The Effect of Deployment on Pulmonary Function in Military Personnel With Asthma

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ABSTRACT
Introduction:
Military personnel with a diagnosis of asthma report increased respiratory symptoms in the deployment and post-deployment periods. The long-term effect of deployment on pulmonary function in this population is unknown. This study sought to determine the effect of deployment on post-deployment pulmonary function in active duty military personnel with asthma.

Materials and Methods:
A retrospective chart review of active duty military personnel with deployment to southwest Asia and an ICD-9 diagnosis of asthma with documented pre- and post-deployment spirometry was performed.

Results:
A total of 642 active duty individuals with a diagnosis of asthma and documented spirometry with deployment to southwest Asia between 2006 and 2015 were identified. Of these, 76 individuals were identified with pre- and post-deployment spirometry. There was no significant change in the post-deployment forced expiratory volume at 1 second (% predicted), from 86.0 ± 14.8 to 87.6 ± 14.4 (P = .30). There was no significant change in post-deployment forced vital capacity (% predicted), from 93.8 ± 12.4 to 94.9 ± 12.1 (P = .42). The absolute change in forced expiratory volume at 1 second (L) after bronchodilator administration was decreased from pre-deployment to post-deployment (+0.31 ± 0.26 to +0.16 ± 0.23; P = .02).

Conclusions:
There was no significant post-deployment change in spirometry in this military population with asthma deployed to southwest Asia. These findings suggest that deployment itself is not associated with any short-term deleterious effect on post-deployment spirometric measures of lung function in many military personnel with asthma.

INTRODUCTION
The effect of deployment on the respiratory health of military personnel deployed to southwest Asia (SWA) is an area of active investigation. Deployment to theaters in SWA is associated with environmental exposures to airborne hazards that include geologic dusts, burn pit smoke, vehicle exhaust emissions, industrial air pollution, and other isolated exposures, which may have deleterious effects on pulmonary function. A 2007 survey of military personnel and contractors deployed in support of operations in Afghanistan and Iraq was notable for an increase in self-reported respiratory symptoms, which was more pronounced in those with a self-reported prior diagnosis of asthma and associated with higher healthcare utilization. Increases in deployment-related respiratory complaints are well documented, though epidemiologic data have failed to show an increase in respiratory disease diagnoses. A prospective evaluation of post-deployment individuals with new respiratory symptoms found that many individuals had evidence of airway hyperreactivity and/or asthma. Some data suggest an increased incidence of asthma in the deployed population; however, undiagnosed pre-deployment lung disease and the lack of objective data to support the diagnosis of asthma may be significant confounding factors. A recent prospective evaluation of military personnel found that deploying soldiers were older, were heavier, frequently smoked, and may have an undiagnosed pre-deployment lung disease. Post-deployment spirometry demonstrated no significant change in forced expiratory volume at 1 second (FEV₁) or forced vital capacity (FVC) in this population. The susceptibility of those military personnel with asthma to the potentially antagonizing effects of airborne exposures in the deployed environment is unknown. A retrospective case–control study of military personnel with asthma who...
underwent a fitness for duty evaluation for asthma compared those deployed individuals with non-deployers. This study demonstrated no difference in spirometry between groups diagnosed with asthma and no difference in spirometry among deployed military personnel who were diagnosed with asthma before and after deployment. While these data suggest no significant relationship between rates of asthma diagnosis or disease severity and history of deployment to SWA, the true effect of deployment on pulmonary function in the military population with a diagnosis of asthma remains unknown. There are no currently reported data that specifically address the effect of deployment on spirometry values in asthmatic military personnel. We hypothesized that military personnel with a diagnosis of asthma will have a reduction in either FVC or FEV₁ following the deployment to SWA because of potential airborne exposures.

METHODS
A retrospective cohort study of military personnel with deployment to SWA between 2006 and 2015 with pre-existing asthma and documented pre- and post-deployment spirometry was performed. The study was reviewed and approved by the Brooke Army Medical Center Institutional Review Board (C.2016.174d). An initial search of the Military Health System database identified individuals in the DoD electronic medical record with (1) an ICD-9 code for asthma (493.xx), (2) a Common Procedural Terminology (CPT) code for spirometry (94010 and/or 94060), and (3) an evaluation in a DoD pulmonary clinic with a minimum of three encounters. Deployment dates to SWA between 2006 and 2015 were verified by the Defense Manpower Data Center. Patient demographics and spirometry data were manually extracted from the electronic medical record, and patients with pre- and post-deployment spirometry were identified. Prescriptions for inhaled corticosteroids (ICS) and long-acting beta agonists (LABA) were extracted from the electronic medical record and compared with dates of spirometry studies to determine pharmacotherapy at the time of those studies. Tobacco use was extracted from the electronic medical record in similar fashion. Data and results were organized using Microsoft Excel (Microsoft, Seattle, WA, USA).

