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Original Research

Self-reported respiratory outcomes associated with blast exposure in post 9/11 veterans

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ABSTRACT

Background: Blast lung overpressure has received interest as a cause of chronic respiratory disease in Service members who deployed in support of U.S. military operations in Southwest Asia and Afghanistan since 2001. We studied whether veterans who experienced blast exposure report more chronic respiratory symptoms and diagnoses compared to deployed veterans who did not.

Methods: 9,000 veterans included in the Department of Veterans Affairs Toxic Embedded Fragment Registry were invited to complete a survey assessing chronic respiratory symptoms, diagnoses, and exposures. Blast exposure was assessed using the Brief Traumatic Brain Injury Screen and by presence of other symptoms such as blast-induced loss of consciousness.

Results: Participants (n = 2147) were predominantly <40 years old, served in the Army, and injured on average 12.8 years previously. 91% reported blast exposure. Blast-exposed veterans were significantly more likely to report cough (OR 1.8), wheeze (OR 2.4), and dyspnea (OR 1.8), even after adjustment for covariates including smoking and occupational exposures to dust, fume, and gas. Veterans reporting higher severity of blast impact, such as traumatic brain injury or loss of consciousness, were more likely to report cough, wheeze, or dyspnea. Veterans with higher severity of blast impact by multiple measures were also more likely to report having COPD. Those reporting a physician-diagnosis of traumatic brain injury were significantly more likely to report having both asthma (OR 1.5) and COPD (OR 1.5).

Conclusions: Blast exposure is associated with respiratory symptoms and COPD. Respiratory system evaluation may warrant inclusion as a standard part of barotrauma health assessment.

1. Introduction

An increasing body of literature has examined respiratory health effects among military Service members who deployed to Southwest Asia[1] and Afghanistan (SAA) following the September 11, 2001 terrorist attacks on the United States [1]. These individuals are known as post 9/11 veterans. The largest study among this body, the Millennium Cohort, showed significant increases in respiratory symptoms among Service members deployed to SAA, compared to those who did not [2]. Other studies have shown similar patterns for symptoms, with conflicting data for respiratory diagnoses [1]. Proposed causes for increased respiratory symptoms in the deployed population include exposures to tobacco and electronic cigarettes, particulate matter, combustion product emissions from burn pits and other industrial pollutants, vehicular exhausts, and allergen exposures [1]. These respiratory insults were common in many different SAA environments, as was potential exposure to blast injury.

Many deployers to SAA in Operation Iraqi Freedom and Operation Enduring Freedom (OIF/OEF) have faced injury from high kinetic

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[1] The US Department of Veterans Affairs defines Southwest Asia to include Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Gulf of Aden, Gulf of Oman, Oman, Qatar, the United Arab Emirates, and the waters of the Persian Gulf, the Arabian Sea, and the Red Sea [40].

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Abbreviations

aOR	Adjusted Odds Ratio
AHOBPR	Airborne Hazards and Open Burn Pit Registry
ATS DLD	American Thoracic Society Division of Lung Disease
BTBIS	Brief Traumatic Brain Injury Screening tool
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
ICD	International Classification of Diseases
IED	Improvised Explosive Device
IRB	Institutional Review Board
Landstuhl	Landstuhl Regional Medical Center
LOC	Loss of Consciousness
NASEM	National Academies of Science, Engineering and Medicine
OIF/OEF	Operation Iraqi Freedom and Operation Enduring Freedom
OR	Odds Ratio
PFT	Pulmonary Function Test
SAA	Southwest Asia and Afghanistan
TBI	Traumatic Brain Injury
TM	Tympanic Membrane
TEF	Toxic Embedded Fragment Registry
US	United States
VA	Department of Veterans Affairs

energy explosive blasts [3,4]. A 2016 review found that incidence of explosion injury between 2005 and 2009 ranged from 1.7/1000 deployed up to 83/1000 in 2007, during the Iraq troop surge [5]. During this period, explosion injuries composed almost 75% of all combat injuries (31 per 10,000 deployed) [5]. Blast-induced injuries range from penetrating trauma injuries to those sustained due to blast wave forces such as Traumatic Brain Injury (TBI), a condition resulting in chronic symptoms and diagnosed in over 450,000 US military Service members since 2000 [6,7]. Other organ systems could sustain similar, chronic injuries from blast.

One such injury is termed blast lung injury. Blast lung injury is one manifestation of barotrauma, or physical damage to body tissues caused by a difference in pressure between a gas space inside, or in contact with, the body, and the surrounding gas or fluid [8]. Blast lung injury is usually acute and diagnosed at time of injury [9]. Estimates from U.S. and U.K. military registries show that 11% of in-theater trauma injuries were from blast lung, and that among all those with primary blast injuries, 30% had lung involvement [4]. Mechanisms for blast lung injury include mechanical trauma-induced epithelial damage and hemorrhage, inflammation, oxidative stress and autonomic nervous system activation [3,9–17]. Manifestations of blast lung injury include conditions such as pneumothorax, pulmonary contusion, pneumo-mediastinum, pulmonary edema and acute respiratory distress syndrome. While these manifestations of blast lung injury may be easily recognized, sub-clinical manifestations are not fully understood. Injury criteria data, such as characterization of “mild” or “sub-clinical” blast lung injury is limited and has been identified as a research need [7].

