

## Supplementary Material

### Air Pollution and Cardiac Biomarkers in Heart Failure: A Scoping Review.

#### 1. SEARCH QUESTIONS, CONCEPTS, AND KEYWORDS

##### *Research question*

What is the association between air pollution and cardiac biomarkers in heart failure?

##### *Concept 1: air pollution*

##### *Keywords*

air pollution, particulate matter, ozone, sulfur dioxide, nitrogen dioxide, carbon monoxide

##### *Mesh*

"Air Pollution"[Mesh]

"Particulate Matter"[Mesh]

"Ozone"[Mesh]

"Sulfur Dioxide"[Mesh]

"Nitrogen Dioxide"[Mesh]

"Carbon Monoxide"[Mesh]

##### *Entree*

'air pollution'/exp

'particulate matter'/exp

'ozone'/exp

'sulfur dioxide'/exp

'nitrogen dioxide'/exp

'carbon monoxide'/exp

***Search terms***

air pollut\* OR particulate matter OR ozone OR sulfur dioxide OR nitrogen dioxide OR  
carbon monoxide

***Concept 2: heart failure***

***Keywords***

heart failure, systolic heart failure, diastolic heart failure

***Mesh***

"Heart Failure"[Mesh]

***Emtree***

'heart failure'/exp

***Search terms***

heart failure\* OR cardiac failure OR congestive cardiac failure OR left ventricular failure OR Heart Decompensation OR Myocardial Failure

**Concept 3: biomarkers**

**Keywords**

Biomarker, Marker, terminal pro brain natriuretic peptide, B-Type Natriuretic Peptide, soluble suppression of tumorigenicity-2, Troponin T, troponin I, IL-1, IL-6, IL-8, C-reactive protein, TNF- $\alpha$ , PAI-1, tPA, plasminogen

**Mesh**

"Biomarkers"[Mesh]

"Interleukin-1"[Mesh]

"Natriuretic Peptides"[Mesh]

"Troponin"[Mesh]

"Interleukins"[Mesh]

"Tumor Necrosis Factors"[Mesh]

"C-Reactive Protein"[Mesh]

"Blood Proteins"[Mesh]

"Protein Kinases"[Mesh]

**Entree**

'amino terminal pro brain natriuretic peptide'/exp

'troponin'/exp

'interleukin receptor'/exp

'cytokine'/de

### ***Search terms***

biomarker\* OR marker\* OR B-Type Natriuretic Peptide OR natriuretic peptide OR Soluble ST2 OR ST2 OR sST2 OR soluble suppression of tumorigenicity-2 OR Troponin T OR Cardiac troponin\* OR troponin\* OR hs-cTn OR cTnI OR cTnT OR cTn OR TnI OR TnT OR interleukin\* OR IL-1\* OR IL-6\* OR IL-8\* OR CRP OR C-reactive protein OR TNF OR tumor necrosis factor\* OR plasminogen activator inhibitor-1 OR PAI-1 OR tissue-type plasminogen activator OR tPA OR plasminogen

## **2. SEARCH STRATEGIES IN DIFFERENT DATABASES**

### ***PubMed***

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<b>Search</b>	<b>Query</b>
#1	air pollut* OR particulate matter OR ozone OR sulfur dioxide OR nitrogen dioxide OR carbon monoxide
#2	"Air Pollution"[Mesh] OR "Particulate Matter"[Mesh] OR "Ozone"[Mesh] OR "Sulfur Dioxide"[Mesh] OR "Nitrogen Dioxide"[Mesh] OR "Carbon

Monoxide"[Mesh]

- #3 biomarker\* OR marker\* OR B-Type Natriuretic Peptide OR natriuretic peptide OR Soluble ST2 OR ST2 OR sST2 OR soluble suppression of tumorigenicity-2 OR Troponin T OR Cardiac troponin\* OR troponin\* OR hs-cTn OR cTnI OR cTnT OR cTn OR TnI OR TnT OR interleukin\* OR IL-1\* OR IL-6\* OR IL-8\* OR CRP OR C-reactive protein OR TNF OR tumor necrosis factor\* OR plasminogen activator inhibitor-1 OR PAI-1 OR tissue-type plasminogen activator OR tPA OR plasminogen
- #4 "Biomarkers"[Mesh] OR "Interleukin-1"[Mesh] OR "Natriuretic Peptides"[Mesh] OR "Troponin"[Mesh] OR "Interleukins"[Mesh] OR "Tumor Necrosis Factors"[Mesh] OR "C-Reactive Protein"[Mesh] OR "Blood Proteins"[Mesh] OR "Protein Kinases"[Mesh]
- #5 heart failure\* OR cardiac failure OR congestive cardiac failure OR left ventricular failure OR Heart Decompensation OR Myocardial Failure
- #6 "Heart Failure"[Mesh]
- #7 #1 OR #2
- #8 #3 OR #4
- #9 #5 OR #6
- #10 #7 AND #8 AND #9