Pre- and post-deployment spirometry were included that met American Thoracic Society/European Respiratory Society standards for acceptability and repeatability. Bronchodilator testing was performed with two to three puffs of albuterol or similar short-acting beta agonists by metered dose inhaler. FEV₁, FVC, and, if performed, post-bronchodilator FEV₁ were recorded as absolute values and reported as percent of predicted values according to patient demographics and the National Health and Nutrition Examination Survey III reference values in accordance with American Thoracic Society/European Respiratory Society guidelines. The FEV₁/FVC ratio was calculated, and obstruction was defined as below the lower limit of normal or 95% CI.

The primary analysis included all identified military personnel with at least one SWA deployment between 2006 and 2015 with an ICD-9 code for asthma, a CPT code for spirometry, and valid pre- and post-deployment spirometric data. The primary outcome of the study was the change in percent of predicted FEV₁ and FVC observed between the pre- and post-deployment spirometry data. Medication use (ICS and LABA) was examined to measure any significant change in pharmacotherapy, which might otherwise confound results of the primary analysis. Subgroup analyses were performed to evaluate spirometric changes in those individuals with tobacco use or spirometric obstruction at the time of pre-deployment spirometry. Analysis of individuals with pre- and post-deployment bronchodilator administration was performed to observe both the absolute change in FEV₁ after bronchodilator administration and the percent of predicted FEV₁ after bronchodilator administration.

Statistical analysis was performed using JMP v13.2 (SAS Corp, Cary NC). Continuous data are expressed as mean ± SD unless otherwise noted. Paired and unpaired two-sided t-tests were used to compare continuous variables as appropriate. McNemar’s test was used on paired nominal data as appropriate. A linear regression model was constructed to estimate the relationship between spirometric variables and cumulative deployment length. Standardized mean difference (Cohen’s d) was calculated to measure the effect size when applicable, and value of 0.2 was considered a small effect size, 0.5 a medium effect size, and 0.8 a large effect size. A P-value of less than .05 was considered statistically significant.

RESULTS
A total of 642 military personnel with documented deployment to locations in SWA between 2006 and 2015 verified by the Defense Manpower Data Center and an established diagnosis of asthma by ICD-9 code with documented spirometry by CPT code were identified. Of these, only 76 (11.8%) individuals were identified with both pre- and post-deployment spirometry (Fig. 1). The average age was 31.9 years, and the cohort was 71% male (n = 54). Tobacco use was noted in 17.1% (n = 13), while ICS use (n = 5, 6.6%) and LABA use (n = 4, 5.3%) were notably low at the time of pre-deployment spirometry. Mean body mass index was 27.4 ± 3.9 kg/m², and 71% (n = 54) of the cohort was overweight or obese.

Pre- and post-deployment spirometry reflected 272 ± 199 total days of deployment. Twenty-one subjects served more than one deployment between spirometry assessments, of which 16 subjects deployed twice, 3 subjects deployed three times, and 2 subjects deployed four times. The average time elapsed between pre- and post-deployment spirometry was 1284 ± 864 days, and the average time between redeployment and post-deployment spirometry was 433 ± 655 days.

