Pulmonary and Critical Care Medicine

Research Article ISSN: 2398-3108

Deployment-related pulmonary symptoms and cardiopulmonary exercise testing in military personnel

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Abstract

Background: The objective of this study was to investigate differences in Cardiopulmonary Exercise Testing (CPET) between deployed and non-deployed military personnel undergoing a clinical evaluation for dyspnea.

Methods: A retrospective electronic medical record review was conducted on active military personnel who underwent CPET at Brooke Army Medical Center during a clinical evaluation for dyspnea from 2007 through 2011. Studies were performed on a cycle ergometer to the point of maximum exercise tolerance. Review of CPET records identified values from expired gas analysis related to cardiac and respiratory exercise limitations and review of medical records identified pre-CPET diagnostic testing and medical and deployment history.

Results: A total of 268 patients were identified. The cohort was predominantly male (78%) and had deployed to Southwest Asia (62%). Demographic comparison of deployed and non-deployed groups showed age (32.2 vs. 30.5 years) and body mass index (28.1 vs. 26.6 kg•m-2) were higher in deployed personnel. Diffusing capacity for carbon monoxide was low in deployed and non-deployed personnel (71.1 vs. 75.0% predicted) and was significantly lower in deployed personnel with onset of dyspnea during or post-deployment (70.0% predicted). Anaerobic threshold was lower in deployed personnel (49.8 vs. 55.8% predicted) but there were no significant differences in maximum work rate, maximum oxygen consumption, maximum heart rate, heart rate response, maximum respiratory rate or other respiratory parameters.

Conclusions: Deployed males in this study were heavier and older than non-deployed males. There were small significant differences between the two groups in some CPET results (all within normal ranges); however, no specific CPET parameters were identified within this study that clearly defined an underlying pulmonary process related to deployment.

Background

Beginning with Operations Desert Shield/Desert Storm in the early 1990s and continuing through Operation Iraqi Freedom and Operation Enduring Freedom, military personnel returning from deployment to Southwest Asia (SWA) have reported new or worsening pulmonary symptoms. Ambient particulate matter levels from this region are elevated mainly due to sandstorms and geologic dusts, but other factors such as burn pit fumes, urban air pollution, vehicle exhaust and the increased rate of cigarette smoking may be environmental airborne hazards to deployed personnel [1]. The relationship between military deployment and these pulmonary symptoms has been the subject of numerous investigations [2,3].

Several surveys have identified a higher incidence of pulmonary complaints in previously deployed personnel. The Iowa Persian Gulf Study Group noted a higher prevalence of self-reported asthma and bronchitis among surveyed veterans of the First Gulf War [4]. During the recent SWA conflicts, the Millennium Cohort Study found a higher rate of new self-reported respiratory symptoms when comparing deployed to non-deployed military members (14% vs. 10%), as well as a direct relationship between deployment length and the frequency of symptoms [5].

These deployment-related pulmonary symptoms have been investigated in the context of inhalational exposures. A 2002 study found the odds ratio for self-reported asthma and bronchitis was higher in veterans who reported oil fire smoke exposure [6]. Later studies described more self-reported pulmonary symptoms in veterans reporting exposures to oil fire smoke, dust storms and sulfur fires, but did not find diminished lung function or an increased rate of chronic respiratory conditions when compared to unexposed veterans [7,8]. Both the 2010 Armed Forces Health Surveillance Center report and 2011 Institute of Medicine report on the potential impacts of burn pits concluded there was no substantial or consistent health effects in personnel assigned near burn pit locations [9,10].

Recent investigations have tried to connect inhalational exposure during military deployment to specific disease processes, including

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Key words: *exercise testing, military deployment, dyspnea and pulmonary function testing*

Received: June 29, 2016; **Accepted:** August 13, 2016; **Published:** August 15, 2016

asthma, acute eosinophilic pneumonia and constrictive bronchiolitis [2,3,11-14]. In patients with post-deployment respiratory symptoms, Cardiopulmonary Exercise Testing (CPET) has been utilized to potentially help identify small groups of individuals with normal or near normal pulmonary function testing for limitations to exercise [2,15]. No specific CPET parameters were identified that clearly defined an underlying pathophysiologic process related to deployment.

