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Title: Traumatic Injury and Atrial Fibrillation Among Deployed Service Members

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Abstract

Introduction. Atrial Fibrillation and Atrial Flutter (AF/AFL), the most common atrial arrhythmias, have never been examined in combat casualties. In this study, we investigated the impact of traumatic injury on AF/AFL among service members with deployment history.

Methods. Sampled from the Department of Defense (DoD) Trauma Registry (n=10,000), each injured patient in this retrospective cohort study was matched with a non-injured service member drawn from the Veterans Affairs/DoD Identity Repository. The primary outcome was AF/AFL diagnosis identified using ICD-9-CM and ICD-10-CM codes. Competing risk regressions based on Fine and Gray subdistribution hazards model with were utilized to assess the association between injury and AF/AFL.

Results. There were 130 reported AF/AFL cases, 90 of whom were injured and 40 were non-injured. The estimated cumulative incidence rates of AF/AFL for injured was higher compared to non-injured patients (HR = 2.04; 95% CI = 1.44, 2.87). After adjustment demographics and tobacco use, the association did not appreciably decrease (HR = 1.90; 95% CI = 1.23, 2.93). Additional adjustment for obesity, hypertension, diabetes, and vascular disorders, the association between injury and AF/AFL was no longer statistically significant (HR: 1.51; 95% CI = 0.99, 2.52).

Conclusion. Higher AF/AFL incidence rate was observed among deployed service members with combat injury compared to servicemembers without injury. The association did not remain significant after adjustment for cardiovascular-related covariates. These findings highlight the need for combat casualty surveillance to further understand the AF/AFL risk within the military population and to elucidate the potential underlying pathophysiologic mechanisms.

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Introduction

Atrial fibrillation (AF) and atrial flutter (AFL), the most common atrial arrhythmias, affect over 3 million adults in the United States (US) (1). Secondary AF increases the risk of new onset AF and is often precipitated by surgery, infection, and myocardial infarction (2, 3). A recent study suggests that combat injury increases risks of hypertension, diabetes mellitus, and coronary heart disease (4), which are risk factors of AF/AFL (5, 6). However, AF and AFL have never been examined in combat casualties. In this study, we investigated the impact of traumatic injury on the incidence of AF or AFL (AF/AFL) among service members with deployment history.

Methods

In this retrospective cohort study, 10,000 service members with combat-related trauma during deployment in Iraq or Afghanistan (February 1, 2002 – June 14, 2016) were sampled from the Department of Defense (DoD) Trauma Registry. Diagnoses within 100 days from injury were excluded as they could represent a complication of the trauma itself. Each injured patient was matched with a non-injured service member drawn from the Veterans Affairs/DoD Identity Repository based on birth year (±1 year), sex (male or female), and service branch (Army, Air Force, Marines, Navy, and Coast Guard). Additional data were queried from the Military Health System Data Repository, the Joint VA-DoD Suicide Data Repository National Death Index extract (7), the Defense Manpower Data Center, and the Veterans Informatics and Computing Infrastructure. Of the 10,000 injured service members, 1,164 patients were excluded due to any of the following: [1] no matched controls were found; [2] death occurred within 90 days from the index date; [3] pre-existing health conditions existed; or [4] outcome information was missing.

The primary outcome was diagnosis of AF or AFL using International Classification of Diseases-9 Clinical Modification (ICD-9-CM) and ICD-10-CM codes (see Supplemental Table).

Competing risk regressions based on Fine and Gray subdistribution hazards model with time-varying covariates were utilized to assess the association between injury and AF/AFL, accounting for mortality (competing risk): (Model 1) bivariate analysis; (Model 2) adjusted for age (in years), race/ethnicity (Hispanic, non-Hispanic White, non-Hispanic Black, Non-Hispanic Asian/Native Hawaiian/Other Pacific Islander, Other including multi-racial), rank [officer, senior (enlisted, E5-E9), junior (enlisted, E1-E4)], marital status (single, married), active status (active duty, national guard/reserve), and tobacco use (yes, no, unknown); and (Model 3) additionally adjusted for obesity (yes, no), hypertension (yes, no), diabetes (yes, no), and vascular disorders such as myocardial infarction (yes, no) as defined by ICD-9-CM and ICD-10-CM codes (see Supplemental Table). The age variable, used as a matching variable, was added to Model 2 to control for potential residual confounding effects by age. The study was approved by the David Grand USAF Medical Center IRB, the University of Utah IRB, and the Research Review Committee of the VA Salt Lake City Health Care System.