There were no significant changes in post-deployment FEV₁ (% predicted) when compared to pre-deployment
values (87.6 ± 14.4 from 86.0 ± 14.8; \( P = .30 \)) and post-deployment FVC (% predicted) when compared to pre-deployment values (94.9 ± 12.1 from 93.8 ± 12.4; \( P = .42 \)) (Table I). The proportion of individuals with obstructive spirometry was also not significantly changed from 28.9% to 26.3% (odds ratio [OR] 0.75, 95% CI 0.21-2.47, \( P = .79 \)). ICS use and LABA use showed no change from 6.6% to 10.5% (OR 1.60, 95% CI 0.46-6.22, \( P = .58 \)) and from 5.3% to 6.6% (OR 1.2, 95% CI 0.27=6.30, \( P = 1.00 \)), respectively. Tobacco use did not significantly change from 17.1% to 11.8% (OR 0.33, 95% CI 0.03-1.86, \( P = .29 \)). Mean body mass index (kg/m\(^2\)) did not change from 27.4 ± 3.9 to 27.7 ± 3.7 (\( P = .16 \)), and the proportion of those who were overweight or obese did not change from 71% to 76% (OR 3.00, 95% CI 0.54-30.39, \( P = .29 \)). An exposure–response plot was constructed to determine the effect of increasing deployment exposure on change in FEV\(_1\) and FVC after deployment. Linear regression failed to show any significant correlation between change in FEV\(_1\) (\( R^2 = 0.000 \)) and change in FVC (\( R^2 = 0.002 \)) with total duration of deployment (Fig. 2).

Subgroup analysis of 22 individuals with spirometric obstruction demonstrated a trend towards statistical significance in the change in FEV\(_1\) (% predicted) from 74.7 ± 10.0 to 80.9 ± 14.4 (\( P = .06 \)), showing a medium effect size (Cohen’s \( d = 0.50 \)); however, no change in FVC (% predicted) from 91.8 ± 11.9 to 96.2 ± 13.8 (\( P = .16 \)) after deployment (Table II), showing a small effect size (Cohen’s \( d = 0.33 \)), was seen. An exposure–response curve (Supplemental Figure S1) did not demonstrate significant correlation between duration of deployment and change in FEV\(_1\) (\( R^2 = 0.008 \)) and FVC (\( R^2 = 0.025 \)). There was no significant change in ICS (\( P = .48 \)) or LABA (\( P = 1.00 \)) use. Tobacco use in this subgroup did not change significantly from 9.1% \((n=2)\) to 13.6% \((n=3)\) at the time of post-deployment spirometry. The obstructed subgroup demonstrated a non-significant change of +6.2 ± 14.0 in FEV\(_1\) (% predicted), while the normal subgroup demonstrated a non-significant change of −0.3 ± 12.7 in FEV\(_1\) (% predicted) \((P = .06)\). The obstructed group demonstrated a non-significant change of +4.3 ± 13.7 in FVC (% predicted), while the normal subgroup demonstrated a non-significant change of −0.02 ± 10.7 in FVC (% predicted) \((P = .13)\).

Further subgroup analyses were performed on individuals with tobacco use and spirometric obstruction at the time of initial pre-deployment spirometry. In the subgroup of 13 individuals with pre-deployment tobacco use, there was no significant change in FEV\(_1\) (% predicted) from 84.9 ± 9.7 to 84.7 ± 9.6 (\( P = .95 \)) or FVC from 91.5 ± 10.7 to 92.8 ± 5.9 (\( P = .59 \)) after deployment. An exposure–response curve did not demonstrate significant correlation between

**TABLE I.** Summary of 76 Active Duty Service Members With Asthma

| Variable     | Pre-deployment | Post-deployment | Odds ratio (95% CI) | \( P \)-value |
|--------------|----------------|-----------------|---------------------|--------------|
| Age (years)  | 31.9 ± 6.7     | 35.4 ± 6.9      | 0.16                |              |
| Male (%      | 54 (71%)       | 54 (71%)        |                     |              |
| BMI (kg/m\(^2\)) | 27.4 ± 3.9  | 27.7 ± 3.7      | 1.00                |              |
| ICS (n)      | 5 (6.6%)       | 8 (10.5%)       | 1.60 (0.46-6.22)    | 0.58         |
| LABA (n)     | 4 (5.3%)       | 5 (6.6%)        | 1.25 (0.27-6.30)    | 1            |
| Tobacco (n)  | 13 (17.1%)     | 9 (11.8%)       | 0.33 (0.03-1.86)    | 0.29         |
| Obstruction (n) | 22 (22.3%)  | 20 (26.3%)      | 0.75 (0.21-2.47)    | 0.79         |
| FEV\(_1\) (%)| 86.0 ± 14.8    | 87.6 ± 14.4     | 0.06                |              |
| FVC (%)      | 93.8 ± 12.4    | 94.9 ± 12.1     | 0.42                |              |
| FEV\(_1\)/FVC| 0.75           | 0.75            |                     |              |

Abbreviations: BMI, body mass index; FEV\(_1\), forced expiratory volume at 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; LABA, long-acting beta agonists.
FIGURE 2. Change in forced expiratory volume at 1 second (FEV\textsubscript{1}) and forced vital capacity (FVC) vs. days deployed.

