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ORIGINAL RESEARCH

OUTCOMES AND QUALITY

Air Pollution and Adverse Cardiovascular Events After Coronary Artery Bypass Grafting

A 10-Year Nationwide Study

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ABSTRACT

BACKGROUND Increased particulate matter <2.5 μm ($PM_{2.5}$) air pollution is associated with adverse cardiovascular outcomes. However, its impact on patients with prior coronary artery bypass grafting (CABG) is unknown.

OBJECTIVES The purpose of this study was to evaluate the association between major adverse cardiovascular events (MACE) (defined as myocardial infarction, stroke, or cardiovascular death) and air pollution after CABG.

METHODS We linked 26,403 U.S. veterans who underwent CABG (2010-2019) nationally with average annual ambient $PM_{2.5}$ estimates using residential address. Over a 5-year median follow-up period, we identified MACE and fit a multivariable Cox proportional hazard model to determine the risk of MACE as per $PM_{2.5}$ exposure. We also estimated the absolute potential reduction in $PM_{2.5}$ attributable MACE simulating a hypothetical $PM_{2.5}$ lowered to the revised World Health Organization standard of 5 $\mu g/m^3$.

RESULTS The observed median $PM_{2.5}$ exposure was 7.9 $\mu g/m^3$ (IQR: 7.0-8.9 $\mu g/m^3$; 95% of patients were exposed to $PM_{2.5}$ above 5 $\mu g/m^3$). Increased $PM_{2.5}$ exposure was associated with a higher 10-year MACE rate (first tertile 38% vs third tertile 45%; $P < 0.001$). Adjusting for demographic, racial, and clinical characteristics, a 10 $\mu g/m^3$ increase in $PM_{2.5}$ resulted in 27% relative risk for MACE (HR: 1.27, 95% CI: 1.10-1.46; $P < 0.001$). Currently, 10% of total MACE is attributable to $PM_{2.5}$ exposure. Reducing maximum $PM_{2.5}$ to 5 $\mu g/m^3$ could result in a 7% absolute reduction in 10-year MACE rates.

CONCLUSIONS In this large nationwide CABG cohort, ambient $PM_{2.5}$ air pollution was strongly associated with adverse 10-year cardiovascular outcomes. Reducing levels to World Health Organization-recommended standards would result in a substantial risk reduction at the population level. (JACC Adv 2024;3:100781) Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

MACE = major adverse cardiovascular event

$PM_{2.5}$ = particulate matter <2.5 μm

SDI = Social deprivation index

VA = Department of Veterans Affairs

VA-PROM = VA projected risk of mortality

VASQIP = VA Surgical Quality Initiative Project

WHO = World Health Organization

Environmental exposures contribute to over 9 million deaths annually with >50% of these events directly related to atherosclerotic cardiovascular disease.[1] Air pollution contributes to the vast preponderance of deaths attributable to environmental exposures. While empirical evidence strongly implicates a gradation of risk with those with underlying risk factors most at risk, the evidence to implicate those at the highest risk, namely individuals with established coronary artery disease (CAD) who have previously also undergone revascularization, is to date lacking.[1,2] With more than 400,000 procedures every year, coronary artery bypass grafting (CABG) is among the most commonly performed adult surgical procedures in the United States.[2] Patients receiving CABG often have complex multivessel CAD and remain at risk of suffering from recurrent major adverse cardiovascular events (MACE) like myocardial infarction (MI), stroke, and cardiovascular mortality.[3-5] While much of this recurrent risk can be reduced by optimal medical therapy and lifestyle/behavioral improvements, some patients continue to have a high residual risk for suffering such adverse events. Traditionally, the construct to think about residual risk has been overwhelmingly in terms of conventional risk factors, but the role of other factors in the environment that may continually amplify and contribute to residual risk has not been systematically considered. In this context, the incremental contribution of air pollution, particularly fine particulate matter ($PM_{2.5}$) exposure, to patients who have undergone CABG with careful consideration of the concomitant comorbidities that many of these individuals suffer from is of particular interest.[6,7] Mechanistically, animal model studies report that air pollution exposure can lead to immune activation, thrombosis, disruption in lipid metabolism, and consequently atherosclerosis, all factors that continue to play a role in the post-CABG patient.[7] This laboratory research has been supported by cohort studies that have reported a strong correlation between increased $PM_{2.5}$ exposure and higher rates of hypertension, stroke, and ischemic heart disease.[6-9] In an earlier nationwide analysis of patients receiving percutaneous coronary intervention, we reported that patients exposed to higher $PM_{2.5}$ levels had higher mortality rates and reduced life expectancy after their procedure.[10] However, in spite of post-CABG patients being at high risk for adverse cardiovascular events, the impact of $PM_{2.5}$ exposure has not been examined in this cohort. Hence, to resolve this question, we analyzed data from a large nationwide cohort of CABG patients.

METHODS

The VA Surgical Quality Initiative Project (VASQIP), our primary data registry, is managed by the National Surgery Office of the Veterans Affairs Administration. This contains rigorously defined, nurse-adjudicated information on the preoperative, intraoperative, and postoperative periods for all patients receiving cardiac surgery at VA medical centers. The VASQIP data was supplemented with information from the corporate data warehouse, which contains data regarding their nonindex in- and out-patient visits, biochemical test results, and echocardiographic data. For this study, we identified US veterans that underwent isolated CABG (excluding patients that received concomitant valve procedures, ascending aorta replacement, or maze procedures) nationwide from 2010 through 2019.