The objective of this study was to evaluate any identifiable relationship between military deployment to SWA and pulmonary symptoms by investigating the differences in CPET results between deployed and non-deployed personnel. Cardiopulmonary exercise testing can be an objective method of assessing functional capacity and may have a role in the evaluation of exertional dyspnea by revealing the underlying etiology, detecting early changes in patients with cardiac or respiratory disease, and determining the limiting disease process in an individual with multiple comorbidities [16,17].

Methods

The Brooke Army Medical Center (BAMC) Institutional Review Board reviewed and approved this study. A retrospective review of BAMC Pulmonary Clinic records was conducted using the clinical CPET database and military electronic medical record. The requirement for informed consent was waived due to the retrospective nature of the study. Patients were included if they were Active Duty (AD) military personnel evaluated at the BAMC Pulmonary Clinic for complaints of dyspnea from 2007 through 2011 who completed a CPET using cycle ergometry. Retired military personnel and dependents were excluded, as were patients who completed a CPET study using a graded treadmill. Treadmill tests were excluded because cycle ergometers have been shown to more accurately quantify work rates and give less variable VO_2 max values at submaximal work rates [18].

Patients were divided into two groups based on prior deployment history. Patients were defined as "deployed" if they deployed for at least three months to SWA from 2003 through 2011 before pulmonary and CPET evaluation, and as "non-deployed" if they had no deployment history or were deployed after pulmonary and CPET evaluation. All patients underwent an evaluation in the clinic to include pulmonary function testing and chest imaging. The remainder of the evaluation varied based on presenting symptoms and preference of the evaluating physician.

All patients had previously completed a standard CPET protocol consisting of exercise on an electromechanically braked cycle ergometer with an increasing workload of 20 watts per minute [18]. Heart rate (HR), blood pressure, 12-lead electrocardiogram, pulse oximetry, oxygen consumption (VO_2), carbon dioxide production (VCO_2) and expired ventilation (V_E) were monitored during exercise and studies were terminated at the point of maximum exercise tolerance [19,20]. The following variables were included for analysis and compared with reference values listed in the American Thoracic Society/American College of Chest Physicians Statement on Cardiopulmonary Exercise Testing: exercise time, Maximum Heart Rate (max HR), Heart Rate Response (HRR), VO_2 max, Anaerobic Threshold (AT), Maximum Respiratory Rate (RR max), tidal volume to inspiratory capacity ratio (V_T/IC), ventilatory equivalent for CO_2 at anaerobic threshold (V_E/VCO_2), ventilatory reserve (V_E max/MVV) maximum work rate and oxygen pulse (O_2 pulse) [21].

Patients' medical records were reviewed to determine the diagnostic pulmonary evaluation prior to CPET completion, including Pulmonary Function Testing (PFT), Chest Radiography (CXR), Chest Computed Tomography (CT), Methacholine Challenge Testing (MCT), transthoracic echocardiogram, laryngoscopy, and bronchoscopy. Forced vital capacity (FVC), Forced Expiratory Volume at one second (FEV_1), total lung capacity (TLC), Residual Volume (RV), and Diffusion Capacity for Carbon Monoxide (DLCO) were recorded from available PFT data. Results of CXR, chest CT, MCT, echocardiogram, and bronchoscopy results were recorded as "normal" or "abnormal" based on documentation of any abnormalities in radiology or procedure reports. Laryngoscopy results were recorded as "normal" if Vocal Cord Dysfunction (VCD) was absent and "abnormal" if VCD was present based on documentation in the procedure note. The final diagnosis given for a patient's dyspnea was determined by reviewing Pulmonary Clinic notes. If the notes attributed symptoms to multiple diagnoses, all diagnoses were included.

