scientific reports

Check for updates

OPEN

Correlation of exposure to volatile organic compounds with myocardial infarction: A Cross-sectional study based on NHANES 2011–2018

Xiangyu Kong[1]✉ & Zhao Qiu[2]

Myocardial infarction (MI), commonly referred to as a heart attack, ranks among the foremost causes of death worldwide. The contribution of exposure to volatile organic compounds (VOCs) to MI is still not well established. This study aims to examine how urinary metabolites of 19 volatile organic compounds (mVOCs) correlate with MI risk in the ordinary population. The data were extracted from the National Health and Nutrition Examination Survey spanning from 2011 to 2018, a nationally representative program conducted by the Centers for Disease Control and Prevention (CDC) to collect and assess the health and nutritional status of the non-institutionalized U.S. population through interviews and physical examinations. The relationship between a single mVOC and MI was analyzed by applying a logistic regression model. The nonlinear relationship between a single mVOC and MI was investigated with the help of a restricted cubic spline regression model. The overall association between mVOCs and MI was examined using a weighted quantile sum (WQS) regression model. The analysis included 5,211 participants, among whom 209 experienced MI, with mVOC levels assessed. A positive association between N-acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA) [OR, 1.95; 95% CI, (1.06, 3.58)] and MI incidence was observed after adjustment for potential confounders. Similarly, N-acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA) was also significantly associated with MI incidence [OR, 1.8; 95% CI, (1.14, 2.83)]. Each incremental unit increase in WQS was linked to a 20.4% rise in MI risk (95% CI, 1.05, 1.38). Among them, N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA), N-acetyl-S-(2-carboxyethyl)-L-cysteine (CEMA), CYMA, N-acetyl-S-(phenyl-2-hydroxyethyl)-L-cysteine (PHEMA), 3HPMA, and 3- and 4-methylhippuric acid (3,4MHA) were identified as key contributors, with DHBMA showing the highest weight (0.27). mVOCs are metabolic derivatives of VOC exposure, with common sources including industrial emissions, environmental pollution, and tobacco combustion. The findings revealed a significant association between urinary mVOCs and MI, implying exposure to these compounds may be linked to an increased MI risk.

Keywords Volatile organic compounds, Myocardial infarction, National Health and Nutrition Examination Survey, Environmental exposure, Metabolomics

Volatile organic compounds (VOCs) are commonly found in both indoor air and outdoor air, arising from sources such as vehicle exhaust, industrial emissions, and household items like cleaners, disinfectants, paints, and tobacco. Smoking, whether using traditional or electronic cigarettes, results in significant exposure to VOCs, which are emitted into the air along with aerosols. Consequently, smoking is a major source of VOC exposure[1–3]. The intrinsic properties of VOCs in toxicology can be directly manifested after inhalation and ingestion of VOCs in the body. Moreover, due to their high photochemical reactivity, VOCs can transform into secondary pollutants in the environment. This process exacerbates environmental pollution and adds to the negative impacts on health[4,5]. The U.S. Agency for Toxic Substances and Disease Registry (ATSDR) has designated several VOCs as chemicals of significant public health concern on its Substance Priority List (SPL)[6]. Existing evidence

[1]Department of Traditional Chinese Medicine, Shanyang Town Community Health Service Center, Jinshan District, Shanghai 201508, China. [2]Department of Rehabilitation Medicine, Shanyang Town Community Health Service Center, Jinshan District, Shanghai 201508, China. ✉email: Kevin_xyKong@163.com

suggests that exposure to certain VOCs is linked to specific pathological mechanisms, including the induction of oxidative stress, pro-inflammatory responses, metabolic disorders, and genotoxicity. These mechanisms can contribute to adverse effects on multiple systems in the body, including the circulatory, respiratory, digestive, and neurological systems[7–10]. Due to their widespread presence and potential health risks, certain VOCs represent a serious public health concern.

Myocardial infarction (MI), commonly referred to as a heart attack, is caused by hypoxia in a certain part of the heart due to interruption of blood flow, leading to damage or death of myocardial cells. Acute myocardial infarction (AMI) ranks among the foremost causes of death worldwide. Despite advanced therapeutic strategies, a large number of patients continue to experience complications and high in-hospital mortality[11] due to the fact that adult cardiomyocytes are terminally differentiated and are incapable of adequate regeneration and proliferation[12]. Between 2017 and 2020, the overall MI prevalence rate among adults aged 20 and older in the U.S. was 3.9%, approximately affecting 10.8 million people. In 2020, the annual adjusted mortality of AMI was about 85.3 per 100,000 people[13]. While percutaneous coronary intervention has enhanced early survival following MI, mortality within 5 years post-MI remains elevated across all ages. Furthermore, post-MI heart failure is increasingly significant in elevating the later incidence rate, mortality rate, and healthcare expenditures[14]. Given the high MI risk and the uncertainty of its prognosis, identifying and managing potential factors associated with MI is an important part of a cardiovascular health strategy.

It has been demonstrated that urinary metabolites of volatile organic compounds (mVOCs) were effective biomarkers for evaluating VOC exposure. Metabolites generally have a longer physiological half-life compared to the parent compounds, with most showing specificity[15]. Therefore, mVOCs can offer valuable guidance for diagnosis, management and monitoring of numerous diseases in clinical practice. The National Health and Nutrition Examination Survey (NHANES) was instituted to investigate the health and nutritional statuses of adults and children across the U.S., and formerly employed urinary metabolites as measurable biomarkers to assess various exposures to VOCs. Due to the uncertainty surrounding the relationship between VOCs exposure and MI, the aim of this study was to investigate the potential association between mVOCs and MI in the U.S. general adult population. Through the evaluation of mVOC levels, the potential risk of VOCs exposure as a contributing factor for MI has been uncovered. This discovery provided clues to help identify those at high MI risk as well as to manage cardiovascular health.

Materials and methods

Study population

The data used in the current study were from NHANES, encompassing demographic characteristics, laboratory biomarkers, physical examination results, and questionnaire responses. NHANES, conducted by the National Center for Health Statistics (NCHS), is a national program instituted to investigate the health and nutritional statuses of adults and children across the U.S.. Four NHANES periods, 2011–2012, 2013–2014, 2015–2016, and 2017–2018, were collected and combined for this study. From the initial sample of 39,156 participants, the study excluded those under 20 years old, those lacking urinary VOCs and creatinine data (n = 29,987), and those lacking MI outcomes (n = 3,280). This left 5,889 participants. 5,211 participants with complete data were included in further analysis. (Fig. 1).

Measurement of mVOCs

Urine samples were collected from each participant during their visit to the Mobile Examination Center (MEC), following standardized NHANES protocols. As NHANES is a cross-sectional study, each participant provided only a single urine sample, which was stored at −30°C before transportation to laboratories for further analysis. After preparation, storage, and shipment, urinary mVOCs were analyzed at the Division of Laboratory Sciences of the National Center for Environmental Health, located at the Centers for Disease Control and Prevention in Atlanta, GA. Urinary mVOC levels were quantified using UPLC-ESI–MS/MS. A total of 19 mVOCs were assessed in this study, including: N-acetyl-S-(2-hydroxypropyl)-L-cysteine (2HPMA), 2-methylhippuric acid (2MHA), 3- and 4-methylhippuric acid (3,4MHA), N-acetyl-S-(3-hydroxypropyl)-L-cysteine (3HPMA), N-acetyl-S-(2-carbamoylethyl)-L-cysteine (AAMA), N-acetyl-S-(N-methylcarbamoyl)-L-cysteine (AMCC), 2-aminothiazoline-4-carboxylic acid (ATCA), N-acetyl-S-(n-propyl)-L-cysteine (BPMA), N-acetyl-S-(2-carboxyethyl)-L-cysteine (CEMA), N-acetyl-S-(2-cyanoethyl)-L-cysteine (CYMA), N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine (DHBMA), N-acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine (GAMA), N-acetyl-S-(2-hydroxyethyl)-L-cysteine (HEMA), N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine (HMPMA), mandelic acid (MA), N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine (MHBMA3), phenylglyoxylic acid (PGA), N-acetyl-S-(phenyl-2-hydroxyethyl)-L-cysteine (PHEMA), and N-acetyl-S-(benzyl)-L-cysteine (SBMA). A detailed summary of the 19 urinary mVOCs, their potential parent VOCs, and associated exposure environments is provided in Extended Data Table 1.Further experimental details can be accessed from the NHANES website (https://www.cdc.gov/nchs/nhanes/index.htm).

Assessment of MI outcomes

MI outcomes are recorded in the medical conditions section of the questionnaire, which collects self-reported data through a single personal interview covering a broad range of health conditions for both children and adults, including whether they have ever been informed of a heart attack (also known as MI). Each participant underwent only one interview, which was conducted by trained interviewers at their homes using a computer-assisted personal interview (CAPI) system.