The main exposure of interest in our study was the annual $PM_{2.5}$ particulate air pollution estimated at the zip code level. Validated $PM_{2.5}$ exposure estimates developed by the Atmospheric Composition Analysis Group were utilized.[11,12] These hybrid estimates combine information from satellite remote sensing, chemical transport modeling, and calibration with ground-based observations to generate concentration estimates. Data are provided in 1 × 1 km grids throughout North America. Raster files were imported to an open-source geographical information system software, QGIS v. 3.16 (Open-Source Geospatial Foundation), and mapped to the 2018 zip code boundaries from the U.S. Census Bureau. The mean zip $PM_{2.5}$ exposure for each zip code was calculated as a simple average over the study period using zonal statistics in QGIS and this was assigned as the $PM_{2.5}$ exposure for each patient.

We obtained demographic, clinical, laboratory, and pharmacy data prior to their procedure for patients

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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from the VASQIP tables; when this information was not directly available in VASQIP, we obtained it from the preoperative outpatient visit (closest to the surgery date) using the International Classification of Disease-9th and-10th editions or Common Procedure Terminology codes. Demographics included age at CABG, sex, and self-reported race and ethnicity. Clinical factors obtained were hypertension, diabetes mellitus, dyslipidemia, obesity (body mass index ≥30 kg/m^2), heart failure, chronic kidney disease (estimated glomerular filtration rate <60 mL/min/m^2), smoking status, and prior MI. We obtained information regarding whether patients had acute coronary syndrome prior to surgery and the urgency of surgery (elective, urgent [performed within the same hospital admission], or emergent [performed within 48 hours of hospital admission]). We additionally also adjusted for area-level socioeconomic variables. The social deprivation index (SDI) is a validated composite metric derived at the level of the zip code tabulation areas to evaluate the socioeconomic condition of that geographical area. The summary SDI score is created based on the following criteria: household income, house ownership, education level, vehicular access, and family composition.[13] The score ranges between 0 and 100, with higher numbers indicative of higher deprivation (lower socioeconomic position).

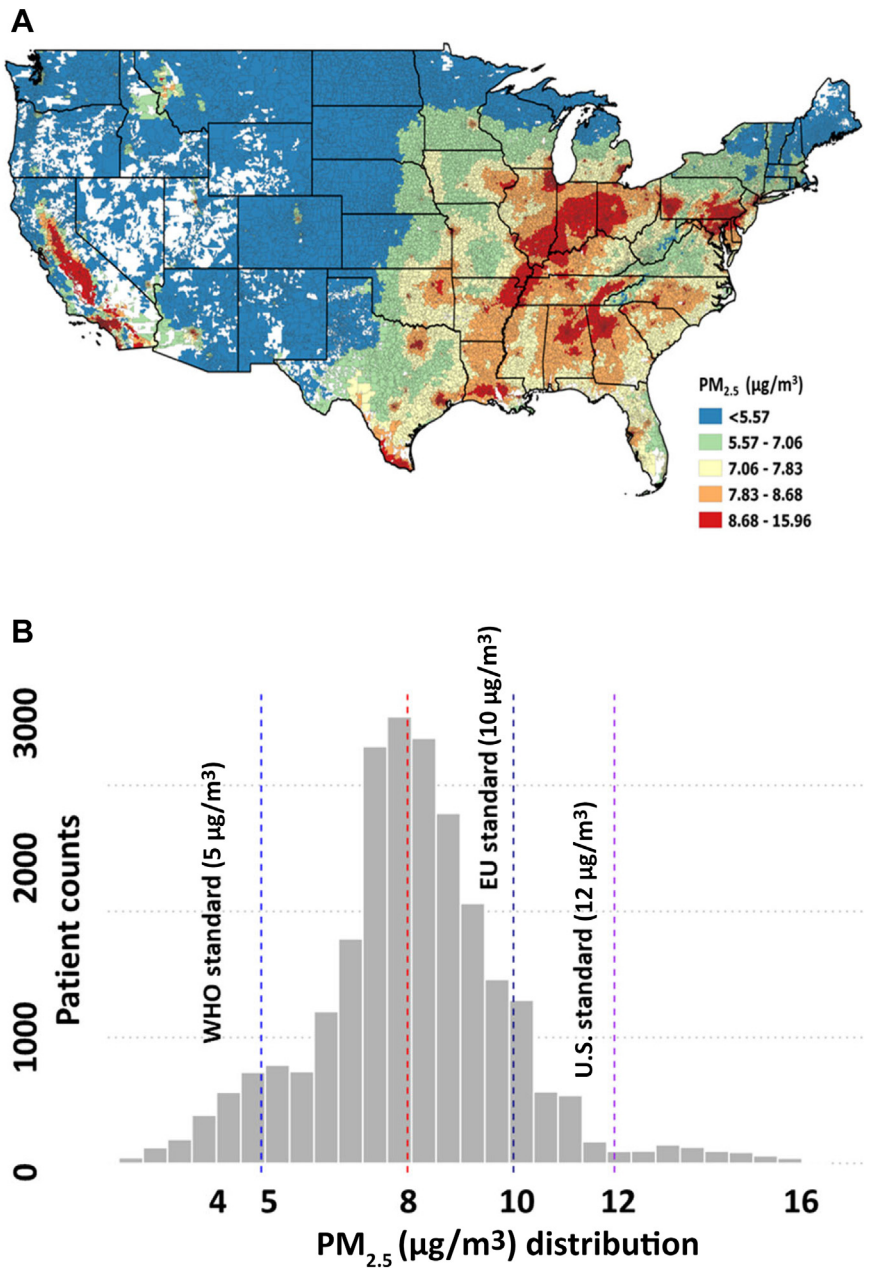
We studied MACE as our primary endpoint. MACE is a composite of cardiovascular mortality and the first instance of nonfatal MI or nonfatal stroke. Nonfatal MI or nonfatal stroke were defined as being admitted to a VA medical center with these conditions as the primary diagnosis. We obtained the dates for these events and calculated the time-to-event as the duration between the surgery date and the event date.