Search	Query
#1	air pollut* OR particulate matter OR ozone OR sulfur dioxide OR nitrogen dioxide OR carbon monoxide
#2	'air pollution'/exp OR 'particulate matter'/exp OR 'ozone'/exp OR 'sulfur dioxide'/exp OR 'nitrogen dioxide'/exp OR 'carbon monoxide'/exp
#3	biomarker* OR marker* OR B-Type Natriuretic Peptide OR natriuretic peptide OR Soluble ST2 OR ST2 OR sST2 OR soluble suppression of tumorigenicity-2 OR Troponin T OR Cardiac troponin* OR troponin* OR hs-cTn OR cTnI OR cTnT OR cTn OR TnI OR TnT OR interleukin* OR IL-1* OR IL-6* OR IL-8* OR CRP OR C-reactive protein OR TNF OR tumor necrosis factor* OR plasminogen activator inhibitor-1 OR PAI-1 OR tissue-type plasminogen activator OR tPA OR plasminogen
#4	'amino terminal pro brain natriuretic peptide'/exp OR 'troponin'/exp OR 'interleukin receptor'/exp OR 'cytokine'/de
#5	heart failure* OR cardiac failure OR congestive cardiac failure OR left ventricular failure OR Heart Decompensation OR Myocardial Failure
#6	'heart failure'/exp
#7	#1 OR #2
#8	#3 OR #4

#9 #5 OR #6

#10 #7 AND #8 AND #9

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### **Web of Science**

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<b>Search</b>	<b>Query</b>
#1	air pollut* OR particulate matter OR ozone OR sulfur dioxide OR nitrogen dioxide OR carbon monoxide
#2	biomarker* OR marker* OR B-Type Natriuretic Peptide OR natriuretic peptide OR Soluble ST2 OR ST2 OR sST2 OR soluble suppression of tumorigenicity-2 OR Troponin T OR Cardiac troponin* OR troponin* OR hs-cTn OR cTnI OR cTnT OR cTn OR TnI OR TnT OR interleukin* OR IL-1* OR IL-6* OR IL-8* OR CRP OR C-reactive protein OR TNF OR tumor necrosis factor* OR plasminogen activator inhibitor-1 OR PAI-1 OR tissue-type plasminogen activator OR tPA OR plasminogen
#3	heart failure* OR cardiac failure OR congestive cardiac failure OR left ventricular failure OR Heart Decompensation OR Myocardial Failure
#4	#1 AND #2 AND #3

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### **CNKI**

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<b>Search</b>	<b>Query</b>
#1	TKA %= '空气污染' + 'PM <sub>2.5</sub> ' + 'PM <sub>10</sub> ' + '颗粒物' + '臭氧' + '二氧化硫' + '

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二氧化氮' + '一氧化碳' + 'air pollution' + 'particulate matter' + 'ozone' +  
'carbon monoxide'

#2 TKA %= '心力衰竭' + '心衰' + '射血分数' + '心功能不全' + 'heart failure'  
+ 'cardiac dysfunction'

#3 TKA %= '生物标志物' + 'BNP' + 'NT-proBNP' + '肌钙蛋白' + 'cTnT' + 'cTnI'  
+ 'troponin' + 'IL-6' + 'CRP' + 'TNF' + 'tPA' + 'PAI-1' + '利钠肽' + '脑钠肽' +  
'白介素' + 'C 反应蛋白' + '肿瘤坏死因子' + '纤溶酶' + 'sST2'

#4 #1 AND #2 AND #3

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### **3. PUBLICATION DATE**

From 1 January 1990 to 31 August 2024

### **4. EXCLUSION CRITERIA**

Reason 1: Heart failure or at least pre-heart failure was not included as a variable

Reason 2: Biomarkers were not included as a variable.

Reason 3: Air pollutant of interest was not measured.

Reason 4: Review or editorial articles.

Reason 5: Repetitive or low-quality.

## 5. BASIC STUDY CHARACTERISTICS

**Supplementary Table S1.** Study characteristics of the included studies

Study	Country	Publication Year	Study Year	Research Object	Data Source	Methods	Outcome	Pollutants	Exposure Window	Exposure Assessment
Barclay, J. L., et al.	Scotland	2009	2003–2005	132 non-smoking patients with stable chronic heart failure	Participants recruited from hospitals in Aberdeen, Scotland	Repeated-measures panel study	arrhythmias, HRV, and RBC, WBC, Fibrinogen, IL-6, hs-CRP, etc.	PM <sub>10</sub> , PM <sub>2.5</sub> , NO <sub>2</sub> , NO <sub>x</sub>	Up to 2-day cumulative exposure	A combination of fixed-site/urban areas, daily background pollution measurements, and estimates or measurements of personal exposure is needed.