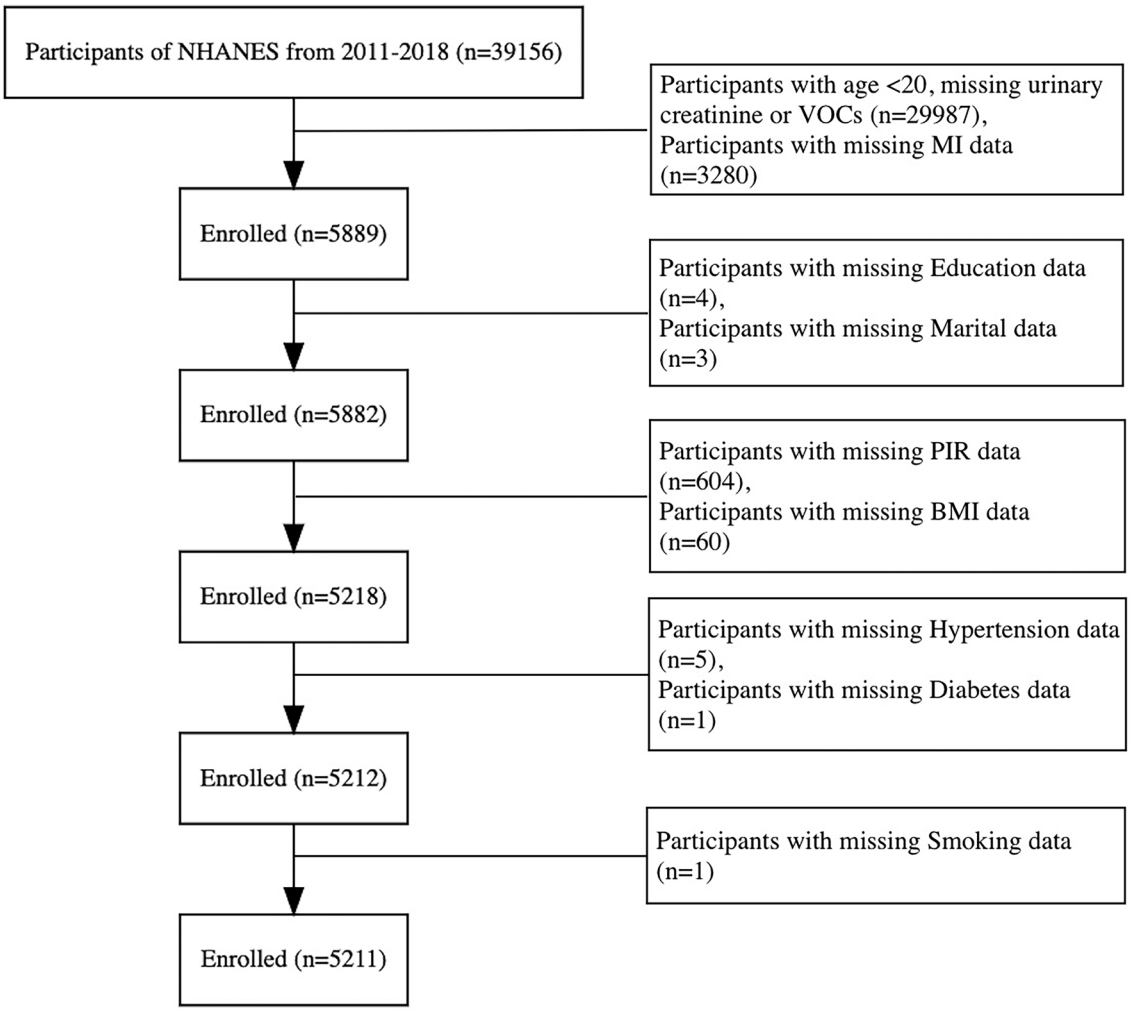


Fig. 1. Flow chart of study participants. Abbreviations: NHANES, National Health and Nutrition Examination Survey; VOCs, volatile organic compounds; MI, myocardial infarction; PIR, income to poverty ratio; BMI, body mass index.

Assessment of covariates

Demographic variables, such as age, gender, race, and education, were obtained through household interviews, which were conducted only once for each participant. The income poverty ratio (PIR) was employed to assess the ratio of family income to the poverty threshold. Information regarding hypertension, diabetes history, and smoking status was gathered via health questionnaires. Body mass index (BMI), calculated as weight divided by the square of height (kg/m^2), was also documented.

Statistical analysis

For continuous variables that exhibited a normal distribution, the data were reported as mean (standard deviation); for skewed continuous variables, the data were reported as median (25%, 75%); for categorical variables, the data were reported as number (%). Continuous variables, assuming independence, normal distribution, and homogeneity of variance, were analyzed using independent samples t-tests. Skewed continuous variables underwent rank-sum tests, while chi-square tests were employed to compare categorical variables and assess differences in demographic and health characteristics between participants with and without MI.

The association between mVOCs and MI was assessed using a multivariate logistic regression model. There were no adjustments in Model 1. Adjustments for gender, age and race were made in Model 2. Model 3 expanded upon these adjustments to additionally include education, marital status, PIR, BMI, hypertension, diabetes, and smoking status. Restricted cubic spline (RCS) regression was applied to explore potential nonlinear relationships between mVOCs and MI. Weighted Quantile Sum (WQS) regression model was utilized to evaluate the overall association between mVOCs and MI. All mVOCs were categorized into deciles, after which the dataset was randomly partitioned into a training dataset (40%) and a validation dataset (60%). The training dataset was subjected to 1000 bootstrap iterations and the weights derived from the WQS index were employed to identify the key mVOCs associated with MI. Creatinine-adjusted mVOC values were used to ensure comparability across

Characteristic	Overall (n = 5211)	Non - MI (n = 5002)	MI (n = 209)	P value
Gender				<0.001 *
Male	2,591(49.7%)	2,448(48.9%)	143(68.4%)	
Female	2,620(50.3%)	2,554(51.1%)	66(31.6%)	
Age	47(33,60)	46(32,59)	67(57,73)	<0.001 *
Race				0.046 *
Mexican American	629(12.1%)	613(12.3%)	16(7.7%)	
Other hispanic	537(10.3%)	513(10.3%)	24(11.5%)	
Non-hispanic white	1,940(37.2%)	1,828(36.5%)	112(53.6%)	
Non-hispanic black	1,211(23.2%)	1,169(23.4%)	42(20.1%)	
Other race - Including multi-racial	894(17.2%)	879(17.6%)	15(7.2%)	
Education				0.009 *
Less than 9 th grade	450(8.6%)	420(8.4%)	30(14.4%)	
9–11 th grade	624(12.0%)	594(11.9%)	30(14.4%)	
High school graduate/GED or equivalent and above	4,137(79.4%)	3,988(79.7%)	149(71.3%)	
Marital				<0.001 *
Never married	1,016(19.5%)	1,001(20.0%)	15(7.2%)	
Living with partner	465(8.9%)	452(9.0%)	13(6.2%)	
Married	2,648(50.8%)	2,539(50.8%)	109(52.2%)	
Married but separated from spouse	1,082(20.8%)	1,010(20.2%)	72(34.4%)	
PIR				0.029 *
≤1.39	1,803(34.6%)	1,709(34.2%)	94(45.0%)	
1.39~=3.49	1,810(34.7%)	1,732(34.6%)	78(37.3%)	
＞3.49	1,598(30.7%)	1,561(31.2%)	37(17.7%)	
BMI				0.2
18.5 kg/m^2 ≤ BMI < 25.0 kg/m^2	1,443(27.7%)	1,394(27.9%)	49(23.4%)	
BMI < 18.5 kg/m^2	75(1.4%)	73(1.5%)	2(1.0%)	
25.0 kg/m^2 ≤ BMI < 30.0 kg/m^2	1,672(32.1%)	1,607(32.1%)	65(31.1%)	
BMI ≥ 30.0 kg/m^2	2,021(38.8%)	1,928(38.5%)	93(44.5%)	
Creatinine	99(55,158)	100(55,158)	93(57,157)	0.7
2MHA	−0.51(−0.84,−0.14)	−0.51(−0.84,−0.14)	−0.44(−0.85,−0.04)	>0.9
3,4MHA	0.23(−0.05,0.68)	0.23(−0.05,0.68)	0.35(−0.02,0.82)	0.14
AAMA	−0.29(−0.48,−0.04)	−0.29(−0.48,−0.04)	−0.17(−0.45,0.06)	0.034 *
AMCC	0.21(−0.03,0.46)	0.21(−0.03,0.46)	0.24(0.02,0.60)	0.07
ATCA	0.07(−0.23,0.34)	0.07(−0.23,0.34)	−0.03(−0.31,0.29)	0.1
SBMA	−1.19(−1.40,−0.95)	−1.19(−1.40,−0.94)	−1.20(−1.40,−1.01)	0.6
BPMA	−1.35(−1.74,−0.95)	−1.35(−1.74,−0.94)	−1.47(−1.79,−1.09)	0.057
CEMA	−0.02(−0.22,0.21)	−0.02(−0.22,0.20)	0.16(−0.11,0.34)	<0.001 *
CYMA	−1.80(−2.02,−1.13)	−1.80(−2.02,−1.16)	−1.67(−1.94,0.04)	0.019 *
DHBMA	0.50(0.39,0.62)	0.50(0.39,0.62)	0.59(0.48,0.71)	<0.001 *
GAMA	−0.96(−1.15,−0.76)	−0.96(−1.15,−0.76)	−0.90(−1.10,−0.73)	0.13
HEMA	−1.98(−2.24,−1.72)	−1.99(−2.24,−1.72)	−1.96(−2.21,−1.65)	0.2
2HPMA	−0.52(−0.73,−0.25)	−0.53(−0.73,−0.26)	−0.39(−0.63,−0.13)	0.002 *
3HPMA	0.35(0.16,0.65)	0.35(0.15,0.64)	0.46(0.29,0.83)	<0.001 *
MA	0.13(−0.01,0.29)	0.13(−0.01,0.29)	0.16(0.01,0.40)	0.12
MHBMA3	−1.34(−1.54,−1.04)	−1.34(−1.54,−1.05)	−1.24(−1.41,−0.65)	0.001 *
PHEMA	−2.06(−2.27,−1.82)	−2.06(−2.27,−1.82)	−2.00(−2.20,−1.69)	0.01 *
PGA	0.33(0.20,0.47)	0.33(0.20,0.47)	0.37(0.25,0.58)	0.05 *
HMPMA	0.33(0.18,0.59)	0.32(0.18,0.58)	0.47(0.29,0.87)	<0.001 *
Hypertension	1,889(36.3%)	1,737(34.7%)	152(72.7%)	<0.001 *
Continued				