STATISTICAL ANALYSIS. We reported continuous data and categorical data as mean ± SD and count (percentage), respectively. We calculated the cumulative incidence of MACE over the study period for the whole cohort and separately for each tertile of $PM_{2.5}$. We then compared the MACE incidence for the $PM_{2.5}$ tertiles by pairwise log-rank tests with the Hochberg correction for multiplicity.[14] To study the association between MACE and $PM_{2.5}$, we used $PM_{2.5}$ as a continuous variable and fit incrementally more complex. Cox proportional hazard models as follows: model 1-unadjusted- only $PM_{2.5}$; model 2-model 1+ age at surgery, sex, race, ethnicity, and social deprivation; model 3-model 2+ preoperative prevalence of diabetes, chronic kidney disease, heart failure, prior MI, prior stroke, left ventricular systolic ejection fraction, urgency of surgery, presence of triple vessel disease, use of multiarterial grafting, need for an intra-aortic balloon pump in the perioperative period, smoking status, chronic obstructive pulmonary disease, and baseline discharge medications. In our initial models, we explored whether using an interaction term between $PM_{2.5}$ and race, a spline term for $PM_{2.5,}$ or an interaction between $PM_{2.5}$ and social deprivation would provide any additional benefit in our explanatory regression model. However, comparing these nested models using the analysis of variance method, we dropped these terms from our final model as they did not significantly improve the model fit at the 95% confidence level. As prior studies have modeled annual $PM_{2.5}$ values using a time-varying approach, we performed a sensitivity analysis to confirm our primary findings using this approach. Using the date of surgery and date of death or censoring, we identified the calendar years that each patient was exposed to and provided each patient with the corresponding annual $PM_{2.5}$ according to their zip code. We then fitted a frailty-type Cox proportional hazards model using this time-varying $PM_{2.5}$ as our primary exposure and included all the variables reported for model 3 as covariates. We further performed subgroup analyses on our primary model according to sex, race, ethnicity, pre-existing diabetes, chronic kidney disease, and heart failure. As we were interested in evaluating the potential benefit of lowering $PM_{2.5}$ to the new Environmental Protection Agency recommendations ($PM_{2.5}$ limit: 8 μg/m^3), we grouped patients into 2 groups ($PM_{2.5}$ <8 μg/m^3 and $PM_{2.5}$ >8 μg/m^3). We then reported the relative risk for MACE in those exposed to $PM_{2.5}$ >8 μg/m^3 using a multivariable Cox proportional hazards model (using variables included in model 3 reported above).

To understand the extent to which $PM_{2.5}$ contributes to the occurrence of MACE, using the adjusted model (M3), we calculated the attributable fraction for $PM_{2.5}$ over the 10-year study period. We then evaluated the potential reduction in MACE that may occur if $PM_{2.5}$ exposure were to be limited to the new Environmental Protection Agency recommendations ($PM_{2.5}$ limit: 8 μg/m^3) or the World Health Organization (WHO) 2021 standard ($PM_{2.5}$ limit: 5 μg/m^3). We calculated CIs for these estimates using bootstrapping approaches.

We observed missing values in the following variables: preoperative left ventricular ejection fraction 16%, preoperative atrial fibrillation 10%, VA-PROM 3%, Hispanic ethnicity 3%, chronic kidney disease <1%, SDI <1%, NYHA functional class <1%, current smoker <1%, and prior heart surgery <1%. To handle missing information, we used the multiple imputation by chained equations approach and fitted a classification and regression tree approach to

FIGURE 1 Annual $PM_{2.5}$ Concentrations Observed in Our Study in the United States

