

Effects of E-Waste Exposure on Biomarkers of Coronary Heart Disease (CHD) and their Associations with Level of Heavy Metals in Blood

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Abstract

Excess heavy metals increase the risk of various diseases. Electronic waste (e-waste) is a potential route to heavy metal exposure, and Taizhou is a large e-waste dismantling area in China. In this study, we acquire blood samples from residents living near an e-waste recycling area (exposed group) and other residents in a selected reference area (reference group) for a comparative study in Taizhou in December 2017. Seven heavy metals, including cobalt (Co), nickel (Ni), cadmium (Cd), tin (Sn), copper (Cu), zinc (Zn), and lead (Pb) are quantitatively determined in all blood samples. It is discovered that the levels of Co, Ni, Sn, and Pb in the exposed group are higher than those in the reference group. Additionally, two crucial biomarkers of coronary heart disease (CHD), i.e., troponin (Tn) and myeloperoxidase (MPO), and two biomarkers of oxidative stress, i.e., malondialdehyde (MDA) and 8-isoprostane (8-I), are measured. We discovered that the levels of these indicators in the exposed group are significantly higher than those in the reference group. Meanwhile, both the Spearman correlation and multiple linear regression analysis show that Ni is positively correlated with Tn, MPO, 8-I, and MDA. Hence, we hypothesize that exposure to e-waste increases the risk of CHD, and that Ni is an important contributor to the initiation of the disease.

Introduction

Coronary heart disease (CHD) is one of the main types of cardiovascular disease. The main cause of CHD is arteriosclerosis (AS), characterized by thickening of arterial walls and narrowing of hemorrhage, which result in myocardial ischemia and increased oxygen demand (Wirtz and von Kanel 2017). Long-term myocardial ischemia can result in acute symptoms such as heart failure, arrhythmia, cardiac infarction, and angina pectoris. CHD is a disease with a high mortality rate (Liao et al. 2017). In 2008, CHD constituted 30% of global deaths, and the total number of deaths increased to 11 million by 2020 (Zhang et al. 2019). Troponin (Tn) is a regulatory protein of myocardial contraction that is vital to muscle contraction and relaxation (He et al. 2020). When cardiomyocytes are damaged, Tn is released rapidly into the bloodstream, resulting in elevated levels of Tn in blood (Chao et al. 1990; Shah et al. 2018). Because of its sensitivity and specificity, Tn can be used as a biomarker of myocardial cell necrosis, and clinical inflammation is regarded as a critical factor in the development of AS. Myeloperoxidase (MPO) is a type of peroxidase formed by the release of neutrophils. It can induce the formation of free radicals, modify low-density lipoprotein, and affect endothelial function, ultimately resulting in unstable AS plaques. MPO levels are assumed to be associated with the severity of CHD (Kurniati et al. 2018; Liu et al. 2012). Elevated levels of oxidative stress (OS), i.e., a series of reaction states caused by an imbalance between oxidation and anti-oxidation in the body, have been shown to be related to the initiation of CHD (Ito et al. 2019). Malondialdehyde (MDA) is a product of the chain reaction of oxygen free radicals, where unsaturated fat in biofilms are attacked and lipid peroxidation that damages tissue cells occurs (Banday et al. 2007). MDA levels are a direct reflection of lipid peroxidation. Meanwhile, 8-isoprostane (8-I) is a lipid peroxidation product catalyzed by arachidonic acid (Patrono et al. 2005; Vassalle et al. 2012). MDA and 8-I are typical biomarkers of OS in the human body.

Heavy metals, which are important raw materials for industrial production, can be released into water, the atmosphere, and soil. Because heavy metals can tolerate decomposition under natural conditions, they persist in the environment (Ra et al. 2013). Heavy metals in the environment can enter the body through various pathways and harm the body through accumulation and biological actions (Ebrahimi et al. 2020). Epidemiological studies have demonstrated relationships between heavy metals and the immune and reproductive systems (Ali et al. 2020; Farkhondeh et al. 2020). Several studies have shown that heavy metals can affect CHD. Long-term exposure to Ni can result in myocardial thickening and hypertrophy (Lou et al. 2013). Chronic accumulation of cobalt (Co) can cause myocardial damage and affect cardiac systolic and diastolic functions (Haga et al. 1996). Meanwhile, heavy metals induce OS, and vascular endothelial dysfunction promotes the formation of AS plaques (Grotto et al. 2010; Vaziri 2008). Exposure to heavy metals is significantly associated with the risk of cardiovascular disease and affects the initiation of CHD (Larsson and Wolk 2016).