TABLE II. Summary of 22 Active Duty Service Members With Asthma and Obstruction

| Variable       | Pre-deployment | Post-deployment | P-value |
|----------------|----------------|-----------------|---------|
| ICS (n)        | 0 (0%)         | 2 (9.1%)        | 0.48    |
| LABA (n)       | 0 (0%)         | 1 (4.5%)        | 1       |
| Tobacco (n)    | 2 (9.1%)       | 3 (13.6%)       |         |
| Obstruction (n)| 22 (100%)      | 14 (63.6%)      |         |
| FEV\textsubscript{1} (%) | 74.7 ± 10.0 | 80.9 ± 14.4 | 0.06    |
| FVC (%)        | 91.8 ± 11.9    | 96.2 ± 13.8     | 0.16    |
| FEV\textsubscript{1}/FVC | 0.66      | 0.68            |         |

Abbreviations: FEV\textsubscript{1}, forced expiratory volume at 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; LABA, long-acting beta agonists.

duration of deployment and change in FEV\textsubscript{1} ($R^2 = 0.014$) and FVC ($R^2 = 0.034$). There was no significant change in ICS ($P = .48$) or LABA ($P = 1.00$) use. Tobacco use within this subgroup declined from 100% ($n = 13$) at the time of pre-deployment spirometry to 54% ($n = 7$) at the time of post-deployment spirometry. The group with pre-deployment tobacco use demonstrated no change in FEV\textsubscript{1} (−0.2 ± 11.3% predicted) and the group without pre-deployment tobacco use also demonstrated no change in FEV\textsubscript{1} (+2.0 ± 13.7% predicted) ($P = .60$). Similarly, pre-deployment tobacco use was associated with no change in FVC (+1.3 ± 8.3% predicted) as well as those without pre-deployment tobacco use demonstrated no change in FVC (+1.1 ± 12.4% predicted) ($P = .94$).

Thirty-three military personnel had pre- and post-deployment spirometry that included bronchodilator administration. The average age of this subgroup was 32.1 years, and the cohort was 67% male ($n = 22$). The absolute change in FEV\textsubscript{1} (L) after bronchodilator administration was significantly decreased from +0.31 ± 0.26 pre-deployment to +0.16 ± 0.23 post-deployment ($P = .02$) (Supplemental Table S1). There was no significant change in the post-bronchodilator FEV\textsubscript{1} (% predicted) from 88.8 ± 14.5 to 89.4 ± 9.8 ($P = .80$) There was no change in pre-bronchodilator FEV\textsubscript{1} (% predicted) from 81.3 ± 14.8 to 85.4 ± 12.9 ($P = .12$). As in the main study group, there was no significant change in ICS use, LABA use, or tobacco use in the subgroup with bronchodilator administration.

DISCUSSION

In this retrospective study, no post-deployment change in FEV\textsubscript{1} or FVC was observed in this population of military personnel with history of deployment to SWA between 2006 and 2015 and an ICD-9 diagnosis of asthma with documented pre- and post-deployment spirometry. No significant change in pre- and post-deployment ICS or LABA use was observed. There was no significant change in pre- and post-deployment tobacco use or mean body mass index. These findings suggest...
that treatment effect, tobacco use, and obesity are unlikely to significantly confound the observed outcome. The primary analysis was supplemented with an exposure–response curve that did not show any significant correlation between duration of deployment and observed changes in spirometry. The negative results of the main study group were also demonstrated in the subgroup analyses of those individuals with tobacco use and without spirometric obstruction before deployment.