Characteristic	Overall (n = 5211)	Non - MI (n = 5002)	MI (n = 209)	P value
Diabetes	706(13.5%)	620(12.4%)	86(41.1%)	<0.001 *
Smoking				<0.001 *
Never smoker	2,959(56.8%)	2,895(57.9%)	64(30.6%)	
Former smoker	1,252(24.0%)	1,167(23.3%)	85(40.7%)	
Current smoker	1000(19.2%)	940(18.8%)	60(28.7%)	

Table 1. Characteristics of the study population. Notes: Data are presented as median (25%, 75%) or n (%). Abbreviations: MI, Myocardial Infarction; BMI, Body Mass Index; PIR, Income to Poverty Ratio; 2HPMA, N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 2MHA, 2-methylhippuric acid; 3,4MHA, 3-and 4-methylhippuric acid; 3HPMA, N-acetyl-S-(3-hydroxypropyl)-L-cysteine; AAMA, N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC, N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; ATCA, 2-aminothiazoline-4-carboxylic acid; BPMA, N-acetyl-S-(n-propyl)-L-cysteine; CEMA, N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA, N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA, N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine; GAMA, N-acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine; HEMA, N-acetyl-S-(2-hydroxyethyl)-L-cysteine; HMPMA, N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine; MA, Mandelic Acid; MHBMA3, N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA, phenylglyoxylic acid; PHEMA, N-acetyl-S-(phenyl-2-hydroxyethyl)-L-cysteine; SBMA, N-acetyl-S-(benzyl)-L-cysteine. *P < 0.05.

participants in statistical analyses. Data analysis and graphical visualization were performed using R version 4.3.0. A statistical significance threshold of a two-sided p-value below 0.05 was established.

Ethical approval and informed consent

The NHANES program was approved by the NCHS Institutional Review Board, and all participants provided written informed consent. Further details about NHANES are available on the official website (https://www.cdc.gov/nchs/nhanes/index.htm). All methods were performed in accordance with the relevant guidelines and regulations.

Results

Baseline characteristics

The median age of the 5,211 participants was 47(33, 60) years old, with 2,591 (49.7%) being male. Table 1 presents the demographic characteristics of the study population according to MI prevalence. Compared to those without MI, participants with MI were more likely to be older, non-Hispanic white, have lower education levels, and exhibit higher rates of hypertension, diabetes, and cigarette smoking. The BMI distribution between the two groups did not show a statistically significant difference. Additionally, the average concentrations of AAMA, CEMA, CYMA, DHBMA, 2HPMA, 3HPMA, MHBMA3, PHEMA, PGA, and HMPMA were significantly higher in participants with MI compared to those without MI ($p < 0.05$).

Association between single VOC and MI

Table 2 presents the findings from multivariate logistic regression, examining the association between mVOCs and MI. In Model 1, a univariate logistic regression between mVOCs and MI revealed significant positive correlations ($p < 0.05$) for concentrations of AAMA, AMCC, CEMA, CYMA, DHBMA, 2HPMA, 3HPMA, MHBMA3, PHEMA, PGA, and HMPMA with MI prevalence. In Model 2, gender, age, and race were included as additional covariates beyond those in Model 1. Model 3 further incorporated education, marital status, PIR, BMI, hypertension, diabetes, and smoking status as additional covariates on top of those in Model 2. After adjustments in Models 2 and 3, higher concentrations of 3HPMA [OR, 1.95; 95% CI, (1.06, 3.58)] and CYMA [OR, 1.80; 95% CI, (1.14, 2.83)] remained significantly associated with MI prevalence.

Figure 2 illustrates the results from a univariate analysis using RCS, depicting the association between mVOCs and MI. The findings indicated a notable correlation between multiple mVOCs and MI. Specifically, 3,4MHA, AMCC, CEMA, DHBMA, 3HPMA, MA, MHBMA3, PGA, and PHEMA demonstrated a significant linear association with MI prevalence, with higher concentrations being observed among participants with MI. HMPMA and 2HPMA showed a significant non-linear relationship with MI risk. Higher concentrations of HMPMA were associated with increased MI prevalence, whereas for 2HPMA, the association initially increased and then plateaued. Higher CYMA concentrations were associated with a non-monotonic trend in MI prevalence, showing an initial decrease followed by an increase. Conversely, ATCA concentrations exhibited a negative association with MI prevalence, which then plateaued at higher levels.

Association between mixed mVOCs and MI

The correlation between the 19 mVOCs and MI is shown in Fig. 3. The Spearman correlation coefficients ranged from −0.03 to 0.84, suggesting intercorrelations among the mVOCs. The overall association between mVOCs and MI was assessed using a Weighted Quantile Sum (WQS) regression model, adjusted for age, gender, race, education, marital status, PIR, BMI, hypertension, diabetes, and smoking. The results revealed that for each one-unit increase in WQS, MI prevalence was associated with a 20.4% increase (95% CI: 1.05, 1.38).DHBMA, CEMA, CYMA, PHEMA, 3HPMA, and 3,4MHA were identified as key compounds among the assessed mVOCs

Variable	Model 1			Model 2			Model 3		
	OR	95% CI	P value	OR	95% CI	P value	OR	95% CI	P value
2MHA	0.99	0.63, 1.57	>0.9	1.09	0.68, 1.76	0.7	0.76	0.47, 1.22	0.2
3,4MHA	1.54	0.99, 2.40	0.055	1.59	0.98, 2.59	0.059	1.09	0.60, 1.97	0.8
AAMA	1.99	1.06, 3.74	0.033	3.37	1.63, 7.00	0.002 *	2.22	0.92, 5.35	0.075
AMCC	2.22	1.24, 3.99	0.008 *	2.15	1.05, 4.37	0.036 *	0.99	0.46, 2.13	>0.9
ATCA	0.73	0.45, 1.17	0.2	1.06	0.62, 1.83	0.8	0.93	0.55, 1.58	0.8
SBMA	0.9	0.54, 1.53	0.7	0.71	0.40, 1.26	0.2	0.7	0.40, 1.25	0.2
BPMA	0.74	0.54, 1.01	0.059	0.84	0.61, 1.17	0.3	0.91	0.65, 1.25	0.5
CEMA	3.61	1.99, 6.53	<0.001 *	2.88	1.46, 5.67	0.003 *	1.72	0.74, 4.04	0.2
CYMA	1.39	1.10, 1.76	0.007 *	1.76	1.39, 2.24	<0.001 *	1.8	1.14, 2.83	0.012 *
DHBMA	16.3	4.95, 53.6	<0.001 *	6.83	1.64, 28.5	0.009 *	3.24	0.73, 14.4	0.12
GAMA	1.58	0.81, 3.05	0.2	2.87	1.38, 5.94	0.005 *	1.71	0.61, 4.80	0.3
HEMA	1.53	0.93, 2.52	0.093	2.85	1.66, 4.90	<0.001 *	2.09	1.06, 4.11	0.034 *
2HPMA	1.62	1.15, 2.29	0.007 *	1.76	1.15, 2.67	0.01 *	1.51	0.89, 2.57	0.13
3HPMA	2.29	1.49, 3.52	<0.001 *	2.87	1.85, 4.46	<0.001 *	1.95	1.06, 3.58	0.032 *
MA	2.05	0.99, 4.26	0.055	2.64	1.23, 5.67	0.014 *	1.31	0.52, 3.30	0.6
MHBMA3	2.07	1.39, 3.10	<0.001 *	2.6	1.64, 4.12	<0.001 *	1.69	0.80, 3.58	0.2
PHEMA	2.25	1.31, 3.88	0.004 *	2.32	1.27, 4.24	0.007 *	1.87	1.00, 3.50	0.05
PGA	3.01	1.40, 6.48	0.006 *	2.61	1.05, 6.51	0.04 *	1.23	0.47, 3.20	0.7
HMPMA	2.52	1.59, 4.00	<0.001 *	2.81	1.72, 4.58	<0.001 *	1.61	0.74, 3.53	0.2