Wellenius, G. A., et al.	United States	2007	2002–2003	28 patients with chronic stable heart failure and impaired systolic function	Outpatient heart failure clinics at the hospital in Boston	Repeated-measures study design; Linear mixed models	BNP levels	PM <sub>2.5</sub> , CO, SO <sub>2</sub> , NO <sub>2</sub> , O <sub>3</sub> , Black carbon	Short-term (0 – 3 days)	Monitoring stations
Vieira, J. L., et al.	Brazil	2016	2013–2015	26 heart failure patients and 15 healthy controls	Randomized, prospective, double-blind controlled trial	Randomized, controlled trial	BNP, reactive hyperemia index (RHi)	Diesel exhaust, PM <sub>2.5</sub>	Short-term, measured across sessions	Controlled exposure
Allaouat, S., et al.	Finland	2024	1997–2012	Finnish residents aged 25 – 74 (42% – 45.3% with cardiovascular disease)	FINRISK study	Cross-sectional analyses with linear and additive models	NT-proBNP, CRP, Troponin I	PM <sub>2.5</sub> , NO <sub>2</sub> , Road-traffic noise	Long-term exposure calculated using 3-year average concentrations	PM <sub>2.5</sub> : Urban Dispersion Model; NO <sub>2</sub> : road network emission and dispersion model;

Noise:  
Nordic  
Prediction  
Method.

Zhang, S. Q., et al.	United States (Duke Hospital)	2021	2001–2012	cardiac catheterized or post-MI patients (pre-heart failure)	CATHGEN cohort	Generalized estimating equations	Troponin T, NT-proBNP, CRP, Fibrinogen, WBC	PM <sub>2.5</sub>	Single-day exposure at 0 – 4 lag days and cumulative exposure of 0 – 4 days	Hybrid exposure prediction model
Brüske et al.	Germany	2011	2003–2004	200 post-MI survivors aged 35 – 80 years, residents within 10 km of a monitoring site	AIRGENE study (Augsburg region)	Prospective longitudinal study with repeated clinical examination s; mixed-effect s models with random	Plasma Lp-PLA2 levels	PM <sub>10</sub> , PM <sub>2.5</sub> , CO, NO, NO <sub>2</sub> , SO <sub>2</sub> , O <sub>3</sub>	Non-cumula tive exposure/ single air pollution lags for Lag 0 to Lag 5 days	Monitoring stations

patient  
effects

Wang, Q., et al.	Europe	2023	2021–2023	European populations from the UK Biobank, comprising 423,796 participants	GWAS data from the UK Biobank	Mendelian randomization	cardiovascular biomarkers (TG, HDL-C, LDL-C, Fasting insulin, Fasting glucose); heart failure and myocardial infarction events, etc.	PM <sub>2.5</sub> , PM <sub>10</sub>	long-term exposure	Two-sample MR analysis using SNPs to determine causal links
Rückerl, R., et al.	Europe (6 cities)	2007	2003–2004	1,003 myocardial infarction survivors	Prospective longitudinal study across six	Mixed-effects models	Interleukin-6, C-Reactive Protein, Fibrinogen	PM <sub>2.5</sub> , PM <sub>10</sub>	Lag 0 – 4 days, cumulative exposure for	Hourly data from fixed monitoring sites

					European cities			PM <sub>10</sub> (5 days)		
Zhang, Z., et al.	China	2020	2018–2020	H9c2 rat myocardial cells	rat myocardial H9c2 cells	Myocardial cell culture exposure experiments	ATP, CPT1/CPT2, MDH, Lactate, Pyruvate, PPAR $\alpha$ , etc.	PM <sub>2.5</sub>	Dose-dependent exposure for 24 hours	Controlled exposure to varying concentrations of PM <sub>2.5</sub>
Wu, F., et al.	China	2018	2017	C57BL/6J mice heart	C57BL/6J mice (Zhengzhou University)	Controlled PM <sub>2.5</sub> exposure	MDA, SOD, iNOS, TNF- $\alpha$ , IL-1 $\beta$ , NOX4, p53, BAX, BCL-2, Caspase-3	PM <sub>2.5</sub>	Acute exposure	PM <sub>2.5</sub> installation in mice
Wang, H., et al.	China	2018	2016	Wild-type and AMPK $\alpha$ 2-deficient mice	Experimental study using multiple rat models	Controlled mouse model study	TNF- $\alpha$ , IL-6, AMPK activity	PM <sub>2.5</sub>	Long-term (6 months)	monitoring station

