BMC Public Health

RESEARCH

Open Access

Association between heavy metal exposure and heart failure incidence and mortality: insights from NHANES data (2003–2018)

Zebin Lin[1†], Yongqi Dong[2†], Xinlong Di[3], Yang Bai[3], Jianmin Tang[3], Guike Lai[4], Shengfang Wang[5], Xiaohu Wang[5], Yuhao Liu[5] and Yipin Zhao[5*]

Abstract

Background Environmental heavy metal exposure is a potential yet understudied risk factor for heart failure (HF), a global health burden with rising prevalence. While toxic metals like cadmium (Cd), mercury (Hg), and arsenic (As) are linked to cardiovascular diseases, their roles in HF incidence and prognosis remain unclear.

Methods The associations between heavy metals and HF outcomes were analyzed using NHANES 2003–2018 data ($n = 11,592$). Metals were measured in blood (Cd, Hg, Pb) and urine (As, Hg, others) using inductively coupled plasma mass spectrometry (ICP-MS). Confounding factors were addressed through propensity score matching (PSM). HF incidence was evaluated using logistic regression, while mortality was assessed via Cox regression. Mechanistic pathways were explored through causal mediation analysis.

Results After PSM ($n = 987$, 337 HF cases), blood Cd showed a positive association with HF incidence (OR:1.35, 95%CI:1.05–1.72), while urinary Hg (OR:0.78, 95%CI:0.63–0.98) and As (OR:0.84, 95%CI:0.72–0.99) exhibited protective effects. Urinary As correlated with elevated cardiovascular mortality in HF patients (HR:1.19, 95%CI:1.04–1.35). Mediation analysis indicated Cd's effect on HF was mediated via CHD/OMI, whereas Hg's protection involved reduced CHD/OMI incidence. As directly lowered HF risk without mediation.

Conclusion These findings underscore cadmium's role as a risk factor and the paradoxical effects of mercury and arsenic: low to moderate concentrations of Hg/As may reduce HF risk through indirect pathways (e.g., reduced CHD/OMI for Hg) or direct cardioprotective mechanisms (for As), yet arsenic's association with mortality highlights its long-term cardiovascular toxicity. Findings advocate for preventive strategies targeting metal exposure and further research integrating cumulative biomarkers.

Keywords Heavy metals, Heart failure, Cardiovascular disease

[†]Zebin Lin and Yongqi Dong equally contributed to this work.

*Correspondence:
Yipin Zhao
zhao1pin@gmail.com
[1]Department of Geriatrics, Zhongshan Hospital Xiamen University, 201 Hubin South Road, Xiamen, Fujian, China
[2]Wushan County People's Hospital of Chongqing, No.168, Guangdongxi Road, Wushan County, Chongqing, China
[3]Department of Cardiology, The Second Affiliated Hospital, School of Medicine, Zhengzhou University, Zhengzhou, Henan, China
[4]Department of Geriatrics Cardiology, The Second Affiliated Hospital, School of Medicine, Xi'an Jiaotong University, Xi'an, Shaanxi 710004, China
[5]Department of Cardiology, Fuwai Central China Cardiovascular Hospital, Henan Provincial People's Hospital Heart Center, Zhengzhou, Henan, China

Introduction

Heart failure (HF), as the terminal stage of cardiovascular disease, has emerged as a significant threat to global public health. In 2017, the global prevalence of HF exceeded 64 million cases. Although HF incidence is stable or declining in high-income countries, its prevalence continues to rise because of population aging, advancements in ischemic heart disease management and survival rates, as well as the implementation of effective evidence-based therapies that extend the lifespan of HF patients. This is inevitably associated with a greater socioeconomic burden. For instance, in the U.S., HF prevalence increased from 2.4% in 2012 to a projected 3.0% by 2030, with HF-related healthcare costs rising from $30.7 billion to $69.8 billion over the same period—a 127% increase—highlighting the growing economic burden [1, 2]. Although significant progress has been made in understanding the risk factors for HF, numerous unknown risks still exist, and traditional risk factors alone are insufficient to account for all potential risks.

Heavy metals are naturally occurring elements characterized by high atomic weight and density (≥ 4.5 g/cm^3). They can be categorized into toxic metals (such as arsenic, cadmium, lead, and mercury) and essential trace metals (such as zinc and selenium). Pollution from heavy metals originates from both natural processes and human activities, including industrial operations, agricultural practices, and fossil fuel combustion [3]. These contaminants can enter the human body through pathways such as air, water, and the food chain. Exposure to heavy metals has been linked to a range of health problems, including cardiovascular diseases [4], kidney damage [5], neurological disorders [6], and cancer [7]. Notably, heavy metal exposure is strongly associated with the development of cardiovascular diseases such as hypertension, atherosclerosis, and myocardial infarction, which are themselves risk factors for HF [8, 9]. These metals have been shown to exert toxic effects on the cardiovascular system by inducing oxidative stress, inflammation, and endothelial dysfunction [10]. For example, cadmium and arsenic promote monocyte infiltration and accelerates atherosclerotic plaque formation by upregulating endothelial cell adhesion molecules [11, 12]. Lead and arsenic are risk factors for hypertension. Lead causes vascular dysfunction by inhibiting the synthesis of calmodulin dependent nitric oxide (NO), while arsenic increases peripheral vascular resistance by activating the renin-angiotensin system (RAS) and inducing oxidative stress [13, 14]. It is also important to note that heavy metals such as cadmium [15], mercury [16], and arsenic [17] can directly damage cardiomyocytes and induce programmed cell death (apoptosis).

While there is growing evidence suggesting a link between heavy metal exposure and cardiovascular disease, limited research has explored the relationship between heavy metal concentration and the occurrence and prognosis of HF. Studies have shown that blood lead levels are associated with left ventricular hypertrophy, while urine arsenic concentration is related to left ventricular wall thickening and hypertrophy [18, 19]. Cadmium exposure demonstrates consistent links to HF risk across cohorts: the Danish Diet cohort identified a 50% elevated HF risk in men (HR: 1.5, 95% CI: 1.2–1.9) [20]. Furthermore, another prospective cohort study compared the highest and lowest quartiles of urinary cadmium concentration with the risk of HF (HR:1.61, 95% CI: 1.10–2.36) [21]. These findings collectively implicate heavy metals in cardiac remodeling and HF pathogenesis. Understanding the impact of heavy metals on HF may provide valuable insights into the pathophysiology of the disease and aid in the development of targeted prevention and treatment strategies [10]. This study, based on data from the National Health and Nutrition Examination Survey (NHANES) (2003–2018), investigates the relationship between environmental heavy metal exposure and the incidence and prognosis of HF. The aim is to determine whether heavy metal exposure is a modifiable risk factor for HF and to provide scientific evidence for future prevention and treatment strategies.

Methods

Study population

The data used in this study is derived from the NHANES (National Health and Nutrition Examination Survey) cycles from 2003 to 2018, which encompassed information from 70,342 participants. To obtain a comprehensive and representative sample, we included participants aged ≥ 20 years (consistent with the NHANES adult sampling framework) and excluded those with missing data in key variables (self-reported heart failure status and heavy metal measurement data), as illustrated in Fig. 1. The research methodology of this study has been approved by the Ethics Review Committee, and the survey adheres to the fundamental principles of the Declaration of Helsinki, with data users strictly complying with data protection and privacy regulations.