Over recent years, links between blast exposure and long-term pulmonary effects have garnered research interest. Pugh et al. observed increased prevalence of COPD and asthma among Department of Veterans Affairs (VA) health care users with TBI, one possible chronic result of blast injury [18]. Jani et al. observed increased odds of dyspnea and self-reported exercise intolerance among registrants of the VA’s Airborne Hazards and Open Burn Pit Registry (AHOBPR) who reported ever being “close enough to feel the blast from an IED or other explosive device” [19]. More recently, Zell-Baran et al. observed more abnormalities in Lung Clearance Index, a test of lung ventilation heterogeneity, associated with blast exposure intensity [20,21]. With these increasing findings, in 2020 the National Academies of Science, Engineering and Medicine (NASEM) recommended that future research on mechanisms of lung disease in military cohorts include study of blast exposure as a contributing factor [1].

Service members who sustain blast exposure often experience injuries from embedded metal fragments. The Department of Veterans Affairs established the Toxic Embedded Fragment (TEF) Surveillance Center and Registry in 2008 at the Baltimore VA Medical Center to identify and track veterans who have retained embedded fragments [22]. As of May 2022, the TEF registry included over 27,000 veterans. Within this population, the majority (92%) report injury due to blasts from IEDs (54%), rocket propelled grenades (20%), or other sources (unpublished data). This population yields a high concentration of blast-exposed veterans who served in SAA since 2001.

The objective of this study was to evaluate TEF registry veterans for associations between respiratory symptoms and diagnoses with blast exposure. We hypothesized that veterans who sustained exposures to blasts would have a greater prevalence of respiratory symptoms and self-reported diagnoses, compared to those who have not sustained exposures to blasts. We also hypothesized that markers of other health effects from blast exposure, such as blast-associated TBI, loss of consciousness (LOC), tympanic membrane (TM) rupture, sinus disease, and other barotrauma effects, would be associated with increased respiratory symptoms and diagnoses.

2. Methods

2.1. Study population and recruitment

Veterans enrolled in the VA’s TEF Registry prior to January 2020 who were identified as at-risk for having an embedded fragment from an injury they received while serving in SAA military conflicts were eligible to participate. We sent study questionnaires to 9,000 eligible veterans enrolled in the TEF registry (9 batches of 1,000) between September 2018 and March 2020. Veterans could complete the questionnaire on paper or electronically using a weblink included in the recruitment letter. Additional details about TEF Registry enrollment and study participant recruitment are included in the supplemental material.

The study was approved by the Baltimore VA Medical Center Research Committee and the affiliated university (University of Maryland-Baltimore) Institutional Review Board (IRB), protocol #HP-00074555, and the US Army Medical Research and Development Command Human Research Protection Office, protocol A-19735.

2.2. Survey instrument

We crafted a survey intended to assess several outcomes, including general health, respiratory, and renal health outcomes among veterans with embedded fragment exposure. This article focuses only on the respiratory outcomes, incorporating respiratory, exposure, and demographic questionnaire data.

We collected demographic and Military Service data using questions from the National Health Study for a New Generation of US Veterans [23]. We collected details on blast exposure and traumatic brain injury (TBI) during deployment using the Brief Traumatic Brain Injury Screening tool (BTBIS), a screening tool designed to identify Service members needing clinician evaluation for TBI (Table 1) [24]. In addition, we asked, “Have you ever been told you had a traumatic brain injury (TBI) by a physician?” We also assessed for presence of injuries related to barotrauma in the lung, ear, or sinuses, as these structures are especially vulnerable to primary blast injury due to air-fluid or air-tissue interfaces and are commonly injured in US military deployers from the

Table 1
First two questions of Brief Traumatic Brain Injury Screen (BTBIS)[a] (22, p379).

1. Did you have any injury(ies) during your deployment from any of the following? *a) Fragment, b) bullet, c) vehicular (any type of vehicle, including airplane), d) fall, e) blast (improvised explosive device, rocket propelled grenade, land mine, grenade, etc.), f) other (specify)*
2. Did any injury received while you were deployed result in any of the following? *a) Being dazed, confused, or "seeing stars", b) not remembering the injury, c) losing consciousness for less than a minute, d) 1-20 min or e) longer than 20 min, f) having any symptoms of concussion afterward (such as headache, dizziness, irritability, etc.), g) head injury, h) none of the above.*

[a] Endorsement of questions 1 or 2a-e indicated a positive screen for TBI.

OEF/OIF cohort [4,25]. These included experience of the following as a result of a blast or explosion: TM rupture, pain around the cheek bones, above the eyes or teeth, nosebleed, or sinus pressure. Subjects were asked about any chest injuries, specifically pneumothorax, lung contusion, rib fracture, or penetrating lung injury that occurred because of a blast or explosion. Finally, as a surrogate measure for severity of injury, we assessed location of medical treatment for injury as described further in the supplemental material.