The CPET and PFT results of the deployed and non-deployed groups were compared as the primary analysis. Results were then compared in three secondary analyses after stratifying the deployed group based on the 1) presence of a diagnosis for a patient's dyspnea 2) duration of deployment and 3) onset of dyspnea symptoms. Military deployment records were queried to separate deployed personnel into two groups: overall deployment length <365 days and overall deployment length ≥365 days. Patients were not included in this analysis if deployment records were unavailable. The onset of dyspnea symptoms for deployed personnel was determined by reviewing Pulmonary Clinic notes. Patients were not included in this secondary analysis if there was no clear documentation of the onset of dyspnea. The percentage of abnormal CXR, chest CTs and other studies in the deployed and non-deployed groups were also compared.

Statistical analyses were performed with SAS version 9.3 software (SAS Institute Inc., Cary, NC) and p values were calculated using Chi-square, Wilcoxon Rank sum, T-test or Fischer Exact Test methods as appropriate for each reported variable. A p value less than 0.05 was considered significant.

Results

A total of 268 active duty military personnel fulfilled the inclusion criteria for analysis. From this group, 103 patients had not been deployed to SWA or were deployed after CPET evaluation ("non-deployed"), and 165 patients were deployed prior to CPET evaluation ("deployed"). There were more males in the deployed group (84 vs. 67, p <0.001), and patients in the deployed group were also older (32.2 ± 8.6 vs. 30.5 ± 10.3 years, p=0.02) with a higher body mass index (28.1 [IQR 25.1, 30.8] vs. 26.6 [IQR 24.1, 29.7] $kg \cdot m^{-2}$, p=0.02). There were no significant differences in other demographics or smoking history, as shown in Table 1. Asthma was the most common diagnosis (n=41), followed by sarcoidosis (n=13), pectus excavatum (n=11) and VCD (n=11) as shown in Table 2.

Among the patients with a chest CT performed, a higher percentage of non-deployed personnel had abnormal results (72 vs. 54%, p=0.024), but there were no other significant differences in the percentage of diagnostic test abnormalities between the two groups (Table 3). In the non-deployed group, chest CT abnormalities included pectus excavatum (6 patients), a localized pulmonary infiltrate (5 patients), bronchial wall thickening (4 patients), hilar and/or mediastinal lymphadenopathy (4 patients), post-cardiac surgery changes (3 patients), apical fibrotic changes (2 patients), multiple pulmonary infiltrates (2 patients), cardiomegaly (2 patients), hyperinflation (2 patients), post-thoracic surgery changes (1 patient), a right-sided

Table 1. Demographic Characteristics by Deployment History.

Variable	Non-Deployed (n=103)	Deployed (n=165)	P value
Gender, n (%)			<0.001[1]
Female	34 (33)	26 (16)	
Male	69 (67)	139 (84)	
Age	30.5 (10.3)	32.2 (8.6)	0.02[2]
Height (in)	69 [66, 71]	69 [67, 71]	0.17[3]
Weight (lbs)	175 [151, 206]	190 [166, 215]	0.03[3]
BMI	26.6 [24.3, 29.7]	28.1 [25.1, 30.8]	0.02[3]
Smoking, n (%)			0.23[1]
No	69 (67)	101 (61)	
Former	15 (15)	38 (23)	
Active	19 (18)	26 (16)	
Total	103	165	

[1] Chi-square; [2]Wilcoxon Rank sum; [3] T-test

Continuous Variables are reported as Mean (SD) or Median [IQR] based on normality of distribution

BMI = (lbs/ht^2) * 703

Table 2. Diagnoses of Dyspnea by Deployment History.

Diagnosis	Non-Deployed	Deployed
Asthma	14	27
Sarcoidosis	6	7
Pectus excavatum	11	0
Vocal cord dysfunction	3	8
Obstructive lung disease[1]	5	8
Diffuse parenchymal lung disease[2]	2	8
Pulmonary vascular disease[3]	1	4
Pleural disease[4]	0	2
Cardiovascular disease[5]	3	0
Occupational[6]	1	6
Acute eosinophilic pneumonia	1	0
Bronchogenic cyst	1	0
Deconditioning	1	3
Diaphragm weakness	1	2
Obstructive sleep apnea	0	1
Pulmonary nodules	1	0
Tuberculosis	1	0