Ramot, Y., et al.	Israel	2015	2014–2015	Male rats (hypertensive, heart failure, obese, diabetic, etc.)	Experimental study using multiple CVD rat models	Controlled ozone exposure	clinical biomarkers (TC, LDL, HDL, TG, RBC, WBC, lymphocytes, fibrinogen, etc.), and lung, heart, and kidney pathologies	O <sub>3</sub>	Acute exposure with 0 h, 20 h post-assessment	Controlled nose-only exposure to varying concentrations of ozone (0, 0.25, 0.5, or 1.0 ppm) for 4 hours
Wold et al.	United States	2012	2003–2012	Adult male mice (C57BL/6 strain)	C57BL/6 mice (Ohio State University, Columbus, OH)	Controlled PM <sub>2.5</sub> exposure	Cardiac function and markers, including ANP, $\alpha$ -tubulin, TGF- $\beta$ , collagen I, collagen, SERCA2a, MHC expression	PM <sub>2.5</sub>	Cumulative exposure over 9 months	Controlled exposure to varying concentrations of PM <sub>2.5</sub>

Wang, Z., et al.	China	2018	2018	Male SD rats	Experimental exposure of rats <i>via</i> tracheal instillation	Controlled PM <sub>2.5</sub> exposure	CK, CK-MB, IL-6, CRP, IL-10, MDA, SOD	PM <sub>2.5</sub>	Short-term dose-dependent exposure for 5 days	PM <sub>2.5</sub> instillation in rat
Xue, B., et al.	China	2020	2018	Rat myocardial H9c2 cells	<i>in vitro</i> exposure to extracted PM <sub>2.5</sub> components	Controlled PM <sub>2.5</sub> exposure	TNF- $\alpha$ and IL-1 $\beta$	PM <sub>2.5</sub>	Short-term exposure (24 h, 48 h)	Controlled exposure to different components of PM <sub>2.5</sub>

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**Note.** PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter  $\leq 2.5 \mu\text{m}$ ; PM<sub>10</sub>, particulate matter with an aerodynamic diameter  $\leq 10 \mu\text{m}$ ; NO<sub>2</sub>, nitrogen dioxide; SO<sub>2</sub>, sulfur dioxide; CO, carbon monoxide; O<sub>3</sub>, ozone; NO<sub>x</sub>, nitrogen oxides; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; sST2, soluble growth stimulation expressed gene 2; HRV, heart rate variability; RBC, red blood cells; WBC, white blood cells; CRP, C-reactive protein; hs-CRP, high-sensitivity C-reactive protein; CK, creatine kinase; CK-MB, creatine kinase-MB isoenzyme; CVD, cardiovascular disease; IL-6, interleukin-6; IL-1 $\beta$ , interleukin-1 beta; Lp-PLA<sub>2</sub>, lipoprotein-associated phospholipase A<sub>2</sub>; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; GWAS, genome-wide association study; SNP, single-nucleotide polymorphism; ATP, adenosine triphosphate; CPT1/CPT2, carnitine palmitoyltransferase 1/2; MDH, malate dehydrogenase; PPAR $\alpha$ , peroxisome proliferator-activated receptor alpha; RHI, reactive hyperemia index; AMPK, adenosine monophosphate-activated protein kinase; MDA, malondialdehyde; SOD, superoxide dismutase; iNOS, inducible nitric oxide synthase; TNF- $\alpha$ , tumor necrosis factor alpha; NOX4, nicotinamide adenine dinucleotide phosphate oxidase 4; p53, tumor protein p53; BAX, Bcl-2-associated X protein; BCL-2, B-cell lymphoma 2; Caspase-3, cysteine-aspartic protease 3; ANP, atrial natriuretic peptide; SERCA2a, sarcoplasmic reticulum Ca<sup>2+</sup> ATPase 2a; TGF- $\beta$ , transforming growth factor beta; MHC, myosin heavy chain



Rückerl, R., et al.	Moderate	Potential exposure misclassification				Potential exposure misclassification weakens the link between exposure and outcome.	Low
Zhang, Z., et al.	High		Cell models yield mechanistic data but lack systemic relevance and clinical extrapolatability.				Low
Wu, F., et al.	High	There is a problem of blindness	Not a heart failure-related animal model				Moderate
Wang, H., et al.	High	Problems with randomization and blinding		Small sample size			Low
Ramot, Y., et al.	High	Problems with randomization, blinding, and selection bias		Small sample size			Low
Wold et al.	High	Problems with randomization, blinding, and selection bias	Not a heart failure-related animal model	Small sample size			Low
Wang, Z., et al.	High	There is a problem of blindness	Not a heart failure-related animal model	Small sample size		Dose-dependent damage observed	
Xue, B., et al.	High	There is a problem of blindness	Cell models yield mechanistic data but lack systemic relevance and clinical extrapolatability.				