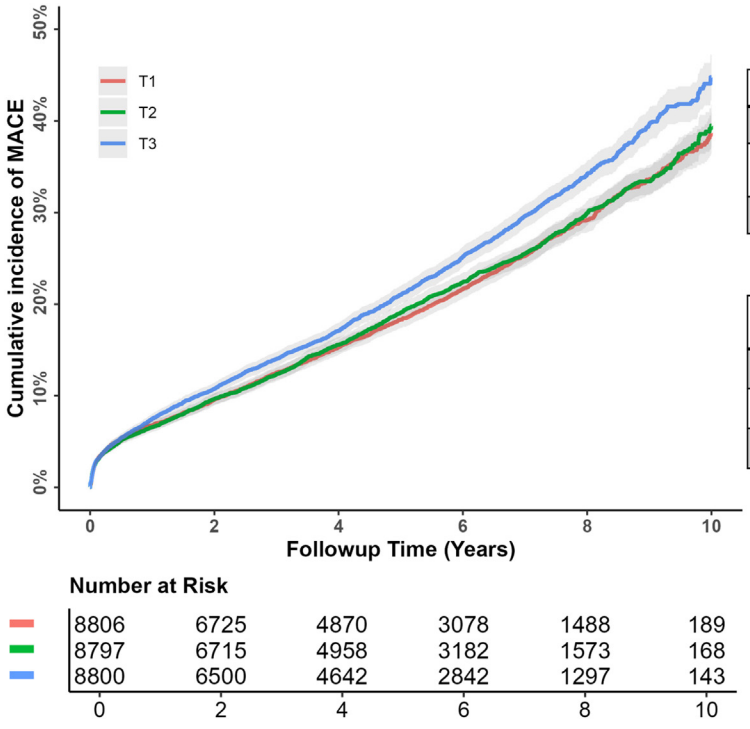


(A) Map of $PM_{2.5}$ distribution according to zip codes in the U.S./histogram for $PM_{2.5}$ (lines at median, WHO, EU, U.S.). (B) Histogram of $PM_{2.5}$ distribution in the study cohort.

impute the missing information.[15] As a sensitivity analysis, we repeated the above model using a complete case method. Patients often have a higher hazard for mortality in the early postoperative period. We therefore repeated our final model with a landmark approach limiting the analysis to only those patients that were MACE-free at 180 days (6 months) after surgery.

DATA AVAILABILITY STATEMENT. Those credentialed to perform research in the Department of Veteran Affairs can directly obtain the data using the

FIGURE 2 The Cumulative Incidence for Major Adverse Cardiovascular Events According to the $PM_{2.5}$ Tertiles



$PM_{2.5}$ Tertile	5-year MACE (%)	10-year MACE (%)
I	18.3 (17.3, 19.2)	38.7 (36.4, 40.9)
II	19 (18.1, 20)	39.5 (37.1, 41.8)
III	21 (20, 21.9)	44.8 (42.2, 47.2)

Pairwise Comparison of the crude rates of cumulative MACE	P-value
Tertile I vs II	< 0.001
Tertile I vs III	< 0.001
Tertile I vs II	0.59

We grouped patients based on their $PM_{2.5}$ into tertiles as follows: tertile I (1.93-7.37 μg/m^3), tertile II (7.37-8.59 μg/m^3), and tertile III (8.59-15.96 μg/m^3). The crude 10-year MACE rate for patients in tertile III for $PM_{2.5}$ was significantly higher than those observed for tertile I ($P < 0.001$) and tertile II ($P < 0.001$). MACE = major adverse cardiovascular events.

regulatory submission methods. Readers can contact the corresponding authors for code used in the analyses presented in this manuscript. The scripts are also available online at the corresponding authors github repository: svd09. We have reported this study according to the Strengthening the Reporting of Observational Studies (STROBE) guidelines.

RESULTS

DESCRIPTION OF THE STUDY COHORT. Between 2010 and 2019, 26,403 U.S. veterans (mean age 65 years, female 1%, Black patients 10%, Hispanic patients 5%) underwent CABG at 42 different VA medical centers nationwide. The prevalence of preoperative diabetes, chronic kidney disease, and heart failure was 46%, 21%, and 3%, respectively. The median $PM_{2.5}$ exposure during the study period was 7.9 μg/m^3 [IQR: 7.0-8.9 μg/m^3] (Figures 1A and 1B); 5% of patients were exposed to $PM_{2.5}$ <5 μg/m^3 (WHO standards), while 12% and 3% were exposed to $PM_{2.5}$ values of >10 μg/m^3 (EU standard) and >12 μg/m^3 (U.S. Environmental Protection Agency standard), respectively. Compared to patients in the lowest tertile (1.93-7.37 μg/m^3), those in the highest tertile (8.59-15.96 μg/m^3) were slightly younger (mean age 65 vs 66 years), more likely to be Black (17% vs 3%), Hispanic (7% vs 4%), and lived in more socially deprived zip codes (mean SDI 61 vs 43).

$PM_{2.5}$ AND MACE RATES. We followed up patients for a median of 4.9 years (maximum 10.4 years). The 5- and 10-year cumulative incidence of MACE was 19.4% (95% CI: 18.9%-19.9%) and 40.9% (95% CI: 39.5%-42.9%), respectively. The cumulative incidence for MACE at 5-years in the lowest and highest $PM_{2.5}$ tertile was 18.3% (95% CI: 17.8%-19.2%) and 21% (95% CI: 20%-21.9%), respectively; at 10 years, the corresponding values were 38.7% (95% CI: 36.4%-40.9%) and 44.8% (95% CI: 42.4%-47.2%), respectively (pairwise log-rank $P < 0.001$) (Figure 2). On crude analysis, an increase in 10 μg/m^3 of $PM_{2.5}$ was associated with a significantly higher relative risk for MACE (1.36 [95% CI: 1.18%-1.55%]). This effect persisted in our fully adjusted model, with every 10 μg/m^3 increase in $PM_{2.5}$ exposure being associated with a significant increase in the relative risk for