[1]Includes allergic bronchopulmonary aspergillosis, bronchiectasis, bronchiolitis, COPD, exercise-induced bronchospasm, reactive airway dysfunction syndrome

[2] Includes Langerhans cell histiocytosis, systemic lupus erythematosus, hypersensitivity pneumonitis, drug-induced parenchymal lung disease, radiation-induced parenchymal lung disease, lymphangioleiomyomatosis, and idiopathic interstitial lung disease

[3] Includes pulmonary embolism, pulmonary hypertension, pulmonary arteriovenous malformation

[4] Includes pleural effusion, pneumothorax

[5]Includes heart failure, aortic valve disease, mitral valve prolapse

[6]Includes inhalational exposure (dust, burn pits, smoke, "toxic cloud"), burns, trauma

aorta (1 patient), pneumothorax (1 patient), pulmonary nodules (1 patient), a prominent left heart border (1 patient), interstitial lung disease (1 patient), prior granulomatous disease (1 patient), an elevated left hemidiaphragm (1 patient), scoliosis (1 patient) and findings suggestive of sarcoidosis (1 patient). In the deployed group, chest CT abnormalities included post-thoracic surgery changes (10 patients), hyperinflation (6 patients), a localized pulmonary infiltrate (5 patients), hilar and/or mediastinal lymphadenopathy (4 patients), interstitial lung disease (3 patients), pulmonary nodules (3 patients), prior granulomatous disease (3 patients), scarring (2 patients), pectus excavatum (2 patients), pneumothorax (2 patients), pleural thickening (2 patients), multiple pulmonary infiltrates (1 patient), bronchial wall thickening (1 patient), atelectasis (1 patient), diaphragm tenting (1 patient), and a pleural effusion (1 patient).

Table 4 displays the CPET and PFT results for the deployed and non-deployed groups, as well as the results after stratification by duration of deployment. Deployed personnel had a significantly lower FEV_1 (86.0 ± 15.2 vs. 91.5 ± 14.2% predicted, p=0.005) and FVC (83.2 ± 15.8 vs. 87.4 ± 14.8% predicted, p=0.04) compared to non-deployed personnel. Both groups had an abnormally low DLCO: 71.1% predicted for deployed personnel and 75.0% predicted for non-deployed personnel. Personnel deployed ≥365 days had a lower FEV_1 than personnel deployed <365 days and non-deployed personnel (85.7 ± 12.5 vs. 86.4 ± 17.6 vs. 91.5 ± 14.2% predicted, p=0.02), but there were no significant differences in any other PFT measurements.

Both the deployed and non-deployed groups had similar max HR (89.1 ± 8.7 and 89.5 ± 7.6% predicted, p=0.72) and a reduced VO_2 max (78.8 ± 18.4 and 79.4 ± 18.1% predicted, p=0.78). The only statistically significant difference was a lower AT in the deployed group (49.8 ± 17.3 vs. 55.8 ± 18.0% predicted, p=0.007). Non-deployed personnel had a significantly higher HRR compared to personnel deployed <365 days and personnel deployed ≥365 days (47.7 ± 14.9 vs. 47.3 ± 14.6 vs. 42.1 ± 13.7, p=0.01). There was also a significantly lower AT in personnel deployed <365 days compared to personnel deployed ≥365 days and non-deployed personnel (47.9 ± 14.9 vs. 51.5 ± 19.1 vs. 55.8 ± 18.0% predicted, p=0.01).

When stratified by the presence of a diagnosis causing dyspnea, deployed personnel with a diagnosis had a significantly lower AT compared to deployed personnel without a diagnosis and non-deployed personnel (48.2 ± 15.4 vs. 51.1 ± 18.6 vs. 55.8 ± 18.0% predicted, p=0.02) (Table 5). There was a significantly higher V_E/VCO_2 in deployed personnel with a diagnosis compared to non-deployed personnel and deployed personnel without a diagnosis (29 [IQR 26, 31] vs. 27 [IQR 25, 30] vs. 26 [IQR 25, 29], p=0.008). Deployed personnel with a diagnosis had lower FEV_1, FVC, and FEV_1/FVC values that were statistically significant when compared to non-deployed personnel and deployed personnel without a diagnosis.

