ORIGINAL RESEARCH

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Cardiovascular Disease Hospitalizations in Relation to Exposure to the September 11, 2001 World Trade Center Disaster and Posttraumatic Stress Disorder

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***Background*—**A cohort study found that 9/11-related environmental exposures and posttraumatic stress disorder increased self-reported cardiovascular disease risk. We attempted to replicate these findings using objectively defined cardiovascular disease hospitalizations in the same cohort.

***Methods and Results*—**Data for adult World Trade Center Health Registry enrollees residing in New York State on enrollment and no cardiovascular disease history (n=46 346) were linked to a New York State hospital discharge–reporting system. Follow-up began at Registry enrollment (2003–2004) and ended at the first cerebrovascular or heart disease (HD) hospitalization, death, or December 31, 2010, whichever was earliest. We used proportional hazards models to estimate adjusted hazard ratios (AHRs) for HD (n=1151) and cerebrovascular disease (n=284) hospitalization during 302 742 person-years of observation (mean follow-up, 6.5 years per person), accounting for other factors including age, race/ethnicity, smoking, and diabetes. An elevated risk of HD hospitalization was observed among women (AHR 1.32, 95% CI 1.01 to 1.71) but not men (AHR 1.16, 95% CI 0.97 to 1.40) with posttraumatic stress disorder at enrollment. A high overall level of World Trade Center rescue and recovery–related exposure was associated with an elevated HD hospitalization risk in men (AHR 1.82, 95% CI 1.06 to 3.13; *P* for trend=0.05), but findings in women were inconclusive (AHR 3.29, 95% CI 0.85 to 12.69; *P* for trend=0.09). Similar associations were observed specifically with coronary artery disease hospitalization. Posttraumatic stress disorder increased the cerebrovascular disease hospitalization risk in men but not in women.

***Conclusions*—**9/11-related exposures and posttraumatic stress disorder appeared to increase the risk of subsequent hospitalization for HD and cerebrovascular disease. This is consistent with findings based on self-reported outcomes. **(*J Am Heart Assoc*. 2013;2:e000431 doi: 10.1161/JAHA.113.000431)**

Key Words: 9/11 World Trade Center disaster • cardiovascular diseases • epidemiology • risk factors • stress

Findings from the World Trade Center Health Registry (the Registry), a longitudinal cohort study of persons exposed to the September 11, 2001, World Trade Center disaster (9/11), have provided preliminary evidence of a link between 9/11-related exposures and cardiovascular disease (CVD) risk, and specifically between event-related posttraumatic stress disorder (PTSD) and CVD. High overall levels of 9/11-related exposure were associated with heart disease–related mortality among Registry enrollees who lived, worked, attended school in, or were commuting through the World Trade Center area on 9/11.[1] Among survivors of collapsed buildings, those exposed to the 9/11 dust and debris cloud had an increased risk of self-reported physician-diagnosed stroke.[2] Moreover, measures of dust cloud exposure, injury on 9/11, and event-related PTSD were associated with an elevated risk of self-reported physician-diagnosed heart disease among Registry enrollees 2 to 6 years after the disaster.[3]

Two of these studies relied on a self-reported history of CVD.[2,3] We therefore linked Registry enrollee data with data from the New York State Department of Health's Statewide Planning and Research Cooperative System (SPARCS), a

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Accompanying Table S1 is available at http://jaha.ahajournals.org/content/2/5/e000431/suppl/DC1

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Received July 17, 2013; accepted August 27, 2013.

hospitalization discharge–reporting system, to obtain objectively defined CVD end points. We sought to determine whether 9/11-related factors were associated with an increased risk of subsequent CVD hospitalization.