Metal measurement

This study analyzed a total of 15 heavy metals, including 3 metals in the blood. Since 2003, Inductively Coupled Plasma Mass Spectrometry (ICP-MS) has been used in NHANES to detect the concentrations of mercury, lead, and cadmium in whole blood. Additionally, urinary metals (Ba, Cd, Co, Cs, Mo, Pb, Sb, Tl, W, and U) were all measured using ICP-MS. Due to extensive missing data, we excluded manganese, tin, and strontium from our analysis of urine samples. Additionally, beryllium and

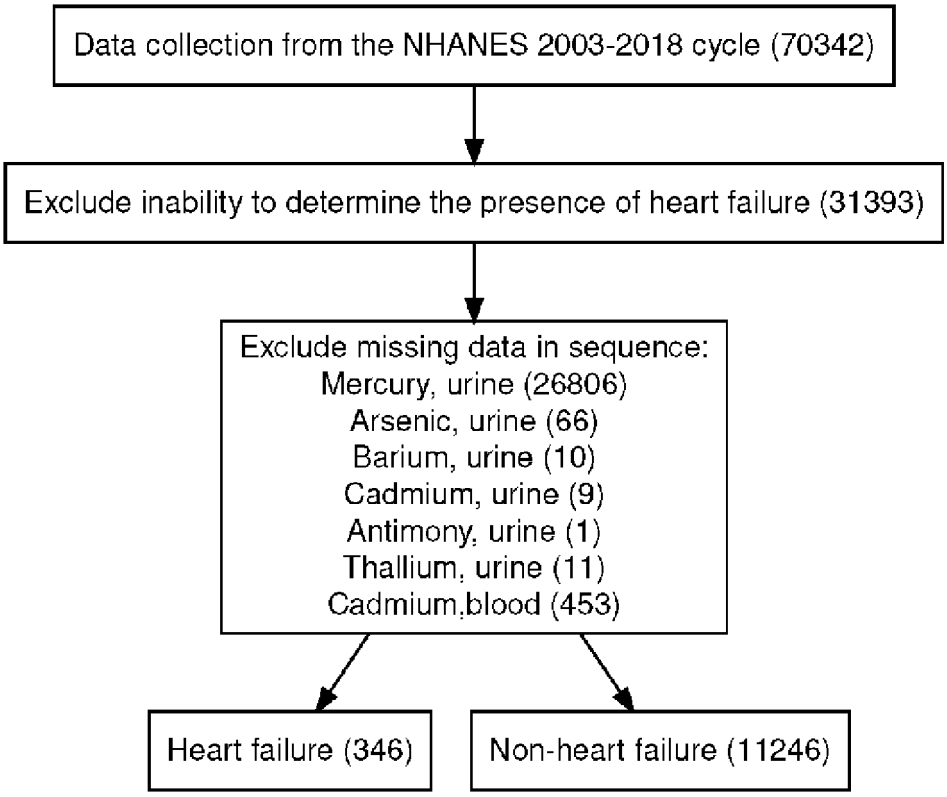

Fig. 1 Baseline Screening Participant Inclusion Flowchart

platinum were not included because their detection rates in urine were below the threshold of the detection limit.

Other definitions

The diagnosis of heart failure was determined by self-reporting by the participants. The public-use linked mortality files of continuous NHANES 2003–2018 were obtained from the NCHS. In the NHANES database, the definition of cardiovascular death (ICD-10 codes: I00-I09, I11, I13, I20-I51) is based on the code of the International Classification of Diseases, 10th edition (ICD-10), as stated in relevant documents in HCHS. Follow-up time has been calculated using person months from the date of interview to the date of death or the end of the mortality period.

Statistical analysis

Any outliers detected in the laboratory results were effectively addressed using the winsorize method. This technique was executed through the STATA winsor2 command, with the 1% and 99% percentiles serving as the designated cut-off points. In addition, any missing values were meticulously filled in using random forest interpolation, a method facilitated by the missForest package [22]. Q-Q plots were utilized to assess the distribution of the data. Group comparisons for continuous variables with a normal distribution were conducted using Welch's t-test, while non-normally distributed variables were compared using the Wilcoxon rank-sum test. Fisher's exact test was used to compare the count data between groups. To minimize the potential impact of confounding factors, we employed propensity score matching. This statistical technique aims to balance the covariates between groups, ensuring that observed differences in outcomes are more likely attributed to the variable of interest rather than the influence of confounders. After adjusting for confounding factors, we proceeded with the Spearman correlation test to evaluate the relationship between variables. Additionally, binary logistic regression and restricted cubic spline plots were utilized to clarify the association between heavy metal concentrations and the risk of HF incidence. To explore additional mechanisms linking heavy metal exposure and the incidence of HF, we conducted causal mediation analysis using the 'mediation' package and estimated the confidence intervals of the mediation effects using the Bootstrap method. To address competing risks (non-cardiovascular deaths), the Fine-Gray subdistribution hazard model was employed to analyze cardiovascular death risk. Proportional Cox regression analysis was employed to evaluate the risk of all-cause mortality in HF patients. Statistical significance was set at $P < 0.05$ (two-sided). In our study, all statistical

analyses were performed using the R software ((R for Mac version 4.2.2, R Foundation for Statistical Computing, Vienna).

Result

Baseline characteristic

In the baseline characteristic analysis of this study, HF was used as the grouping variable to compare various characteristics between the two groups. The results showed that the HF group was significantly older (mean age 68 ± 12 years) than the non-HF group (49 ± 18 years), with a statistically significant difference ($p < 0.001$). The HF group also had a higher proportion of males (60.4%). In terms of ethnicity, the proportion of non-Hispanic whites in the HF group was significantly higher (60.7%), while the proportion of other ethnic minorities, such as Mexican Americans, was lower (7.2%). The proportion of individuals with higher education in the HF group (38.7%) was lower than in the non-HF group (50.9%). In terms of health risks, the prevalence of diabetes (44.5%), coronary heart disease (CHD) (37.0%), angina (22.3%), old myocardial infarction (OMI) (44.8%) and stroke (22.3%) in the HF group was significantly higher than in the control group ($p < 0.001$). Biochemical indicators showed that the red blood cell count, hemoglobin, and albumin levels were lower in the HF group compared to the control group, with all indicators showing p-values less than 0.001. Additionally, the levels of uric acid, creatinine, blood urea nitrogen, and concentrations of various trace metals such as urinary mercury, blood cadmium, and blood lead were significantly elevated in the HF group. The detailed baseline situation is shown in Table 1.

Propensity score matching (PSM)

Considering the substantial differences between groups at baseline that could potentially interfere with our research results, we utilized propensity score matching (PSM) to mitigate the impact of potential confounding factors. We conducted 1:2 greedy nearest neighbor matching with a caliper of 0.2 using the "MatchIt" R package. A distance was calculated between units in one group and the other, with each unit being assigned a control unit as a match. The matching process was considered "greedy" as no attempt was made to optimize an overall criterion; each match was chosen independently without considering potential subsequent matches. The covariates included in the PSM and the standardized mean differences (SMD) before and after matching can be found in the supplementary materials (Table S1). A significant decrease in SMDs can be observed after matching, indicating that propensity score matching effectively improves the balance of covariates between the two groups. Following the matching process, we compared clinical outcomes between the two groups using the same statistical methods as in the baseline analysis section. The post propensity matching baseline data is displayed in Table 2, revealing significant discrepancies in CHD, angina pectoris, OMI, all-cause mortality, and cardiovascular mortality between the compared groups. These variations are highly statistically significant, with all P-values being less than 0.001. Conversely, no significant variations were found in other characteristics such as diabetes, stroke history, and most laboratory indicators. Among laboratory parameters, urinary mercury and arsenic, as well as blood cadmium and mercury levels, showed significant differences, with the HF group generally indicating lower levels. These findings suggest distinct clinical and biochemical profiles associated with HF, underscoring the potential importance of these factors in its context.