Owing to developments in science and technology, many electrical and electronic equipment have been developed. In China, several large electronic waste (e-waste) recycling locations exist, including Guiyu and Taizhou. Many metals are released during e-waste recycling, including mercury (Hg) Co, Ni, Sn, Zn, and Cu (Guo et al. 2020; Li et al. 2020; Xu et al. 2018; Yu et al. 2017). Nevertheless, to prevent further environmental degradation, manual and scattered e-waste disassembling workshops in Taizhou were closed in 2015. In December 2017, we collected blood samples from residents living near an e-waste dismantling area and a reference area in Taizhou.

The aim of the present study is to investigate the potential effects of e-waste exposure on the risk of CHD, as well as the contribution of heavy metals to the disease by analyzing the concentrations of heavy metals, biomarkers (Tn and MPO) of CHD, and the correlation among them in blood.

Material And Method

Study Areas and Sample Collection

In the present study, we selected Luqiao District as the exposure site (exposed group), which is a well-known e-waste dismantling area in Taizhou. Huangyan District was selected as the reference site (reference group), which is approximately 20 km from Luqiao and is extremely similar to Luqiao in terms of population, transportation, lifestyle, and socio-economic status. The age of all participants was between 30 and 50 years. Informed consent was obtained for acquiring information such as sex, weight, career history, and residence. The age, height, weight, and body mass index (BMI) of the two groups were similar, as shown in Table 1. The study was approved by the Ethics Review Committee of the Peking University Health Science Center in Beijing, China. After blood collection, all samples were stored at -80°C in an anticoagulant tube.

Table 1
Descriptive statistics of residents in reference and exposed groups

	Reference group (n = 51)	Exposed group (n = 62)	p-value
gender	male (29, 57%)	male (35, 58%)	
	female (22, 43%)	female (25, 42%)	
Age (mean ± SD, years)	43.0	41.0	0.14
Height (mean ± SD, cm)	167.0	167.0	0.11
Weight (mean ± SD, kg)	66.0	64.8	0.62
BMI	22.6	23.6	0.06

Instrumentation And Metal Determination

Venous whole blood samples were acquired from a vacuum blood collection tube containing K2EDTA. The plasma was preserved at -20°C after centrifugation (3000 rpm, 2°C–8°C). Subsequently, 1.5 mL of HNO₃ was added to the sample at room temperature and predigested for 2 h. Next, 0.5 mL of H₂O₂ was added for further digestion (Microwave Digestion System; mws-2; Bergholt, Germany) and diluted with deionized water to 7 mL. The concentrations of metals in the pretreated samples were determined via inductively coupled plasma mass spectrometry (ELAN DRCII PerkinElmer, USA). The quantitative limit of all target metals was 0.002-1 ng/mL. Seven heavy metals were determined quantitatively.

Biomarkers Analyses

Human blood plasma acquired via the procedures above was used as a biomarker. The expression of the following markers of myocardial injury (Tn and MPO) and OS markers (MDA and 8-I) was determined using ELISA based on the manufacturer's instructions.

Statistical Analysis

The concentrations of heavy metals and biomarkers are expressed as medium values. Univariate analysis indicated a partial normal distribution for all data in this study. We performed a Spearman correlation analysis (two tailed) to investigate the relationships between different variables. In addition, we used a multiple linear regression model to estimate the relationship between the concentrations of metals and each of Tn, MPO, MDA, and 8-I and used a t-test to evaluate their significance. Statistical significance was set at $p < 0.05$. The data analysis software used was SPSS version 25.0.