Methods

Study Population

The Registry's methods have been described previously.[4,5] Briefly, rescue/recovery workers and volunteers; lower Manhattan area residents, workers, and school attendees and staff; and commuters or passersby on 9/11 were recruited through building or employee lists or encouraged to enroll via a website or toll-free telephone number. Between September 12, 2003, and November 24, 2004, 71 434 persons completed a telephone (95%) or in-person (5%) enrollment questionnaire on exposures occurring on and after 9/11, sociodemographic factors, and health status. All participants gave verbal informed consent to participate in the Registry. The US Centers for Disease Control and Prevention and the New York City Department of Health and Mental Hygiene institutional review boards approved the Registry protocol.

Procedures

The New York State Department of Health's SPARCS program is an administrative reporting system that records data, including discharge diagnoses and dates, for all patients discharged from acute care hospitals in New York State, excluding psychiatric and federal hospitals. SPARCS data have been used for health research in the past, including studies of CVD hospitalizations.[6–9]

Personal identifying data for Registry enrollees were electronically linked to SPARCS records from January 1, 2000, through December 31, 2010. Records that matched on parts of key identifying information, such as name, date of birth, Social Security number, or address, were considered matches. Deaths were identified through data linkages to New York City vital records (through December 31, 2010) and the National Death Index (through December 31, 2008), as described previously.[1]

CVD Outcomes

We defined cardiovascular hospitalizations based on *International Classification of Disease*, *9th Revision* (ICD-9) codes for the principal discharge diagnosis. CVD hospitalizations were categorized as either heart disease or cerebrovascular disease hospitalizations. Heart disease hospitalizations included those for hypertension (ICD codes 401 to 405), acute coronary artery disease (410, 411), chronic coronary artery disease (412 to 414), dysrhythmia (427), and congestive heart failure (428). We also studied a more narrowly defined subset of these outcomes, coronary artery disease hospitalizations (ICD codes 410 to 414). Cerebrovascular disease was defined as ICD codes 430 to 438.

Exposure Assessment

Because objective measures of 9/11-related exposures are not available for most persons exposed to the disaster, we defined exposure based on responses to the enrollment questionnaire, as summarized in Table 1. Dust cloud exposure was defined as answering "yes" to having been caught in the dust and debris cloud on 9/11. Injury was defined as reporting any of the following: eye injury or irritation; cut, abrasion, or puncture wound; sprain or strain; burn; broken or dislocated bone; or concussion or head injury. Rescue/recovery workers were asked questions about arrival time, location, type, and duration of work. Area residents and workers were asked about evacuation of their homes and workplaces. Because enrollees were queried about many different but overlapping exposures, we summarized the overall level of 9/11-related exposure as high, intermediate, or low, separately for rescue/recovery and nonrescue/recovery enrollees, as described previously.[1]

Table 1. Definitions of Overall Levels of Exposure to the World Trade Center Disaster and Its Aftermath[1]

Rescue/recovery workers
• High—Was present in Manhattan south of Chambers Street between the time of the first plane impact and noon on 9/11 (encompassing the WTC towers' collapse) *and* at least one of the following:
○ Worked on the dust and debris pile on 9/11 and/or
○ Worked for >90 days starting before September 18, 2001
• Low—Met all of the following conditions
○ Began work on or after September 18, 2001, *and*
○ Did not work on pile *and*
○ Worked fewer than 30 days *and*
○ Was not present south of Chambers Street between the first plane impact and noon on 9/11
• Intermediate—Neither high nor low
Residents of lower Manhattan, area workers, and commuters or passersby on 9/11.
• High—Reported at least two 9/11-related injuries and, if a lower Manhattan resident, did not evacuate home
• Low—Reported no injuries related to 9/11 and, if a lower Manhattan resident, also evacuated home
• Intermediate—Neither high nor low

WTC indicates World Trade Center.

Additional Study Variables

Study participants were hierarchically categorized as rescue /recovery workers (including volunteers) or nonrescue /recovery workers (including lower Manhattan area residents or workers and passersby or commuters). A history of self-reported, physician-diagnosed hypertension or diabetes was obtained from the enrollment questionnaire. Posttraumatic stress disorder (PTSD) was assessed with the PTSD Checklist (PCL), a validated, 17-item scale that inquired about 9/11-specific psychological symptoms within the 30 days preceding the enrollment questionnaire.[10–12] We used a score ≥ 44[10] to define probable PTSD, which we subsequently refer to as PTSD for simplicity. If an enrollee was missing responses to PCL items but had a score from the remaining items that could only be compatible with a total score of less than or ≥ 44, he or she was categorized accordingly. Otherwise, PTSD was considered missing.

