

Original Article

# Relationship Between Blood Mercury Concentration and Waist-to-Hip Ratio in Elderly Korean Individuals Living in Coastal Areas

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**Objectives:** This study investigated the relationship between the blood mercury concentration and cardiovascular risk factors in elderly Korean individuals living in coastal areas.

**Methods:** The sample consisted of 477 adults (164 males, 313 females) aged 40 to 65 years who visited a Busan health promotion center from June to September in 2009. The relationship between blood mercury concentration and cardiovascular risk factors including metabolic syndrome, cholesterol profiles, blood pressure, body mass index (BMI), waist circumference and waist-to-hip ratio (WHR), was investigated. Variables related to blood mercury concentration were further evaluated using multiple regression analysis.

**Results:** The blood mercury concentration of the study population was 7.99 (range, 7.60 to 8.40)  $\mu\text{g/L}$ . In males, the blood mercury concentration was 9.74 (8.92 to 10.63)  $\mu\text{g/L}$ , which was significantly higher than that in females (7.21, [6.80 to 7.64]  $\mu\text{g/L}$ ). The blood mercury concentration of the study population was related to several cardiovascular risk factors including low-density lipoprotein (LDL) cholesterol ( $p=0.044$ ), high-density lipoprotein (HDL) cholesterol ( $p=0.034$ ), BMI ( $p=0.006$ ), waist circumference ( $p=0.031$ ), and WHR ( $p<0.001$ ). In males, the blood mercury concentration was significantly correlated with WHR in the multiple regression analysis.

**Conclusions:** In males, the blood mercury concentration was related to waist-to-hip ratio, which is a central obesity index and cardiovascular risk factor. Our finding suggests that cardiovascular disease risk in males was increased by mercury exposure via an obesity-related mechanism.

**Key words:** Cardiovascular risk factor, Mercury, Obesity, Waist-to-hip ratio  
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## INTRODUCTION

The metal mercury is used in thermometers, fluorescent lamps and batteries; however, over-exposure to mercury is harmful to human health [1]. In aqueous ecosystems, this metal is converted into methylmercury, which accumulates in fish and shellfish. Contaminated fish and shellfish are the main source of mercury exposure in humans and methylmercury is readily absorbed by the alimentary tract. Dietary exposure of fertile women to mercury increases the risk of neurological problems in the fetus during pregnancy [2-4]. In 2004, the U.S. Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) recommended that fertile women reduce their consumption of mercury-contaminated seafood [5]. In

2009, human biomonitoring (HBM) established two safety criteria for blood mercury levels: HBM I, 5  $\mu\text{g/L}$ , an alert level under which no risk of adverse health effects, and HBM II, 15  $\mu\text{g/L}$ , an action level above which an increased risk of adverse health effects does exist [6].

Wiggers et al. [7] observed that low level of exposure to mercury altered vascular activity and induced endothelial cell dysfunction in animals. De Marco et al, [8] observed that the blood mercury level of humans was significantly association with the plasma nitric oxide level, but the effect of mercury on cardiovascular disease has not established [9]. Indeed, Guallar et al, [10] reported that the mercury level in patients suffering from myocardial infarction was associated with the mortality rate in this group, whereas Yoshizawa et al. [11] did not observe this association. It is difficult to understand the effects of mercury exposure on cardiovascular disease

because fish and shellfish contained unsaturated fats, which protect against cardiovascular disease and act in a manner opposite to the adverse effect of mercury exposure [12,13]. A recent study of mercury exposure and cardiovascular disease integrated the adverse effects of mercury exposure and the protective effect of unsaturated fats [14].

Busan, Korea is located in coastal area and has the highest standardized mortality ratio (SMR) for cardiovascular disease compared with other provinces in Korea: Busan, 31.6; Incheon, 26.5; Ulsan, 24.2; Deagu, 23.9; Daejeon, 20.3; Gwangju, 19.6; and Seoul, 18.7 [15]. We found that the mortality from cardiovascular disease was higher in coastal areas (Busan, Incheon and Ulsan) than inland (Deagu, Daejeon, and Gwangju) areas [15]. However, no study has evaluated the health effects of mercury exposure on the risk for cardiovascular disease in coastal areas. In Korea, research on mercury has been limited to evaluating the mercury exposure by region or investigating pathological mechanisms as heart rate variability [16-21]. Investigations in other countries have compared the cardiovascular disease risk of subjects with high and low level of mercury, although studies on factors that are intermediate between mercury levels and risk for cardiovascular disease are insufficient [22]. Therefore, this study evaluates the relationship between the mercury exposure level and risk for cardiovascular disease in Korea, by comparing blood mercury concentrations with presence and parameters of metabolic syndrome, including cholesterol profiles, blood pressure, body mass index (BMI), waist circumference, waist-to-hip ratio (WHR) and fasting blood sugar levels.