We assessed respiratory health through the American Thoracic Society and the Division of Lung Disease (ATS-DLD-78) questionnaire [26]. Cough was defined as presence of a usual cough as much as 4 to 6 times a day, 4 or more days out of the week. Wheeze was defined as wheezing most days and nights, or having wheezing attacks causing shortness of breath that required medicine or treatment for these attacks. Dyspnea was defined as having to walk slower than people of your age on the level (a flat surface) because of breathlessness, having to stop for breath when walking at your own pace on the level, or being too breathless to leave the house or breathless on dressing and undressing. Details of the ATS-DLD-78 respiratory symptom questions used in this study are shown in the supplement. Participants were also questioned on any history of doctor-confirmed chronic bronchitis, emphysema, or asthma, or any other chest illness. We included limited occupational exposure questions from the ATS-DLD-78. These included "Have you ever worked for a year or more in a dusty job?" and "Have you ever been exposed to gas or chemical fumes in your work?" If respondents answer "yes" to the either question, they were asked to report whether exposure was mild, moderate, or severe.

2.3. Analysis

All analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC). Descriptive statistics and t or chi-square tests were performed to examine differences in demographic and exposure factors between the blast exposure groups. Logistic regression was used to adjust for covariates (age, sex, race, income, marital status, Service branch, time since injury, history of smoking or vaping, work in dusty job or occupational exposure to gas or fumes) in assessment of respiratory symptoms and diagnoses in blast-exposed compared to unexposed veterans. For this analysis, work for a year or more in a dusty job or exposure to gas or fumes was categorized as none or mild versus moderate or severe.

Among the survey respondents, only those veterans who reported a date of injury in 2001 or later, and who had sustained their injury in Afghanistan or Iraq were analyzed. If a veteran reported multiple dates of injury including prior to 2001, they were excluded from further analyses to eliminate any contribution to respiratory symptoms from conflicts outside of OIF/OEF.

Certain demographic categories were collapsed to facilitate analysis, such as current age (<30 years old, 30-39, 40-49, 50+), race, (white vs. non-white including Latinx), Service branch (Army vs. other), and income level (< or ≥$75,000). Smoking status was evaluated using pack-years, categorized as 0, >0-10, >10 pack-years, or missing. Vaping status was evaluated as ever vs. never. Exposure for one year or more in a dusty job or to gas or fume was grouped as moderate or higher severity vs. mild or none.

Respondents were classified as "blast-exposed" if they noted any injuries during their deployment from a blast, corresponding to question 1 of the BTBIS tool (Table 1) with a qualifying answer choice of "blast" (n = 1834). Veterans who answered affirmatively to BTBIS questions 2a-2e, regardless of their response to question 1, were also included in the "blast-exposed" group (n = 111) Finally, any respondent not already included who endorsed the following sequelae of a blast or explosion were deemed blast-exposed (n = 14): pneumothorax; lung contusion; rib fracture; penetrating lung injury; ruptured ear drum; pain around the cheek bones, above the eyes, or in the teeth; nose bleeds; or sinus pressure. All other veterans were classified as "blast unexposed."

To further clarify the effect of blast trauma on respiratory outcomes, analysis utilizing the degree of blast exposure was performed. One surrogate for blast exposure severity was LOC, with mild LOC defined as being dazed or confused, not remembering the injury, or LOC for less than 1 min; moderate defined as LOC for 1–20 min; and severe as LOC over 20 min. Other surrogates for severe exposure were presence of any of the following resulting from a blast or explosion: a history of physician-diagnosed TBI, ruptured TM, sinus problems (pain in the periorbital region or in teeth, nosebleed, sinus pressure), and chest trauma. Details on how chest trauma was categorized are included in the supplement.

Self-reported proximity to blast was assessed after dividing into four quartiles: a) 0–5 m from blast, b) 6–15 m, c) 16–40 m, and d) > 40 m, based on a review of blast studies by Champion et al. [7]. Hypothesizing that treatment for injury at Landstuhl Regional Medical Center (Landstuhl), Germany indicated a more severe blast injury warranting evacuation from military theater, we compared outcomes among veterans who were treated at Landstuhl versus elsewhere.

For analysis of respiratory health outcomes, respondents were defined to have respiratory symptoms if they endorsed any usual cough, wheezing, or dyspnea, with severity levels previously defined. Respondents were defined to have respiratory diagnoses if they reported ever having doctor-confirmed chronic bronchitis, emphysema (combined as "COPD"), or asthma, or any other chest illness added as a free-text response.

3. Results

A total of 2396 veterans completed the survey, yielding a 31% response rate (Fig. 1). Most respondents (71%) completed the paper survey instead of the electronic option. After excluding respondents who were injured before 2001 or not in SAA, or who did not complete questions about blast exposure, the final sample for analysis included 2147 veterans.