Statistical Analysis

The observation period began at Registry enrollment and ended at the first cerebrovascular or heart disease hospitalization, death, or December 31, 2010, whichever was earliest. The analysis was limited to enrollees who lived in New York State on Registry enrollment (54 650, 76.5%) because SPARCS reflects only New York State hospitalizations. Participants who reported a history of stroke or heart disease before Registry enrollment (n=4443) or with a preenrollment cardiovascular or cerebrovascular disease hospitalization (n=338) were excluded. We also excluded enrollees who withdrew from the Registry (n=470), who were <18 years old on 9/11 (n=2740) or had missing age data (n=242), or were lower Manhattan area school students or staff but did not belong to other eligibility groups (n=71), due to small numbers. Enrollees with a first cerebrovascular disease hospitalization during the study period were excluded from analyses of heart disease hospitalizations, and vice versa. We stratified the analysis on sex due to well-established differences in cardiovascular risk profiles for men and women.

Proportional hazards regression models were used to examine associations of 9/11-related exposures and PTSD with heart disease and cerebrovascular hospitalizations accounting for factors that were theoretically and statistically associated with the outcomes in bivariate analysis: age, race/ethnicity, education, smoking, history of hypertension, and history of diabetes. We evaluated linear trends in the hazards ratios by including each exposure as a continuous variable in a multivariable analysis and testing whether its coefficient differed significantly from zero. The low, intermediate, and high levels were assigned values of 1, 2, and 3, respectively. The assumption of proportional hazards over time was tested for all models presented by using time-dependent variables to assess interactions between each predictor of interest and a function of survival time and by using the Kolmogorov–Smirnov test.

We considered *P*-values <0.05 or CIs that did not include 1 to be statistically significant. Analyses used SAS version 9.2 (SAS Institute Inc).

Results

Table 2 shows characteristics of the study group. Mean age on 9/11 was 41.6 years for women and 40.7 years for men. Compared with women, a higher proportion of men were non-Hispanic white. A higher proportion of women were college graduates. Twenty-two percent of women and 15% of men screened positive for PTSD at study enrollment. Among rescue/recovery enrollees, a larger proportion of men had a high overall level of 9/11-related exposure.

We identified 1151 heart disease and 284 cerebrovascular hospitalizations from the SPARCS system during 302 742 person-years of observation (mean follow-up, 6.5 years per person). The most common heart disease admissions were for coronary atherosclerosis (ICD-9 codes 411 [n=62], 413 [n=16], and 414 [n=401]), dysrhythmia (ICD-9 code 427, n=269), and acute myocardial infarction (ICD-9 code 410, n=223). Most cerebrovascular hospitalizations were for acute cerebrovascular disease (ICD-9 codes 430 to 434, n=145) or transient ischemic attacks (ICD-9 code 435, n=100).

Heart Disease Hospitalizations

Table 3 shows multivariable adjusted hazard ratios (AHRs) for relationships between 9/11-related exposures and PTSD and heart disease hospitalization. Accounting for other factors, women with PTSD at enrollment had an elevated risk of heart disease hospitalization (AHR 1.32, 95% CI 1.01 to 1.71). Among men, this relationship did not reach statistical significance (AHR 1.16, 95% CI 0.97 to 1.40). Male rescue /recovery workers with a high overall level of 9/11-related exposure were at an 82% higher risk of heart disease hospitalization compared with those with a low level of exposure (*P* for trend 0.05). The hazard ratios for female rescue/recovery workers with high or intermediate levels of exposure were also elevated, but this was not statistically significant (*P* for trend 0.09).