## METHODS

### I. Study Population

The samples recruited from subjects who had participated in Korean Genome and Epidemiology Study (KoGES) and consisted of 477 middle-aged people (40 - 65 years; 164 males, 313 females) who visited a health promotion center in Busan from June to September, 2009. All the participants were informed of the study purpose and provided consent for blood sampling and the use of a personal data. This study was performed after approval from the Institutional Review Board of the Dong-A Medical Center.

### II. Questionnaire

A questionnaire survey was administered in face-to-face interviews. The questionnaire gathered information on demographic factors (sex and age), smoking status, drinking habits, menopause, and history of diseases.

### III. Blood Sampling and Anthropometric Measurements

Blood was sampled after an 8-hour fast and the samples were transported to a diagnostic center in Seoul. The cholesterol profiles and fasting blood sugar levels were analyzed using an enzymatic method. Blood pressure was checked twice by a trained examiner after participants rested for 5 minutes in a sitting position. Waist circumference was determined with a measuring tape placed midway between the lowest rib and the iliac crest during expiration. Hip circumference was measured at the level of the greater trochanters. The WHR equaled the waist circumference divided by the hip circumference. Metabolic syndrome was determined by the National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATP III) criteria, using the waist circumference for Koreans (males, 90 cm; females, 85 cm) [23].

### IV. Measuring the Blood Mercury Concentration

The blood mercury concentration was analyzed using the double-amalgam method with cold vapor atomic absorption spectrometry (CV-AAS) using a mercury analyzer (SP-3DS, NIC, Tokyo, Japan). Blood samples were collected in an EDTA-treated 3 -mL vacuum tube, transported on dry ice and stored in a refrigerator at - 70 °C. Before analysis, the blood samples were thawed slowly at room temperature and homogenized with a roller-mixer for 1 hour. The blood samples were premixed with 0.001 % L-cysteine solution, the hg-BHT, and the hg-MHT reagents (NIC, Tokyo, Japan) were added, and the sample was introduced into the analyzer. After the samples were heated at 650 °C, the mercury in the samples was evaporated and captured by gold amalgam. The captured mercury was evaporated and introduced into a spectrometer by reheating gold amalgam at 700 °C. The blood mercury concentration was determined by the value absorbed at 253.7 nm. The L-cysteine solution was produced by mixing 10 mg of L-cysteine and 2 mL of 60 % nitric acid. A calibration curve was plotted by 2, 4, 6, and 8- ppb solutions made from a 1000 ppm mercury standard solution (Wako,

**Table 1.** General characteristics of study population

n (%)