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## 7. LIST OF EXCLUDED STUDIES

***Reason 1: Heart failure or at least pre-heart failure was not included as a variable.***

***(N = 21)***

1. Balmes, J. R., et al. (2019). "Ozone effects on blood biomarkers of systemic inflammation, oxidative stress, endothelial function, and thrombosis: The Multicenter Ozone Study in older Subjects (MOSES)." *PLoS One* 14(9).
2. Brugge, D., et al. (2021). "A randomized crossover trial of HEPA air filtration to reduce cardiovascular risk for near highway residents: Methods and approach." *Contemp Clin Trials* 108: 106520.
3. de Oliveira-Fonoff, A. M., et al. (2017). "The role of air pollution in myocardial remodeling." *PLoS One* 12(4).
4. Graff, D. W., et al. (2009). "Exposure to concentrated coarse air pollution particles causes mild cardiopulmonary effects in healthy young adults." *Environmental Health Perspectives* 117(7): 1089-1094.
5. Kristovich, R., et al. (2004). "Macrophage-mediated endothelial inflammatory responses to airborne particulates: Impact of particulate physicochemical properties." *Chemical Research in Toxicology* 17(10): 1303-1312.
6. Li, H. Y., et al. (2011). "Oxidative stress, endothelial dysfunction and inflammatory response in rat heart to NO<sub>2</sub> inhalation exposure." *Chemosphere* 82(11): 1589-1596.
7. Liao, D. P., et al. (1999). "Daily variation of particulate air pollution and poor cardiac autonomic control in the elderly." *Environmental Health Perspectives*

107(7): 521-525.

8. Liu, X. M., et al. (2018). "Particulate Matter Triggers Depressive-Like Response Associated With Modulation of Inflammatory Cytokine Homeostasis and Brain-Derived Neurotrophic Factor Signaling Pathway in Mice." *Toxicological Sciences* 164(1): 278-288.
9. Macchi, C., et al. (2023). "Pollution from fine particulate matter and atherosclerosis: A narrative review." *Environment International* 175.
10. Muñoz Jimenez, L. D., et al. (2010). "Elevated troponin levels predictive role in coronary revascularization surgery postoperative management." *Intensive Care Medicine* 36: S266.
11. Muñoz-Rodríguez, A., et al. (2021). "Prenatal Particulate Matter (PM) Exposure and Natriuretic Peptides in Newborns from Mexico City." *International Journal of Environmental Research and Public Health* 18(12).
12. Pope, C. A., et al. (2004). "Ambient particulate air pollution, heart rate variability, and blood markers of inflammation in a panel of elderly subjects." *Environmental Health Perspectives* 112(3): 339-345.
13. Rehman, A., et al. (2023). "Cell-free circulating mitochondrial DNA: An emerging biomarker for airborne particulate matter associated with cardiovascular diseases." *Free Radical Biology and Medicine* 195: 103-120.
14. Rich, D. Q., et al. (2018). "Cardiovascular function and ozone exposure: The Multicenter Ozone Study in oldEr Subjects (MOSES)." *Environment International* 119: 193-202.

15. Sivakumar, B. and G. A. Kurian (2023). "PM<sub>2.5</sub> from diesel exhaust attenuated fisetin mediated cytoprotection in H9c2 cardiomyocytes subjected to ischemia reoxygenation by inducing mitotoxicity." *Drug Chem Toxicol* 46(1): 15-23.
16. Villarreal-Calderon, R., et al. (2013). "Up-Regulation of mRNA Ventricular PRNP Prion Protein Gene Expression in Air Pollution Highly Exposed Young Urbanites: Endoplasmic Reticulum Stress, Glucose Regulated Protein 78, and Nanosized Particles." *International Journal of Molecular Sciences* 14(12): 23471-23491.
17. Villarreal-Calderon, R., et al. (2012). "Urban air pollution produces up-regulation of myocardial inflammatory genes and dark chocolate provides cardioprotection." *Experimental and Toxicologic Pathology* 64(4): 297-306.
18. Xing, Q. S., et al. (2021). "Comparative studies on regional variations in PM<sub>2.5</sub> in the induction of myocardial hypertrophy in mice." *Science of the Total Environment* 775.
19. Yang, W. Y., et al. (2017). "Left ventricular function in relation to chronic residential air pollution in a general population." *European Journal of Preventive Cardiology* 24(13): 1416-1428.
20. Yuan, S. M. (2017). "Sudden cardiac death in the young: Cytokines and pathways." *Periodicum Biologorum* 119(1): 17-25.
21. Pan, X.X., et al., Urban Particulate Matter Induces Changes in Gene Expression in Vascular Endothelial Cells that Are Associated with Altered Clot Structure In Vitro. *Thrombosis and Haemostasis*, 2018. 118(2): p. 266-278.

