Cardiovascular Risk Factors in Deployed Service Members With and Without Acute Coronary Syndromes

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Background: Acute coronary syndromes (ACSs) occur in deployed military personnel, yet little is known about the cardiovascular (CV) risk profile of deployed US military service members who experience ACS. Stress and socioeconomic status (SES) as risk factors for ACS in service members deployed in ongoing Overseas Contingency Operations have not been considered. Research Objective: To compare CV risk factors between service members who experienced ACS and healthy service members who did not experience ACS while deployed while controlling for nontraditional CV risk factors. Subjects: Deployed service members who experienced ACS (n = 93) and matched controls who did not experience ACS (n = 137). Methods: Healthy controls and ACS cases were matched on rank, area of operations, and ethnicity to control for confounding effects of SES, combat stress exposure, and ethnicity. Results: Acute myocardial infarction occurred in 81.7% of the cases, and 18.3% had unstable angina. Most major CV risk factors were different between the 2 groups except blood sugar and history of dyslipidemia. In a univariate conditional logistic regression model, all CV risk factors except blood sugar were significant predictors of ACS. In a multivariate logistic regression model, older age (odds ratio [OR], 1.25; 95% confidence interval [CI], 1.11–1.40), higher total cholesterol/high density lipoprotein cholesterol ratio (OR, 2.87; 95% CI, 1.65–4.97), and family history of premature coronary artery disease (OR, 4.83 [95% CI, 1.64–14.26]) independently predicted ACS in deployed service personnel. Conclusion: Controlling for SES, combat stress exposure, and ethnicity, traditional CV risk factors remain independent predictors of ACS in deployed service members.

KEY WORDS: acute coronary syndromes, military personnel, risk factors

After the terrorist attacks on September 11, 2001, the United States responded with military operations in Afghanistan in October 2001, followed in March 2003 with military action in Iraq. Today, the US government continues to deploy military personnel to conduct counterinsurgency and counterterrorism missions as part of the larger effort in Overseas Contingency Operations, formerly known as the Global War on Terror. Deployments are unquestionably stressful for service members. The negative psychological effects of combat on deployed military personnel are well documented; however, consideration for the effects of stress on the cardiovascular (CV) health of deployed personnel has largely gone unnoticed.

Acute CV events occur in deployed military personnel, and although stress is recognized as a potential confounder of CV events, the investigators chose to examine only the major CV risk factors in these studies. In a potentially volatile, chaotic, and unpredictable combat environment, it is conceivable that the physiological changes that occur with physical and psychological stress are associated with acute
coronary syndromes (ACS) in a vulnerable individual. Increased heart rate, blood pressure, endothelial dysfunction, arrhythmias, increased platelet aggregation, and cardiac ischemia occur with stress exposure. Theoretical models suggest stress is associated with myocardial ischemia, arrhythmias, thrombosis, and vulnerable plaque formation; indeed, war-related stressors are associated with ACS and angiographically confirmed coronary artery disease (CAD) in civilian cohort studies.

In addition to combat stress exposure, evaluation of the relationship between major CV risk factors and ACS in deployed service members must also consider socioeconomic status (SES) as a nontraditional risk factor known to affect CAD. In deployed service members, combat stress exposure and SES are captured with assessment of 2 variables: location and rank. The specific area of deployment likely affects the level of combat-related stress experienced while overseas. Compared with other Overseas Contingency Operation locations, Hoge and colleagues report increased psychological sequelae in combat veterans from Iraq and Afghanistan. Rank is associated with both income and education, and generally officer ranks have both higher income and higher education levels than do enlisted ranks, and rank is used as a surrogate measure of SES.

The purpose of this study was to compare traditional CV risk factors between military personnel who deployed in support of Overseas Contingency Operations and experienced ACS and those who deployed in support of Overseas Contingency Operations and did not experience ACS while controlling for nontraditional CV risk factors of combat stress exposure and SES.