TABLE 1 Baseline Characteristics of the Study Cohort

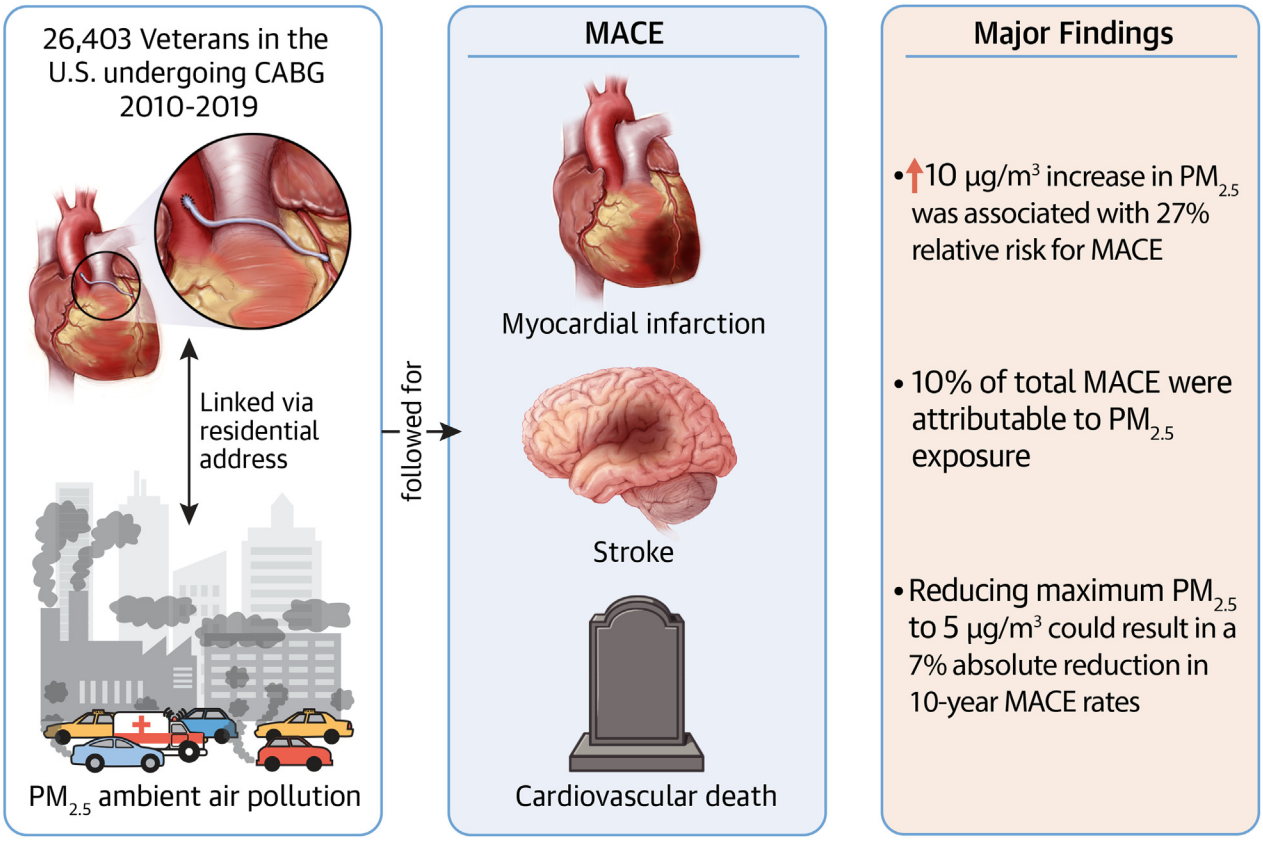
	Whole Cohort (N = 26,403)	Tertile of Average $PM_{2.5}$ ($\mu g/m^3$) During the Study Period			*P* Value
		Tertile I 1.93-7.37 (n = 8,806)	Tertile II 7.38-8.59 (n = 8,797)	Tertile III 8.60-15.96 (n = 8,800)	
Sociodemographic data					
Age, y	65.67 ± 7.60	66.54 ± 7.45	65.32 ± 7.64	65.17 ± 7.62	<0.001
Men	26,122 (98.9)	8,718 (99.0)	8,703 (98.9)	8,701 (98.9)	0.718
Race					<0.001
Black	2,714 (10.3)	264 (3.0)	881 (10.0)	1,569 (17.8)	
White	19,923 (75.5)	7,097 (80.6)	6,810 (77.4)	6,016 (68.4)	
Others	3,766 (14.3)	1,445 (16.4)	1,106 (12.6)	1,215 (13.8)	
Hispanic ethnicity	1,305 (5.1)	344 (4.1)	337 (3.9)	624 (7.3)	<0.001
Body mass index (kg/m^2)	30.09 ± 5.36	30.24 ± 5.35	30.13 ± 5.38	29.90 ± 5.34	<0.001
Social deprivation index	52.33 ± 26.63	43.85 ± 23.94	51.80 ± 25.15	61.35 ± 27.71	<0.001
Clinical characteristics					
Triple vessel coronary stenosis	20,025 (75.8)	6,789 (77.1)	6,594 (75.0)	6,642 (75.5)	0.007
Chronic obstructive pulmonary disease	6,027 (22.8)	1,980 (22.5)	2,086 (23.7)	1,961 (22.3)	0.05
Diabetes					<0.001
No diabetes	14,220 (53.9)	4,992 (56.7)	4,721 (53.7)	4,507 (51.2)	
Noninsulin-treated diabetes	5,089 (19.3)	1,570 (17.8)	1,739 (19.8)	1,780 (20.2)	
Insulin-treated diabetes	7,094 (26.9)	2,244 (25.5)	2,337 (26.6)	2,513 (28.6)	
Smoking	6,525 (24.7)	1,911 (21.7)	2,308 (26.2)	2,306 (26.2)	<0.001
Acute coronary syndrome	3,469 (13.1)	1,209 (13.7)	1,086 (12.3)	1,174 (13.3)	0.02
Atrial fibrillation	3,014 (11.4)	1,129 (12.8)	1,044 (11.9)	841 (9.6)	<0.001
Chronic kidney disease	5,731 (21.7)	1,851 (21.0)	1,922 (21.9)	1,958 (22.3)	0.133
Prior myocardial infarction	2,725 (10.3)	980 (11.1)	860 (9.8)	885 (10.1)	0.008
Peripheral artery disease	5,048 (19.1)	1,779 (20.2)	1,691 (19.2)	1,578 (17.9)	0.001
Priority status for surgery (%)					<0.001
Elective	22,364 (84.7)	7,301 (82.9)	7,559 (85.9)	7,504 (85.3)	
Urgent (within the same hospital admission)	3,420 (13.0)	1,232 (14.0)	1,072 (12.2)	1,116 (12.7)	
Emergent (within 48 h of the same hospital admission)	619 (2.3)	273 (3.1)	166 (1.9)	180 (2.0)	
Prior heart surgery	439 (1.7)	159 (1.8)	156 (1.8)	124 (1.4)	0.074
Cerebrovascular disease	6,377 (24.2)	2,016 (22.9)	2,203 (25.0)	2,158 (24.5)	0.002
Heart failure	781 (3.0)	229 (2.6)	278 (3.2)	274 (3.1)	0.052
Recent acute coronary syndrome	1,597 (6.0)	541 (6.1)	504 (5.7)	552 (6.3)	0.287
Laboratory and echocardiographic data					
Serum creatinine	1.20 ± 1.10	1.15 ± 0.79	1.18 ± 0.86	1.26 ± 1.50	<0.001
Hemoglobin A1c	6.80 ± 4.33	6.70 ± 1.45	6.77 ± 1.47	6.95 ± 7.31	0.002
LDL cholesterol (mg/dL)	93.25 ± 37.26	94.86 ± 37.31	94.10 ± 36.72	90.84 ± 37.63	<0.001
Preoperative LVEF	48.97 ± 13.90	48.83 ± 14.18	49.00 ± 13.72	49.08 ± 13.80	0.53
Ozone 2014 (ppm)	38.32 ± 3.95	38.58 ± 4.31	38.11 ± 3.05	38.28 ± 4.34	<0.001