Variables	Males (n = 164) Mean ± SD	Females (n = 313) Mean ± SD	p-value
Mean age (y)	54.60 ± 8.69	53.37 ± 7.77	0.127 <sup>1</sup>
40 - 49	52 (31.7)	99 (31.6)	0.176 <sup>2</sup>
50 - 59	62 (37.8)	141 (45.0)	
60 >	50 (30.5)	73 (23.3)	
Total cholesterol (mg/dL)	194.91 ± 32.17	198.71 ± 35.15	0.249 <sup>1</sup>
Triglycerides (mg/dL)	141.59 ± 79.53	113.70 ± 74.20	<0.001 <sup>1</sup>
LDL cholesterol (mg/dL)	118.80 ± 29.52	121.58 ± 32.52	0.361 <sup>1</sup>
HDL cholesterol (mg/dL)	47.84 ± 11.10	54.48 ± 13.04	<0.001 <sup>1</sup>
Fasting blood sugar (mg/dL)	99.08 ± 21.02	92.44 ± 21.40	0.001 <sup>1</sup>
Systolic blood pressure (mmHg)	120.02 ± 11.58	117.90 ± 12.75	0.075 <sup>1</sup>
Diastolic blood pressure (mmHg)	78.83 ± 7.21	77.88 ± 7.78	0.194 <sup>1</sup>
Body mass index (kg/m <sup>2</sup> )	24.24 ± 2.91	23.38 ± 2.99	0.003 <sup>1</sup>
Waist circumference (cm)	84.01 ± 8.08	76.86 ± 8.24	<0.001 <sup>1</sup>
Waist to hip ratio	0.93 ± 0.05	0.82 ± 0.04	<0.001 <sup>1</sup>
Smoking			
Yes	63 (38.4)	101 (61.6)	<0.001 <sup>2</sup>
No	11 (3.5)	302 (96.5)	
Drinking			
Yes	123 (75.0)	41 (25.0)	<0.001 <sup>2</sup>
No	105 (33.5)	208 (66.5)	
Hair tail (Cutlass fish)			
Less than once a week	103 (62.8)	61 (37.2)	0.554 <sup>2</sup>
More than once a week	187 (59.7)	126 (40.3)	
Eel			
Less than once a week	144 (87.8)	20 (12.2)	0.266 <sup>2</sup>
More than once a week	285 (91.1)	28 (8.9)	
Yellow corbina (Croaker, Pacific)			
Less than once a week	114 (69.5)	50 (30.5)	0.917 <sup>2</sup>
More than once a week	219 (70.0)	94 (30.0)	
Tuna			
Less than once a week	153 (93.3)	11 (6.7)	1.000 <sup>2</sup>
More than nce a week	291 (93.0)	22 (7.0)	
Sushi (raw fish)			
Less than once a week	150 (91.5)	14 (8.5)	0.110 <sup>2</sup>
More than once a week	298 (95.2)	15 (4.8)	

LDL: low-density lipoprotein, HDL: cholesterol, high-density lipoprotein.

<sup>1</sup> The p-value was calculated using t-test to compare males and females, <sup>2</sup>The p-value was calculated using Fisher's exact test to compare males and females.

Osaka, Japan) diluted with L-cysteine solution. External quality control was provided by the Korea Occupational Safety & Health Agency (KOSHA) and the German External Quality Assessment Scheme (G-EQUAS).

## V. Statistical Analysis

Data on blood mercury concentrations had a leftward-skewed distribution and were analyzed using logarithmic transformation. The blood mercury concentration was compared with the cardiovascular risk factors including blood pressure, cholesterol profiles, BMI, waist circumference and WHR, using a one-way analysis of variance (ANOVA). The association between blood mercury concentration and cardiovascular risk factors was evaluated using multiple regression analysis. All statistical analyses were performed with SPSS version

18.0 (SPSS Inc., Chicago, IL, USA), and  $p < 0.05$  was considered to be statistically significant.

## RESULTS

### I. General Characteristics of the Study Population

The study population consisted of 477 adults including 164 males and 313 females. The mean age of study population was  $53.79 \pm 8.11$  years and that of male ( $54.60 \pm 8.69$ ) and female ( $53.37 \pm 7.77$ ) subjects did not differ significantly. The age distribution and frequency of fish intake of men and women did not differ, but smoking status and drinking habits differed significantly (Table 1).

**Table 2.** Blood mercury levels of the study population by sex and age

Variable	n	GM (95% CI)	Mercury concentration by percentiles				
			5	25	50	75	95
Total	477	7.99 (7.60, 8.40)	3.23	5.55	7.83	11.71	18.45
Sex							
Male	164	9.74 (8.92, 10.63)	3.91	6.77	9.66	14.59	19.56
Female	313	7.21 (6.80, 7.64)	3.04	5.19	7.12	10.49	14.04
Age (y)							
40 - 49	151	8.87 (7.95, 9.80)	2.57	5.09	7.53	10.93	15.37
50 - 59	203	9.84 (8.98, 10.71)	3.52	5.86	7.96	12.08	16.60
60 ≥	123	9.06 (8.19, 9.94)	2.84	4.10	7.91	11.28	16.70

GM: Geometric mean, CI: confidence interval.

## II. Blood Mercury Concentration

The blood mercury concentration of the study population, males and females were 7.99 (range 7.60 to 8.44), 9.74 (8.92 to 10.63) and 7.21 (6.80 to 7.64)  $\mu\text{g/L}$ , respectively. The blood mercury concentration of males was significantly higher than that of females. The blood mercury concentrations of subjects in their 40s, 50s, and 60s were 8.87 (7.95 to 9.80), 9.84 (8.98 to 10.71), and 9.06 (8.91 to 9.94)  $\mu\text{g/L}$ , respectively (Table 2).