Table 3. Diagnostic Test Abnormalities by Deployment History.

	Non-Deployed			Deployed			
Diagnostic Test	**Abnormal (n)**	**Total (n)**	**Percent Abnormal (%)**	**Abnormal (n)**	**Total (n)**	**Percent Abnormal (%)**	**P value[1]**
Chest x-ray	37	94	39	44	158	28	0.070
Chest CT	44	61	72	64	119	54	0.024
Methacholine	11	47	23	12	75	16	0.35
Echocardiogram	32	52	62	38	84	45	0.078
Laryngoscopy	4	22	18	8	32	25	0.74
Bronchoscopy	5	7	71	6	8	75	1.0

[1] Fischer Exact Test

Table 4. CPET and PFT Results by Deployment History and Duration of Deployment.

Variable	Reference Value	Non-Deployed (n=103)	Deployed (n=165)	P-value	Deployed <365 days (n=77)	Deployed ≥365 days (n=88)	P value
Exercise time (min)	None	9.67 (2.47)	9.60 (2.11)	0.82[1]	9.36 (2.04)	9.81 (2.16)	0.42[1]
Max HR (% predicted)	>90	89.5 (7.6)	89.1 (8.7)	0.72[1]	89.0 (8.1)	89.2 (9.2)	0.92[1]
Heart rate response	≤50	47.7 (14.9)	44.5 (14.3)	0.08[1]	47.3 (14.6)	42.1 (13.7)	0.01[1]
VO_2 max (% predicted)	>84	79.4 (18.1)	78.8 (18.4)	0.78[1]	76.4 (17.3)	80.9 (19.2)	0.27[1]
AT (% predicted VO_2 max)	>40	55.8 (18.0)	49.8 (17.3)	0.007[1]	47.9 (14.9)	51.5 (19.1)	0.01[1]
RR max (breaths/min)	<60	39 [34, 45]	37 [31, 46]	0.47[2]	37 [31, 48]	37 [32, 44]	0.73[2]
V_T/IC	<0.80	0.63 [0.54, 0.74]	0.68 [0.57, 0.80]	0.1[2]	0.65 [0.52, 0.75]	0.71 [0.58, 0.82]	0.05[2]
V_E/VCO_2(at AT)	<34	27 [25, 30]	27 [25, 30]	0.62[2]	27 [25, 29]	27 [25, 30]	0.82[2]
V_E max/MVV	0.72 ± 0.12	0.62 [0.53, 0.77]	0.65 [0.51, 0.76]	0.97[2]	0.62 [0.49, 0.76]	0.68 [0.54, 0.78]	0.42[2]
Max work rate (watts)	None	183.85 (53.72)	184.74 (42.94)	0.88[1]	178.49 (40.62)	190.28 (44.39)	0.28[1]
O_2 pulse (% predicted)	>80	86.8 [75.8, 99.6]	88.0 [73.1, 101.8]	0.98[2]	85.6 [73.0, 95.6]	90.8 [74.0, 108.4]	0.29[2]
FEV_1 (% predicted)	80 - 120	91.5 (14.2)	86.0 (15.2)	0.005[1]	86.4 (17.6)	85.7 (12.5)	0.02[1]
FVC (% predicted)	80 - 120	87.4 (14.8)	83.2 (15.8)	0.04[1]	82.9 (17.8)	83.4 (13.7)	0.11[1]
FEV_1/FVC (actual)	>70	80.2 [77.2, 82.9]	80.1 [75.5, 84.2]	0.78[2]	79.3 [75.7, 84.0]	81.3 [75.3, 84.3]	0.71[2]
TLC (% predicted)	80 - 120	89.4 (15.6)	86.9 (15.8)	0.33[1]	84.5 (15.1)	88.8 (16.2)	0.24[1]
DLCO (% predicted)	80 - 120	75.0 [66.5, 86.3]	71.1 [63.5, 81.8]	0.12[2]	70.0 [63.1, 82.8]	71.5 [63.6, 79.7]	0.3[2]

[1] T-test

[2] Wilcoxon Rank sum

Continuous Variables are reported as Mean (SD) or Median [IQR] based on normality of distribution

Table 5: CPET and PFT Results by Presence of a Diagnosis.