Values are mean ± SD or n (%).
LDL = low-density lipoprotein; LVEF = left ventricular ejection fraction.

MACE (HR: 1.18 [95% CI: 1.02-1.37]; $P < 0.001$) (Table 1, Central Illustration). The sensitivity analysis, where the $PM_{2.5}$ was treated as time-varying value, supported our primary model, and each 10 $\mu g/m^3$ $PM_{2.5}$ was associated with a comparable relative MACE risk (HR: 1.34 [95% CI: 1.27-1.42]; $P < 0.001$). With patients exposed to $PM_{2.5} \leq 8$ $\mu g/m^3$ as a reference, those exposed to $PM_{2.5} > 8$ $\mu g/m^3$ had a significantly higher MACE risk (HR: 1.10 [95% CI: 1.05-1.16]; $P < 0.001$). We observed that our primary results were supported by the landmark analysis of patients free of MACE for at least 180 days after surgery (HR: 1.30 [95% CI: 1.11-1.54]).

SUBGROUP ANALYSES. Overall, the association between $PM_{2.5}$ and MACE was consistent with the main results in the examined subgroups (Table 2). Specifically, we did not find any statistically significant difference in the point estimates of the main model according to age, race, sex, left ventricular function, and social deprivation status (Table 2).

CENTRAL ILLUSTRATION **Ambient Particulate Air Pollution Exposure and Adverse Cardiovascular Events After Coronary Artery Bypass Grafting**



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ATTRIBUTABLE FRACTION AND SIMULATED IMPACT UNDER LOWER THRESHOLDS OF PM2.5. After adjusting for specified covariates, $PM_{2.5}$ was attributed to 10.2% (95% CI: 4.7%-15.4%) and 9.7% (95% CI: 3.8%-15.9%) of all MACE events at 5 and 10 years, respectively (Figure 3). A hypothetical scenario where maximum $PM_{2.5}$ exposure is limited to 8 μg/m³ will result in an absolute reduction of 1.7% (95% CI: 0.7%-2.6%) and 1.6% (95% CI: 0.6%-2.5%) in the MACE rates at 5 and 10 years, respectively. If $PM_{2.5}$ were further limited to 5 μg/m³, this would result in a potential absolute risk reduction in MACE of 6.9 (95% CI: 3.1-11.2) and 6.6 (95% CI: 2.9-10.7) at 5 and 10 years, respectively.