## III. Cardiovascular Risk Factors

Comparison of blood mercury with cardiovascular risk factors showed that low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, BMI, waist circumference and WHR differed significantly, whereas the prevalence of metabolic syndrome, total cholesterol, triglycerides, blood pressure, and fasting blood sugar levels did not differ in this regard. BMI and WHR were significant variables among men, whereas LDL cholesterol level, menopause, and WHR were significant variables among women (Table 3).

## IV. Association between Cardiovascular Risk Factors and Blood Mercury Concentration

Multiple regression analysis showed that WHRs ( $p < 0.001$ ) and LDL cholesterol ( $p = 0.028$ ) levels for the group who met the HBM I criterion were associated with blood mercury concentration after adjusting for age, sex, alcohol intake, and smoking status (Table 4). Specifically, the WHRs of males whose scores met HBM I threshold were associated with their blood mercury concentration ( $p < 0.001$ ).

## DISCUSSION

In this study, we found that the blood mercury concentration differed significantly according to the several cardiovascular risk factors as BMI, LDL cholesterol, waist circumference and WHR. By contrast, HDL cholesterol showed no correlation with blood mercury concentration. The WHRs of males were significantly related to their blood mercury concentrations. Therefore, males with heavy mercury exposure may be susceptible to cardiovascular disease based on their WHR.

Typically, hair, urine and blood are used to evaluate mercury exposure. The mercury level in hair and urine reflects long-term exposure, although the mercury concentration in hair samples is prone to error because of external contamination such as with dyes, and varies with length of the hair. It is inconvenient to collect urine samples to determine mercury levels, and the urine creatinine level should be 30-300 mg/dL [24]. Although blood mercury level reflects recent mercury exposure, it is used widely for monitoring the mercury exposure of population at risk and for comparison with other populations. The Second National Human Exposure and Biomonitoring Examination of Mercury measured the exposure level of 2369 Koreans at 3.80 (3.66 to 3.93)  $\mu\text{g/L}$ , whereas the Third Korean Health Examination Survey found a level of 4.15 (3.94 to 4.36)  $\mu\text{g/L}$  in 1997 adults [16-18]. The geometric mean of blood mercury concentration in our study was 7.99 (7.60 to 8.40)  $\mu\text{g/L}$ , which was higher than the range of 3.80 to 4.15  $\mu\text{g/L}$  in the previous Korean National Studies. The blood mercury concentration of previous studies of coastal population was 6.54 to 8.63  $\mu\text{g/L}$  [19,20], which is similar to the mean value in our study.

Mahaffey reported that the distributions of mercury levels in a single country differed by geographic location and high mercury level in coastal areas were a result of the ready access to fresh seafood [25]. The HBM has

