic regression using Model 2 to predict myocardial infarction among never smokers.

3. Results

Mean urinary cadmium concentrations by smoking status and gender are given in Table 1. Former smokers had cadmium concentrations that were intermediate between never smokers and current smokers even though they had quit for a mean of 16.5 years for men and 15.4 years for women. Women had higher cadmium concentrations than men regardless of smoking status.

Results of our logistic regressions are given in Table 2. When covariates were included as separate variables (Model 1), urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine had an odds ratio of 1.46 (95% CI 1.01–2.13) compared to urinary cadmium $<0.43\,\mu g/g$ creatinine. Looking at Model 1 by gender, neither men nor women had a significant association between myocardial infarction and urinary cadmium. Using the Framingham risk score (Model 2), urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine had an odds ratio of 1.86 (95% CI 1.26–2.75) compared to urinary cadmium $<0.43\,\mu g/g$ creatinine. Using Model 2, men did not have a significant association between myocardial infarction and

Table 1
Mean urinary cadmium concentrations by smoking status and gender

	Urinary cadmium ($\mu g/g$ creatinine)	
	Men	Women
Never smoker	0.35 (0.02)[a]	0.70 (0.02)
Former smoker[b]	0.66 (0.02)	1.01 (0.04)
Current smoker	1.01 (0.03)	1.45 (0.06)

[a]Standard error of the mean.
[b]Quit for a mean of 16.5 years for men, and 15.4 years for women.

Table 2
Association of urinary cadmium with myocardial infarction

Urinary cadmium ($\mu g/g$ creatinine)	Odds ratio	95% CI
Model 1[a]		
<0.43	1.00	–
0.43–0.87	1.13	0.79–1.63
$\geqslant 0.88$	1.46	1.01–2.13
Model 1—men		
<0.43	1.00	–
0.43–0.87	1.04	0.55–1.98
$\geqslant 0.88$	1.32	0.74–2.35
Model 1—women		
<0.43	1.00	–
0.43–0.87	1.22	0.75–2.00
$\geqslant 0.88$	1.63	0.95–2.80
Model 2[b]		
<0.43	1.00	–
0.43–0.87	1.32	0.91–1.90
$\geqslant 0.88$	1.86	1.26–2.75
Model 2—men		
<0.43	1.00	–
0.43–0.87	1.09	0.60–2.00
$\geqslant 0.88$	1.26	0.71–2.26
Model 2—women		
<0.43	1.00	–
0.43–0.87	1.27	0.77–2.09
$\geqslant 0.88$	1.80	1.06–3.04

[a]Model 1 adjusted for age, gender, total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, hypertension medications, smoking status, pack-years of smoking, race-ethnicity, family history of heart attack, and diabetes.
[b]Model 2 adjusted for the Framingham risk score, pack-years of smoking, race-ethnicity, family history of heart attack, and diabetes.

urinary cadmium, but women did. Using Model 2, women with urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine had an odds ratio of 1.80 (95% CI 1.06–3.04) compared to urinary cadmium $<0.43\,\mu g/g$ creatinine.

When never smokers were analyzed separately (using Model 2), there was still a significant association between myocardial infarction and urinary cadmium. There were a total of 2187 never smokers in our sample, 653 men and 1534 women. The mean urinary cadmium was $0.35\,\mu g/g$ creatinine for men, and $0.70\,\mu g/g$ creatinine for women (Table 1). A total of 18.6% of the never smokers had urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine. Urinary cadmium $\geqslant 0.88\,\mu g/g$ creatinine had an odds ratio of 1.85 (95% CI 1.10–3.14) compared to urinary cadmium $<0.43\,\mu g/g$ creatinine. These results support the hypothesis that cadmium is associated with coronary heart disease, especially among women.

4. Discussion

Our results indicate a possible role for cadmium in coronary heart disease. A limitation of our study is that it

is cross-sectional in nature like many of the previous studies. Therefore, we cannot determine the temporal relationship or causality of these associations. Persons diagnosed with myocardial infarction are more likely to change dietary and smoking behaviors, which would be reflected in total cholesterol and smoking status. In particular, persons who were smoking at the time of their myocardial infarction may have subsequently quit smoking and their urinary cadmium concentration deceased by the time of the NHANES III examination. Such an occurrence would have skewed our results. However, urinary cadmium concentrations are higher in former smokers than never smokers, so the effect of quitting is not the same as never smoking. A strength of our study is that it is nationally representative; another is that we included the relevant covariates in a sophisticated way by using the Framingham risk score. We hope to follow-up this study with a longitudinal investigation using the NHANES III linked mortality file to look at coronary heart disease mortality.

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