Table 2. Logistic regression associations of mVOC with MI in adults. Notes: Model 1 was a univariate logistic regression model; Model 2 was adjusted for age, race, gender;Model 3 was adjusted for age, race, gender, education, ratio of family income to poverty, marital, BMI, hypertension, diabetes, smoking.* P < 0.05. Abbreviations:OR, Odds Ratio; 95% CI, 95% Confidence Interval; VOC, Volatile Organic Compounds; MI, Myocardial Infarction; 2HPMA, N-acetyl-S-(2-hydroxypropyl)-L-cysteine; 2MHA, 2-methylhippuric acid; 3,4MHA, 3- and 4-methylhippuric acid; 3HPMA, N-acetyl-S-(3-hydroxypropyl)-L-cysteine; AAMA, N-acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC, N-acetyl-S-(N-methylcarbamoyl)-L-cysteine; ATCA, 2-aminothiazoline-4-carboxylic acid; BPMA, N-acetyl-S-(n-propyl)-L-cysteine; CEMA, N-acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA, N-acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA, N-acetyl-S-(3,4-dihydroxybutyl)-L-cysteine; GAMA, N-acetyl-S-(2-carbamoyl-2-hydroxyethyl)-L-cysteine; HEMA, N-acetyl-S-(2-hydroxyethyl)-L-cysteine; HMPMA, N-acetyl-S-(3-hydroxypropyl-1-methyl)-L-cysteine; MA, mandelic acid; MHBMA3, N-acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine; PGA, phenylglyoxylic acid; PHEMA, N-acetyl-S-(phenyl-2-hydroxyethyl)-L-cysteine; SBMA, N-acetyl-S-(benzyl)-L-cysteine.

(Fig. 4). DHBMA had the highest relative weight in the combined association, with a weight of 0.27. The weights of CEMA and CYMA were 0.16 and 0.14, respectively, also contributing substantially to the combined association. The weights of PHEMA, 3HPMA, and 3,4MHA were 0.12, 0.08, and 0.05, respectively.

Discussion

This study analyzed data from 5,211 U.S. adults between 2011 and 2018, indicating a significant positive association between mVOCs and MI. After comprehensive adjustment for confounders—including gender, age, race, education, marital status, PIR, BMI, hypertension, diabetes, and smoking status—levels of 3HPMA and CYMA remained statistically associated with MI prevalence. Additionally, CEMA and DHBMA showed significant associations with increased MI occurrence across multiple analyses.WQS analysis further demonstrated a significant overall association between mVOCs and MI prevalence. Based on these findings, VOC exposure may be a potential environmental concern in MI health management.

CYMA

Multivariate logistic regression analysis demonstrated a significant association between CYMA and MI prevalence, which was also significant in both RCS and WQS analyses. CYMA is a primary urinary metabolite of acrylonitrile[16], a high-production industrial chemical widely used in textiles, plastics, and medical pipelines[17]. Occupational exposure to acrylonitrile primarily occurs via inhalation and skin contact[18], while the general population may be exposed through residual commercial materials, fires, vehicle exhaust, and tobacco smoke. Among these sources, tobacco smoke is a major contributor, with approximately 1–2 mg of acrylonitrile per 100 cigarettes[19].Acrylonitrile is classified as a genotoxic and carcinogenic compound, largely due to its metabolite, cyanoethylene oxide (CEO)[19]. Experimental studies suggest that acrylonitrile and CEO may interfere with cellular signaling by interacting with key proteins[20]. CEO has also been implicated in DNA alkylation, mutations, oxidative stress-induced DNA damage, immune dysregulation, and inflammation[21]. Animal studies indicate that acrylonitrile exposure can elevate oxidative stress[22–24], which has been associated with cardiovascular disease (CVD) in certain experimental models[25]. While acrylonitrile is considered the primary precursor of

CYMA, the potential contribution of other VOCs remains unclear. Further research is warranted to evaluate the specificity of CYMA as a biomarker, identify alternative VOC sources, and refine exposure assessment strategies for improved air quality management.

3HPMA

In multivariate logistic regression, 3HPMA was significantly associated with MI prevalence and was also statistically significant in RCS analysis. It also showed a notable association in WQS analysis (weight: 0.08). As the primary urinary metabolite of acrolein, 3HPMA serves as an indicator of exposure to this highly electrophilic α,β-unsaturated carbonyl VOC. Acrolein is widely detected in industrial emissions, vehicle exhaust, building materials, tobacco smoke, overheated cooking oils, biocides, biomass burning, incense, and wildfires, with inhalation being the predominant exposure route for the general population[26–28].Due to its strong pulmonary toxicity, acrolein is classified as a hazardous air pollutant and has been epidemiologically linked to increased respiratory disease prevalence[29,30]. The U.S. Environmental Protection Agency (EPA) has identified it as an important environmental factor associated with non-cancerous respiratory conditions[30–32].Beyond exogenous exposure, acrolein can be endogenously generated through lipid peroxidation and polyamine oxidation[33]. It is primarily metabolized via conjugation with glutathione (GSH) in the liver, followed by N-acetylation in the kidneys to form S-(3-oxopropyl)-N-acetylcysteine, which is further metabolized into 3HPMA. Additionally, acrolein undergoes oxidative metabolism, producing the minor metabolite CEMA[34–36].

Acrolein has been reported to interact with proteins, lipids, and DNA, contributing to oxidative damage, cell death, and mitochondrial dysfunction[37–45]. Additionally, it may interfere with the antioxidant system by binding to sulfhydryl groups[41,42].Acrolein exposure has also been associated with alterations in cellular signaling pathways, where the PI3 K/AKT pathway may promote cell survival in acrolein-induced cytotoxicity, while the MAPK-ERK pathway is thought to facilitate cell death[46,47]. Moreover, acrolein exposure has been linked to endothelial dysfunction[48].Studies further suggest that acrolein may influence blood pressure regulation[49,50], and epidemiological evidence indicates potential associations with systemic inflammation and dyslipidemia[51.]