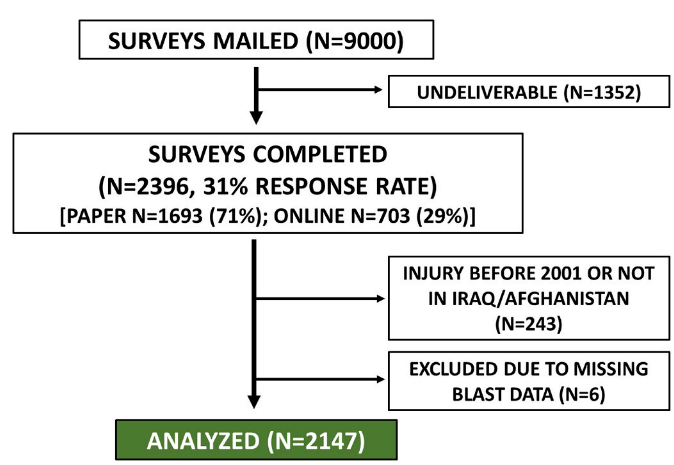

Fig. 1. Description of participant response rates and inclusion in final analysis.

Table 2
Demographic characteristics of veteran respondents reported as number (%) unless otherwise specified.

	TOTAL	No Blast	Blast	p value
Respondents	2147 (100)	188 (8.8)	1959 (91.2)	
Age				
- <30	94 (4.4)	23 (12.2)	71 (3.6)	<0.001
- 30–39.9	981 (45.7)	85 (45.2)	896 (45.7)	
- 40–49.9	550 (25.6)	47 (25.0)	503 (25.7)	
- ≥50	318 (14.8)	19 (10.1)	299 (15.3)	
- No response	204 (9.6)	14 (7.5)	190 (9.7)	
Sex				
- Male	2070 (96.5)	183 (97.3)	1887 (96.5)	0.53
- Female	74 (3.5)	5 (2.66)	69 (3.5)	
Race				
- White	1728 (81.1)	154 (82.3)	1575 (81.0)	0.68
- Non-White	402 (18.9)	33 (17.7)	369 (19.0)	
Household annual income				
- <$75,000	1144 (53.3)	88 (46.8)	1056 (53.9)	0.18
- ≥$75,000	757 (35.3)	75 (39.9)	682 (34.8)	
- No answer/missing	246 (11.5)	25 (13.3)	221 (11.3)	
Branch				
- Army	1507 (70.2)	118 (62.8)	1389 (70.9)	0.02
- Other Branch	640 (29.8)	70 (37.2)	570 (29.1)	
Marital status				
- Married	1464 (68.4)	114 (60.6)	1350 (69.2)	0.02
- Unmarried	675 (31.6)	74 (39.4)	601 (30.8)	
Smoking status (pack years)				
- Zero (0)	952 (47.6)	99 (55.0)	853 (46.9)	0.01
- ≤10	592 (29.6)	36 (20.0)	556 (30.6)	
- >10	455 (22.8)	45 (25.0)	410 (22.5)	
- Missing	148 (6.9)			
Ever vape user	292 (13.8)	23 (12.4)	269 (14.0)	0.57
Dusty job >1 year (moderate or greater exposure)	888 (41.9)	68 (36.8)	820 (42.4)	0.14
Ever exposed to "chemical fume"/gas at work (moderate or greater exposure)	649 (30.8)	40 (21.5)	609 (31.7)	0.004
Years since injury [mean (SD)]	12.8 (2.9)	11.8 (3.5)	12.9 (2.8)	<0.001

Participants were predominantly male and white and had served in the Army (Table 2). Most respondents (91%) reported blast exposure. Blast-exposed veterans differed from those without blast exposure in age, military branch, marital status, pack-years of smoking, occupational fume or gas exposure, and time since injury. The groups did not differ based on sex, race, income, work for a year or more in a dusty job, or ever vaping. Reported source of blast is presented in Supplemental Table S1.

Overall, many of the participants reported respiratory symptoms and diagnoses (Table 3). Blast-exposed veterans were more likely to report respiratory symptoms than unexposed veterans, even with adjustment for covariates of age, race, marital status, income, military branch, smoking status, vaping status, occupational exposure to dust, gas or fume, or years since injury. This included usual cough, wheezing, and dyspnea, and an aggregate assessment of reporting any severe respiratory symptom (OR 2.2, 95% CI [1.6–3.0]). Blast-exposed veterans were

Table 3
Frequency of respiratory symptoms and diagnoses in blast-exposed versus blast-unexposed veterans as number (%).

