Comparison of questionnaire-based estimates of dietary cadmium exposure with concentrations of cadmium in urine

Introduction

We evaluated the comparability of the average long-term dietary cadmium exposure with urinary cadmium (reflecting the long-term kidney accumulation) using two approaches: cross-classification (sensitivity and specificity) and correlation of the dietary cadmium estimates, taking into account within-person variation (reproducibility) in the self-reports of intake.

Population

To assess the sensitivity and specificity of the dietary cadmium estimates and the comparability between these estimates and a biomarker, we used the food frequency questionnaire (FFQ) that the women had completed in 1987 as a part of their participation in the Swedish Mammography Cohort (SMC). In addition, urine was collected for cadmium analysis from totally 1519 women, 56-70 years of age during 2004-2007, as previously described in detail in Amzal et al., 2009. After exclusions of those who reported to have ever smoked (n=813) and those with implausible values for total energy intake (n=26), 680 women were left for analysis.

To assess the reproducibility (random variation) of questionnaire-based dietary cadmium intake, women randomly selected from the SMC were asked to complete two identical FFQs one year apart (during 2004-2005); 300 returned a complete questionnaire. The study was approved by the Regional Ethical Review Board in Stockholm, Sweden, and written informed consent was obtained from each participant.

Urinary cadmium

The concentration of cadmium was determined in the first voided morning urine. Cadmium isotope 111 concentrations were measured using inductively coupled plasma mass spectrometry (ICPMS; Agilent 7500ce, Agilent Technologies, Waldbronn, Germany), with high analytical quality. The limit of detection, calculated as three times the standard deviation of the blank values, was 0.003µg/L. All urinary cadmium concentrations were expressed as µg per g creatinine. The mean urinary cadmium concentration in the 680 women was 0.34 µg/g creatinine (range 0.09-1.23 µg/g creatinine) (1).

Because a one-compartment model with a standard first-order elimination takes the exponential shape of the elimination rate of cadmium as well as physiological factors such as the gastrointestinal absorption and kidney weight into account, we also assessed the link between model-predicted urinary cadmium and measured urinary cadmium concentration (1). The prediction of urinary concentration by the model was based on individual data for dietary cadmium intake, age and weight, while unknown factors such as the gastrointestinal cadmium absorption and the cadmium half-life were set to 3% and 11.6 years, respectively (1). The mean predicted urinary cadmium concentration from the FFQ-based dietary cadmium intake estimates was 0.21 ± 0.07 µg/g creatinine and the mean urinary cadmium concentration was 0.34 ± 0.16 µg/ g creatinine.

Statistical methods

Cross-classification was assessed by comparing extreme tertiles (high and low) of FFQ-based dietary cadmium estimates with extreme tertiles (high and low) of urinary cadmium concentrations. We calculated the sensitivity (defined as the probability of being classified as high in the FFQ-estimated dietary cadmium if also urinary cadmium was high), and specificity (defined as the probability of being classified as low in FFQ-cadmium if also urinary cadmium was low).

The reproducibility of the dietary cadmium intake was assessed by calculating the intraclass correlation between the two identical FFQs. We compared long-term dietary cadmium exposure with urinary cadmium using the partial Pearson correlation coefficient for continuous data (residuals showed no major deviation from a linear pattern). Because physiological factors, such as gastrointestinal absorption, age and body weight, affect the concentration of cadmium in urine and thus the link between dietary and urinary cadmium, we adjusted the correlation for dietary iron and fiber intake (as approximations for gastrointestinal absorption), age and weight. To account for the exponential shape of the elimination rate, we also compared the one-compartment model-based predicted urinary cadmium concentrations (which were based on the individual dietary cadmium intake) with the actual measured urinary cadmium concentrations. In a final step, the correlation was adjusted for the within-person variation of the FFQ-based dietary cadmium estimates (deattenuated correlation) (2). Statistical analyses were performed with SAS (version 9.2; SAS Institute, Cary, NC) and STATA (version 11; STATA Corp, College Station, TX) software.

Results

Cross-classification

The cross-classification of the extreme tertiles of FFQ-based dietary cadmium estimates and measured urinary cadmium is shown in Table S1. The sensitivity of the FFQ-based dietary cadmium was 58% (86/149) and the specificity was 51% (76/149).

Reproducibility and correlation

The reproducibility of the FFQ-based dietary cadmium estimates was 0.58 (P = <0.0001). We observed a partial Pearson correlation of 0.1 (95% CI: 0.01-0.21) between questionnaire-based estimates of dietary cadmium and measured urinary cadmium concentration when accounting for within-person variation in the FFQ-based estimates. When comparing, predicted urinary cadmium concentration with measured urinary cadmium concentration, the Pearson correlation was 0.2 (95% CI: 0.1-0.3), accounting for within-person variation in the FFQ-based estimates.

References

1. Amzal B, Julin B, Vahter M, Wolk A, Johanson G, Akesson A. Population toxicokinetic modeling of cadmium for health risk assessment. Environ Health Perspect. 2009 Aug;117(8):1293-301.
2. Willett W, editor. Nutritional Epidemiology: Implications of Total Energy Intake for Epidemiologic Analyses. second ed. Oxford: Oxford University Press; 1998.

Table S1. Cross-classification, numbers (column %), of women according to FFQ-based dietary cadmium estimates and urinary cadmium concentration.

	Urinary cadmium concentration		
FFQ-based dietary cadmium estimates	Low	High	Total
Low	76 (51)	63 (42)	139
High	73 (49)	86 (58)	159
Total	149	149	298