CEMA

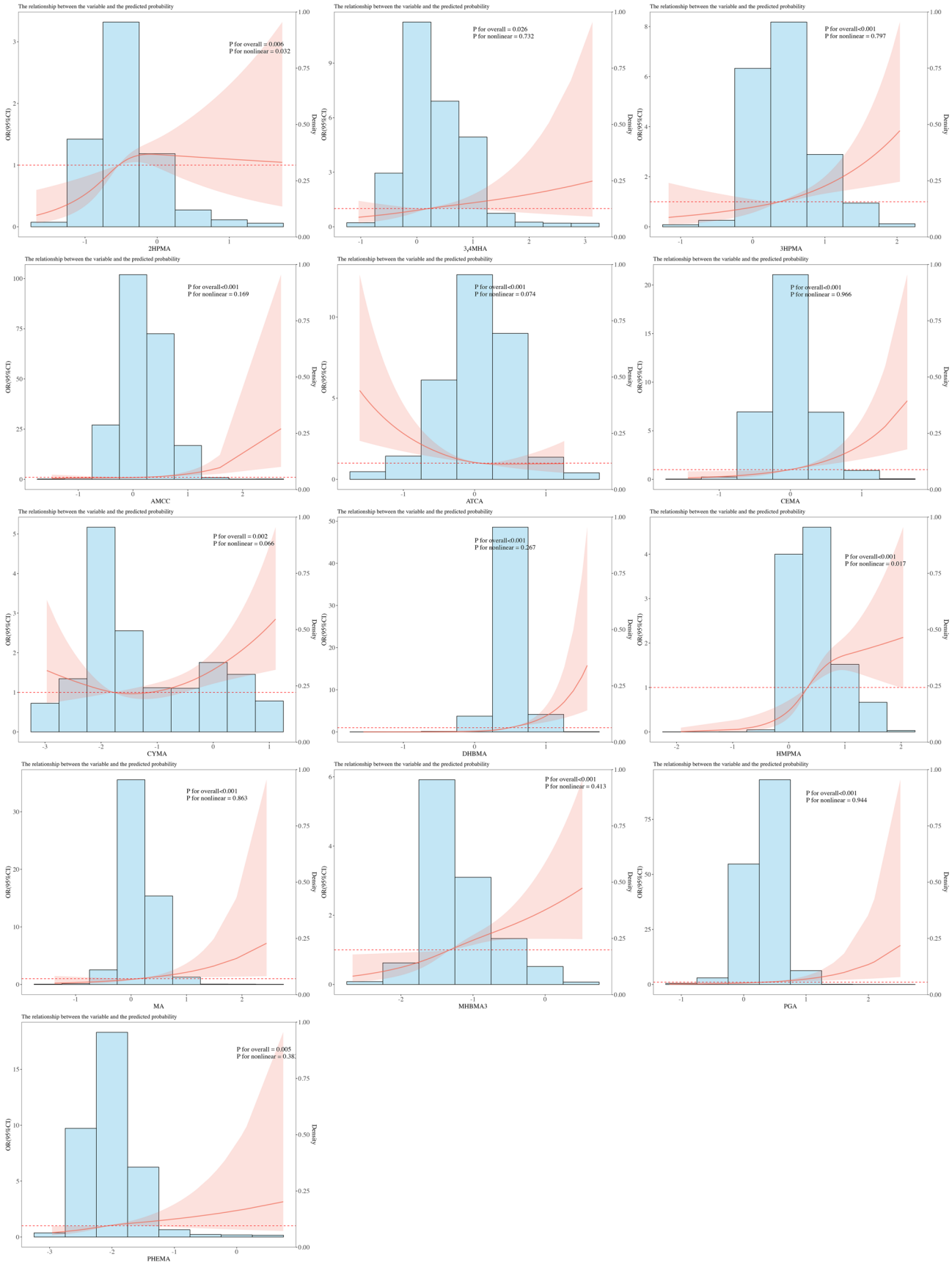
CEMA had a high weight of 0.16 in WQS and showed a statistically significant association with MI in RCS. It primarily originates from both vinyl chloride and acrolein metabolism, where cytochrome P450 2E1 (CYP2E1) oxidizes vinyl chloride into a reactive epoxide, which can bind to DNA and proteins or be further metabolized into CEMA[52.] Additionally, acrolein metabolism may contribute to urinary CEMA formation through oxidative pathways[34–36].Vinyl chloride, widely used in polyvinyl chloride production, is an environmental contaminant found in groundwater, air, and indoor environments[53–55.] Due to its prevalence and potential health risks, it ranks high on the ATSDR hazardous substances list[56]. Biologically, vinyl chloride is mutagenic, linked to chromosomal aberrations, and classified by the IARC as a risk factor for hepatic angiosarcoma and hepatocellular carcinoma[57]. It has also been associated with insulin resistance (IR) in both occupational and experimental settings[58,59]. IR contributes to carotid atherosclerosis, endothelial dysfunction, and inflammation, all of which are linked to CVD risk[60–64].The association between CEMA and MI may reflect contributions from mutagenicity, IR, oxidative stress, and atherosclerosis-related pathways. Further research is needed to delineate these mechanisms and clarify the relative contributions of vinyl chloride and acrolein metabolism to urinary CEMA levels.

DHBMA

DHBMA had the highest weight in WQS analysis and was significantly associated with MI in RCS analysis. Urinary DHBMA is a biomarker of 1,3-butadiene (BD) exposure[65]. BD, a synthetic gas, is primarily used in rubber manufacturing and rapidly evaporates in air[66]. Major sources include vehicle exhaust, industrial activities, forest fires, rubber and plastic combustion, drinking water contamination, and tobacco smoke[67]. Indoor BD levels vary based on smoking, traffic infiltration, vehicle emissions, and cooking[68]. BD exposure mainly occurs through inhalation. Once absorbed, BD undergoes CYP2E1-catalyzed oxidation to form 1,2-epoxy-3-butene, which reacts with GSH to produce mercapturic acids. If hydrolyzed before conjugation, it forms DHBMA, the predominant urinary BD biomarker, accounting for over 97%[69,70]. BD exposure has been linked to hematologic and lymphatic malignancies[71], oxidative stress[72], and genotoxicity. It can induce DNA adducts, double-strand breaks, and chromatin modifications[73,74].One study associated environmental BD exposure with blood pressure changes in pregnant women[75], while another found a significant link between BD exposure, endothelial dysfunction, and increased diastolic blood pressure[76]. Future research should further investigate the biological mechanisms linking BD exposure to cardiovascular health and assess the potential of DHBMA as a specific biomarker for BD-related effects.

The WQS analysis showed that the risk of MI increased by approximately 20.4% (95% CI: 1.05,1.38) for each unit increase in WQS. In recent years, accumulating evidence suggested that environmental chemical carcinogens may contribute to atherosclerosis development by causing DNA damage in circulating and blood vessel wall cells. Moreover, these chemicals can induce mitochondrial DNA damage, which serves as an endogenous source of oxidative stress. This endogenous oxidative stress was considered the primary mechanism of mutation-related atherosclerosis, resulting in the development and instability of plaques[77]. Therefore, exposure to VOCs may be a risk factor for MI, especially promoting atherosclerosis and MI by inducing oxidative stress and DNA damage. Future research should further clarify the correspondence between mVOCs and their precursor VOCs and investigate the specific mechanisms by which certain VOCs affect the cardiovascular system. This will facilitate more precise identification of emission sources and the optimization of air quality management strategies.

There are several strengths in our study. According to available information, this is the first study examining the correlation between 19 urinary mVOCs and MI using a nationally representative sample of U.S. adults. In addition, the four positives, CYMA, 3HPMA, CEMA, and DHBMA, showed positive results related to MI


The relationship between the variable and the predicted probability
P for overall = 0.006
P for nonlinear = 0.032
OR(95%CI)
Density
2HPMA
The relationship between the variable and the predicted probability
P for overall = 0.026
P for nonlinear = 0.732
OR(95%CI)
Density
3,4MHA
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.797
OR(95%CI)
Density
3HPMA
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.169
OR(95%CI)
Density
AMCC
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.074
OR(95%CI)
Density
ATCA
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.966
OR(95%CI)
Density
CEMA
The relationship between the variable and the predicted probability
P for overall = 0.002
P for nonlinear = 0.066
OR(95%CI)
Density
CYMA
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.267
OR(95%CI)
Density
DHBMA
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.017
OR(95%CI)
Density
HMPMA
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.863
OR(95%CI)
Density
MA
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.413
OR(95%CI)
Density
MHBMA3
The relationship between the variable and the predicted probability
P for overall<0.001
P for nonlinear = 0.944
OR(95%CI)
Density
PGA
The relationship between the variable and the predicted probability
P for overall = 0.005
P for nonlinear = 0.38
OR(95%CI)
Density
PHEMA

◂**Fig. 2**. Restricted cubic spline regression analysis of urinary metabolites of volatile organic compounds and myocardial infarction. **Note:** The solid red line represents the estimated association between urinary metabolite levels and the odds of myocardial infarction (MI), based on restricted cubic spline regression analysis. The shaded red area indicates the 95% confidence interval (CI). The blue histogram shows the distribution of urinary metabolite concentrations. The dashed black line at zero represents the reference point for no association. P-values for the overall association and nonlinearity are provided for each metabolite.