Correlation analysis

Spearman correlation analysis was used to explore the correlations among heavy metals. The results are illustrated in Fig. 2. It is evident that there exists a small to moderate correlation between the concentrations of these heavy metals, as detailed in Table S2.

Heavy metal exposure and risk of HF

Logistic regression was utilized to assess the relationship between heavy metal exposure and the occurrence of HF (Table 3). The findings revealed that mercury (Hg) (OR: 0.78,,95%CI:0.63–0.98, $P = 0.022$) and standardized arsenic (As) (OR $_{\text{per 29ug/L}}$: 0.84, 95%CI:0.72–0.99, $P = 0.031$) levels in urine after adjustment for age, gender, and creatinine exhibited a statistically significant "protective" association with the incidence of HF, while cadmium (Cd) (OR: 1.35, 95%CI: 1.05–1.72, $P = 0.013$, adjusted for the same covariates) concentration in blood was a risk factor. The increase of mercury (Hg) concentration in blood and the risk of HF showed a downward trend. After adjustment for age, gender and creatinine, there was no significant correlation between urinary cesium and the risk of HF. Furthermore, the relationship between the concentrations of the aforementioned four forms of heavy metals and the incidence of HF was demonstrated using a restricted cubic spline graph. The results indicated a linear relationship, as shown in Fig. 3.

Mediation analysis

The modeling approach was based on a Bootstrap method with 100 simulations to estimate the indirect effect, direct effect of heavy metals (Cd, As and Hg) on HF, with CHD and OMI as a mediator, as shown in Table 4. With CHD and OMI as mediators, the levels of blood cadmium[coefficient (95%CI): 0.043 (0.009, 0.062),CHD as mediator; 0.042 (0.012, 0.059),OMI as mediator] and urinary mercury[coefficient (95%CI):

Table 1 Patient demographics and baseline characteristics

Characteristic	Non-HF, *N* = 11,246	HF *N* = 346	*p*-value
Age(years)	49 ± 18	68 ± 12	< 0.001
Gender			< 0.001
Male	5,463 (48.6%)	209 (60.4%)	
Female	5,783 (51.4%)	137 (39.6%)	
Race			< 0.001
Non-Hispanic Black	2,351 (20.9%)	77 (22.3%)	
Non-Hispanic White	4,986 (44.3%)	210 (60.7%)	
Mexican American	1,852 (16.5%)	25 (7.2%)	
Other Hispanic	932 (8.3%)	19 (5.5%)	
Other Race	1,125 (10.0%)	15 (4.3%)	
Higher education			< 0.001
No	5,519 (49.1%)	212 (61.3%)	
Yes	5,727 (50.9%)	134 (38.7%)	
Smoking			0.358
No	8,938 (79.5%)	282 (81.5%)	
Yes	2,308 (20.5%)	64 (18.5%)	
Drinking			0.026
Yes	978 (8.7%)	42 (12.1%)	
No	10,268 (91.3%)	304 (87.9%)	
DM			< 0.001
Yes	1,820 (16.2%)	154 (44.5%)	
No	9,426 (83.8%)	192 (55.5%)	
CHD			< 0.001
No	10,792 (95.4%)	145 (41.9%)	
Yes	517 (4.6%)	201 (58.1%)	
OMI			< 0.001
No	10,911 (97.0%)	191 (55.2%)	
Yes	335 (3.0%)	155 (44.8%)	
History of stroke			< 0.001
No	10,885 (96.8%)	269 (77.7%)	
Yes	361 (3.2%)	77 (22.3%)	
Pulmonary emphysema			< 0.001
No	11,053 (98.3%)	304 (87.9%)	
Yes	193 (1.7%)	42 (12.1%)	
Hepatopathy			0.001
No	11,015 (97.9%)	330 (95.4%)	
Yes	231 (2.1%)	16 (4.6%)	
Malignancy			< 0.001
No	10,222 (90.9%)	273 (78.9%)	
Yes	1,024 (9.1%)	73 (21.1%)	
WBC (1000 cells/uL)	6.90 (5.70, 8.40)	7.10 (5.90, 8.60)	0.083
RBC (million cells/uL)	4.67 ± 0.50	4.49 ± 0.57	< 0.001
Hemoglobin (g/dL)	14.12 ± 1.53	13.72 ± 1.71	< 0.001
Platelet count (1000 cells/uL)	244 (206, 288)	215 (180, 260)	< 0.001
Albumin (g/L)	42.1 ± 3.6	40.6 ± 3.2	< 0.001
Alanine Aminotransferase (ALT) (U/L)	21 (16, 28)	19 (15, 24)	< 0.001
Aspartate Aminotransferase (AST) (U/L)	23 (19, 27)	24 (19, 28)	0.086
Cholesterol (mmol/L)	5.06 ± 1.08	4.61 ± 1.19	< 0.001
Glucose (mmol/L)	5.16 (4.72, 5.72)	5.72 (5.05, 7.11)	< 0.001
Total Bilirubin (umol/L)	10.3 (8.6, 13.7)	12.0 (8.6, 13.7)	0.078
Triglycerides (mmol/L)	1.34 (0.90, 2.06)	1.50 (1.08, 2.18)	< 0.001
Uric acid (umol/L)	315 (262, 375)	369 (309, 440)	< 0.001

Table 1 (continued)

Characteristic	Non-HF, *N* = 11,246	HF *N* = 346	*p*-value
Creatinine (umol/L)	79 ± 28	108 ± 51	< 0.001
Blood Urea Nitrogen (mmol/L)	4.28 (3.57, 5.71)	6.07 (4.64, 8.21)	< 0.001
Mercury, urine (ug/L)	0.34 (0.15, 0.77)	0.23 (0.10, 0.48)	< 0.001
Arsenic, urine (ug/L)	8 (4, 17)	7 (3, 14)	0.030
Barium, urine (ng/mL)	1.18 (0.58, 2.29)	0.83 (0.43, 1.72)	< 0.001
Cadmium, urine (ng/mL)	0.24 (0.12, 0.48)	0.35 (0.19, 0.63)	< 0.001
Cobalt, urine (ng/mL)	0.35 (0.21, 0.56)	0.33 (0.22, 0.53)	0.977
Cesium, urine (ng/mL)	4.6 (2.8, 6.8)	3.8 (2.4, 5.7)	< 0.001
Molybdenum, urine (ng/mL)	41 (22, 70)	38 (22, 64)	0.165
Lead, urine (ng/mL)	0.48 (0.26, 0.87)	0.53 (0.28, 0.97)	0.062
Antimony, urine (ng/mL)	0.05 (0.03, 0.09)	0.05 (0.03, 0.09)	0.558
Thallium, urine (ng/mL)	0.16 (0.09, 0.25)	0.12 (0.07, 0.18)	< 0.001
Tungsten, urine (ng/mL)	0.07 (0.03, 0.13)	0.07 (0.04, 0.14)	0.143
Uranium, urine (ng/mL)	0.006 (0.004, 0.012)	0.006 (0.004, 0.012)	0.749
Blood cadmium (ug/L)	0.33 (0.20, 0.60)	0.47 (0.30, 0.80)	< 0.001
Blood lead (ug/dL)	1.23 (0.78, 1.98)	1.72 (1.10, 2.71)	< 0.001
Blood mercury, total (ug/L)	0.86 (0.45, 1.71)	0.69 (0.41, 1.33)	< 0.001

Mean ± SD; n (%); Median (IQR)

-0.017 (-0.050, -0.003),CHD as mediator; -0.020 (-0.059, -0.001),OMI as mediator] have indirect effects on the occurrence of HF, but there is no direct effect. Moreover, urinary arsenic (As) concentration has a significant direct effect on the occurrence of HF. However, the analysis did not reveal any mediating effect of CHD or OMI on the relationship between blood mercury (Hg).