Results

Of the 10,000 patients originally queried, 8,836 were matched to uninjured service members and did not meet the exclusion criteria, resulting in a total study sample of 17,672. Among these patients, 98% were males and 72% in the Army. The median age was 24 (IQR = 17-59). **Table 1** shows demographic distributions by injury status. For both groups, the majority were non-Hispanic Whites, junior enlisted (E1-E4), single (or unmarried), and active component (as opposed to reserves or National Guard). Over a third of both groups had unknown tobacco use.

There were 130 reported AF/AFL cases, 90 of whom were injured (cumulative incidence: 10.2 cases per 1,000 injured, deployed servicemembers) and 40 were non-injured (cumulative incidence: 4.5 cases per 1,000 injured, deployed servicemembers). **Figure 1** shows higher estimated unadjusted cumulative incidence rates of AF/AFL for injured versus non-injured patients, with a statistically significant unadjusted hazard ratio (HR) of 2.04 (Model 1: 95% CI = 1.44, 2.87) as shown in **Table 2**. The association did not appreciably decrease with adjustment of demographic covariates and tobacco use (Model 2: HR = 1.90; 95% CI = 1.23, 2.93). After adjustment for obesity, hypertension, diabetes, and vascular disorders, the association between injury and AF/AFL was no longer significant (Model 3: HR: 1.51; 95% CI = 0.99, 2.52).

Conclusions

Our findings suggest increased AF/AFL incidence among deployed service members with combat injury compared to members without injury. The association remained statistically significant after controlling for demographics. However, it did not remain significant after adjustment for cardiovascular-related covariates. Differences in obesity, hypertension, diabetes, and vascular disorders could explain the observed association between injury and AF/AFL. Alternatively, it is possible that the robust HR of 1.51 might have been statistically significant with longer follow-up.

In the general population, patients with traumatic injury, particularly to the nervous system, have increased risk of developing AF/AFL (8). To our knowledge, no prior study has investigated the relationship between any traumatic injury and AF/AFL among deployed service members. Our results may provide some evidence of AF/AFL as a potential mechanism linking traumatic injury and neurologic disorders (e.g., stroke) (9). After adjusting for cardiovascular-

related covariates, the shift of HR towards the null suggests potential mediating effects of the cardiovascular covariates on the increased incidence rate of AF/AFL after traumatic injury. The mechanisms between combat injury and AF/AFL remain to be established, as multiple pathways are possible. Several post-combat factors are associated with AF/AFL. For example, a recent prospective study on young and middle-aged veterans showed post-traumatic stress disorder and emotional distress increased risk of AF/AFL (10).

Several limitations of our study are worth noting. First, AF/AFL, although they share very similar symptoms, have different pathogenesis. Our study did not differentiate the two conditions due to our inclusion of certain ICD codes that combine atrial fibrillation and atrial flutter, potentially resulting in different AF-specific and AFL-specific incidence rates. Second, the samples from the military components do not necessarily represent the US population. Casualties from military combat are a unique group of patients, and our results may not be generalizable to patients from the general population. Third, the available information on tobacco use was limited, with unknown tobacco use in 37.5% of the sample. Lastly, although we have carefully controlled for effects of potential confounders through matching and statistical analysis, unmeasured or unknown residual confounding remains possible (4).

In conclusion, our findings provide some evidence of increased incidence of AF/AFL among service members with combat-related traumatic injury. It is important to note that this cohort is relatively young and will develop further risk factors for AF/AFL over time. This implies that surveillance of combat casualties is required to further define AF/AFL risk and to elucidate the potential underlying pathophysiologic mechanisms.

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