Results And Discussion

E-waste exposure elevated levels of biomarkers of CHD and OS in blood

Tn and MPO are markers of inflammation and CHD, respectively. In the present study, we analyzed the levels of Tn and MPO in blood. The results showed that the concentrations of the two biomarkers in the exposed group were significantly higher than those in the reference group (Table 2). Furthermore, we discovered that the concentrations of the two OS markers (MDA and 8-I) in the exposed group were significantly higher than those in the reference group.

Table 2
Concentrations of biomarkers (ng/mL) and heavy metals in blood from reference and exposed groups

	Reference group (Huangyan)	Exposed group(Luqiao)	P-value
8-I (pg/ml)	1021.72	1210.94	0.003
MDA(pg/mL)	5.24	6.43	0.000
Tn(ng/mL)	523.18	576.11	0.037
MPO(ng/mL)	163.13	183.38	0.000

CHD is a chronic disease characterized by OS and inflammation. When the body is stimulated by external stimulation, the imbalance of OS result in the formation of significant amounts of lipid products and oxides in the arterial walls, which induces an immune response and an inflammatory reaction (Abraham and Marchuk 2014). Several studies have shown that MPO mediates the formation of OS and inflammatory reactions and is a significant inflammatory marker (Love et al. 2017; Zhang et al. 2020). Moreover, the oxidative modification of MPO causes the formation of arterial plaques, and the level of MPO is closely associated with CHD (Gorudko et al. 2012). During the initiation of CHD, inflammatory cell infiltration and OS can cause oxidative damage to cardiomyocytes and other tissues. When cardiomyocytes are slightly damaged, membrane rupture occurs, and Tn is released from the cardiomyocytes into the peripheral blood (Mair et al. 1994). Our results showed that e-waste exposure elevated the blood levels of CHD and OS biomarkers, i.e., Tn, MPO, 8-I, and MDA, which indicates an elevated risk of CHD in residents living near e-waste recycling sites, and that OS is involved in the process.

Associations Between Biomarkers And Heavy Metal Exposure

The results of the levels of the seven heavy metals in the blood samples are shown in Table 3. Compared with the reference group, the concentrations of Co, Ni, and Sn in the exposed group were significantly higher than those in the reference group (Table 3).

Table 3
Concentrations of heavy metals (ng/mL) in blood from reference and exposed groups

	Reference group (Huangyan)	Exposed group(Luqiao)	P-value
Co	0.32	0.40	0.000
Ni	2.10	4.79	0.000
Cd	1.56	1.60	0.892
Sn	0.23	0.32	0.013
Cu	735.14	763.85	0.261
Zn	5312.01	4831.19	0.084
Pb	32.85	37.93	0.066
SUM	6084.21	5640.08	0.930

The results of Spearman correlation analysis showed that the concentrations of Co, Ni, and Sn were significantly positively correlated in the exposed group, indicating that the concentrations of heavy metals in human blood were affected by exposed e-waste. To investigate the contributions of heavy metals to the risk of CHD, we analyzed the relationships between altered heavy metals and biomarkers of CHD and OS using Spearman correlation analysis and multiple linear regression. In the exposed group, the Spearman correlation analysis showed that the concentration of Ni was positively correlated with the concentrations of Tn, MPO, MDA and 8-I. Meanwhile, the concentration of Co was positively correlated with 8-I and MDA, and 8-I and MPO were positively correlated with Sn (Table 4, Fig. 1). In addition, the linear regression analysis showed that Ni was correlated with Tn, MPO, and MDA, whereas Co was correlated with Tn (Table 5). In the reference group, both the Spearman correlation and linear regression analyses did not indicate any association between heavy metals and the biomarkers of CHD and OS (Tables 4 and 5).