Heavy metals concentration and prognosis of HF

During the follow-up period (median follow-up time of 105 months), 337 HF patients experienced 175 all-cause death events, of which 78 were cardiovascular deaths. In the competing risk analysis (Fine-Gray model), non-cardiovascular deaths were treated as competing events. After adjusting for these competing risks and covariates (age, gender, DM, CHD, pulmonary emphysema, hepatopathy, and malignancy.), urinary arsenic remained a significant predictor of cardiovascular mortality. Specifically, each standard deviation (23.9 μg/L) increase in standardized urinary arsenic concentration was associated with a 26% elevated risk of cardiovascular death ($HR_{adjusted}$:1.19, 95%CI: 1.04–1.35, $P = 0.009$). In contrast, no significant association was observed between arsenic exposure and all-cause mortality risk ($HR_{adjusted}$: 1.09, 95%CI:0.84–1.41, $P = 0.526$).). Additionally, neither mercury nor cadmium demonstrated statistically significant associations with cardiovascular or all-cause mortality outcomes in HF patients (Table 5).

Discussion

In this study, we identified three heavy metals (Hg, As and Cd) that have a significant association with the occurrence of HF. Furthermore, through causal mediation analysis, we clarified that Cd-blood may contribute to the development of HF by inducing CHD and OMI. In contrast, As-urine appears to directly lower the incidence of HF. Similarly, Hg-urine may reduce HF risk by indirectly decreasing the occurrence of CHD and OMI. In addition, the results of further competitive risk model analysis also showed that As-urine was significantly positively associated with the risk of cardiovascular death in HF patients.

Previous studies have shown a positive linear correlation between blood cadmium and the occurrence of HF, which is consistent with our finding. Its mechanism is likely to damage the heart by increasing oxidative stress and inflammation, inducing mitochondrial damage, endothelial dysfunction, enhancing lipid synthesis, and up regulating adhesion molecules to promote atherosclerosis [23]. However, there are also studies suggesting that blood cadmium directly damages myocardial cells [24, 25]. It is important to note that our study found, blood cadmium is associated with HF risk, potentially mediated through its role in CHD or OMI development, rather than directly mediating HF. This finding was not mentioned in previous studies. Although Hsu'et al. have demonstrated a connection between cadmium excretion and mortality risk in patients with severe acute HF [26], we did not identify a correlation between mortality risk and cadmium concentration in our own study. This discrepancy is likely attributed to variations in the study population and the methods used to quantify cadmium exposure. Therefore, we anticipate more robust cohort studies and more comprehensive toxicology research in the future.

Mercury is a well-known harmful heavy metal that is highly associated with neurotoxicity and nephrotoxicity.

Table 2 Patient demographics and baseline characteristics after PSM

Characteristic	Overall *N* = 987	Non-HF *N* = 650	HF *N* = 337	*p*-value
Age (years)	68 ± 13	68 ± 13	68 ± 12	0.621
Gender				0.798
Male	600 (60.8%)	397 (61.1%)	203 (60.2%)	
Female	387 (39.2%)	253 (38.9%)	134 (39.8%)	
Race				0.911
Non-Hispanic White	595 (60.3%)	390 (60.0%)	205 (60.8%)	
Other Hispanic	60 (6.1%)	41 (6.3%)	19 (5.6%)	
Other Race	52 (5.3%)	37 (5.7%)	15 (4.5%)	
Non-Hispanic Black	209 (21.2%)	135 (20.8%)	74 (22.0%)	
Mexican American	71 (7.2%)	47 (7.2%)	24 (7.1%)	
Higher education				0.343
No	583 (59.1%)	377 (58.0%)	206 (61.1%)	
Yes	404 (40.9%)	273 (42.0%)	131 (38.9%)	
Smoking				0.063
No	832 (84.3%)	558 (85.8%)	274 (81.3%)	
Yes	155 (15.7%)	92 (14.2%)	63 (18.7%)	
Drinking				0.636
Yes	130 (13.2%)	88 (13.5%)	42 (12.5%)	
No	857 (86.8%)	562 (86.5%)	295 (87.5%)	
DM				0.662
Yes	547 (55.4%)	357 (54.9%)	190 (56.4%)	
No	440 (44.6%)	293 (45.1%)	147 (43.6%)	
CHD				< 0.001
No	676 (68.5%)	534 82.2%)	142 (42.1%)	
Yes	311 (31.5%)	116 (17.8%)	195 (57.9%)	
OMI				< 0.001
No	771 (78.1%)	583 (89.7%)	188 (55.8%)	
Yes	216 (21.9%)	67 (10.3%)	149 (44.2%)	
History of stroke				0.530
No	790 (80.0%)	524 (80.6%)	266 (78.9%)	
Yes	197 (20.0%)	126 (19.4%)	71 (21.1%)	
Pulmonary emphysema				0.071
No	893 (90.5%)	596 (91.7%)	297 (88.1%)	
Yes	94 (9.5%)	54 (8.3%)	40 (11.9%)	
Hepatopathy				0.751
No	943 (95.5%)	622 (95.7%)	321 (95.3%)	
Yes	44 (4.5%)	28 (4.3%)	16 (4.7%)	
Malignancy				0.656
No	774 (78.4%)	507 (78.0%)	267 (79.2%)	
Yes	213 (21.6%)	143 (22.0%)	70 (20.8%)	
All cause death				< 0.001
No	576 (58.4%)	414 (63.7%)	162 (48.1%)	
Yes	411 (41.6%)	236 (36.3%)	175 (51.9%)	
Cardiovascular death				< 0.001
No	842 (85.3%)	583 (89.7%)	259 (76.9%)	
Yes	145 (14.7%)	67 (10.3%)	78 (23.1%)	
WBC(1000cells/uL)	7.10 (5.80, 8.40)	7.00 (5.70, 8.30)	7.10 (5.90, 8.60)	0.189
RBC (million cells/uL)	4.53 ± 0.56	4.54 ± 0.55	4.51 ± 0.57	0.453
Hemoglobin (g/dL)	13.83 ± 1.65	13.86 ± 1.64	13.78 ± 1.67	0.502
Platelet count (1000 cells/uL)	228 ± 68	229 ± 64	226 ± 75	0.514
Albumin (g/L)	40.8 ± 3.4	40.8 ± 3.5	40.7 ± 3.2	0.688
Alanine Aminotransferase (ALT) (U/L)	20 (15, 25)	20 (15, 26)	19 (15, 24)	0.446
Aspartate Aminotransferase (AST) (U/L)	23 (20, 28)	23 (19, 28)	24 (20, 28)	0.427

Table 2 (continued)