**Table 3.** Blood mercury concentration according to cardiovascular risk factors by sex

	Total			Male			Female		
	n	GM (95% CI) <sup>1</sup>	p-value	n	GM (95% CI) <sup>1</sup>	p-value	n	GM (95% CI) <sup>1</sup>	p-value
<b>Total cholesterol (mg/dL)</b>									
< 200	263	7.70 (7.20, 8.23)	0.241	99	9.16 (8.17, 10.27)	0.210	164	6.94 (6.42, 7.50)	0.343
200 - 240	161	8.28 (7.62, 8.99)		51	10.48 (8.92, 12.31)		110	7.42 (6.78, 8.12)	
> 240	53	8.63 (7.21, 10.33)		14	11.46 (8.65, 15.19)		39	7.80 (6.27, 9.71)	
<b>LDL cholesterol (mg/dL)</b>									
< 130	286	7.66 (7.19, 8.17)	0.044	100	9.31 (8.32, 10.42)	0.360	186	6.90 (6.41, 7.42)	0.039
130 - 160	147	8.24 (7.55, 9.01)		53	10.21 (8.70, 11.98)		94	7.32 (6.62, 8.08)	
> 160	44	9.46 (7.86, 11.40)		11	11.65 (8.38, 16.20)		33	8.84 (7.05, 11.08)	
<b>HDL cholesterol (mg/dL)</b>									
< 40 (or 50) <sup>2</sup>	170	7.43 (6.86, 8.06)	0.034	39	9.67 (8.24, 11.34)	0.930	131	6.88 (6.29, 7.52)	0.175
≥ 40 (or 50) <sup>2</sup>	307	8.32 (7.81, 8.86)		125	9.75 (8.78, 10.84)		182	7.45 (6.91, 8.04)	
<b>Triglyceride (mg/dL)</b>									
< 150	362	7.77 (7.34, 8.21)	0.125	110	9.12 (8.18, 10.16)	0.100	252	7.25 (6.80, 7.72)	0.452
150 - 200	47	9.01 (7.58, 10.72)		18	11.66 (8.74, 15.54)		29	7.68 (6.23, 9.47)	
> 200	68	8.56 (7.39, 9.90)		36	10.87 (9.08, 13.00)		32	6.54 (5.31, 8.05)	
<b>Fasting blood sugar (mg/dL)</b>									
< 110	423	7.94 (7.52, 8.37)	0.725	135	9.62 (8.69, 10.66)	0.820	288	7.25 (6.83, 7.70)	0.614
110 - 126	21	8.57 (6.86, 10.71)		13	10.63 (8.25, 13.69)		8	6.04 (4.35, 8.41)	
> 126	33	8.38 (6.91, 10.17)		16	10.04 (8.23, 12.23)		17	7.07 (5.11, 9.79)	
<b>Systolic blood pressure (mg/dL)</b>									
< 130	327	7.76 (7.30, 8.26)	0.090	106	9.58 (8.58, 10.70)	0.630	221	7.02 (6.54, 7.53)	0.159
≥ 130	150	8.51 (7.82, 9.28)		58	10.02 (8.66, 11.62)		95	7.68 (6.95, 8.50)	
<b>Diastolic blood pressure (mg/dL)</b>									
< 85	327	7.82 (7.35, 8.31)	0.200	110	9.72 (8.74, 10.82)	0.960	217	7.00 (6.53, 7.51)	0.136
≥ 85	150	8.39 (7.68, 9.16)		54	9.76 (8.34, 11.45)		96	7.70 (6.94, 8.53)	
<b>Metabolic syndrome</b>									
Yes	420	7.97 (7.57, 8.40)	0.722	148	9.48 (8.64, 10.41)	0.07	272	7.25 (6.83, 7.71)	0.586
No	57	8.15 (6.90, 9.64)		16	12.43 (9.52, 16.24)		41	6.91 (5.72, 8.36)	
<b>Body mass index (kg/m<sup>2</sup>)</b>									
< 18.5	11	5.22 (3.67, 7.43)	0.006	5	4.87 (2.11, 11.24)	0.001	6	5.53 (3.54, 8.64)	0.419
18.5 - 25.0	326	7.74 (7.30, 8.21)		91	9.04 (8.07, 10.14)		235	7.29 (6.82, 7.80)	
≥ 25.0	140	8.90 (8.09, 9.79)		68	11.31 (9.93, 12.88)		72	7.10 (6.31, 7.98)	
<b>Waist circumference (cm)</b>									
< 90 (or 80) <sup>2</sup>	425	7.84 (7.44, 8.26)	0.031	129	9.51 (8.62, 10.50)	0.31	296	7.21 (6.79, 7.65)	0.991
≥ 90 (or 80) <sup>2</sup>	52	9.35 (7.96, 10.99)		35	10.61 (8.69, 12.97)		17	7.20 (5.60, 9.25)	
<b>Waist-to-hip ratio</b>									
< 0.9 (or 0.8) <sup>2</sup>	132	6.65 (6.13, 7.21)	0.001	38	7.05 (6.06, 8.20)	<0.001	94	6.49 (5.89, 7.16)	0.019
0.9 - 0.95 (or 0.8-0.85) <sup>2</sup>	240	8.37 (7.80, 8.98)		79	9.68 (8.54, 10.98)		161	7.79 (7.17, 8.47)	
≥ 0.95 (or 0.85) <sup>2</sup>	105	9.08 (8.08, 10.20)		47	12.77 (10.94, 14.91)		58	6.89 (6.02, 7.88)	
<b>Menopause</b>									
Yes	181	7.20 (6.64, 7.81)	0.974				181	7.20 (6.64, 7.81)	0.974
No	132	7.22 (6.65, 7.83)					132	7.22 (6.65, 7.83)	

GM: geometric mean, CI: confidence interval, LDL: low-density lipoprotein, HDL: cholesterol, high-density lipoprotein.