	TOTAL	No Blast	Blast	p value[a]	OR[a] (95% CI)
Respondents	2147 (100)	188 (8.8)	1959 (91.2)		
SYMPTOMS					
Cough[b]	984 (46.13)	62 (33.2)	922 (47.4)	<0.001	1.8 (1.3–2.5)
Wheeze[c]	964 (46.5)	50 (27.3)	914 (48.3)	<0.0001	2.5 (1.8–3.5)
- Wheeze most days/nights	901 (42.4)	49 (26.3)	852 (43.9)	<0.0001	2.2 (1.6–3.1)
- Wheezing requiring medicine/treatment	294 (14.4)	15 (8.3)	279 (15.0)	0.02	1.9 (1.1–3.4)
Dyspnea[d]	893 (41.9)	48 (26.0)	845 (43.4)	0.0022	1.8 (1.2–2.6)
- Walking slower than same age on level	798 (37.5)	39 (21.1)	759 (39.0)	<0.0001	2.4 (1.7–3.5)
- Stop for breath walking on level	635 (29.8)	30(16.1)	605 (31.1)	<0.0001	2.3 (1.6–3.5)
- Too breathless to leave house/dress	368 (17.2)	21 (11.3)	347 (17.8)	0.03	1.7 (1.1–2.7)
Any symptom (cough, wheeze, dyspnea)	1430 (68.2)	94 (51.1)	1336 (69.8)	<0.0001	2.2 (1.6–3.0)
DIAGNOSES					
COPD confirmed by Dr.	296 (14.5)	23 (12.6)	273 (14.7)	0.46	1.2 (0.8–1.9)
Asthma confirmed by Dr.	285 (14.0)	23 (12.5)	262 (14.1)	0.54	1.2 (0.7–1.8)
Other chest illnesses[e]	217 (10.3)	10 (5.4)	207 (10.7)	0.03	2.1 (1.1–4.0)
Dr-confirmed Asthma or COPD + other chest illness	652 (31.8)	45 (24.7)	607 (32.5)	0.03	1.5 (1.0–2.1)

[a] Comparisons adjusted for age, race, marital status, income, military branch, smoking status, vaping status, >1year occupational dust exposure, ever occupational gas/vapor exposure, years since injury.
[b] Cough defined as occurring 4-6 times per day, 4 or more days per week.
[c] Wheeze defined as occurring most days and nights or requirement medicine or treatment.
[d] Dyspnea defined as any of the listed symptoms subsequently.
[e] Includes free-text responses.

Table 4

Odds ratios (95% Confidence Intervals) of respiratory symptoms and diagnoses in blast-exposed veterans, stratified by markers of blast severity.

		Symptoms				Diagnoses		
	Responses n (%)	Cough[a]	Wheeze[b]	Dyspnea[c]	Any Symptom	Asthma[d]	COPD[e]	Any Resp Diagnosis[f]
Blast-induced loss of consciousness (LOC)[g]								
None	300 (14.0)	1	1	1	1	1	1	1
Mild	1156 (54.3)	***2.0 (1.5–2.6)	***2.2 (1.7–2.9)	***2.2 (1.7–3.0)	***2.2 (1.7–2.9)	1.1 (0.7–1.6)	1.2 (0.8–1.7)	*1.4 (1.0–1.9)
Moderate	516 (24.0)	***2.4 (1.8–3.3)	***3.5 (2.6–4.8)	***3.8 (2.7–5.2)	***3.7 (2.7–5.1)	1.4 (0.9–2.1)	**1.9 (1.3–2.9)	***1.9 (1.4–2.7)
Severe	166 (7.7)	***2.2 (1.5–3.3)	***2.3 (1.6–3.5)	***4.4 (2.9–6.7)	***3.4 (2.2–5.3)	1 (0.6–1.8)	1.2 (0.6–2.2)	1.5 (1.0–2.3)
Presence of physician-diagnosed TBI								
Absent	696 (32.7)	1	1	1	1	1	1	1
Present	1431 (67.3)	***1.6 (1.3–1.9)	***1.9 (1.5–2.2)	***2.3 (1.9–2.7)	***2.0 (1.6–2.4)	**1.5 (1.1–2.0)	**1.5 (1.1–1.9)	***1.5 (1.3–1.9)
Blast-induced tympanic membrane rupture								
Absent	1653 (77.0)	1	1	1	1	1	1	1
Present	494 (23.0)	**1.4 (1.1–1.7)	**1.4 (1.1–1.7)	*1.3 (1.1–1.6)	**1.5 (1.2–1.8)	0.8 (0.6–1.1)	*1.3 (1.0–1.7)	1.0 (0.8–1.2)
Blast-induced sinonasal problems (pain, pressure, or nosebleed)								
Absent	824 (38.4)	1	1	1	1	1	1	1
Present	1323 (61.6)	***2.5 (2.1–3.1)	***2.5 (2.1–3.0)	***2.5 (2.1–3.0)	***2.8 (2.4–3.4)	1.1 (0.9–1.4)	***1.8 (1.4–2.4)	***1.6 (1.3–1.9)
Blast-induced pneumothorax, lung contusion, rib fracture, or penetrating chest trauma								
None	1893 (88.2)	1	1	1	1	1.0	1	1
Non-penetrating	170 (7.9)	**1.6 (1.2–2.3)	***1.9 (1.4–2.6)	***2.1 (1.5–2.9)	***2.2 (1.5–3.3)	1.1 (0.7–1.8)	*1.5 (1.0–2.3)	1.4 (1.0–1.9)
Penetrating	84 (3.9)	1.4 (0.9–2.1)	1.4 (0.9–2.3)	**2.0 (1.3–3.2)	**2.1 (1.2–3.7)	1.0 (0.5–2.0)	1.4 (0.8–2.5)	1.2 (0.8–2.0)
Any blast-induced problem (Yes to any of the above)								
Absent	211 (9.8)	1	1	1	1	1	1	1
Present	1936 (90.2)	***2.4 (1.8–3.3)	***2.9 (2.1–4.1)	***3.3 (2.3–4.8)	***3.0 (2.3–4.1)	1.2 (0.8–1.8)	*1.6 (1.0–2.6)	**1.6 (1.2–2.3)
Treatment at Landstuhl, Germany								
Elsewhere[h]	1502 (70)	1	1	1	1	1	1	1
Yes	645 (30)	0.9 (0.7–1.1)	***0.7 (0.6–0.8)	***0.7 (0.6–0.9)	**0.7 (0.6–0.9)	0.8 (0.6–1.1)	**0.7 (0.5–0.9)	**0.7 (0.6–0.9)
Reported distance from blast (n=1682)[i]								
>40 m	168 (10.0)	1	1	1	1	1	1	1
15–40 m	215 (12.8)	*0.7 (0.5–1.0)	0.8 (0.5–1.2)	*0.6 (0.4–0.9)	0.7 (0.5–1.2)	0.8 (0.4–1.5)	1.1 (0.7–1.9)	1.1 (0.7–1.7)
5–15 m	329 (19.6)	0.8 (0.6–1.2)	0.8 (0.5–1.1)	**0.5 (0.3–0.8)	0.7 (0.4–1.1)	0.9 (0.5–1.5)	0.7 (0.4–1.1)	0.9 (0.6–1.4)
0–5 m	970 (57.7)	0.8 (0.5–1.2)	***0.6 (0.4–0.8)	***0.5 (0.3–0.6)	**0.6 (0.4–0.9)	1.0 (0.6–1.6)	**0.5 (0.3–0.8)	0.8 (0.6–1.2)