Variable	Reference Value	Non-Deployed (n=103)	Deployed with Diagnosis (n=73)	Deployed without Diagnosis (n=92)	P value
Exercise time (min)	None	9.67 (2.47)	9.16 (2.06)	9.95 (2.10)	0.08[1]
Max HR (% predicted)	>90	89.5 (7.6)	89.1 (8.7)	89.1 (9.6)	0.94[1]
Heart rate response	≤50	47.7 (14.9)	45.6 (14.0)	43.7 (14.6)	0.15[1]
VO_2 max (% predicted)	>84	79.4 (18.1)	76.5 (17.9)	80.6 (18.7)	0.34[1]
AT (% predicted VO_2 max)	>40	55.8 (18.0)	48.2 (15.4)	51.1 (18.6)	0.02[1]
RR max (breaths/min)	<60	39 [34, 45]	40 [30, 51]	36 [32, 42]	0.19[2]
V_T/IC	<0.80	0.63 [0.54, 0.74]	0.67 [0.50, 0.76]	0.69 [0.59, 0.82]	0.07[2]
V_E/VCO_2 (at AT)	<34	27 [25, 30]	29 [26, 31]	26 [25, 29]	0.008[2]
V_E max/MVV	0.72 ± 0.12	0.62 [0.53, 0.77]	0.66 [0.52, 0.81]	0.65 [0.51, 0.73]	0.77[2]
Max work rate (watts)	None	183.85 (53.72)	177.79 (40.86)	190.32 (43.96)	0.24[1]
O_2pulse (% predicted)	>80	86.8 [75.8, 99.6]	84.3 [70.6, 101.3]	89.2 [79.4, 103.0]	0.29[2]
FEV_1(% predicted)	80 - 120	91.5 (14.2)	84.4 (13.1)	87.4 (16.6)	0.009[1]
FVC (% predicted)	80 - 120	87.4 (14.8)	79.9 (15.1)	85.7 (16.0)	0.007[1]
FEV_1/FVC (actual)	>70	80.2 [77.2, 82.9]	78.4 [73.8, 83.6]	82.1 [77.6, 84.5]	0.03[2]
TLC (% predicted)	80 - 120	89.4 (15.6)	87.0 (13.2)	86.8 (17.9)	0.62[1]
DLCO (% predicted)	80 - 120	75.0 [66.5, 86.3]	70.0 [63.4, 80.8]	71.6 [63.6, 82.0]	0.28[2]

[1] T-test; [2] Wilcoxon Rank sum

Continuous Variables are reported as Mean (SD) or Median [IQR] based on normality of distribution

Stratification of CPET results by the onset of dyspnea revealed that non-deployed personnel had a significantly higher HRR compared to deployed personnel with onset pre-deployment and deployed personnel with onset during or post-deployment (47.7 ± 14.9 *vs.* 47.1 ± 14.3 vs. 42.4 ± 12.9, p=0.04) (Table 6). Anaerobic threshold was significantly lower in deployed personnel with onset pre-deployment compared to deployed personnel with onset during or post-deployment and non-deployed personnel (45.3 ± 20.8 vs. 52.1 ± 16.4 vs. 55.8 ± 18.0% predicted, p= 0.02). Deployed personnel with onset of dyspnea during or post-deployment had significantly lower DLCO values than non-deployed personnel or personnel with onset pre-deployment (70.0 [IQR 63.6, 77.6] *vs.* 75.0 [IQR 66.5, 86.3] vs. 75.7 [IQR 68.4, 93.5] % predicted, p=0.03). The medical record did not specify the onset of dyspnea for 57 deployed personnel, so those patients were excluded from this secondary analysis.