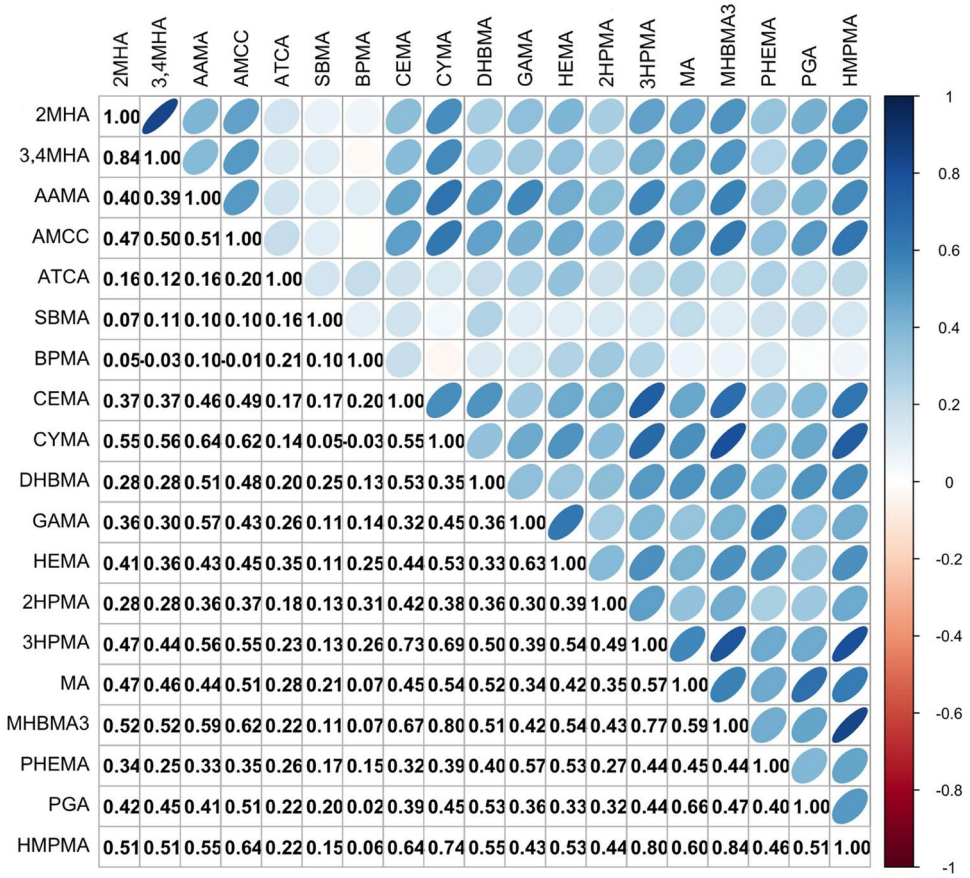


Fig. 3. Spearman correlation coefficients of 19 volatile organic compound metabolite concentrations.

in multiple modeling analyses. Furthermore, we explored the interaction between mVOCs. However, there are several limitations in this study. Firstly, since this study was designed as an observational study, causal relationships cannot be inferred from these data. Secondly, despite adjusting for covariates in regression models, potential unmeasured confounding effects may have influenced the results. Factors such as genetic predisposition, medication dosage and type, adequacy of CVD medications, and adherence to treatment were not fully accounted for. Thirdly, the exact pathogenic mechanisms of VOCs and their metabolites in animals or humans regarding MI have not been studied. Finally, since the study participants were adults from the U.S., it is essential to ascertain the transferability of the results to other populations.

Conclusion

This study identified a significant association between urinary mVOCs and MI incidence, suggesting that VOC exposure may be related to MI risk. However, further research is required to elucidate the underlying mechanisms and validate these findings.

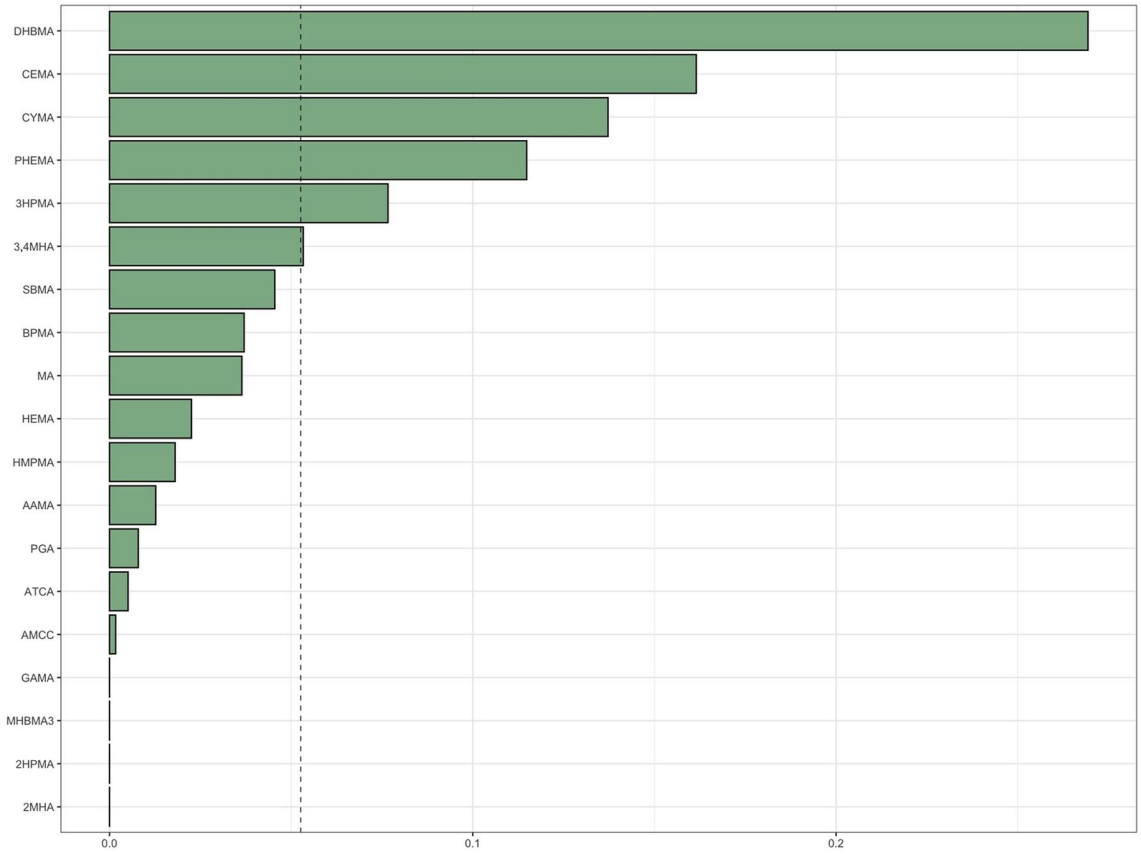


Fig. 4. Mixed effects of urinary metabolites of volatile organic compounds on myocardial infarction assessed by weighted quantile sum regression. Note: The bar plot displays the weights of individual mVOCs in the WQS index, indicating their relative contribution to the overall association with MI. The dashed horizontal line represents the cutoff above which the weights are considered relatively influential within the WQS model.

Data availability

The datasets analysed during the current study are available in the National Health and Nutrition Examination Survey (NHANES), https://www.cdc.gov/nchs/nhanes/index.htm.

Received: 14 August 2024; Accepted: 8 May 2025
Published online: 22 May 2025

References

1. Lorkiewicz, P. et al. Comparison of urinary biomarkers of exposure in humans using electronic cigarettes, combustible cigarettes, and smokeless tobacco. *Nicotine. Tob. Res.* **21**, 1228–1238. https://doi.org/10.1093/ntr/nty089 (2019).
2. Keith, R. J. et al. Characterization of volatile organic compound metabolites in cigarette smokers, electronic nicotine device users, dual users, and nonusers of tobacco. *Nicotine. Tob. Res.* **22**, 264–272. https://doi.org/10.1093/ntr/ntz021 (2020).
3. St Helen, G. et al. Comparison of systemic exposure to toxic and/or carcinogenic volatile organic compounds (VOC) during vaping, smoking, and abstention. *Cancer Prev. Res. (Phila)* **13**(153), 162. https://doi.org/10.1158/1940-6207.Capr-19-0356 (2020).
4. Hanna, G. B., Boshier, P. R., Markar, S. R. & Romano, A. Accuracy and methodologic challenges of volatile organic compound-based exhaled breath tests for cancer diagnosis: A systematic review and meta-analysis. *JAMA Oncol.* **5**, e182815. https://doi.org/10.1001/jamaoncol.2018.2815 (2019).
5. Lei, T., Qian, H., Yang, J. & Hu, Y. The association analysis between exposure to volatile organic chemicals and obesity in the general USA population: A cross-sectional study from NHANES program. *Chemosphere* **315**, 137738. https://doi.org/10.1016/j.chemosphere.2023.137738 (2023).
6. *ATSDR's Substance Priority List*, <https://www.atsdr.cdc.gov/spl/> (2023).
7. Wang, Y. et al. Associations between the compositional patterns of blood volatile organic compounds and chronic respiratory diseases and ages at onset in NHANES 2003–2012. *Chemosphere* **327**, 138425. https://doi.org/10.1016/j.chemosphere.2023.138425 (2023).
8. Wahlang, B. et al. Associations between residential volatile organic compound exposures and liver injury markers: The role of biological sex and race. *Environ. Res.* **221**, 115228. https://doi.org/10.1016/j.envres.2023.115228 (2023).
9. Annavarapu, R. N. & Kathi, S. Cognitive disorders in children associated with urban vehicular emissions. *Environ. Pollut.* **208**, 74–78. https://doi.org/10.1016/j.envpol.2015.09.036 (2016).
10. Wang, X. et al. Association between urinary metabolites of volatile organic compounds and cardiovascular disease in the general population from NHANES 2011–2018. *Ecotoxicol. Environ. Saf.* **264**, 115412. https://doi.org/10.1016/j.ecoenv.2023.115412 (2023).
11. Curry, L. A. et al. What distinguishes top-performing hospitals in acute myocardial infarction mortality rates? A qualitative study. *Ann. Intern. Med.* **154**, 384–390. https://doi.org/10.7326/0003-4819-154-6-201103150-00003 (2011).