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

[a] Cough defined as occurring 4-6 times per day, 4 or more days per week.

[b] Wheeze defined as occurring most days and nights or requirement medicine or treatment.

[c] Dyspnea defined as walking slower than those of same age on level or greater limitation.

[d] Asthma confirmed by a doctor.

[e] COPD confirmed by a doctor.

[f] Asthma or COPD confirmed by a doctor or other chest illness.

[g] mild LOC = being dazed or confused, not remembering the injury, or LOC for < 1 min; moderate defined as LOC for 1–20 min; and severe as LOC >20 min.

[h] Includes in the field, at a combat support hospital, at a U.S. based medical treatment facility, or at a VA Medical Center.

[i] Distance from blast n = 1682 includes only veterans who reported a distance; Does not include 140 who stated they were injured by blast but did not report a distance, or those who were not injured by blast.

more likely to report other chest illness and were more likely than unexposed veterans to report any respiratory diagnosis (OR 1.5, 95% CI [1.0–2.1]) when diagnoses were combined as an aggregate outcome.

Table 4 shows respiratory outcomes associated with severity markers of blast. Veterans were more likely to report usual cough, wheeze, or dyspnea if they had experienced more severe blast-induced LOC. These symptoms were also more likely among veterans reporting a physician diagnosis of TBI, blast-induced TM rupture and other sinonasal problems. Additionally, reporting any respiratory symptom was associated with these severity markers of blast physiologic impact. Among types of chest trauma, odds of having usual cough, wheeze, or dyspnea were highest in association with non-penetrating chest trauma.

Among diagnoses, doctor-diagnosed COPD was more likely to be reported among veterans with moderately severe LOC, physician-diagnosed TBI, blast-induced TM rupture and sinonasal problems, and non-penetrating chest trauma. Doctor-diagnosed asthma was only significantly reported among veterans reporting physician-diagnosed TBI. When combined in aggregate, having any respiratory diagnosis was associated with moderately severe LOC, doctor-diagnosed TBI, and blast-induced sinonasal problems, and a combined exposure assessment of "any blast-induced problem." Care for injury at Landstuhl was inversely associated with reporting of all symptoms and all diagnoses. Reported distance from blast was not associated with increased respiratory symptoms or diagnoses, and closest proximity (0–5 m) was significantly inversely associated with wheezing, dyspnea, any symptom, and COPD (Table 4).

Occupational exposure to dust for a year or more or ever exposure to fume or gas was significantly associated with wheezing, dyspnea, and aggregate presence of symptoms. Occupational exposure to fume or gas was also significantly associated with doctor-confirmed COPD or aggregate presence of diagnosis, even when adjusted for co-variates including blast exposure (Supplemental Table S2). Similar effects were observed in adjusted analysis of respiratory outcomes by blast severity markers (data not shown).

4. Discussion

In this study of post-9/11 U S. veterans who deployed to SAA, veterans who reported exposure to blast reported more respiratory symptoms, including cough, wheeze, and dyspnea than unexposed veterans. Markers of other severe effects of blast exposure, such as LOC, physician-diagnosed TBI, blast-induced TM rupture, sinonasal problems or chest trauma, also correlated with increased respiratory symptoms. Veterans who experienced severe markers of blast impact, such as physician-diagnosed TBI, blast-induced sinonasal problems or non-penetrating chest trauma more often reported COPD and pulmonary diagnoses in aggregate. Overall, these findings support our hypothesis that blast exposure is associated with adverse respiratory outcomes.