Discussion

The intent of this study was to evaluate the relationship between military deployment and pulmonary symptoms by comparing the CPET results of deployed and non-deployed personnel undergoing an evaluation for dyspnea. The primary analysis revealed no significant differences in CPET results between the two groups, with the exception of a lower AT in the deployed group that was within the accepted range of normal based on established reference values [21]. The VO_2 max was lower than predicted in both groups; however, this is not unexpected in a group of patients being evaluated for dyspnea.

Demographic differences may have affected the ability to detect a significant difference in VO_2 max and max HR, as deployed personnel were older and VO_2 max and max HR linearly regress with age [22-24]. The increased weight and BMI in the deployed group could have had a similar effect, as peak VO_2 max prediction is also dependent on weight

Table 6: CPET and PFT Results by Onset of Dyspnea.

Variable	Reference Value	Non-Deployed (n=103)	Deployed with Onset Pre-deployment (n=34)	Deployed with Onset During/ Post-deployment (n=74)	P value
Exercise time (min)	None	9.67 (2.47)	9.15 (2.31)	9.81 (1.97)	0.41[1]
Max HR (% predicted)	>90	89.5 (7.6)	85.7 (9.1)	89.9 (8.0)	0.05[1]
Heart rate response	≤50	47.7 (14.9)	47.1 (14.3)	42.4 (12.9)	0.04[1]
VO_2 max (% predicted)	>84	79.4 (18.1)	77.7 (22.9)	81.2 (17.4)	0.65[1]
AT (% predicted VO_2 max)	>40	55.8 (18.0)	45.3 (20.8)	52.1 (16.4)	0.02[1]
RR max (breaths/min)	<60	39 [34, 45]	37 [30, 55]	38 [35, 44]	0.92[2]
V_T/IC	<0.80	0.63 [0.54, 0.74]	0.69 [0.54, 0.84]	0.66 [0.57, 0.76]	0.58[2]
V_E/VCO_2 (at AT)	<34	27 [25, 30]	28 [26, 32]	27 [25, 30]	0.17[2]
V_E max/MVV	0.72 ±0.12	0.62 [0.53, 0.77]	0.65 [0.46, 0.78]	0.67 [0.55, 0.75]	0.46[2]
Max work rate (watts)	None	183.85 (53.72)	174.63 (47.74)	191.78 (41.08)	0.25[1]
O_2 pulse (% predicted)	>80	86.8 [75.8, 99.6]	87.3 [74.7, 107.7]	90.4 [79.6, 102.4]	0.76[2]
FEV_1 (% predicted)	80 - 120	91.5 (14.2)	89.0 (17.5)	86.6 (13.8)	0.1[1]
FVC (% predicted)	80 - 120	87.4 (14.8)	86.7 (17.0)	84.3 (14.6)	0.41[1]
FEV_1/FVC (actual)	>70	80.2 [77.2, 82.9]	80.5 [77.8, 84.6]	81.3 [74.6, 84.8]	0.72[2]
TLC (% predicted)	80 - 120	89.4 (15.6)	85.3 (9.7)	88.2 (17.6)	0.7[1]
DLCO (% predicted)	80 - 120	75.0 [66.5, 86.3]	75.7 [68.4, 93.5]	70.0 [63.6, 77.6]	0.03[2]

[1] T-test; [2]Wilcoxon Rank sum

Continuous Variables are reported as Mean (SD) or Median [IQR] based on normality of distribution

[19,25-27]. If these demographic differences did have an impact, they could have lowered both the VO_2 max and max HR in the deployed group. The age difference would not have been expected to significantly impact cardiovascular and respiratory variables, as the change in those variables with age is minimal until age 50 [27,28]. Additionally, the number of cigarette smokers in the two groups was not significantly different, which is important because smoking may impact CPET respiratory variables [23].