Characteristic	Overall *N* = 987	Non-HF *N* = 650	HF *N* = 337	*p*-value
Cholesterol (mmol/L)	4.64 ± 1.09	4.64 ± 1.05	4.65 ± 1.18	0.858
Glucose (mmol/L)	5.72 (5.11, 7.11)	5.77 (5.11, 7.22)	5.69 (5.05, 7.03)	0.374
Triglycerides (mmol/L)	1.50 (1.03, 2.21)	1.51 (1.00, 2.25)	1.50 (1.08, 2.17)	0.611
Total Bilirubin (umol/L)	12.0 ± 4.9	12.0 ± 5.0	12.0 ± 4.5	0.966
Uric acid (umol/L)	376 ± 95	376 ± 92	377 ± 102	0.864
Blood Urea Nitrogen (mmol/L)	6.07 (4.64, 7.85)	6.07 (4.64, 7.85)	6.07 (4.64, 8.21)	0.858
Creatinine (umol/L)	93 (78, 115)	93 (76, 112)	95 (80, 117)	0.118
Mercury, urine (ug/L)	0.27 (0.12, 0.60)	0.29 (0.13, 0.66)	0.23 (0.11, 0.48)	0.016
Arsenic, urine (ug/L)	8 (4, 17)	9 (4, 18)	7 (4, 14)	0.007
Barium, urine (ng/mL)	0.87 (0.44, 1.81)	0.88 (0.45, 1.82)	0.85 (0.43, 1.78)	0.415
Cadmium, urine (ng/mL)	0.35 (0.19, 0.64)	0.35 (0.19, 0.66)	0.36 (0.19, 0.63)	0.853
Cobalt, urine (ng/mL)	0.34 (0.21, 0.54)	0.34 (0.21, 0.54)	0.33 (0.22, 0.53)	0.576
Cesium, urine (ng/mL)	4.17 (2.60, 6.17)	4.36 (2.68, 6.25)	3.90 (2.47, 5.72)	0.044
Molybdenum, urine (ng/mL)	39 (22, 65)	40 (22, 66)	39 (22, 65)	0.484
Lead, urine (ng/mL)	0.55 (0.30, 0.99)	0.55 (0.31, 0.99)	0.53 (0.28, 0.98)	0.340
Antimony, urine (ng/mL)	0.05 (0.03, 0.09)	0.05 (0.03, 0.09)	0.05 (0.03, 0.09)	0.903
Thallium, urine (ng/mL)	0.13 (0.08, 0.19)	0.13 (0.08, 0.20)	0.13 (0.07, 0.18)	0.131
Tungsten, urine (ng/mL)	0.07 (0.04, 0.13)	0.07 (0.04, 0.13)	0.07 (0.04, 0.14)	0.611
Uranium, urine (ng/mL)	0.011 ± 0.014	0.011 ± 0.013	0.011 ± 0.015	0.770
Blood cadmium (ug/L)	0.41 (0.29, 0.70)	0.40 (0.27, 0.70)	0.46 (0.30, 0.80)	0.006
Blood lead (ug/dL)	1.70 (1.14, 2.67)	1.70 (1.15, 2.64)	1.71 (1.10, 2.71)	0.814
Blood mercury, total (ug/L)	0.80 (0.44, 1.63)	0.86 (0.45, 1.70)	0.70 (0.41, 1.35)	0.012

Mean ± SD; n (%); Median (IQR)

However, the findings of this study suggest that mercury levels in urine may actually serve as a protective factor against HF, and there was also a trend towards protection with mercury levels in blood. In fact, this result is controversial. The study by Mozaffarian et al. indicated that mercury exposure did not significantly increase the risk of coronary heart disease and overall cardiovascular disease in American adults [27]. In addition, two cohort studies also found that there was no significant correlation between blood mercury concentration and the risk of all-cause death or death from cardiovascular disease, which was consistent with our results [28, 29]. A Gothenburg female cohort study with a follow-up period of 32 years showed a negative correlation between blood mercury and the risk of death and myocardial infarction [30]. The contentious findings appear to be resolved by a recent meta-analysis, which suggests that there is an J-shaped relationship between mercury exposure and both fatal and non-fatal cardiovascular outcomes [31]. This is likely to be the reason why low concentrations of mercury exposure show up as a protective factor for HF. There are three forms of human exposure to mercury: elemental mercury, inorganic mercury, or organic mercury (mainly methylmercury). In the NHANES database, the total mercury concentration in urine is the main biological indicator of exposure to elemental mercury and inorganic mercury, while the total mercury in blood is mainly methylmercury. The median urinary mercury of our study population was 0.27 ug/L, while the median blood mercury was 0.80ug/L, indicating low concentration exposure.

The mediation analysis suggested a potential indirect pathway linking urinary mercury levels to reduced HF risk. This association may be mediated through a lower incidence of CHD or OMI. While mercury is widely recognized as a toxicant, our findings align with emerging evidence of a non-linear dose-response relationship. Specifically, under low-to-moderate exposure conditions, the body's natural elimination of mercury through urine may reflect a protective mechanism, potentially interacting with beneficial dietary components such as selenium from marine fish consumption [32]. Adaptive antioxidant responses or synergistic effects with trace elements could paradoxically attenuate cardiovascular risk at these exposure levels [33]. However, this observation should be interpreted cautiously, as residual confounding (e.g., unmeasured dietary habits, socioeconomic factors) or temporal variations in exposure might influence the observed associations. We cannot rule out the possibility that other protective factors (e.g., omega-3 fatty

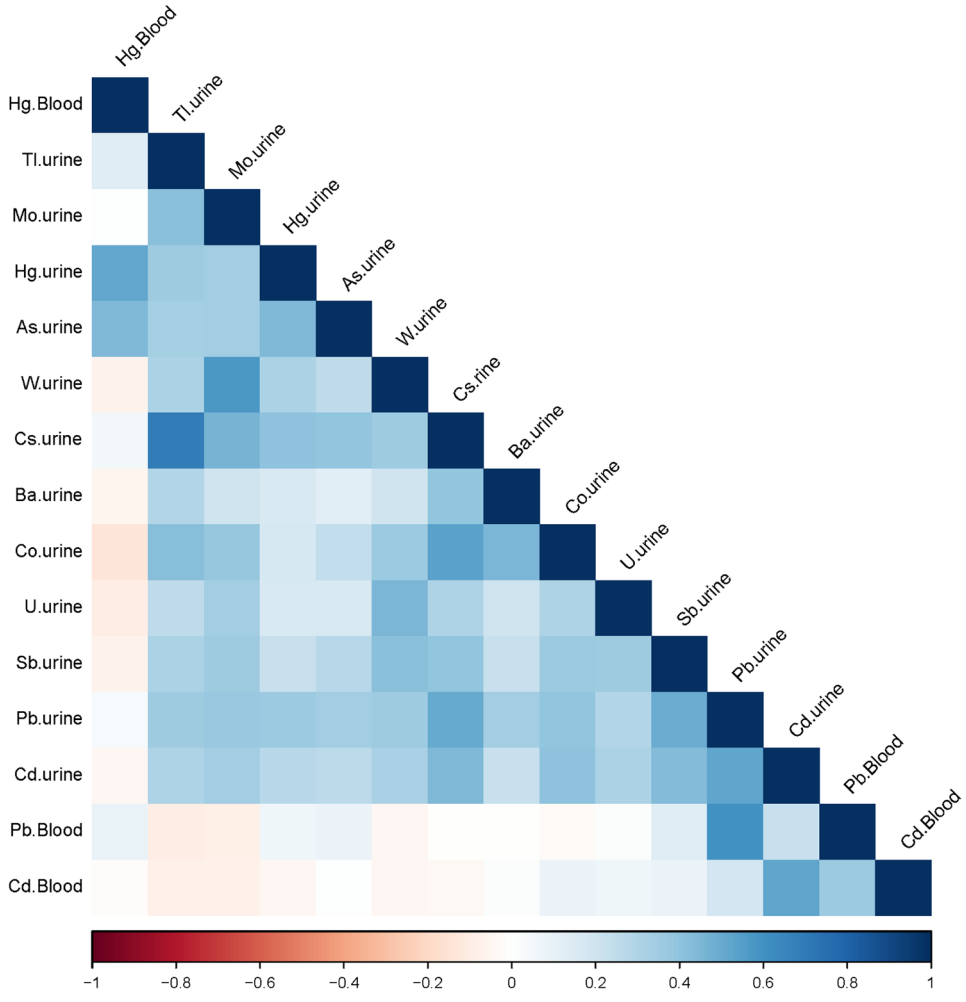

Fig. 2 Correlation heat map between heavy metals exposure

acids from fish) confounded the relationship [34]. Further mechanistic studies are warranted to clarify whether mercury excretion directly contributes to cardioprotection or merely serves as a biomarker of healthier lifestyles or nutrient-rich diets.