We repeated this analysis restricting the outcome to coronary artery disease hospitalizations (Table S1). The hazard ratios for associations between the various predictor variables and coronary artery disease hospitalization were

Table 2. Characteristics of Study Participants*

	Women (n=18 679), %	Men (n=27 667), %
Age on September 11, 2001, y		
<25	8.1	5.4
25 to 44	51.5	60.8
45 to 64	36.6	31.7
65+	3.8	2.1
Race/ethnicity		
Non-Hispanic white	49.4	66.6
Non-Hispanic black	20.1	9.8
Hispanic	16.1	13.7
Asian	9.3	6.2
Other/multiracial	5.0	3.8
Education		
Less than high school	5.2	6.0
High school	16.7	22.0
Some college	22.9	26.1
College graduate	53.5	44.5
Marital status		
Married	38.5	63.0
Widowed/divorced/separated	21.3	9.8
Never married	30.3	18.8
Living with a partner	7.9	6.9
Smoking history		
Never	58.8	54.3
Current	15.7	17.9
Former	24.1	26.5
History of hypertension		
Yes	15.3	15.6
No	84.2	83.9
History of diabetes		
Yes	4.0	4.0
No	95.6	95.6
9/11 dust cloud exposure		
Yes	59.8	53.1
No	39.7	46.5
Injured on 9/11†		
Yes	40.9	42.1
No	59.1	57.9
PTSD at enrollment		
Yes	21.6	14.7
No	77.0	84.0
Rescue/recovery workers/volunteers	n=3634	n=16 137
Overall level of exposure‡		
Low	16.7	4.3
Intermediate	73.6	77.1
High	5.5	15.7
Nonrescue/recovery participants	n=15 045	n=11 530
Overall level of exposure‡		
Low	48.5	54.6
Intermediate	41.4	37.5
High	8.7	6.9

PTSD indicates posttraumatic stress disorder.
*Percentages may not sum to 100 due to missing values.
†Injury was defined as reporting any of the following: eye injury or irritation; cut, abrasion, or puncture wound; sprain or strain; burn; broken or dislocated bone; or concussion or head injury.
‡Please see Table 1 for definition of exposure levels.

similar to those for the more inclusively defined heart disease hospitalizations.

Cerebrovascular Disease Hospitalizations

An analysis of associations between 9/11-related exposures and PTSD and cerebrovascular hospitalizations is shown in Table 4. AHRs for cerebrovascular disease hospitalization were elevated among both women and men with PTSD at enrollment, although the relationship was only statistically significant among men. None of the other exposures examined were significantly associated with cerebrovascular hospitalization.

Discussion

Among female members of the WTC Health Registry cohort, the presence of PTSD at study enrollment was associated with an elevated risk of subsequent heart disease hospitalization. We also found an association between PTSD and cerebrovascular disease hospitalization among male enrollees. Additionally, male rescue/recovery enrollees with a high overall level of 9/11-related exposure were at a higher risk of heart disease hospitalization compared with those with a low level of exposure. While the AHRs for these associations were not statistically significant for both men and women, the hazard ratios were of similar magnitude for the 2 sexes, suggesting that the associations identified may exist for both, although our study may be underpowered to detect this. These results, based on objectively defined cardiovascular end points, suggest that persons with 9/11-related PTSD and

Table 3. Sex-Specific Associations of 9/11-Related Exposures and PTSD With Heart Disease Hospitalization Among Participants in the World Trade Center Health Registry residing in New York State, 2003–2010