***Reason 2: Biomarkers were not included as a variable. (N = 18)***

1. Aung, N., et al. (2018). "Association Between Ambient Air Pollution and Cardiac Morpho-Functional Phenotypes: Insights From the UK Biobank Population Imaging Study." *Circulation* 138(20): 2175-2186.
2. Carll, A. P., et al. (2012). "Whole and particle-free diesel exhausts differentially affect cardiac electrophysiology, blood pressure, and autonomic balance in heart failure-prone rats." *Toxicol Sci* 128(2): 490-499.
3. Gerber, Y., et al. (2010). "Cumulative exposure to air pollution and long term outcomes after first acute myocardial infarction: A population-based cohort study. Objectives and methodology." *Bmc Public Health* 10.
4. Goldberg, M. S., et al. (2003). "Associations between ambient air pollution and daily mortality among persons with congestive heart failure." *Environmental Research* 91(1): 8-20.
5. Guo, Y. M., et al. (2009). "The association between fine particulate air pollution and hospital emergency room visits for cardiovascular diseases in Beijing, China." *Science of the Total Environment* 407(17): 4826-4830.
6. Koton, S., et al. (2013). "Cumulative exposure to particulate matter air pollution and long-term post-myocardial infarction outcomes." *Preventive Medicine* 57(4): 339-344.
7. Leary, P. J., et al. (2014). "Traffic-related Air Pollution and the Right Ventricle The Multi-ethnic Study of Atherosclerosis." *American Journal of Respiratory and Critical Care Medicine* 189(9): 1093-1100.

8. Sinkovic, A., et al. (2021). "The role of environmental PM<sub>2.5</sub> in admission acute heart failure in st-elevation myocardial infarction patients-an observational retrospective study." *International Journal of General Medicine* 14: 8473-8479.
9. Steinvil, A., et al. (2013). "Environmental exposure to combustion-derived air pollution is associated with reduced functional capacity in apparently healthy individuals." *Clinical Research in Cardiology* 102(8): 583-591.
10. Tankersley, C. G., et al. (2013). "Effects of Ozone and Particulate Matter on Cardiac Mechanics: Role of the Atrial Natriuretic Peptide Gene." *Toxicological Sciences* 131(1): 95-107.
11. Wang, T., et al. (2012). "Particulate Matter Induces Cardiac Arrhythmias via Dysregulation of Carotid Body Sensitivity and Cardiac Sodium Channels." *American Journal of Respiratory Cell and Molecular Biology* 46(4): 524-531.
12. Zanobetti, A., et al. (2009). "Fine particulate air pollution and its components in association with cause-specific emergency admissions." *Environmental Health* 8.
13. Zhang, L., et al., Long-term effects of air quality on hospital readmission for heart failure in patients with acute myocardial infarction. *International Journal of Cardiology*, 2024. 412.
14. Donzelli, G., et al., A systematic review and meta-analysis of human population studies on the association between exposure to toxic environmental chemicals and left ventricular dysfunction (LVD). *Environ Res*, 2024. 249: p. 118429.
15. Yu, Y., et al., Adverse outcome pathway of fine particulate matter leading to increased cardiovascular morbidity and mortality: An integrated perspective

from toxicology and epidemiology. *Journal of Hazardous Materials*, 2022. 430.

16. Murray, C.J.L., et al., Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*, 2020. 396(10258): p. 1223-1249.
17. Bates, J.T., et al., Reactive Oxygen Species Generation Linked to Sources of Atmospheric Particulate Matter and Cardiorespiratory Effects. *Environmental Science & Technology*, 2015. 49(22): p. 13605-13612.
18. Forastiere, F. and N. Agabiti, Assessing the link between air pollution and heart failure. *The Lancet*, 2013. 382(9897): p. 1008-1010.