Table 4

Spearman correlation coefficients among individual heavy metals and hormones in blood samples acquired from reference and exposed groups

	8-I	MDA	Tn	MPO	Co	Ni	Sn
Reference group							
8-I	1.000						
p-value							
MDA	0.350*	1.000					
p-value	0.015						
Tn	0.162	0.145	1.000				
p-value	36	39	39				
MPO	0.230	0.100	0.314	1.000			
p-value	0.138	0.51	0.052				
Co	0.256	-0.16	0.016	-0.075	1.000		
p-value	0.079	0.262	0.925	0.619			
Ni	-0.085	-0.275	-0.063	-0.065	0.078	1.000	
p-value	0.565	0.051	0.702	0.669	0.586		
Sn	-0.160	-0.245	0.029	-0.047	0.104	0.298*	1.000
p-value	0.277	0.083	0.861	0.756	0.469	0.034	
exposed group							
8-I	1.000						
p-value	.						
MDA	0.399**	1.000					
p-value	0.002	.					
Tn	0.166	0.018	1.000				
p-value	0.249	0.900	.				
MPO	0.331*	0.132	-0.013	1.000			
p-value	0.018	0.357	0.928	.			
Co	0.308*	0.399**	-0.176	0.235	1.000		

*significance level of 0.1, **significance level of 0.05, ***significance level of 0.001.

	8-I	MDA	Tn	MPO	Co	Ni	Sn
p-value	0.020	0.002	0.209	0.091	.		
Ni	0.327*	0.367**	.339*	0.427**	0.354**	1.000	
p-value	0.013	0.005	0.013	0.001	0.005	.	
Sn	0.329*	0.127	0.066	0.314*	0.487**	0.420**	1.000
p-value	0.012	0.348	0.639	0.022	0	0.001	.
*significance level of 0.1, **significance level of 0.05, ***significance level of 0.001.							

Table 5

Multiple linear regression analysis for analyzing associations between hormones and metals in participants of reference and exposed groups

	Reference group(Huangyan)			Exposed group(Luqiao)		
	β	95% CI	p-value	β	95% CI	p-value
MDA						
Ni	-0.240	(-0.562) - 0.082	0.141	0.274	(- 0.023) - 0.525	0.033
Co	-1.246	(-3.993) - 1.500	0.366	1.932	(- 0.026) - 3.890	0.053
Sn	-0.881	(-2.397) - 0.635	0.248	-0.238	(-0.771) - 0.296	0.375
8-I						
Ni	-14.971	(-94.64) - 64.707	0.707	48.533	(-22.783) - 119.849	0.178
Co	579.139	(-15.682) - 1173.959	0.707	229.903	(-327.439) - 787.246	0.412
Sn	-184.84	(-517.551) - 147.872	0.056	5.126	(-148.03) - 158.282	0.947
Tn						
Ni	-5.615	(-31.160) - 19.929	0.658	49.048	12.278-85.818	0.010
Co	5.845	(-250.984) - 262.673	0.963	-556.678	(-903.143) -(210.213)	0.002
Sn	17.518	(-97.539) - 132.574	0.759	64.852	(-15.409) - 145.114	0.111
MPO						
Ni	-1.459	(-10.084) - 7.166	0.735	6.797	0.674-12.921	0.03
Co	-21.134	(-108.193) - 65.924	0.627	7.018	(-34.52) - 48.557	0.736
Sn	-3.670	(-44.071) - 36.732	0.855	-2.892	(-14.085) - 8.302	0.606

Meanwhile, the results showed that exposure to heavy metals can affect OS in the body, as well as increase the corresponding levels of CHD markers. The results showed a significant correlation among MPO, 8-I, and MDA (Table 4).