Subgroup analyses were performed on those with pre-deployment tobacco use and those with pre-deployment spirometric obstruction to determine if these populations may be more likely to experience lasting effects of deployment on pulmonary function. Of interest, there was a non-significant increase of 6.2 in FEV1 (% predicted) in those individuals with pre-deployment spirometric obstruction. This is contrasted with a non-significant 0.3 decrease in FEV1 (% predicted) in those individuals without initial spirometry obstruction. Unpaired intergroup comparison of those with and without pre-deployment spirometric obstruction demonstrates a +6.5 change in FEV1 (% predicted) after deployment in favor of those with pre-deployment obstruction (P = .06). Although this was not statistically significant, there was a medium effect size (Cohen’s d = 0.50). This trend is not intuitive, and one may expect any difference to favor those without pre-deployment obstruction. It is possible that asthma control in the subgroup with pre-deployment obstruction improved with the simple passage of time as improvement over time is well-documented in the natural history of asthma.13,14 Although we were not able to assess the level of exercise in this population, frequent exercise is less common in the deployed environment and aerobic endurance can decline;15 a meta-analysis of physical training in the asthmatic population demonstrated no significant effect on FEV1 and FVC.16 Our observed trend to improve post-deployment FEV1 in the asthmatic population with pre-deployment obstruction cannot be easily explained as an effect of deployment, but its presence does suggest that deployment is not associated with any deleterious effect on post-deployment spirometric measures of lung function in this population.

Our retrospective study population included those military personnel with an ICD-9 diagnosis of asthma who may be more susceptible to respiratory symptoms and spirometric changes associated with airborne hazards in the SWA deployment environment. Our findings in this population mirror those reported in a prospective study of soldiers deploying to SWA recruited from the pre-deployment processing center in Fort Hood, TX, which reported non-significant increases in both FEV1 and FVC after deployment.9

The present study makes several important contributions to the existing literature. It provides the first pre- and post-deployment spirometric evaluation of lung function in the military population with history of asthma and deployment to SWA. Although baseline lung function is lower in the asthmatic population we studied (FEV1 86.0% predicted), when compared with the general population (FEV1 95.2% predicted) of the Study of Active Military Personnel for Pulmonary Disease Related to Environmental Deployment Exposure II trial, a non-significant increase in FEV1 and FVC is seen in both populations. These data sets both provide evidence that there is no measurable effect of deployment on post-deployment spirometric measures of lung function, even among military personnel with existing asthma and reduced baseline spirometry.

The present study also provides the first pre- and post-deployment spirometric evaluation of lung function that includes bronchodilator administration. Notably, in the subgroup of individuals with bronchodilator administration, there was a statistically significant reduction in the absolute change in FEV1 (L) after bronchodilator administration. While this result may suggest reduced bronchodilator efficacy after deployment, there was no significant difference in the post-bronchodilator FEV1 (% predicted). Taken together, these results assume an improved pre-bronchodilator FEV1 (% predicted) after deployment in line with that reported in the subgroup with bronchodilator administration for the same reasons offered for the post-deployment improvement in FEV1 (% predicted) in the obstructed subgroup.

The retrospective nature of our study introduces selection bias. We identified relatively few asthmatic individuals (12% of the initial cohort) with documented pre- and post-deployment spirometry. While our findings may not reflect the larger population of military personnel with asthma, they do support the prior finding of no significant difference in the spirometry data of military personnel diagnosed with asthma before and after deployment.10 The ICD-9 diagnosis of asthma was confirmed by airway obstruction and bronchodilator response or reactive bronchoprovocation testing in many, though not all, patients. Rates of ICS and LABA use were low and suggest mild or intermittent disease. It is unknown if these individuals with mild or intermittent disease may be less susceptible to any effects of deployment. The differences in time elapsed between spirometry dates and deployment dates reduce the ability to detect transient acute and subacute changes in pulmonary function associated with deployment. Strengths of our study include the requirement for three encounters in DoD pulmonary clinics, objective measurements of pre- and post-deployment pulmonary function, and inclusion of available bronchodilator data.

CONCLUSION
There was no change in FEV1 and FVC in the small group of military personnel with SWA deployment between 2006 and 2015 with an ICD-9 diagnosis of asthma and documented pre- and post-deployment spirometry. Furthermore, no change in asthma control regimen was noted. There was also no readily apparent correlation between duration of deployment exposure and change in pulmonary function. These data do not suggest any detrimental effect of deployment on post-deployment spirometric measures of lung function in this limited population with both pre-/post-measurements. More
careful monitoring of asthmatics post-deployment is clearly warranted.

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J.W. contributed to data collection and data analysis and was the primary manuscript author; B.B. contributed to data collection; R.W. contributed to data analysis and presentation; M.H. was the tertiary manuscript author; M.M. contributed to protocol development, data collection, and data analysis and was the secondary manuscript author.

SUPPLEMENTARY MATERIAL
Supplementary material is available at Military Medicine online.

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CONFLICT OF INTEREST STATEMENT
Dr. Morris is paid speaker for GSK and Janssen Pharmaceuticals.

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