DISCUSSION

In this national cohort of U.S. veterans undergoing CABG, we showed that 10-year MACE rates were significantly higher among those exposed to high ambient $PM_{2.5}$ air pollution levels. Adjusting for multiple factors only strengthened these associations with every 10 μg/m³ increasing the relative risk for MACE by 18%. This association was consistent across age, race, social deprivation, and clinically important subgroups. Approximately 10% of the currently observed MACE rates were attributable to $PM_{2.5}$ exposure confirming the high attributable fraction related to a common environmental factor even at relatively lower levels of the dose response curve.[3] A hypothetical scenario of reducing $PM_{2.5}$ exposure to 5 μg/m³ as recommended in 2021 by the WHO could lead to a 6% absolute reduction in 10-year MACE in patients post-CABG. The evidence in this work is consistent with a large body of empirical evidence, both in animal models and in humans.[4,6-9] In human studies, both acute time series and chronic prospective cohort studies have clearly implicated a role for air pollution exposure in MACE.[2,5]

TABLE 2 Association Between $PM_{2.5}$ and Major Adverse Cardiovascular Events in Subgroups

	Adjusted HR for MACE (95% CI)	*P* Value for Interaction
Overall	1.18 (1.02-1.37)	
Age		0.52
<70 y	1.19 (1.00-1.41)	
≥70 y	1.11 (0.86-1.44)	
Race		0.70
White	1.34 (1.13-1.59)	
Black	1.24 (0.75-2.04)	
Nonelective surgery		0.05
No	1.34 (1.13-1.58)	
Yes	0.98 (0.74-1.30)	
Chronic kidney disease		
Yes	1.10 (0.84-1.43)	0.21
No	1.40 (1.20-1.65)	
Diabetes		
Yes	1.29 (1.07-1.56)	0.54
No	1.23 (1.00-1.50)	
LVEF		
<40%	1.30 (1.09-1.54)	0.83
≥40%	1.25 (0.98-1.60)	
Social deprivation index		0.15
Quartile 1	1.09 (0.75-1.57)	
Quartile 2	1.15 (0.86-1.55)	
Quartile 3	1.16 (0.88-1.52)	
Quartile 4	1.32 (1.02-1.72)	

LVEF = left ventricular ejection fraction; MACE = major adverse cardiovascular events.

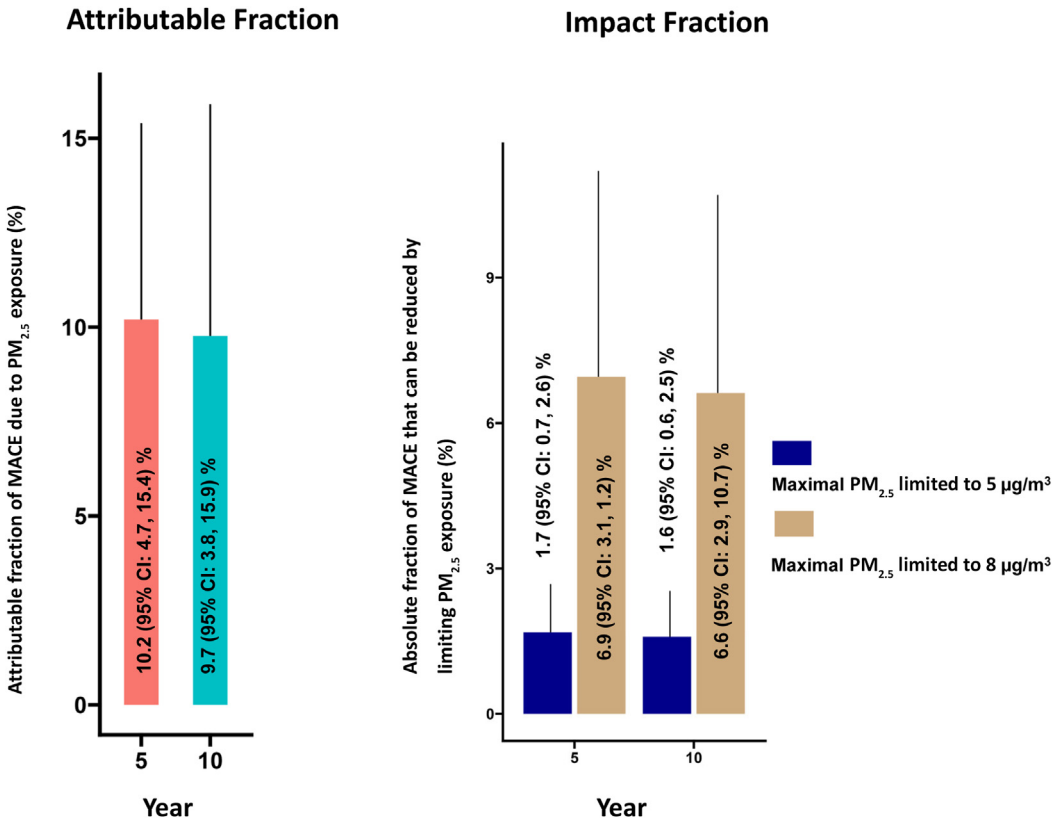
The present study, therefore, builds on prior evidence to support the possibility that air pollution may disproportionately affect the more clinically vulnerable subgroups. However, there have been no studies in CABG patients, who often have multiple comorbidities and a high atherosclerotic burden. The best early evidence of a graded response to air pollution based on underlying risk came from Utah (n = 16,314), where concurrent-day $PM_{2.5}$ was associated with an increase in suffering from acute coronary syndrome.[6] The excess risk was observed only among individuals with angiographic CAD, and led to an increase in ST-segment elevation MI. Additional evidence from a variety of cohort studies have also demonstrated that factors such as age, diabetes, obesity, and cardiac transplantation are all additional risk factors that increase the risk of adverse MACE in response to $PM_{2.5}$.[2,4,5,7] Comparing results obtained in our prior study analyzing data from patients receiving coronary percutaneous interventions (PCIs), it may appear that the deleterious impact of $PM_{2.5}$ exposure is higher after PCI than CABG.[10]