Epidemiological and toxicological studies have shown that exposure to heavy metals is associated with cardiovascular mortality (Houston 2011). Heavy metals contribute significantly to CHD (Myong et al. 2014). Heavy metal-rich monocytes accumulate in the aortic wall through blood circulation and induce endothelial cell injury and apoptosis (Kukongviriyapan et al. 2014). Excessive amounts of heavy metals cause cardiotoxicity through apoptosis and DNA damage (Owumi et al. 2020). Metals can cause OS and inflammation, increase blood pressure, and affect thrombosis (Valera et al. 2012). After exposure to heavy metals, the body produces an inflammatory response, resulting in elevated levels of MPO, which increases the risk of CHD (Reisgen et al. 2020; Xiao et al. 2019). In a study pertaining to the cardiac toxicity of heavy metals, it was discovered that heavy metals can cause an increase in serum Tn levels (Ali et al. 2020). Our results showed that e-waste exposure elevated the blood levels of Ni, and that Ni was positively correlated with the biomarkers of CHD and OS, including Tn, MPO, MDA, and 8-I. Ni can promote LDL oxidation and affect AS (Wu et al. 2015). Furthermore, Ni damages the vascular endothelium and alters vasoconstriction/vasodilation, which are important symptoms of CHD (Cuevas et al. 2010). Occupational Ni exposure can increase lipid peroxidation and decrease antioxidant levels (Kalahasthi et al. 2006). Moreover, OS is vital to the pathogenesis of CHD (Yang et al. 2019). Elevated levels of MDA and 8-I suggest that exposure to heavy metals can result in lipid peroxidation, which can subsequently cause cell and tissue damage and hence the formation of plaques in the arteries. Based on the findings above, we infer that Ni can increase the risk of CHD and OS.

Conclusion

In summary, although almost all e-waste workshops have been closed for two years, the effect of exposure to heavy metals persists in the associated areas. Compared with the reference group, the levels of Co, Ni, and Sn in the exposed group were higher. This indicates that e-waste exposure can result in the accumulation of heavy metals and increase the level of heavy metals in the body. Therefore, the problem of heavy metal exposure mediated by e-waste must be investigated comprehensively.

In addition, it was discovered some critical biomarkers of CHD and OS in blood were elevated in residents living near the e-waste recycling area. Furthermore, a significant correlation was discovered among Ni, Tn, MPO, MDA, and 8-I, indicating that e-waste exposure increased the risk of CHD, and that Ni is an important contributor to the initiation of the disease.

Declarations

Authors' contributions

Wang and Xue is mainly responsible for the data analysis and drafts the manuscript. Li and Wei curated the study and oversaw the coordination. All authors were involved this study and read and approved the final manuscript.

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Data availability

Available on request.

Ethics approval and consent to participate

The study was approved by the Ethics Review Committee of Peking University Health Science Center in Beijing, China.

Consent to participate

Not applicable.

Consent to publish

All of the authors have reviewed and approved the manuscript for publication.

Competing interests

The authors declare that they have no competing interests.

References

1. Abraham DM, Marchuk DA. 2014. Inhibition of the cardiomyocyte-specific troponin i-interacting kinase limits oxidative stress, injury, and adverse remodeling due to ischemic heart disease. *Circulation Research* 114:938-940.
2. Ali S, Awan Z, Mumtaz S, Shakir HA, Ahmad F, Ulhaq M, et al. 2020. Cardiac toxicity of heavy metals (cadmium and mercury) and pharmacological intervention by vitamin c in rabbits. *Environmental Science and Pollution Research* 27:29266-29279.
3. Banday AA, Muhammad AB, Fazili FR, Lokhandwala M. 2007. Mechanisms of oxidative stress-induced increase in salt sensitivity and development of hypertension in sprague-dawley rats. *Hypertension* 49:664-671.
4. Chao SH, Bu CH, Cheung WY. 1990. Activation of troponin-c by cd-2+ and pb-2+. *Archives of Toxicology* 64:490-496.