	Women (n=18 551)				Men (n=27 511)			
	Number of Events*	Person-Years	AHR	95% CI	Number of Events*	Person-Years	AHR	95% CI
9/11 Dust cloud exposure								
Yes	178	73 826	0.96	0.75 to 1.22	450	95 219	0.96	0.84 to 1.11
No	118	48 488	Ref.		402	82 794	Ref.	
Injured on 9/11[†]								
Yes	126	50 418	0.93	0.74 to 1.19	377	75 256	1.11	0.97 to 1.28
No	170	72 544	Ref.		478	103 512	Ref.	
PTSD at enrollment								
Yes	94	26 413	1.32	1.01 to 1.71	146	25 947	1.16	0.97 to 1.40
No	197	94 878	Ref.		698	150 597	Ref.	
Rescue/recovery enrollees	Women (n=3 634)				Men (n=16 137)			
Overall level of exposure[‡§]								
Low	4	4036	Ref.		16	4468	Ref.	
Intermediate	36	17 616	1.72	0.60 to 4.94	407	80 225	1.63	0.99 to 2.69
High	5	1317	3.29	0.85 to 12.69	82	16 242	1.82	1.06 to 3.13
Nonrescue/recovery enrollees	Women (n=15 045)				Men (n=11 530)			
Overall level of exposure[‡]								
Low	98	48 223	Ref.		164	41 003	Ref.	
Intermediate	125	40 755	0.94	0.71 to 1.25	140	27 775	0.92	0.72 to 1.16
High	20	8661	0.88	0.54 to 1.43	22	5157	0.94	0.60 to 1.47

Hospitalizations were identified through data linkage with the New York State Department of Health Statewide Planning and Research Cooperative System (SPARCS). Each predictor was examined in a separate model. HRs were adjusted for race/ethnicity, education, marital status, smoking, diabetes, and hypertension. AHR indicates adjusted hazard ratio; PTSD, posttraumatic stress disorder; Ref., reference group.

*Number of heart disease hospitalizations may not sum to 1151 due to missing exposure data.

[†]Injury was defined as reporting any of the following: eye injury or irritation; cut, abrasion, or puncture wound; sprain or strain; burn; broken or dislocated bone; or concussion or head injury.

[‡]Please see Table 1 for definition of exposure levels.

[§]*P* value for trend=0.09 among women, 0.05 among men.

those who performed intensive rescue/recovery work may be at an elevated risk of chronic CVD.

A growing body of literature, including prospective studies of well-defined cardiovascular end points such as mortality, links PTSD to CVD in both military and civilian populations.[13–17] A number of feasible explanations for this association have been proposed, including chronic dysregulation of the hypothalamic-pituitary-adrenal axis and autonomic nervous system leading to long-term physiological changes that promote atherosclerosis.[18,19] Adverse effects of PTSD on blood pressure and lipid metabolism have been reported, each of which could play an important role in the causal pathway.[20–22] Behaviors associated with PTSD, such as smoking and alcohol consumption, may also contribute.[23,24] Studies of PTSD and cerebrovascular disease, although fewer, also support a potential link.[17,24] Since PTSD is 1 of the most commonly reported 9/11-related health outcomes, it could have a considerable influence on CVD risk in this population.[4]

In contrast to results of our previous study of self-reported heart disease in this cohort,[3] we did not identify an association between measures of dust cloud exposure or injury on 9/11 and heart disease hospitalization. It is possible that our analysis of hospitalized cases was underpowered to detect this relationship, whereas the larger number of self-reported cases enabled us to identify such an association. It is also possible that a relationship exists between these 9/11-related exposures and milder manifestations of CVD, as reflected in self-reported heart disease, but not between 9/11-related exposures and more severe CVD that would tend to result in hospitalization. Additional years of study may help clarify the nature of the relationship between 9/11-related exposures and chronic CVD risk.

Although this study builds on our previous work by using a more objective case definition, our findings remain limited by a lack of information on several CVD risk factors,

Table 4. Sex-Specific Associations of 9/11-Related Exposures and PTSD With Cerebrovascular Disease Hospitalization Among Participants in the World Trade Center Health Registry Residing in New York State, 2003–2010