Human exposure to arsenic primarily occurs through contaminated drinking water and the consumption of rice and grains. High levels of arsenic (> 100ug/L) are positively correlated with the incidence of cardiovascular diseases (CVD) [35]. Nonetheless, the existing body of evidence is insufficient to establish a definitive correlation between exposure to low to moderate concentrations of arsenic and the development of cardiovascular disease. In this study, the indicator used to assess arsenic exposure was the total arsenic in urine, mainly inorganic arsenic. Exposure to low to moderate levels of arsenic appears to exhibit a negative correlation with the incidence of HF. Concurrently, mediation analysis has not revealed any significant mediating effects associated with CHD and OMI. In addition, urinary arsenic was significantly positively correlated with cardiovascular related death events. This finding is not surprising. The SHFS study involved 1337 young participants without cardiovascular disease. The findings indicated that low to moderate levels of urinary arsenic may contribute to cardiac remodeling, although symptomatic HF was not observed [18]. Although our research findings suggest that urinary arsenic may be a protective factor for HF, this is likely due to the fact that participants without HF are likely experiencing cardiac compensation. Furthermore, our study does not account for potential biases stemming from factors such as seafood consumption, medication use, and other variables [36]. Therefore, caution is advised when interpreting the impact of low urinary arsenic concentrations on HF.

Table 3 Association between heavy metals and HF (Logistic regression)

Characteristic	Model 1			Model 2			Model 3		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Hg-urine	0.77	0.62, 0.96	0.022	0.77	0.62, 0.96	0.022	0.78	0.63, 0.98	0.030
As-urine	0.99	0.99, 1.00	0.032	0.99	0.99, 1.00	0.034	0.99	0.99, 1.00	0.031
As-urine (per 29 ug/L)	0.84	0.72, 0.98	0.032	0.84	0.72, 0.99	0.034	0.84	0.72, 0.99	0.031
Ba-urine	0.98	0.91, 1.05	0.516	0.98	0.91, 1.05	0.483	0.99	0.92, 1.06	0.681
Cd-urine	0.97	0.73, 1.29	0.839	0.98	0.73, 1.30	0.871	0.98	0.74, 1.31	0.916
Co-urine	1.11	0.87, 1.42	0.388	1.12	0.87, 1.42	0.376	1.14	0.89, 1.45	0.298
Cs-urine	0.95	0.91, 1.00	0.043	0.95	0.91, 1.00	0.044	0.96	0.92, 1.01	0.086
Mo-urine	1.00	1.00, 1.00	0.514	1.00	1.00, 1.00	0.539	1.00	1.00, 1.00	0.618
Pb-urine	0.94	0.78, 1.12	0.483	0.94	0.78, 1.14	0.544	0.95	0.79, 1.15	0.625
Sb-urine	0.79	0.15, 4.22	0.784	0.78	0.14, 4.19	0.770	0.67	0.12, 3.67	0.643
Tl-urine	0.46	0.13, 1.62	0.230	0.44	0.13, 1.57	0.209	0.51	0.14, 1.83	0.305
W-urine	1.19	0.41, 3.43	0.748	1.17	0.40, 3.37	0.777	1.10	0.38, 3.20	0.863
U-urine	4.26	0.00, 46,584.52	0.760	4.17	0.00, 45,747.17	0.764	1.63	0.00, 19,788.22	0.919
Cd-Blood	1.36	1.07, 1.74	0.013	1.36	1.06, 1.73	0.014	1.35	1.05, 1.72	0.018
Pb-Blood	1.03	0.95, 1.12	0.531	1.04	0.95, 1.13	0.399	1.03	0.94, 1.12	0.551
Hg-Blood	0.91	0.82, 1.00	0.052	0.91	0.82, 1.00	0.055	0.91	0.82, 1.00	0.055
Hg-Blood (Categorical variable)									
Q1 [0.14,0.44)	—	—		—	—		—	—	
Q2 [0.44,0.8)	1.05	0.73, 1.51	0.797	1.05	0.73, 1.52	0.782	1.07	0.74, 1.54	0.721
Q3 [0.8,1.63)	0.75	0.52, 1.09	0.129	0.75	0.52, 1.09	0.132	0.76	0.52, 1.11	0.151
Q4 [1.63,11.8]	0.71	0.49, 1.04	0.076	0.71	0.49, 1.04	0.080	0.72	0.49, 1.05	0.086
P for trend			0.025			0.026			0.028

OR = Odds Ratio, CI = Confidence Interval

Model 1: no covariates were adjusted; Model 2: adjusted for Age and Gender; Model 3: adjusted for Age, Gender, and Creatinine

This study comprehensively evaluated the impact of heavy metal exposure on the incidence and mortality of HF. However, there are some deficiencies in our research that need to be pointed out. Firstly, although this study has greatly reduced the confounding factors through PSM, it is possible that many potential confounding factors may have been omitted due to the nature of it being an observational study. Secondly, all patients with HF included in this study self-reported their condition, therefore, memory bias was inevitable. Third, blood heavy metal levels primarily reflect recent exposure, whereas HF is a chronic condition shaped by long-term risk factors. For example, blood lead (half-life ~ 30 days) may not fully capture cumulative exposure, potentially introducing misclassification bias. While blood cadmium's longer half-life (about several decades) better aligns with chronic disease timelines, urinary metals (e.g., arsenic, mercury) represent a mix of recent excretion and historical exposure. Future studies incorporating biomarkers of cumulative exposure (e.g., bone lead, toenail metals) or longitudinal metal measurements would strengthen causal inferences.

Conclusion

This study revealed significant correlations between concentration of mercury and arsenic in urine, as well as cadmium in blood, and the risk of HF. In addition, even exposure to low to moderate levels of arsenic was