5. Cuevas AK, Liberda EN, Gillespie PA, Allina J, Chen LC. 2010. Inhaled nickel nanoparticles alter vascular reactivity in c57bl/6 mice. *Inhalation Toxicology* 22:100-106.
6. Ebrahimi M, Khalili N, Razi S, Keshavarz-Fathi M, Khalili N, Rezaei N. 2020. Effects of lead and cadmium on the immune system and cancer progression. *Journal of Environmental Health Science and Engineering* 18:335-343.
7. Farkhondeh T, Afshari R, Mehrpour O, Samarghandian S. 2020. Mercury and atherosclerosis: Cell biology, pathophysiology, and epidemiological studies. *Biological trace element research* 196:27-36.
8. Gorudko IV, Kostevich VA, Sokolov AV, Shamova EV, Buko IV, Konstantinova EE, et al. 2012. Functional activity of neutrophils in diabetes mellitus and coronary heart disease: Role of myeloperoxidase in the development of oxidative stress. *Bulletin of Experimental Biology and Medicine* 154:23-26.
9. Grotto D, Valentini J, Fillion M, Passos CJS, Garcia SC, Mergler D, et al. 2010. Mercury exposure and oxidative stress in communities of the Brazilian Amazon. *Science of the Total Environment* 408:806-811.
10. Guo C, Wei YJ, Yan LL, Li ZG, Qian Y, Liu HJ, et al. 2020. Rare earth elements exposure and the alteration of the hormones in the hypothalamic-pituitary-thyroid (hpt) axis of the residents in an e-waste site: A cross-sectional study. *Chemosphere* 252.
11. Haga Y, Clyne N, Hatori N, HoffmanBang C, Pehrsson SK, Ryden L. 1996. Impaired myocardial function following chronic cobalt exposure in an isolated rat heart model. *Trace Elements and Electrolytes* 13:69-74.
12. He Y, Liu Q, Wang J, Wang DW, Ding H, Wang W. 2020. Prognostic value of elevated cardiac troponin I in patients with intracerebral hemorrhage. *Clinical Cardiology* 43:338-345.
13. Houston MC. 2011. Role of mercury toxicity in hypertension, cardiovascular disease, and stroke. *Journal of Clinical Hypertension* 13:621-627.
14. Ito F, Sono Y, Ito T. 2019. Measurement and clinical significance of lipid peroxidation as a biomarker of oxidative stress: Oxidative stress in diabetes, atherosclerosis, and chronic inflammation. *Antioxidants* 8.
15. Kalahasthi RB, Rao RHR, Murthy RBK. 2006. Plasma lipid peroxidation and erythrocyte antioxidants status in workers exposed to nickel. *Biomarkers* 11:241-249.
16. Kukongviriyapan U, Pannangpetch P, Kukongviriyapan V, Donpunha W, Sompamit K, Surawattanawan P. 2014. Curcumin protects against cadmium-induced vascular dysfunction, hypertension and tissue cadmium accumulation in mice. *Nutrients* 6:1194-1208.
17. Kurniati NF, Angelia T, Artarini AA, Nurfatwa M. 2018. Myocardial infarction elevates inflammation and contributes to the formation of atheroma plaques in the aorta of hypercholesterolaemic rats. *Makara Journal of Health Research* 22:40-45.
18. Larsson SC, Wolk A. 2016. Urinary cadmium and mortality from all causes, cancer and cardiovascular disease in the general population: Systematic review and meta-analysis of cohort studies. *International Journal of Epidemiology* 45:782-791.