	Women (n=18 383)				Men (n=26 812)			
	Number of Events*	Person-Years	AHR	95% CI	Number of Events*	Person-Years	AHR	95% CI
9/11 Dust cloud exposure								
Yes	76	73 441	0.84	0.58 to 1.22	85	94 007	1.03	0.75 to 1.42
No	51	48 277	Ref.		71	81 680		
Injured on 9/11[†]								
Yes	64	50 213	1.31	0.91 to 1.89	68	74 221	1.14	0.82 to 1.57
No	64	72 160	Ref.		88	102 214	Ref.	
PTSD at enrollment								
Yes	37	26 231	1.38	0.92 to 2.07	35	25 585	1.53	1.03 to 2.27
No	87	94 471	Ref.		121	148 665	Ref.	
Rescue/recovery enrollees	Women (n=3 586)				Men (n=15 613)			
Overall level of exposure[‡§]								
Low	2	4029	Ref.		4	4426	Ref.	
Intermediate	14	17 538	1.40	0.31 to 6.39	60	79 061	1.33	0.42 to 4.27
High	0	1303			12	15 998	1.66	0.46 to 5.95
Nonrescue/recovery enrollees	Women (n=14 797)				Men (n=11 199)			
Overall level of exposure[‡]								
Low	39	47 990	Ref.		32	40 584	Ref.	
Intermediate	60	40 550	1.34	0.87 to 2.08	41	27 457	1.16	0.71 to 1.90
High	11	8629	1.22	0.60 to 2.47	4	5086	0.83	0.29 to 2.36

Hospitalizations were identified through data linkage with the New York State Department of Health Statewide Planning and Research Cooperative System (SPARCS). Each predictor was examined in a separate model. HRs were adjusted for race/ethnicity, education, marital status, smoking, diabetes, and hypertension. AHR indicates adjusted hazard ratio; PTSD, posttraumatic stress disorder; Ref., reference group.

*Number of cerebrovascular disease hospitalizations may not sum to 284 due to missing exposure data.

[†]Injury was defined as reporting any of the following: eye injury or irritation; cut, abrasion, or puncture wound; sprain or strain; burn; broken or dislocated bone; or concussion or head injury.

[‡]Please see Table 1 for definition of exposure levels.

[§]*P* value for trend=0.38 among men.

including family history and dyslipidemia. The Registry has begun collecting data on hypercholesterolemia and body mass index among its enrollees, which will enable future studies to incorporate this information. However, epidemiological studies based on in-depth clinical examination may be needed to further clarify the relation of 9/11-related exposures and PTSD to heart disease and stroke, fully accounting for factors such as family history, physical activity level, and metabolic markers of cardiovascular risk factors. An additional limitation is potential underascertainment of hospitalizations among study participants, since personal identifying data used in the data linkage were incomplete for some Registry enrollees; SPARCS does not include federal or psychiatric hospitals; and study participants may have been hospitalized outside of New York State during the study period, which would not be reflected in SPARCS. This may have diminished the power of our study. Furthermore, our study did not determine whether PTSD was part of the causal pathway between 9/11-related environmental exposures and CVD hospitalizations or whether PTSD and rescue/recovery-related exposures were independent risk factors; we hope to explore this further when additional years of observation are available for study.

Limitations notwithstanding, these results are consistent with our previous finding of an association of 9/11-related exposures and PTSD with CVD, and with a larger body of literature that has established environmental and psychological stressors as CVD risk factors.[25–30] Our results suggest that medical follow-up of persons who performed intensive rescue/recovery work in response to the disaster or developed 9/11-related PTSD should include screening for modifiable CVD risk factors, including smoking, hypertension, and dyslipidemia.

Acknowledgments

We thank Jiehui Li, James Stark, Wei-Yann Tsai, and Sukhminder Osahan for their guidance on the statistical analysis, and John Piddock and Mike Zdeb for their assistance with preparation and cleaning of the data.

Sources of Funding

This publication was supported by Cooperative Agreement numbers 2U50OH009739 and 1U50OH009739 from the Centers for Disease Control and Prevention (CDC)-National Institute for Occupational Safety and Health, and U50/ATU272750 from CDC-Agency for Toxic Substances and Disease Registry which included support from CDC-National Center for Environmental Health, and the New York City Department of Health and Mental Hygiene. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC.

Disclosures

None.

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