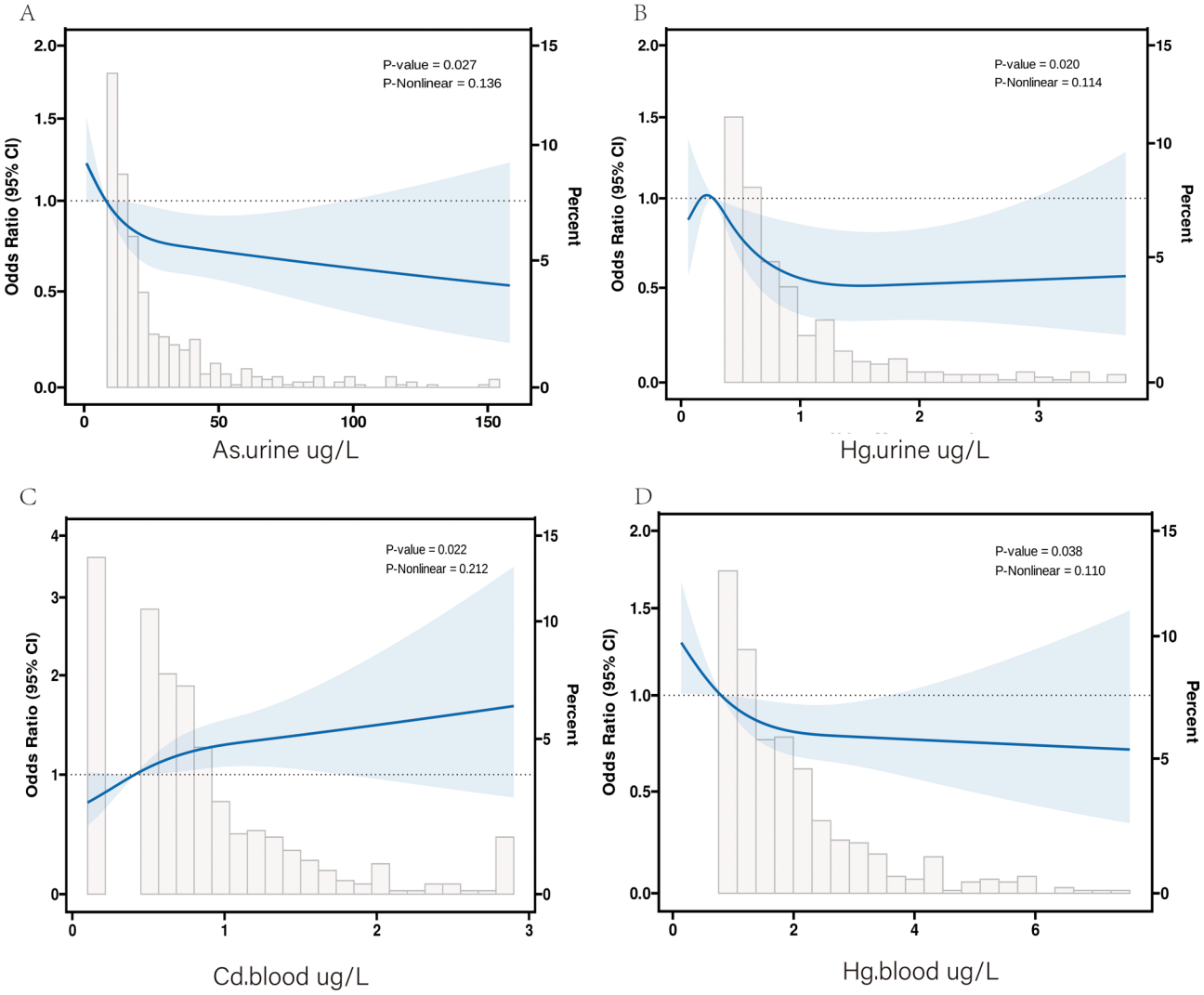

Fig. 3 Restricted cubic spline plot for the association between heavy metal exposure and the risk of heart failure

Table 4 Mediation analysis for the associations between heavy metals and HF

Independent variable	Mediator	Indirect effect		Direct effect		Proportion mediated, % (95% CI)
		Coefficient (95% CI)	P value	Coefficient (95% CI)	P value	
Cd blood	CHD	0.043 (0.009, 0.062)	< 0.001	0.032 (-0.017, 0.072)	0.240	57.9 (12.1, 184.2)
	OMI	0.042 (0.012, 0.059)	< 0.001	0.029 (-0.026, 0.073)	0.240	59.3 (21.2, 218.1)
As urine	CHD	0.005 (-0.017, 0.013)	0.900	-0.001 (-0.003, -0.000)	0.020	136.7 (-85.2, 335.2)
	OMI	-0.000 (-0.020, 0.012)	0.860	-0.001 (-0.002, -0.000)	0.020	30.9 (-47.0, 206.8)
Hg urine	CHD	-0.017 (-0.050, -0.003)	0.020	-0.032 (-0.087, 0.007)	0.120	34.9 (7.7, 134.9)
	OMI	-0.020 (-0.059, -0.001)	0.040	-0.032 (-0.087, 0.009)	0.140	38.0 (1.6, 128.4)
Hg Blood	CHD	0.000 (-0.027, 0.008)	> 0.999	-0.015 (-0.042, 0.002)	0.100	-0.0 (-159.1, 134.5)
	OMI	-0.011 (-0.045, 0.006)	0.240	-0.011 (-0.037, 0.003)	0.200	50.3 (-176.2, 109.1)

Table 5 Univariate and multivariate Cox regression analysis of heavy metals for prognosis

Characteristic	Cardiovascular death							
	N	Event *N*	HR	95% CI	*p*-value	$HR_{Adjusted}$	95% CI	*p*-value
Hg-urine	337	78	0.66	0.45, 0.96	0.028	0.73	0.50, 1.07	0.100
As-urine	337	78	1.01	1.00, 1.02	< 0.001	1.01	1.00, 1.01	0.009
As-urine (per 23.9ug/L)	337	78	1.26	1.11, 1.44	< 0.001	1.19	1.04, 1.35	0.009
Cd-Blood	337	78	0.75	0.52, 1.10	0.140	0.71	0.43, 1.17	0.180
Hg-Blood	337	78	0.98	0.84, 1.14	0.770	0.98	0.84, 1.15	0.830
All cause death								
Hg-urine	337	175	0.80	0.55, 1.15	0.220	0.88	0.58, 1.34	0.556
As-urine	337	175	1.01	1.00, 1.02	0.202	1.00	0.99, 1.01	0.526
As-urine (per 23.9ug/L)	337	175	1.17	0.92, 1.48	0.202	1.09	0.84, 1.41	0.526
Cd-Blood	337	175	1.15	0.79, 1.69	0.470	1.19	0.75, 1.87	0.459
Hg-Blood	337	175	0.95	0.82, 1.11	0.530	0.93	0.78, 1.10	0.375

HR = Hazard Ratio, CI = Confidence Interval

*Adjusted for Age, Gender, DM, CHD, pulmonary emphysema, hepatopathy, malignancy

significantly associated with cardiovascular mortality in patients with HF. These findings underscore the potential impact of heavy metal exposure on the onset of HF, and future research should adopt longitudinal designs incorporating cumulative exposure biomarkers and integrate mechanistic studies to explore interactions between low-dose metals and cardiac pathways. Clinically, targeted metal screening in high-risk populations and public health policies to reduce environmental contamination are recommended.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-23177-2.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
Not Applicable.

Author contributions
ZBL: Conceptualization, Methodology, Writing- Original draft preparation; YQD: Software, validation, Writing- Original draft preparation; XLD, BY, JMT, GKL and SFW: Visualization, Investigation. YPZ, XHW and YHL: Supervision, Writing-Reviewing and Editing.

Funding
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability
The study utilized NHANES data, which is publicly accessible(https://www.cdc.gov/nchs/nhanes/index.html). Restricted data are available upon request following NHANES protocols. Contact the corresponding author for further information.

Declarations

Ethics approval and consent to participate
The protocol was approved by the Institutional Review Board of National Center for Health Statistics and no new data was added.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