<sup>1</sup> Mercury concentration, <sup>2</sup> The values in bracket are the reference for females for HDL cholesterol, waist circumference and waist-to-hip ratio.

**Table 4.** Multiple regression analysis between blood mercury level and cardiovascular risk factors in the total population, males and females

		Total <sup>1</sup>		Males <sup>2</sup>		Females <sup>3</sup>				
		Variable	$\beta$	p-value	Variable	$\beta$	p-value	Variable	$\beta$	p-value
HBM I ( $\mu\text{g/L}$ )	< 5	WHR	0.231	0.117	WHR	0.516	0.067	WHR	0.125	0.380
		LDLc	-0.006	0.957	LDLc	-0.210	0.432	LDLc	0.037	0.774
	≥ 5	WHR	0.332	<0.001 <sup>4</sup>	WHR	0.362	<0.001 <sup>4</sup>	WHR	0.063	0.353
		LDLc	0.107	0.028 <sup>4</sup>	LDLc	0.094	0.232	LDLc	0.107	0.102

HBM: human biomonitoring, WHR: Waist-to-hip ratio, LDLc: low-density lipoprotein cholesterol.

<sup>1</sup> The model for the total population was adjusted for age, sex, frequency of fish intake, drinking, and smoking, <sup>2</sup> The model for males was adjusted for age, frequency of fish intake, drinking, and smoking, <sup>3</sup> The model for females was adjusted for age, frequency of fish intake, menopause, drinking and smoking, <sup>4</sup> The p-value was statistically significant.



suggested two criteria for mercury exposure: HBM I as an alert level and HBM II as an action level [6]. The highest quartile of blood mercury concentrations (14.59  $\mu\text{g/L}$ ) in males corresponds to HBM II, and the population at risk for mercury exposure comprised one-quarter of the male population. The mean blood mercury level may have been higher if more participated in our study. Virtanen et al. [26] reported that Hallgren et al. observed no association between the mercury level and cardiovascular risk because females with low mercury concentrations participated in their study, and the distribution of mercury concentrations in the study population was too narrow to identify the association of mercury exposure with cardiovascular risk. In our study, blood mercury levels ranged from 1.48 to 45.54  $\mu\text{g/L}$  and a sufficient numbers of subjects above the criterion for HBM II participated in our study.

Among the cardiovascular risk factors, BMI and WHR, indices of obesity differed according to mercury concentrations. BMI is related to general adiposity and WHR is related to central obesity [27]. In a multiple regression analysis, WHR was associated with blood mercury concentration, whereas BMI was not. Additionally, the WHRs of men were correlated with their mercury levels. This result concurred with a study of Brazilian natives in a mercury-contaminated area that found mercury exposure from fish consumption was not associated with BMI [28]. Hu et al. reported that the WHRs of men were significantly associated with cardiovascular disease risk, whereas BMIs were associated with increased cardiovascular risk in both sexes [27]. In a study of Faroe islanders and inhabitants of Nunavik who traditionally consume fish, mercury exposure was associated with blood pressure as cardiovascular risk factor in males only [29,30]. In a European study targeting adult men, an increased risk of mortality was observed in newly diagnosed patients with myocardial infarction with high mercury concentrations. Those results were consistent with our findings of significant association between blood mercury concentration and cardiovascular disease risk in males.

The mercury concentration was reported to be higher in males than in females. In our study, mercury concentrations were significantly higher in males than in females, and an association between mercury exposure and cardiovascular disease risk was observed in males. Blood mercury concentration was not significantly associated with menopause, and we postulate that estrogen has a limited effect on mercury levels. It is possible that this limited significance derived from differences in the alcohol intake and smoking status by

sex, whereas fish consumption was excluded because no differences in the frequency of fish consumption according to sex were observed. Kim et al. reported that drinking alcohol affected mercury concentration [14], whereas Son et al. reported found no association between alcohol consumption and mercury concentration [17]. Smoking status has not been associated with mercury concentration. Therefore, the differences of mercury concentrations by sex require further investigation.