Our findings support results from other epidemiologic studies exploring respiratory outcomes and blast exposure. Jani et al. also observed that self-reported exposure to blast independently predicted presence of dyspnea and exercise intolerance among registrants of the AHOBPR (aOR 1.66, [95% CI 1.5–1.7]) even when adjusted for occupational exposure to vapors, gases, dusts, fumes, smoking status, and other covariates, including burn pit smoke exposure [19]. Pugh et al. studied trends in ICD-9 codes among veterans receiving VA care between 2002 and 2011. Using TBI as a surrogate measure for blast exposure, they found that veterans diagnosed with TBI were more likely to be diagnosed with any chronic lung disease [18]. Controlled for covariates including tobacco use and multiple deployments, veterans with TBI were more likely to have diagnoses of asthma (aOR 1.47, [95% CI 1.42–1.53]), COPD (aOR 1.51, [95% CI 1.38–1.64], and interstitial lung disease (aOR 1.88, [95% CI 1.62–2.19]). Like Pugh's findings, we saw increased odds of asthma (aOR 1.5, [95% CI 1.1–2.0] and COPD (aOR 1.4, [95% CI 1.1–1.9]) among veterans reporting TBI in our study. Additionally, in a population of symptomatic deployers with asthma or distal lung disease (defined as bronchiolitis, small airways inflammation, peribronchiolar fibrosis, emphysema, or granulomatous pneumonitis), 55% reported exposure to blasts from IEDs, and 73% reported exposures to controlled detonations during deployment [21,27]. In another retrospective study evaluating veterans who had deployed and were discharged from military service between 2004 and 2010, TBI was highly prevalent (92.5%) among symptomatic veterans undergoing spirometry [28]. Our study supports findings from prior studies linking adverse respiratory outcomes and markers of blast exposure.

Chronic respiratory insults could plausibly result from the consequences of acute blast exposure. During acute exposure, mechanical trauma from the primary blast wave may result in shearing of the airway or alveolar epithelium [9,29]. Such damage from mechanical trauma might result in a chronic airway or parenchymal injury. In early studies, initial blast insult led to hemorrhage, resolution, emphysema and scarring around alveolar ducts that persisted at 2 months post-injury [13]. Other mechanisms involving neuroendocrine and autonomic pathways stemming from acute blast exposure may also impact chronic respiratory dysfunction [3,30].

Limitations of this study include several important issues. First, the data are self-reported. Our study does not include confirmation of physician diagnosis from medical records, markers of physiologic impairment or imaging. Additionally, our study population was recruited from TEF registry veterans who have sought VA care. The experiences of VA health care users may differ from the broader population of post 9/11 veterans who may also have experienced blast exposure and not suffered adverse respiratory effects [31]. While the generalizability of the interpretation of the exposure effect among all who experience blast may be limited, these findings likely do reflect the impact among those who have suffered more severe blast consequences, such as those with confirmed diagnoses of TBI. Additionally, recall bias may impact these self-reported responses [32]. However, responses among our study population participants were similar in magnitude to that reported by AHOBPR participants, who found overall prevalence of dyspnea or exercise intolerance of 61%, reported by 65% of blast exposed and 47% of non-blast exposed registrants [19]. Thus, we see similar patterns in a different veteran registry population.

Furthermore, it is unclear what the best measure of blast exposure is, when assessed historically. We did not quantify frequency of blast exposure or cumulative blast exposure, which limits our assessment of this exposure. Other researchers have attempted to do this, finding associations with abnormal pulmonary physiology in an unadjusted evaluation [21]. Although we did not assess cumulative blast exposure, we did evaluate outcomes associated with surrogate markers for severity of blast, such as LOC and physician-diagnosed TBI. Importantly, we saw higher ORs for cough, wheeze, and dyspnea with moderate and severe LOC. Other researchers have shown that recall of LOC and greater injury severity can predict the presence of TBI [33]. These findings support use of a surrogate marker for a physiologic impact of blast exposure, like LOC and TBI, in predicting exposure intensity. Therefore, we feel that our findings provide an important contribution in understanding associations between blast exposure and respiratory outcomes. Several instruments are under development and testing to assess career low level blast exposure [34,35]. These tools may better characterize exposure and could have applications to assessment of respiratory health.

TBI and LOC can result from non-blast trauma sources, such as falls or vehicular collisions. Thus, using TBI alone as a marker for blast exposure could lead to exposure misclassification. Importantly, of the 1959 participants classified as blast-exposed, 94% were included based on affirmative response to being injured specifically by blast. Therefore, we have taken efforts to reduce misclassification of blast exposure that reliance solely on TBI or LOC may create. Even so, we also saw patterns for adverse respiratory outcomes associated with the less specific measures of TBI and LOC. This may suggest that an underlying neurologic mechanism may also lead to an adverse respiratory outcome, instead of, or perhaps in addition to, the physical impact of the blast. Additional study to determine whether these patterns are replicated is needed.

We evaluated whether care for injury at Landstuhl, the nearest and largest U.S. military hospital to operations in SAA, predicted respiratory outcomes. Counter to our hypothesis, those treated at Landstuhl were less likely to have adverse respiratory outcomes. Possible explanation for these findings could be that the high level of medical care and expertise present at Landstuhl may allow for earlier recognition and treatment of findings that, if unabated, could result in chronic disease.