However, differences in the baseline characteristics of patient cohorts included in both studies may partly explain the observed difference in effect estimates. Hence, to better understand the differential association between procedure and the effect of $PM_{2.5,}$ we need a single study of both CABG and PCI patients with statistical adjustments for cohort differences.

In this study, we observed that as much as 10% of the observed MACE rates may be attributable to $PM_{2.5}$ exposure. Therefore, this residual risk would not be reduced by addressing traditional risk factors. Furthermore, reducing $PM_{2.5}$ levels to the Environmental Protection Agency (<8 μg/m^3) and WHO (<5 μg/m^3) standards may hypothetically result in an absolute reduction in MACE rates of 2% and 7%, respectively.[16,17] While the cumulative MACE rates increased between 5 and 10 years, we observed that the $PM_{2.5}$ attributable fraction for MACE remained constant and the potential impact of reducing the maximal $PM_{2.5}$ levels decreased over the same time-frame. A possible explanation is that the burden of MACE attributable to traditional endogenous cardiovascular risk factors (like diabetes, hypertension, dyslipidemia, and smoking) may have increased between 5 and 10 years. However, lowering the $PM_{2.5}$ has also been observed to reduce the incidence of these traditional cardiovascular risk factors. Therefore, the mechanistic pathways between $PM_{2.5}$ are complex; therefore, our model may have underestimated the true effect of reducing $PM_{2.5}$ levels. Therefore, in high-risk patients, it may be prudent to consider air pollution mitigation strategies such as portable air cleaners that have high-efficiency filters; studies have already reported improved cardiometabolic parameters with the use of these devices.[18-21] However, randomized trials in this area are lacking, and we feel that future studies should address this knowledge gap.[8,9] In fact, applying such strategies to reduce $PM_{2.5}$ exposure may synchronously also reduce prevalent traditional cardiovascular risk factors among patients.[22]

STUDY LIMITATIONS AND STRENGTHS. These findings should be considered on the background of certain study limitations. We have studied a U.S. veteran cohort that often has more comorbidities than the general population. Yet, while the overall event rates may be lower in the civilian population, we believe that the incremental risk associated with increased $PM_{2.5}$ levels may be similar to what we observed. Our cohort is also predominantly male, and therefore we were unable to study whether any

FIGURE 3 Percentage of MACE Attributable to $PM_{2.5}$ at 5- and 10-Year Follow-Up Observed in Our Cohort



We further fit 2 hypothetical situations ($PM_{2.5}$, 5 and 8 $\mu g/m^3$) and calculated the possible absolute reduction in MACE that we may predict at 5- and 10-year follow-up. MACE = major adverse cardiovascular events.

sex-based differences exist. We chose to model $PM_{2.5}$ exposure based on patients' residential zip-code at the time of surgery and therefore did not account for address and zipcode changes during the study period. Lastly, we modeled $PM_{2.5}$ exposure as the simple average at the residential zip-code level, a method that is a validated approach in such situations. Furthermore, we acknowledge that analysis for isolated exposures (ie, $PM_{2.5}$) is a somewhat simplistic representation of the overall exposome, and thus the effect estimate of $PM_{2.5}$ on MACE may be overestimated or underestimated. Acute extreme weather events may substantially impact MACE rates over a short time span. However, studies (like ours) that model event rates associated with averaged chronic exposure may not reliably capture such variation. Future studies should incorporate multiexposure models, potentially using evolving data science approaches, to better characterize the impact of air pollution within the context of the total external exposome.[23] The strengths of our study, apart from likely being the first to evaluate this issue in a CABG cohort, are the large sample size, long follow-up, and our ability to accurately map the patient's longitudinal trajectory using data from a single large nationwide healthcare system.

CONCLUSIONS

In this large, contemporary, national study of patients undergoing isolated CABG in the United States, ambient $PM_{2.5}$ air pollution exposure was strongly associated with higher 10-year adverse cardiovascular outcomes. This harmful effect was consistent across age, race, social deprivation, and important clinical subgroups. Future studies should investigate the applicability of scalable mitigation

strategies against air pollution, especially in these high-risk cohorts.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Exposure to particulate matter pollution is associated with higher 10-year cardiovascular events after CABG. In the studied cohort, reaching WHO-recommended limits may result in a 7% reduction in 10-year MACE rates.

TRANSLATIONAL OUTLOOK: To improve long-term health quality for patients post-CABG, we must investigate the impact of nontraditional risk factors like air pollution in greater details.

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