***Reason 3: Air pollutant of interest was not measured. (N=18)***

1. Buyuklu, M., et al. (2017). "Beneficial Effects of Ozone Therapy on Oxidative Stress, Cardiac Functions and Clinical Findings in Patients with Heart Failure Reduced Ejection Fraction." *Cardiovascular Toxicology* 17(4): 426-433.
2. Cerkauskaite, S., et al. (2024). "Association between greenery and health indicators in urban patients with symptomatic heart failure: a retrospective cohort study in Lithuania." *International Journal of Environmental Health Research* 34(7): 2801-2812.
3. Chien, P. T. Y., et al. (2015). "Induction of HO-1 by carbon monoxide releasing molecule-2 attenuates thrombin-induced COX-2 expression and hypertrophy in primary human cardiomyocytes." *Toxicology and Applied Pharmacology* 289(2): 349-359.
4. El-Sawalhi, M. M., et al. (2013). "Modulation of age-related changes in oxidative

stress markers and energy status in the rat heart and hippocampus: a significant role for ozone therapy." *Cell Biochemistry and Function* 31(6): 518-525.

5. Gandini, C., et al. (2001). "Carbon monoxide cardiotoxicity." *Journal of Toxicology-Clinical Toxicology* 39(1): 35-44.
6. Jin, Y. F., et al. (2016). "Association of EGF Receptor and NLRs signaling with Cardiac Inflammation and Fibrosis in Mice Exposed to Fine Particulate Matter." *Journal of Biochemical and Molecular Toxicology* 30(9): 429-437.
7. Kim, H. H. and S. Choi (2018). "Therapeutic aspects of carbon monoxide in cardiovascular disease." *International Journal of Molecular Sciences* 19(8).
8. Lu, L., et al. (2015). "The Inflammatory Heart Diseases: Causes, Symptoms, and Treatments." *Cell Biochemistry and Biophysics* 72(3): 851-855.
9. Ndisang, J. F., et al. (2014). "Oxidative stress and inflammation in obesity, diabetes, hypertension, and related cardiometabolic complications." *Oxidative Medicine and Cellular Longevity* 2014.
10. Pandolfi, S., et al. (2024). "Insights into the use of oxygen-ozone therapy in ischemic cardiopathy and cardiovascular disease: a role for mitochondria?" *Medical Gas Research* 14(4): 164-166.
11. Payne, F. M., et al. (2024). "The carbon monoxide prodrug oCOm-21 increases Ca<sup>2+</sup> sensitivity of the cardiac myofilament." *Physiological Reports* 12(6).
12. Saucy, A., et al. (2021). "The role of extreme temperature in cause-specific acute cardiovascular mortality in Switzerland: A case-crossover study." *Science of the Total Environment* 790.

13. Taghdiri, A. (2024). "Cardiovascular biomarkers: exploring troponin and BNP applications in conditions related to carbon monoxide exposure." *Egyptian Heart Journal* 76(1).
14. Vanderpool, R. R., et al. (2018). "Association Between Hemodynamic Markers of Pulmonary Hypertension and Outcomes in Heart Failure With Preserved Ejection Fraction." *JAMA Cardiol* 3(4): 298-306.
15. Wang, Q. S., et al. (2017). "Carbon Monoxide-Saturated Hemoglobin-Based Oxygen Carriers Attenuate High-Altitude-Induced Cardiac Injury by Amelioration of the Inflammation Response and Mitochondrial Oxidative Damage." *Cardiology* 136(3): 180-191.
16. Wilker, E. H., et al. (2012). "Ambient Temperature and Biomarkers of Heart Failure: A Repeated Measures Analysis." *Environmental Health Perspectives* 120(8): 1083-1087.
17. Xie, X., et al. (2024). "Inflammation Links Cardiac Injury and Renal Dysfunction: A Cardiovascular Magnetic Resonance Study." *Reviews in Cardiovascular Medicine* 25(4).
18. Liu, X., et al. (2023). "Improvement effect of SO<sub>2</sub> on myocardial fibrosis after acute myocardial ischemic injury in rats and its mechanism." *Journal of Jilin University (Medicine Edition)*, 49(5): 1125–1133. (in Chinese)

***Reason 4: Review or editorial articles. (N=8)***

1. Roth, G. A., et al. (2018). "Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a

systematic analysis for the Global Burden of Disease Study 2017." *Lancet* 392(10159): 1736-1788.