We did not observe an association between self-reported distance from blast and adverse respiratory outcomes. Physiologic impacts of blast are affected not only by distance from blast, but by other factors we were unable to assess. This includes power and size of ordnance, space characteristics of the location of exposure, including presence of blast reflective and shielding factors, and by presence of protective gear [10, 29].

We observed consistently high associations between chest trauma, especially non-penetrating trauma, with adverse respiratory outcomes. Previous research among active-duty Service members with history of trauma showed high prevalence of abnormal pulmonary function test (PFT) results [36]. Although no significant differences were observed in prevalence of PFT abnormality based on mechanism of injury, obstructive abnormalities were seen most often following burn injuries, followed by penetrating and then blunt injuries. Further analysis of chest trauma and type of chest trauma in populations with pulmonary physiologic testing may shed additional insight into this observation.

Our questionnaire did not ask for cumulative deployment or military service time; thus, we are unable to account for these variables in our analysis. Interestingly, however, multiple other studies have not identified correlations between cumulative deployment time and health effects [1]. Some have theorized that specific exposures, rather than deployment in general, are important in predicting adverse respiratory health. Blast may represent one of these specific exposures that deserves additional study, particularly in how best to assess exposure.

This study has several strengths. First, this large study analyzed over 2100 participants from a national sample. This increases generalizability to the broader sample of US veterans injured by blasts with chronic conditions such as TBI. Comparing our study population to the overall TEF registry population, we saw similar distributions of sex, race, and most age strata. We see a difference between the populations for the 30–39-year age group, but we note more non-respondents in the study group, also (Supplemental Table S1). Furthermore, our response rate of 31% is similar to response rates in other large studies of OEF/OIF veterans, such as the Millennium Cohort Study baseline survey (34%) and the VA NewGen Study (34%) [23]. This supports consistency in reporting patterns among OEF/OIF veterans, our target population. Second, the strengths and consistencies of the associations across multiple outcome measures support the link between blast exposure and respiratory outcome. Third, even though the unexposed group was notably smaller than the blast-exposed group, it was sufficiently large to detect relatively small differences between the groups with 80% power. Finally, we also accounted for tobacco smoking, vaping, and occupational exposure to vapor, gas, dust, and fume. Respiratory health analyses among SAA deployers have often not accounted for these important risk factors, limiting their interpretation [1]. While the purpose of this study was not to evaluate the effects of exposure to airborne hazards from military service, such as burn pit emissions and dust storms, we did see impacts of exposures to dust, gas, and fume on respiratory outcomes. Even accounting for these elements, we saw blast-associated respiratory outcomes. This suggests that both airborne hazards and blast exposures have important associations with respiratory health outcomes in previously deployed populations that deserve additional study.

5. Significance

Estimates suggest that 86% of OIF/OEF wounded in action injuries involved blasts [37]. Over 450,000 US Service members since 2000 have been diagnosed with TBI alone [6]. Knowing that chronic pulmonary health effects are a possible consequence of blast exposure, thousands of veterans may face risk for chronic lung disease. An expanding body of epidemiologic research has shown mixed findings for increased presence of pulmonary diagnoses and objective abnormalities in SAA deployers [1,38,39]. Respiratory symptoms, however, seem to consistently be reported among deployers to SAA, although not consistently correlated with burn pit smoke or other proposed causal airborne hazards. This raises two key questions: 1) Is the airborne hazards exposure assessment sufficiently comprehensive, and 2) are veterans undergoing the correct clinical diagnostic evaluation for their symptoms? In their 2020 report, the NASEM highlighted the potential role of blast exposure as a contributor or even facilitator in a respiratory health effect resulting from deployment. They recommended that future research on mechanisms of lung disease in military cohorts include study of blast exposure as a contributing factor [1]. If future mechanistic and epidemiologic research confirms that blast exposure leads to chronic respiratory disease, this highlights the need to evaluate the respiratory system in assessing those who have experienced blast injuries. Additional study is needed to clarify what that assessment might include, such as symptom surveys, pulmonary physiological testing and chest imaging.

6. Conclusion

Even years after traumatic injury, self-reported blast exposure significantly predicts respiratory symptoms in post-9/11 veterans deployed to SAA. Additionally, veterans reporting greater severity of blast exposure were more likely to have adverse respiratory outcomes. These patterns exist independent of other important predictors of adverse respiratory outcomes, such as tobacco exposure and exposure to vapors, gas, dust, or fume. Future studies should further investigate mechanistic hypotheses for chronic lung injury from pulmonary barotrauma. Further, respiratory system evaluation may warrant inclusion as a standard part of barotrauma health assessment.

Guarantor

Stella E. Hines, MD, MSPH, claims responsibility for the content of the manuscript.

Author contributions

Clinical data acquisition: SEH, JMG, DRG, KHC, MAR. Study design: SEH, JMG, MAM, CHB. Data analysis: CHB, JMG. Interpretation of results: SEH, JMG, CHB, DRG, KHC, MAR, MAM. Manuscript preparation and review. All authors reviewed, revised, and approved the manuscript for submission.

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Disclaimer

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Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2022.106963.

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