The three secondary analyses revealed some statistically significant differences in AT, V_E/VCO_2, HRR and max HR, but the values for these variables were all within the accepted range of normal [20]. Although these differences were statistically significant, they are not likely clinically significant because the mean values were still within predicted range of normal. While deployment length has been associated with increased pulmonary symptoms, this study did not identify an impact of deployment length on CPET results [5]. The similar CPET results among deployed personnel stratified by the onset of dyspnea argue against a significant sustained impact from potential inhalational exposures experienced during deployment [2,6,8]. Deployed personnel were specifically stratified by the presence of a dyspnea diagnosis to look for a pattern of CPET or PFT abnormalities among deployed personnel without a diagnosis, but the results for this group revealed a decreased VO_2 max, minimally decreased max HR, and low DLCO, not suggestive of any particular disease process.

Pulmonary function data were notable for lower, but still normal FEV_1 and FVC values in the deployed group. Deployed personnel with a specific diagnosis had a significantly lower and slightly decreased FVC; this is not an unexpected finding in patients with established pulmonary disease. The DLCO was significantly lower in deployed personnel with onset of dyspnea during or post-deployment, which could indicate the development of interstitial or emphysematous lung changes related to inhalational exposures during deployment; however, this finding did not correlate with a reduction in TLC or the presence of imaging abnormalities, and there was actually a significantly higher percentage of abnormal chest CTs in non-deployed personnel. Additionally, other PFT values in the secondary analysis were not suggestive of an obstructive or restrictive process. There were 13 more diagnoses of asthma in deployed personnel, but asthma is typically associated with a normal or increased DLCO [29].

Cardiopulmonary exercise testing may not be the ideal modality to diagnose the etiology of a patient's dyspnea in this population. The 2002 study by Morris *et al.* of 105 active duty patients with exertional dyspnea concluded that CPET added little to the diagnostic evaluation compared to pulmonary function tests, methacholine challenge, laryngoscopy and chest imaging [15]. A 2009 study of the same cohort used age-matched controls when interpreting CPET results of the patients with exertional dyspnea. Compared to established reference values using age-matched controls resulted in statistically significant differences in the sensitivity (53% vs. 12%) and specificity (31% vs. 96%) of V_T/IC, which suggests CPET may be insensitive in detecting mild pulmonary disease in young healthy adults [30]. Finally, the 2011 King study of deployed military personnel found to have constrictive bronchiolitis on surgical lung biopsy utilized CPET in some of the patients evaluated and there were significant decreases in VO_2 max and AT (compared to published normal controls) but no increase in measured respiratory parameters [2].

This study has several limitations. The retrospective design subjects the study to confounding variables. There is a lack of final diagnoses in many patients and incomplete data sets to ideally compare differences between groups. Due to the lack of documentation of specific inhalational exposures, onset of dyspnea symptoms was used as a surrogate measure to investigate the effect of any deployment exposures, which is not an exact substitute. Lastly, the diagnostic utility of CPET is not absolute, as previous studies have demonstrated that it has a limited diagnostic yield, especially in young healthy adults with mild disease [30]. Both the 2002 Morris *et al.* study of exertional dyspnea and the recent 2014 STAMPEDE study are examples of this, as a diagnosis was not established in 25% and 42% of patients in those studies, respectively [3,15].

Conclusions

This review of CPET values in military personnel evaluated for dyspnea revealed small significant differences in specific CPET

values between deployed and non-deployed personnel; however, the values in both groups were within normal limits (based on published reference values) and CPET interpretation did not indicate an increase in pulmonary abnormalities in the deployed population. The utility of CPET evaluation in this population may be limited and may only establish exercise capacity. Future prospective trials investigating CPET in the relationship between military deployment and pulmonary symptoms are warranted to help further characterize any association.

Authors' contributions

Dr. Hiles conducted the electronic medical record review and drafted the manuscript. Dr. Morris designed the study and reviewed and edited the manuscript. Dr. Porr and Dr. Hannah reviewed and edited the manuscript.

Acknowledgements

The authors would like to thank LeeAnn Zarzabal for performing the statistical analysis.

Competing interest

Dr. Morris is part of the Speaker's Bureau for Spiriva (Boehringer-Ingelheim). Dr. Hiles, Dr. Porr and Dr. Hannah have no competing interests.

Disclosure

The view(s) expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army, the Department of the Air Force and Department of Defense or the U.S. Government.

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