Metabolic syndrome is a cardiovascular risk factor and is related to obesity. We found that the metabolic syndrome was not correlated with mercury concentration. Park et al. [31] reported that those in highest quartile of hair-mercury concentration had an increased risk of metabolic syndrome compared with those in the lowest quartile. These findings were based on differences in the mercury concentrations in hair specimens, which were used as an index of previous exposure to mercury [32], or on the significance of differences between the lowest and the highest quartiles of mercury concentrations. In our results, waist circumference was the only variable of five diagnostic criteria for metabolic syndrome (NCEP ATP-III) associated with mercury level. Thus, metabolic syndrome was not related to mercury level because a diagnosis of metabolic syndrome must meet three additional diagnostic criteria.

Kim et al. [33] reported that urinary mercury in children was associated with serum cholesterol and suggested that heavy metal was as a risk factor for cardiovascular disease. We found that a blood mercury concentration in males above HBM I was correlated with WHR as an index of central obesity. Based on this finding, we postulated that the risk for cardiovascular disease of men with a high mercury exposure was increased by WHR. However, a significant confounding effect, that obese subjects may eat more mercury-contaminated seafood resulting in a high mercury exposure, should also be considered. Dietary data are essential to answer this problem, but one weakness of our study was that its design did not include such data for analysis. A future study should examine dietary data and the adverse health effects of mercury exposure. In addition, no definite pathological mechanism has been identified to explain the relationship between the mercury level in males and their WHRs, an index of central obesity. Further investigations into the mechanisms related mercury exposure and central obesity or a cohort study of a population with heavy mercury exposure should contribute to our

understanding of the effect of mercury on cardiovascular disease.

## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest related to this study.

## REFERENCES

- National Research Council (U.S.). Committee on the Toxicological Effects of Methylmercury. *Toxicological effects of methylmercury*. Washington, DC: National Academy Press; 2000.
- Grandjean P, Satoh H, Murata K, Eto K. Adverse effects of methylmercury: environmental health research implications. *Environ Health Perspect* 2010; 118(8): 1137-1145.
- Oken E, Wright RO, Kleinman KP, Bellinger D, Amarasi riwardena CJ, Hu H, et al. Maternal fish consumption, hair mercury, and infant cognition in a U.S. Cohort. *Environ Health Perspect* 2005; 113(10): 1376-1380.
- Clarkson TW. The three modern faces of mercury. *Environ Health Perspect* 2002; 110 (Suppl 1): 11-23.
- United States Environmental Protection Agency. What you need to know about mercury in fish and shell fish. [cited 2011 July 18]. Available from: [http://water.epa.gov/scitech/swguidance/outreach/advice\\_index.cfm](http://water.epa.gov/scitech/swguidance/outreach/advice_index.cfm).
- Schulz C, Angerer J, Ewers U, Kolossa-Gehring M. The German Human Biomonitoring Commission. *Int J Hyg Environ Health* 2007; 210(3-4): 373-382.
- Wiggers GA, Pecanha FM, Briones AM, Perez-Giron JV, Miguel M, Vassallo DV, et al. Low mercury concentrations cause oxidative stress and endothelial dysfunction in conductance and resistance arteries. *Am J Physiol Heart Circ Physiol* 2008; 295(3): H1033-H1043.
- de Marco KC, Passos CJ, Sertorio J, Tanus-Santos JE, Barbosa F Jr. Environmental exposure to methylmercury is associated with a decrease in nitric oxide production. *Basic Clin Pharmacol Toxicol* 2010; 106(5): 411-415.
- Stern AH. A review of the studies of the cardiovascular health effects of methylmercury with consideration of their suitability for risk assessment. *Environ Res* 2005; 98(1): 133-142.
- Guallar E, Sanz-Gallardo MI, van't Veer P, Bode P, Aro A, Gomez-Aracena J, et al. Mercury, fish oils, and the risk of myocardial infarction. *N Engl J Med* 2002; 347(22): 1747-1754.
- Yoshizawa K, Rimm EB, Morris JS, Spate VL, Hsieh CC, Spiegelman D, et al. Mercury and the risk of coronary heart disease in men. *N Engl J Med* 2002; 347(22): 1755-1760.
- Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. *Circulation* 2002; 106(21): 2747-2757.
- Konig A, Bouzan C, Cohen JT, Connor WE, Kris-Etherton PM, Gray GM, et al. A quantitative analysis of fish consumption and coronary heart disease mortality. *Am J Prev Med* 2005; 29(4): 335-346.
- Ström S, Helmfrid I, Glynn A, Berglund M. Nutritional and toxicological aspects of seafood consumption-an integrated exposure and risk assessment of methylmercury and polyunsaturated fatty acid. *Environ Res* 2011; 111(2): 274-280.
- Korean National Statistical Office. *Annual report in the cause of death statistics*. Daejeon: Korean National Statistical Office; 2010. (Korean)
- Kim NS, Lee BK. National estimates of blood lead, cadmium, and mercury levels in the Korean general adult population. *Int Arch Occup Environ Health* 2011; 84(1): 53-63.
- Son JY, Lee J, Paek D, Lee JT. Blood levels of lead, cadmium, and mercury in the Korean population: results from the Second Korean National Human Exposure and Bio-monitoring Examination. *Environ Res* 2009; 109(6): 738-744.
- Kim NS, Lee BK. Blood total mercury and fish consumption in the Korean general population in KNHANES III, 2005. *Sci Total Environ* 2010; 408(20): 4841-4847.
- Kim CW, Kim YW, Chae CH, Son JS, Park SH, Koh JC, et al. The effects of the frequency of fish consumption on blood mercury levels in Koreans. *Korean J Occup Environ Med* 2010; 22(2): 114-121. (Korean)
- Jo EM, Kim BG, Kim YM, Yu SD, You CH, Kim JY, et al. Blood mercury concentration and related factors in an urban coastal area in Korea. *J Prev Med Public Health* 2010; 43(5): 377-386.
- Lim S, Chung HU, Paek D. Low dose mercury and heart rate variability among community residents nearby to an industrial complex in Korea. *Neurotoxicology* 2010; 31(1): 10-16.
- Rissanen T, Voutilainen S, Nyyssonen K, Lakka TA, Salonen JT. Fish oil-derived fatty acids, docosahexaenoic acid and docosapentaenoic acid, and the risk of acute coronary events: the Kuopio ischaemic heart disease risk factor study. *Circulation* 2000; 102(22): 2677-2679.
- Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, et al. Appropriate waist circumference cutoff points for central obesity in Korean adults. *Diabetes Res Clin Pract* 2007; 75(1): 72-80.
- Nuttall KL. Interpreting hair mercury levels in individual patients. *Ann Clin Lab Sci* 2006; 36(3): 248-261.
- Mahaffey KR. Mercury exposure: medical and public health issues. *Trans Am Clin Climatol Assoc* 2005; 116: 127-153.
- Virtanen JK, Rissanen TH, Voutilainen S, Tuomainen TP. Mercury as a risk factor for cardiovascular diseases. *J Nutr Biochem* 2007; 18(2): 75-85.