12. Pasumarthi, K. B. & Field, L. J. Cardiomyocyte cell cycle regulation. *Circ. Res.* **90**, 1044–1054. https://doi.org/10.1161/01.res.0000020201.44772.67 (2002).
13. Martin, S. S. et al. 2024 heart disease and stroke statistics: A report of US and global data from the American heart association. *Circulation* **149**, e347–e913. https://doi.org/10.1161/cir.0000000000001209 (2024).
14. Virani, S. S. et al. Heart disease and stroke statistics-2020 Update: A report from the American heart association. *Circulation* **141**, e139–e596. https://doi.org/10.1161/cir.0000000000000757 (2020).
15. Qian, X. et al. Urinary metabolites of multiple volatile organic compounds among general population in Wuhan, central China: Inter-day reproducibility, seasonal difference, and their associations with oxidative stress biomarkers. *Environ. Pollut.* **289**, 117913. https://doi.org/10.1016/j.envpol.2021.117913 (2021).
16. Lin, C. Y., Lee, H. L., Sung, F. C. & Su, T. C. Investigating the association between urinary levels of acrylonitrile metabolite N-acetyl-S-(2-cyanoethyl)-L-cysteine and the oxidative stress product 8-hydroxydeoxyguanosine in adolescents and young adults. *Environ. Pollut.* **239**, 493–498. https://doi.org/10.1016/j.envpol.2018.04.010 (2018).
17. Watcharasit, P., Suntararuks, S., Visitnonthachai, D., Thiantanawat, A. & Satayavivad, J. Acrylonitrile induced apoptosis via oxidative stress in neuroblastoma SH-SY5Y cell. *J. Appl. Toxicol.* **30**, 649–655. https://doi.org/10.1002/jat.1535 (2010).
18. Marsh, G. M. & Zimmerman, S. D. Mortality among chemical plant workers exposed to acrylonitrile: 2011 follow-up. *J. Occup. Environ. Med.* **57**, 134–145. https://doi.org/10.1097/jom.0000000000000369 (2015).
19. Léonard, A. et al. Mutagenicity, carcinogenicity, and teratogenicity of acrylonitrile. *Mutat. Res.* **436**, 263–283. https://doi.org/10.1016/s1383-5742(99)00006-x (1999).
20. Walker, V. E., Walker, D. M., Ghanayem, B. I. & Douglas, G. R. Analysis of biomarkers of DNA Damage and mutagenicity in mice exposed to acrylonitrile. *Chem. Res. Toxicol.* **33**, 1623–1632. https://doi.org/10.1021/acs.chemrestox.0c00154 (2020).
21. Kamendulis, L. M. et al. The effect of acrylonitrile on gap junctional intercellular communication in rat astrocytes. *Cell. Biol. Toxicol.* **15**, 173–183. https://doi.org/10.1023/a:1007685504941 (1999).
22. el El-Sayed, S. M., Abo-Salem, O. M., Abd-Ellah, M. F. & Abd-Alla, G. M. Hesperidin, an antioxidant flavonoid, prevents acrylonitrile-induced oxidative stress in rat brain. *J. Biochem. Mol. Toxicol.* **22**, 268–273. https://doi.org/10.1002/jbt.20237 (2008).
23. Pu, X., Wang, Z., Zhou, S. & Klaunig, J. E. Protective effects of antioxidants on acrylonitrile-induced oxidative stress in female F344 rats. *Environ. Toxicol.* **31**, 1808–1818. https://doi.org/10.1002/tox.22182 (2016).
24. Rongzhu, L. et al. Effects of acrylonitrile on antioxidant status of different brain regions in rats. *Neurochem. Int.* **55**, 552–557. https://doi.org/10.1016/j.neuint.2009.05.009 (2009).
25. Csányi, G. & Miller, F. J. Jr. Oxidative stress in cardiovascular disease. *Int. J. Mol. Sci.* **15**, 6002–6008. https://doi.org/10.3390/ijms15046002 (2014).
26. Cahill, T. M. Ambient acrolein concentrations in coastal, remote, and urban regions in California. *Environ. Sci. Technol.* **48**, 8507–8513. https://doi.org/10.1021/es5014533 (2014).
27. Lunderberg, D. M. et al. High-resolution exposure assessment for volatile organic compounds in two California residences. *Environ. Sci. Technol.* **55**, 6740–6751. https://doi.org/10.1021/acs.est.0c08304 (2021).
28. Seaman, V. Y., Bennett, D. H. & Cahill, T. M. Origin, occurrence, and source emission rate of acrolein in residential indoor air. *Environ. Sci. Technol.* **41**, 6940–6946. https://doi.org/10.1021/es0707299 (2007).
29. Annesi-Maesano, I. et al. Poor air quality in classrooms related to asthma and rhinitis in primary schoolchildren of the French 6 Cities Study. *Thorax* **67**, 682–688. https://doi.org/10.1136/thoraxjnl-2011-200391 (2012).
30. Kuang, H. et al. Exposure to volatile organic compounds may be associated with oxidative DNA damage-mediated childhood asthma. *Ecotoxicol. Environ. Saf.* **210**, 111864. https://doi.org/10.1016/j.ecoenv.2020.111864 (2021).
31. Alwis, K. U., de Castro, B. R., Morrow, J. C. & Blount, B. C. Acrolein exposure in U.S. tobacco smokers and non-tobacco users: NHANES 2005–2006. *Environ. Health Perspect.* **123**, 1302–1308. https://doi.org/10.1289/ehp.1409251 (2015).
32. *Summary of Results for the 2002 National-Scale Assessment*, <https://archive.epa.gov/nata2002/web/html/risksum.html> (2016).
33. Alfarhan, M., Jafari, E. & Narayanan, S. P. Acrolein: A potential mediator of oxidative damage in diabetic retinopathy. *Biomolecules* https://doi.org/10.3390/biom10111579 (2020).
34. Stevens, J. F. & Maier, C. S. Acrolein: Sources, metabolism, and biomolecular interactions relevant to human health and disease. *Mol. Nutr. Food Res.* **52**, 7–25. https://doi.org/10.1002/mnfr.200700412 (2008).
35. Burcham, P. C. Acrolein and human disease: Untangling the knotty exposure scenarios accompanying several diverse disorders. *Chem. Res. Toxicol.* **30**, 145–161. https://doi.org/10.1021/acs.chemrestox.6b00310 (2017).
36. Carmella, S. G. et al. Quantitation of acrolein-derived (3-hydroxypropyl)mercapturic acid in human urine by liquid chromatography-atmospheric pressure chemical ionization tandem mass spectrometry: Effects of cigarette smoking. *Chem. Res. Toxicol.* **20**, 986–990. https://doi.org/10.1021/tx700075y (2007).
37. Uchida, K. et al. Acrolein is a product of lipid peroxidation reaction: Formation of free acrolein and its conjugate with lysine residues in oxidized low density lipoproteins. *J. Biol. Chem.* **273**, 16058–16066. https://doi.org/10.1074/jbc.273.26.16058 (1998).
38. Li, L., Jiang, L., Geng, C., Cao, J. & Zhong, L. The role of oxidative stress in acrolein-induced DNA damage in HepG2 cells. *Free Radic. Res.* **42**, 354–361. https://doi.org/10.1080/10715760802008114 (2008).
39. Wang, Y. T. et al. Acrolein acts as a neurotoxin in the nigrostriatal dopaminergic system of rat: Involvement of α-synuclein aggregation and programmed cell death. *Sci. Rep.* **7**, 45741. https://doi.org/10.1038/srep45741 (2017).
40. Lovell, M. A. & Markesbery, W. R. Amyloid beta peptide, 4-hydroxynonenal and apoptosis. *Curr. Alzheimer Res.* **3**, 359–364. https://doi.org/10.2174/156720506778249506 (2006).
41. Furuhata, A., Nakamura, M., Osawa, T. & Uchida, K. Thiolation of protein-bound carcinogenic aldehyde. An electrophilic acrolein-lysine adduct that covalently binds to thiols. *J. Biol. Chem.* **277**, 27919–27926. https://doi.org/10.1074/jbc.M202794200 (2002).
42. Qin, W. S., Deng, Y. H. & Cui, F. C. Sulforaphane protects against acrolein-induced oxidative stress and inflammatory responses: Modulation of Nrf-2 and COX-2 expression. *Arch. Med. Sci.* **12**, 871–880. https://doi.org/10.5114/aoms.2016.59919 (2016).
43. Shi, R., Rickett, T. & Sun, W. Acrolein-mediated injury in nervous system trauma and diseases. *Mol. Nutr. Food Res.* **55**, 1320–1331. https://doi.org/10.1002/mnfr.201100217 (2011).
44. Sun, L., Luo, C., Long, J., Wei, D. & Liu, J. Acrolein is a mitochondrial toxin: Effects on respiratory function and enzyme activities in isolated rat liver mitochondria. *Mitochondrion* **6**, 136–142. https://doi.org/10.1016/j.mito.2006.04.003 (2006).
45. Luo, J. & Shi, R. Acrolein induces axolemmal disruption, oxidative stress, and mitochondrial impairment in spinal cord tissue. *Neurochem. Int.* **44**, 475–486. https://doi.org/10.1016/j.neuint.2003.09.006 (2004).
46. Dong, L. et al. Magnolol protects against oxidative stress-mediated neural cell damage by modulating mitochondrial dysfunction and PI3K/Akt signaling. *J. Mol. Neurosci.* **50**, 469–481. https://doi.org/10.1007/s12031-013-9964-0 (2013).
47. Huang, M. H. et al. MEK inhibitors reverse resistance in epidermal growth factor receptor mutation lung cancer cells with acquired resistance to gefitinib. *Mol. Oncol.* **7**, 112–120. https://doi.org/10.1016/j.molonc.2012.09.002 (2013).
48. DeJarnett, N. et al. Acrolein exposure is associated with increased cardiovascular disease risk. *J. Am. Heart Assoc.* **3**, e000934. https://doi.org/10.1161/jaha.114.000934 (2014).
49. Perez, C. M. et al. Hypoxia stress test reveals exaggerated cardiovascular effects in hypertensive rats after exposure to the air pollutant acrolein. *Toxicol. Sci.* **132**, 467–477. https://doi.org/10.1093/toxsci/kft008 (2013).
50. McGraw, K. E. et al. Exposure to volatile organic compounds—acrolein, 1,3-butadiene, and crotonaldehyde—is associated with vascular dysfunction. *Environ. Res.* **196**, 110903. https://doi.org/10.1016/j.envres.2021.110903 (2021).