19. Li Z, Guo C, Li X, Wang Z, Wu J, Qian Y, et al. 2020. Associations between metal exposure and global DNA methylation in potentially affected people in e-waste recycling sites in taizhou city, china. *Sci Total Environ* 711:135100.
20. Liao JW, Huang W, Liu G. 2017. Animal models of coronary heart disease. *Journal of Biomedical Research* 31:3-10.
21. Liu CG, Xie GM, Huang WF, Yang YC, Li P, Tu ZG. 2012. Elevated serum myeloperoxidase activities are significantly associated with the prevalence of atherosclerosis and high ldl-c levels in chd patients. *Journal of Atherosclerosis and Thrombosis* 19:435-443.
22. Lou SY, Zhong LK, Yang XC, Xue T, Gai RH, Zhu DF, et al. 2013. Efficacy of all-trans retinoid acid in preventing nickel induced cardiotoxicity in myocardial cells of rats. *Food and Chemical Toxicology* 51:251-258.
23. Love D, Barrett T, Hawkins C. 2017. Role of the myeloperoxidase oxidant hypochlorous acid (hosc) in the adaptation of cells to oxidative stress during inflammation. *Free Radical Biology and Medicine* 108:S29-S30.
24. Mair J, Thomekromer B, Wagner I, Lechleitner P, Dienstl F, Puschendorf B, et al. 1994. Concentration-time courses of troponin and myosin subunits after acute myocardial-infarction. *Coronary Artery Disease* 5:865-872.
25. Myong JP, Kim HR, Jang TW, Lee HE, Koo JW. 2014. Association between blood cadmium levels and 10-year coronary heart disease risk in the general korean population: The korean national health and nutrition examination survey 2008-2010. *Plos One* 9.
26. Owumi SE, Olayiwola YO, Alao GE, Gbadegesin MA, Odunola OA. 2020. Cadmium and nickel co-exposure exacerbates genotoxicity and not oxido-inflammatory stress in liver and kidney of rats: Protective role of omega-3 fatty acid. *Environmental Toxicology* 35:231-241.
27. Patrono C, Falco A, Davi G. 2005. Isoprostane formation and inhibition in atherothrombosis. *Current Opinion in Pharmacology* 5:198-203.
28. Ra K, Kim ES, Kim KT, Kim JK, Lee JM, Choi JY. 2013. Assessment of heavy metal contamination and its ecological risk in the surface sediments along the coast of korea. *Journal of Coastal Research*:105-110.
29. Reisgen M, Thomas K, Beilmann V, Markert A, Gerhards B, Krichel T, et al. 2020. Increased neutrophil granulocyte and myeloperoxidase (mpo) levels indicate acute inflammation due to the exposure of zinc- and copper-containing welding fumes. *Journal of occupational and environmental medicine*.
30. Shah KS, Maisel AS, Fonarow GC. 2018. Troponin in heart failure. *Heart Failure Clinics* 14:57+.
31. Valera B, Muckle G, Poirier P, Jacobson SW, Jacobson JL, Dewailly E. 2012. Cardiac autonomic activity and blood pressure among inuit children exposed to mercury. *Neurotoxicology* 33:1067-1074.
32. Vassalle C, Bianchi S, Bianchi F, Landi P, Battaglia D, Carpeggiani C. 2012. Oxidative stress as a predictor of cardiovascular events in coronary artery disease patients. *Clinical Chemistry and Laboratory Medicine* 50:1463-1468.

33. Vaziri ND. 2008. Mechanisms of lead-induced hypertension and cardiovascular disease. *American Journal of Physiology-Heart and Circulatory Physiology* 295:H454-H465.
34. Wirtz PH, von Kanel R. 2017. Psychological stress, inflammation, and coronary heart disease. *Current Cardiology Reports* 19.
35. Wu SW, Yang D, Wei HY, Wang B, Huang J, Li HY, et al. 2015. Association of chemical constituents and pollution sources of ambient fine particulate air pollution and biomarkers of oxidative stress associated with atherosclerosis: A panel study among young adults in Beijing, China. *Chemosphere* 135:347-353.
36. Xiao LL, Zhou Y, Ma JX, Cao LM, Zhu CM, Li W, et al. 2019. Roles of C-reactive protein on the association between urinary cadmium and type 2 diabetes. *Environmental Pollution* 255.
37. Xu X, Liao W, Lin Y, Dai Y, Shi Z, Huo X. 2018. Blood concentrations of lead, cadmium, mercury and their association with biomarkers of DNA oxidative damage in preschool children living in an e-waste recycling area. *Environmental Geochemistry and Health* 40:1481-1494.
38. Yang X, He T, Han S, Zhang X, Sun Y, Xing Y, et al. 2019. The role of traditional Chinese medicine in the regulation of oxidative stress in treating coronary heart disease. *Oxid Med Cell Longev* 2019:3231424.
39. Yu EA, Akormedi M, Asampong E, Meyer CG, Fobil JN. 2017. Informal processing of electronic waste at Agbogbloshie, Ghana: Workers' knowledge about associated health hazards and alternative livelihoods. *Global Health Promotion* 24:90-98.
40. Zhang YN, Yan FH, Jiang WH. 2019. Relationship between self-management behaviors and health-related quality of life among Chinese patients with coronary heart disease: A cross-sectional study. *Contemporary Nurse* 55:554-564.
41. Zhang YQ, Jiang YF, Chen M, Zhang NN, Zhou YF. 2020. Association between myeloperoxidase rs2333227 polymorphism and susceptibility to coronary heart disease. *Archives of Medical Science* 16:1231-1238.