27. Hu G, Tuomilehto J, Silventoinen K, Sarti C, Mannisto S, Jousilahti P. Body mass index, waist circumference, and waist-hip ratio on the risk of total and type-specific stroke. *Arch Intern Med* 2007; 167(13): 1420-1427.
28. Barbosa AC, Jardim W, Dorea JG, Fosberg B, Souza J. Hair mercury speciation as a function of gender, age, and body mass index in inhabitants of the Negro River basin, Amazon, Brazil. *Arch Environ Contam Toxicol* 2001; 40(3): 439-444.
29. Valera B, Dewailly E, Poirier P. Environmental mercury exposure and blood pressure among Nunavik Inuit adults. *Hypertension* 2009; 54(5): 981-986.
30. Choi AL, Weihe P, Budtz-Jorgensen E, Jorgensen PJ, Salonen JT, Tuomainen TP, et al. Methylmercury exposure and adverse cardiovascular effects in Faroese whaling men. *Environ Health Perspect* 2009; 117(3): 367-372.
31. Park SB, Choi SW, Nam AY. Hair tissue mineral analysis and metabolic syndrome. *Biol Trace Elem Res* 2009; 130(3): 218-228.
32. Nuttall KL. Interpreting mercury in blood and urine of individual patients. *Ann Clin Lab Sci* 2004; 34(3): 235-250.
33. Kim DS, Lee EH, Yu SD, Cha JH, Ahn SC. Heavy metal as risk factor of cardiovascular disease--an analysis of blood lead and urinary mercury. *J Prev Med Public Health* 2005; 38(4): 401-407. (Korean)