2. Routledge, H. C. and J. G. Ayres (2005). "Air pollution and the heart." *Occupational Medicine-Oxford* 55(6): 439-447.
3. Stanaway, J. D., et al. (2018). "Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017." *Lancet* 392(10159): 1923-1994.
4. Visseren, F. L. J., et al. (2022). "2021 ESC Guidelines on cardiovascular disease prevention in clinical practice." *European Journal of Preventive Cardiology* 29(1): 5-115.
5. Scapellato, M.L. and M. Lotti, Short-term effects of particulate matter: An inflammatory mechanism? *Critical Reviews in Toxicology*, 2007. 37(6): p. 461-487.
6. 8. Ji, X., et al., Potential role of inflammation in associations between particulate matter and heart failure. *Current Pharmaceutical Design*, 2018. 24(3): p. 341-358.
7. Jia, Y., et al., Effect of Air Pollution on Heart Failure: Systematic Review and Meta-Analysis. *Environmental Health Perspectives*, 2023. 131(7).
8. Goodman, J.E., et al., Weight-of-evidence evaluation of short-term ozone exposure and cardiovascular effects. *Critical Reviews in Toxicology*, 2014. 44(9): p.

725-790.

***Reason 5: Repetitive. (N=3)***

1. Kodavanti, U. P., et al. (2015). "Variability in ozone-induced pulmonary injury and inflammation in healthy and cardiovascular-compromised rat models." *Inhal Toxicol* 27 Suppl 1: 39-53.
2. Soeiro, A., et al. (2015). "Intermediate levels of BNP were related with cardiogenic shock in acute coronary syndromes." *European Heart Journal: Acute Cardiovascular Care* 4: 164.
3. Franchini, M. and P.M. Mannucci, Short-term effects of air pollution on cardiovascular diseases: Outcomes and mechanisms. *Journal of Thrombosis and Haemostasis*, 2007. 5(11): p. 2169-2174.

***List of included studies. (N = 15)***

1. Allaouat, S., et al., Long-term exposures to low concentrations of source-specific air pollution, road-traffic noise, and systemic inflammation and cardiovascular disease biomarkers. *Environmental Research*, 2024. 262.
2. Wang, Q., et al., Causality of particulate matter on cardiovascular diseases and cardiovascular biomarkers. *Front Public Health*, 2023. 11: p. 1201479.
3. Zhang, S.Q., et al., association between short-term exposure to ambient fine particulate matter and myocardial injury in the CATHGEN cohort. *Environmental Pollution*, 2021. 275.

4. Zhang, Z., et al., Critical biomarkers for myocardial damage by fine particulate matter: Focused on PPAR $\alpha$ -regulated energy metabolism. *Environmental Pollution*, 2020. 264: p. 114659.
5. Wu, F. and J.Y. Zhang, The involvement of Nox4 in fine particulate matter exposure-induced cardiac injury in mice. *Journal of Toxicological Sciences*, 2018. 43(1-3): p. 171-181.
6. Wang, H., et al., AMPK $\alpha$ 2 deficiency exacerbates long-term PM<sub>2.5</sub> exposure-induced lung injury and cardiac dysfunction. *Free Radic Biol Med*, 2018. 121: p. 202-214.
7. Vieira, J.L., et al., Respiratory Filter Reduces the Cardiovascular Effects Associated With Diesel Exhaust Exposure: A Randomized, Prospective, Double-Blind, Controlled Study of Heart Failure: The FILTER-HF Trial. *JACC Heart Fail*, 2016. 4(1): p. 55-64.
8. Ramot, Y., et al., Clinical and pathological manifestations of cardiovascular disease in rat models: the influence of acute ozone exposure. *Inhalation Toxicology*, 2015. 27: p. 26-38.
9. Barclay, J.L., et al., A panel study of air pollution in subjects with heart failure: negative results in treated patients. *Occupational and Environmental Medicine*, 2009. 66(5): p. 325-334.
10. Wellenius, G.A., et al., Effects of ambient air pollution on functional status in patients with chronic congestive heart failure: a repeated-measures study. *Environmental Health*, 2007. 6.

11. R ckerl, R., et al., Air pollution and inflammation (interleukin-6,C-reactive protein, fibrinogen) in myocardial infarction survivors. *Environmental Health Perspectives*, 2007. 115(7): p. 1072-1080.
12. Bruske, I., et al., Ambient air pollution and lipoprotein-associated phospholipase A(2) in survivors of myocardial infarction. *Environmental Health Perspectives*, 2011. 119(7): p. 921-6.
13. Wold, L.E., et al., Cardiovascular Remodeling in Response to Long-Term Exposure to Fine Particulate Matter Air Pollution. *Circulation-Heart Failure*, 2012. 5(4): p. 452-461.
14. Wang, Z., et al., Acute injury and mechanisms of cardiovascular system induced by exposure to fine particulate matter in rats[J]. *Journal of Environmental Health*, 2018, 35(11): 962–965. (in Chinese).
15. Xue, B., et al., The main toxic components of fine particulate matters on cardiocytes: Focused on the cell viability and inflammatory response[J]. *Acta Scientiae Circumstantiae*, 2020, 40(1): 306–314. (in Chinese)