Figures

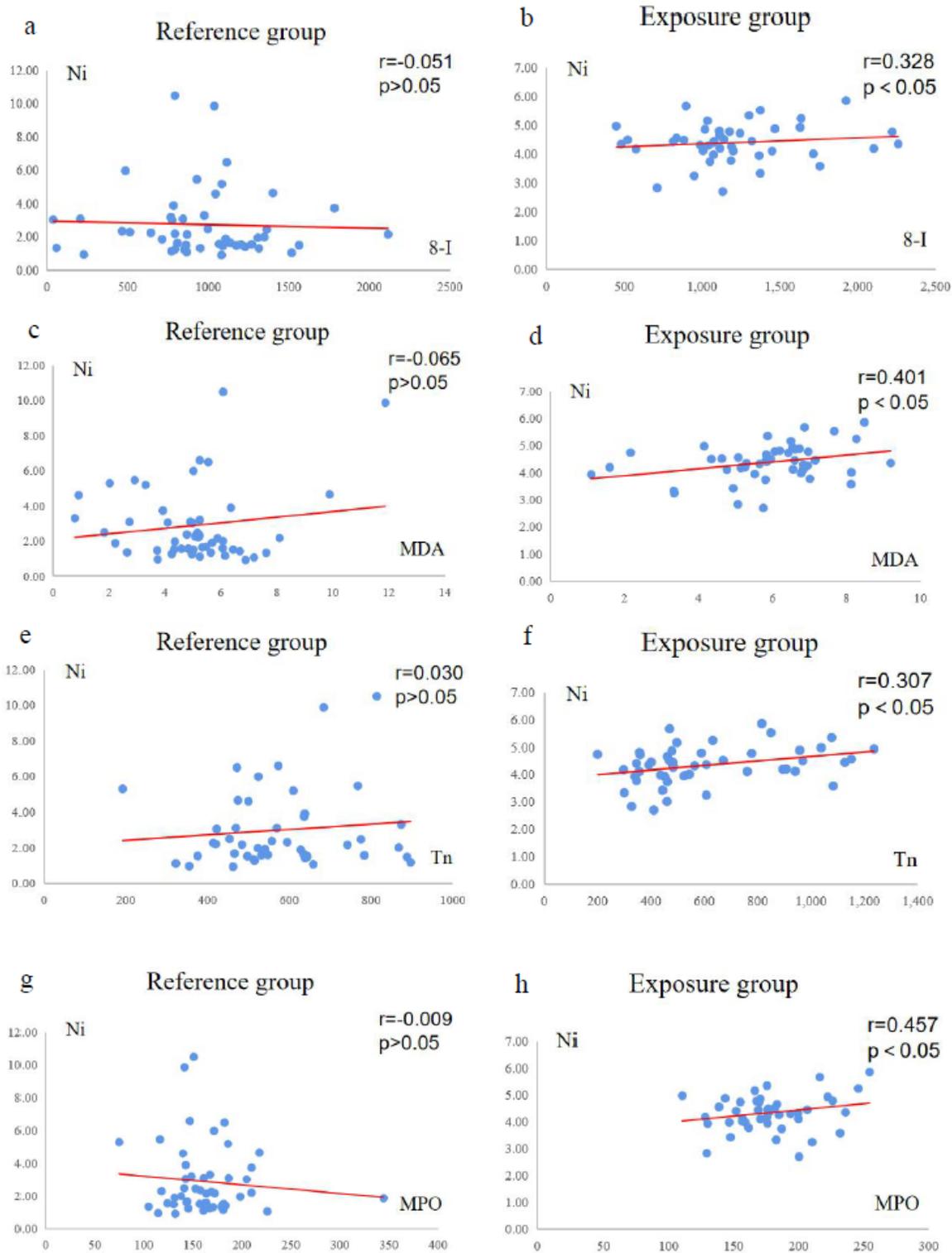


Figure 1

Correlations of blood Ni with indicators of OS (8-I and MDA) and CHD (Tn and MPO). Ni was positively correlated with the level of these indicators in exposed group.