51. Feng, X. et al. Urinary acrolein metabolites, systemic inflammation, and blood lipids: Results from the national health and nutrition examination survey. *Chemosphere* **286**, 131791. https://doi.org/10.1016/j.chemosphere.2021.131791 (2022).
52. Studies, C. o. A. E. G. L. C. o. T. B. o. E. S. a. T. D. o. E. a. L. in *Acute Exposure Guideline Levels for Selected Airborne Chemicals: Volume 11* Vol. 11 (The National Academies Press, 2012).
53. Kielhorn, J., Melber, C., Wahnschaffe, U., Aitio, A. & Mangelsdorf, I. Vinyl chloride: Still a cause for concern. *Environ. Health Perspect* **108**, 579–588. https://doi.org/10.1289/ehp.00108579 (2000).
54. Cleary, E., Asher, M., Olawoyin, R. & Zhang, K. Assessment of indoor air quality exposures and impacts on respiratory outcomes in river rouge and dearborn. *Michigan. Chemosphere* **187**, 320–329. https://doi.org/10.1016/j.chemosphere.2017.08.091 (2017).
55. El-Metwally, D. et al. Urinary metabolites of volatile organic compounds of infants in the neonatal intensive care unit. *Pediatr. Res.* **83**, 1158–1164. https://doi.org/10.1038/pr.2018.52 (2018).
56. *Toxicological Profile for Vinyl Chloride*, <https://wwwn.cdc.gov/TSP/ToxProfiles/ToxProfiles.aspx?id=282&tid=51> (
57. IARC monographs on the evaluation of carcinogenic risks to humans. Volume 97. 1,3-butadiene, ethylene oxide and vinyl halides (vinyl fluoride, vinyl chloride and vinyl bromide). *IARC Monogr Eval Carcinog Risks Hum* **97**, 3–471 (2008).
58. Cave, M. et al. Toxicant-associated steatohepatitis in vinyl chloride workers. *Hepatology* **51**, 474–481. https://doi.org/10.1002/hep.23321 (2010).
59. Lang, A. L. et al. Vinyl chloride dysregulates metabolic homeostasis and enhances diet-induced liver injury in mice. *Hepatol. Commun.* **2**, 270–284. https://doi.org/10.1002/hep4.1151 (2018).
60. Bonora, E. et al. Impaired glucose tolerance, Type II diabetes mellitus and carotid atherosclerosis: Prospective results from the Bruneck study. *Diabetologia* **43**, 156–164. https://doi.org/10.1007/s001250050024 (2000).
61. Meigs, J. B., Nathan, D. M., D'Agostino, R. B. Sr. & Wilson, P. W. Fasting and postchallenge glycemia and cardiovascular disease risk: The Framingham Offspring Study. *Diabet. Care* **25**, 1845–1850. https://doi.org/10.2337/diacare.25.10.1845 (2002).
62. Bornfeldt, K. E. & Tabas, I. Insulin resistance, hyperglycemia, and atherosclerosis. *Cell Metab.* **14**, 575–585. https://doi.org/10.1016/j.cmet.2011.07.015 (2011).
63. Ceriello, A. Postprandial hyperglycemia and diabetes complications: Is it time to treat?. *Diabetes* **54**, 1–7. https://doi.org/10.2337/diabetes.54.1.1 (2005).
64. Meshkani, R. & Adeli, K. Hepatic insulin resistance, metabolic syndrome and cardiovascular disease. *Clin. Biochem.* **42**, 1331–1346. https://doi.org/10.1016/j.clinbiochem.2009.05.018 (2009).
65. Albertini, R. J. et al. Biomarkers for assessing occupational exposures to 1,3-butadiene. *Chem. Biol. Interact.* **135–136**, 429–453. https://doi.org/10.1016/s0009-2797(01)00181-8 (2001).
66. *Public Health Statement for 1,3-Butadiene*, <https://wwwn.cdc.gov/TSP/PHS/PHS.aspx?phsid=457&toxid=81> (2011).
67. ,3-Butadiene. <https://www.epa.gov/sites/production/files/2016-08/documents/13-butadiene.pdf>.
68. Environmental, C. P. *A report on multimedia exposures to selected PSL2 substances*. (Health Canada, 1998).
69. Sapkota, A., Halden, R. U., Dominici, F., Groopman, J. D. & Buckley, T. J. Urinary biomarkers of 1,3-butadiene in environmental settings using liquid chromatography isotope dilution tandem mass spectrometry. *Chem. Biol. Interact.* **160**, 70–79. https://doi.org/10.1016/j.cbi.2005.12.006 (2006).
70. Penn, A. & Snyder, C. A. 1,3-Butadiene exposure and cardiovascular disease. *Mutat. Res.* **621**, 42–49. https://doi.org/10.1016/j.mrfmmm.2006.12.011 (2007).
71. Kirman, C. R., Albertini, R. J., Sweeney, L. M. & Gargas, M. L. 1,3-Butadiene: I. Review of metabolism and the implications to human health risk assessment. *Crit. Rev. Toxicol.* **40**(1), 1–11. https://doi.org/10.3109/10408444.2010.507181 (2010).
72. Arayasiri, M., Mahidol, C., Navasumrit, P., Autrup, H. & Ruchirawat, M. Biomonitoring of benzene and 1,3-butadiene exposure and early biological effects in traffic policemen. *Sci. Total Environ.* **408**, 4855–4862. https://doi.org/10.1016/j.scitotenv.2010.06.033 (2010).
73. Walker, V. E. et al. 1,3-Butadiene metabolite 1,2,3,4-diepoxybutane induces DNA adducts and micronuclei but not t(9;22) translocations in human cells. *Chem. Biol. Interact.* **312**, 108797. https://doi.org/10.1016/j.cbi.2019.108797 (2019).
74. Lewis, L. et al. Sex-specific differences in genotoxic and epigenetic effects of 1,3-butadiene among mouse tissues. *Arch. Toxicol.* **93**, 791–800. https://doi.org/10.1007/s00204-018-2374-x (2019).
75. Männistö, T. et al. Acute and recent air pollution exposure and cardiovascular events at labor and delivery. *Heart* **101**, 1491–1498. https://doi.org/10.1136/heartjnl-2014-307366 (2015).
76. Hyun, S. H. et al. Associations between personal exposures to VOCs and alterations in cardiovascular physiology: Detroit exposure and aerosol research study (DEARS). *Atmos. Environ.* **104**, 246–255. https://doi.org/10.1016/j.atmosenv.2015.01.016 (2015).
77. Pulliero, A. et al. Environmental carcinogens and mutational pathways in atherosclerosis. *Int. J. Hyg. Environ. Health* **218**, 293–312. https://doi.org/10.1016/j.ijheh.2015.01.007 (2015).

Author contributions

All authors contributed to the study conception and design. Writing—original draft preparation: Xiangyu Kong; Writing—review and editing: Xiangyu Kong, Zhao Qiu; Conceptualization: Xiangyu Kong; Methodology: Xiangyu Kong; Formal analysis and investigation: Xiangyu Kong, Zhao Qiu; Resources: Xiangyu Kong; Supervision: Xiangyu Kong, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-025-01773-x.

Correspondence and requests for materials should be addressed to X.K.