Received: 11 February 2025 / Accepted: 14 May 2025
Published online: 26 May 2025

References

1. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, et al. Heart disease and stroke Statistics-2021 update: A report from the American heart association. Circulation. 2021;143(8):e254–743.
2. Heidenreich PA, Albert NM, Allen LA, Bluemke DA, Butler J, Fonarow GC, Ikonomidis JS, Khavjou O, Konstam MA, Maddox TM, et al. Forecasting the impact of heart failure in the united States: a policy statement from the American heart association. Circ Heart Fail. 2013;6(3):606–19.
3. Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ. Heavy metal toxicity and the environment. Exp Suppl. 2012;101:133–64.
4. Pan Z, Gong T, Liang P. Heavy metal exposure and cardiovascular disease. Circ Res. 2024;134(9):1160–78.
5. Yin G, Xin M, Zhao S, Zhao M, Xu J, Chen X, Xu Q. Heavy metals and elderly kidney health: A multidimensional study through Enviro-target Mendelian randomization. Ecotoxicol Environ Saf. 2024;281:116659.
6. Lee KS, Min WK, Choi YJ, Jin S, Park KH, Kim S. The effect of maternal exposure to air pollutants and heavy metals during pregnancy on the risk of neurological disorders using the National health insurance claims data of South Korea. Med (Kaunas) 2023;59(5).
7. Khoshakhlagh AH, Mohammadzadeh M, Gruszecka-Kosowska A. The preventive and carcinogenic effect of metals on cancer: a systematic review. BMC Public Health. 2024;24(1):2079.
8. Mohammadifard N, Haghighatdoost F, Rahimlou M, Rodrigues APS, Gaskarei MK, Okhovat P, de Oliveira C, Silveira EA, Sarrafzadegan N. The effect of ketogenic diet on shared risk factors of cardiovascular disease and Cancer. Nutrients 2022;14(17).
9. Rahimlou M, Mousavi MA, Chiti H, Peyda M, Mousavi SN. Association of maternal exposure to endocrine disruptor chemicals with cardio-metabolic risk factors in children during childhood: a systematic review and meta-analysis of cohort studies. Diabetol Metab Syndr. 2024;16(1):82.
10. Lamas GA, Bhatnagar A, Jones MR, Mann KK, Nasir K, Tellez-Plaza M, Ujueta F, Navas-Acien A. Contaminant metals as cardiovascular risk factors: A scientific statement from the American heart association. J Am Heart Association. 2023;12(13):e029852.
11. States JC, Srivastava S, Chen Y, Barchowsky A. Arsenic and cardiovascular disease. Toxicol Sci. 2009;107(2):312–23.

12. Fagerberg B, Barregard L. Review of cadmium exposure and smoking-independent effects on atherosclerotic cardiovascular disease in the general population. J Intern Med. 2021;290(6):1153–79.
13. Vaziri ND. Mechanisms of lead-induced hypertension and cardiovascular disease. Am J Physiol Heart Circ Physiol. 2008;295(2):H454–465.
14. Rahaman MS, Mise N, Ikegami A, Zong C, Ichihara G, Ichihara S. The mechanism of low-level arsenic exposure-induced hypertension: Inhibition of the activity of the angiotensin-converting enzyme 2. Chemosphere. 2023;318:137911.
15. Chatterjee S, Kundu S, Sengupta S, Bhattacharyya A. Divergence to apoptosis from ROS induced cell cycle arrest: effect of cadmium. Mutat Res. 2009;663(1–2):22–31.
16. Amin A, Saadatakhtar M, Mohajerian A, Marashi SM, Zamanifard S, Keshavarzian A, Molaee P, Keshmiri MS, Nikdoust F. Mercury-Mediated cardiovascular toxicity: mechanisms and remedies. Cardiovasc Toxicol. 2025;25(3):507–22.
17. Zhao X, Feng T, Chen H, Shan H, Zhang Y, Lu Y, Yang B. Arsenic trioxide-induced apoptosis in H9c2 cardiomyocytes: implications in cardiotoxicity. Basic Clin Pharmacol Toxicol. 2008;102(5):419–25.
18. Pichler G, Grau-Perez M, Tellez-Plaza M, Umans J, Best L, Cole S, Goessler W, Francesconi K, Newman J, Redon J, et al. Association of arsenic exposure with cardiac geometry and left ventricular function in young adults. Circ Cardiovasc Imaging. 2019;12(5):e009018.
19. Navas-Acien A, Guallar E, Silbergeld EK, Rothenberg SJ. Lead exposure and cardiovascular disease–a systematic review. Environ Health Perspect. 2007;115(3):472–82.
20. Sears CG, Eliot M, Raaschou-Nielsen O, Poulsen AH, Harrington JM, Howe CJ, James KA, Roswall N, Overvad K, Tjønneland A, et al. Urinary cadmium and incident heart failure: A Case-Cohort analysis among Never-Smokers in Denmark. Epidemiology. 2022;33(2):185–92.
21. Tellez-Plaza M, Guallar E, Howard BV, Umans JG, Francesconi KA, Goessler W, Silbergeld EK, Devereux RB, Navas-Acien A. Cadmium exposure and incident cardiovascular disease. Epidemiology. 2013;24(3):421–9.
22. Stekhoven DJ, Bühlmann P. MissForest–non-parametric missing value imputation for mixed-type data. Bioinformatics. 2012;28(1):112–8.
23. Verzelloni P, Urbano T, Wise LA, Vinceti M, Filippini T. Cadmium exposure and cardiovascular disease risk: A systematic review and dose-response meta-analysis. Environ Pollut. 2024;345:123462.
24. Ghosh K, N I. Cadmium treatment induces echinocytosis, DNA damage, inflammation, and apoptosis in cardiac tissue of albino Wistar rats. Environ Toxicol Pharmacol. 2018;59:43–52.
25. Chou SH, Lin HC, Chen SW, Tai YT, Jung SM, Ko FH, Pang JS, Chu PH. Cadmium exposure induces histological damage and cytotoxicity in the cardiovascular system of mice. Food Chem Toxicol. 2023;175:113740.
26. Hsu CW, Weng CH, Lee CC, Lin-Tan DT, Chu PH, Chen KH, Yen TH, Huang WH. Urinary cadmium levels predict mortality of patients with acute heart failure. Ther Clin Risk Manag. 2017;13:379–86.
27. Mozaffarian D, Shi P, Morris JS, Spiegelman D, Grandjean P, Siscovick DS, Willett WC, Rimm EB. Mercury exposure and risk of cardiovascular disease in two U.S. Cohorts. N Engl J Med. 2011;364(12):1116–25.
28. Duan W, Xu C, Liu Q, Xu J, Weng Z, Zhang X, Basnet TB, Dahal M, Gu A. Levels of a mixture of heavy metals in blood and urine and all-cause, cardiovascular disease and cancer mortality: A population-based cohort study. Environ Pollut. 2020;263Pt A:114630.
29. Sun Y, Liu B, Rong S, Zhang J, Du Y, Xu G, Snetselaar LG, Wallace RB, Lehmler HJ, Bao W. Association of seafood consumption and mercury exposure with cardiovascular and All-Cause mortality among US adults. JAMA Netw Open. 2021;4(11):e2136367.
30. Bergdahl IA, Ahlqwist M, Barregard L, Björkelund C, Blomstrand A, Skerfving S, Sundh V, Wennberg M, Lissner L. Mercury in serum predicts low risk of death and myocardial infarction in Gothenburg women. Int Arch Occup Environ Health. 2013;86(1):71–7.
31. Hu XF, Lowe M, Chan HM. Mercury exposure, cardiovascular disease, and mortality: A systematic review and dose-response meta-analysis. Environ Res. 2021;193:110538.
32. Raymond LJ, Ralston NVC. Mercury: selenium interactions and health implications. Neurotoxicology. 2020;81:294–9.
33. Mieiro CL. Pereira Me Fau - Duarte AC, Duarte Ac Fau - Pacheco M, Pacheco M: Brain as a critical target of mercury in environmentally exposed fish (Dicentrarchus labrax)--bioaccumulation and oxidative stress profiles. Electronic. 1879– 1514.
34. Mozaffarian D, Rimm EB. Fish intake, contaminants, and human health: evaluating the risks and the benefits. Electronic. 1538–3598.
35. Kaur G, Desai KP, Chang IY, Newman JD, Mathew RO, Bangalore S, Venditti FJ, Sidhu MS. A clinical perspective on arsenic exposure and development of atherosclerotic cardiovascular disease. Cardiovasc Drugs Ther. 2023;37(6):1167–74.
36. Nigra AE, Moon KA, Jones MR, Sanchez TR, Navas-Acien A. Urinary arsenic and heart disease mortality in NHANES 2003–2014. Environ Res. 2021;200:111387.

Publisher's note