Methods

The institutional review boards at Walter Reed Army Medical Center, Washington, District of Columbia; Madigan Army Medical Center, Tacoma, Washington; and the University of California, San Francisco, approved this study.

Sample

This case-control study was composed of 93 cases with ACS and at least 1 and up to 3 matched healthy controls for every case (n = 137). Cases and controls were matched by rank (officer or enlisted) to minimize the effects of SES, by area of operations (Iraq/Afghanistan or other Overseas Contingency Operation location) to mitigate variation in combat stress exposure, and ethnicity (white, African American, or other) to control for well-documented differences in heart disease between ethnic groups. Age was not a matching factor because it was controlled for in the multivariate analysis.

Inclusion criteria for participants in the study included male sex, active duty, reserve or National Guard military members of any service deployed overseas in support of Overseas Contingency Operations, and having no known history of CAD. Individuals were excluded if they were missing 3 or more variables of interest.

Cases

The cases were obtained from a query list at a military medical center in Europe. The query list was generated using 4 criteria: (1) International Classification of Diseases, Ninth Revision codes suggestive of ACS; (2) a prefix code identifying them as a service member; (3) a unique identifier used for service members deployed in Overseas Contingency Operations; and (4) treated at the facility for ACS between October 2001 and July 2007. Cases met inclusion criteria and had a primary diagnosis of ACS. Evaluation of information in the medical record confirmed that the subject met the eligibility criteria.

Controls

Controls were recruited through placement of posters in medical clinics servicing military personnel at a large military installation in the Pacific Northwest. Additionally, service members returning from an overseas deployment were provided with information on the research study by the primary investigator at their redeployment briefings.

Data Collection

A record review was conducted using electronic records and medical records. Information on age, ethnicity, branch of service, duty status (active or reserve), family history of premature CAD in first-degree family members, and personal history of hypertension, diabetes or impaired fasting glucose, and dyslipidemia was annotated. If no history of dyslipidemia was reported, but predeployment values revealed a high-density lipoprotein (HDL) cholesterol of less than 40 mg/dL, low-density lipoprotein (LDL) cholesterol of 160 mg/dL or greater, or triglycerides of 150 mg/dL or greater, an additional variable of corrected history of dyslipidemia was created to reflect the actual history of dyslipidemia. Predeployment glucose, blood pressure, height, and weight were also obtained if available. Individuals were classified as former smokers if they had not smoked in the past 12 months. If a participant smoked any form of tobacco, including pipes and cigars in the previous 12 months, they were categorized as smokers. Because the participants in the case group are now considered “high risk” based on their clinical...
status, Framingham risk scores were calculated only on participants in the control group using age, LDL cholesterol, HDL cholesterol, systolic and diastolic blood pressure, presence of diabetes, and smoking status.19 To measure dyslipidemia, a total cholesterol–HDL cholesterol ratio was calculated. For ACS cases, blood pressure, lipid panel, blood sugar, height, and weight were the first values obtained after the CV event.

In addition to the record review, a face-to-face interview and assessment of the following clinical characteristics were obtained on all the controls.

### Blood Pressure

Blood pressure was obtained with the patient seated using a Baum (Copiague, NY) aneroid sphygmomanometer and appropriate-size cuff. The participant’s arm was bare and at heart level. The mean of 2 blood pressure measurements was used for the final analysis.

### Anthropometric Measurements

Height and weight were measured on a Detecto (Webb City, MO) manual physician scale with height rod. Height was measured without shoes to the nearest 0.64 cm, and weight was measured in the lightweight army combat uniform with pockets emptied and without boots to the nearest 0.11 kg.

### Lipid Profile and Fasting Blood Sugar

After an overnight fast, participants returned for a venous blood draw. Approximately 5 mL of blood was drawn in a Vacutainer (BD, Franklin Lakes, NJ) with serum separator. Blood was centrifuged for 20 minutes, and serum was extracted and stored in cryovials at −57°C until shipment to a central laboratory. Lipid values were measured using the Vertical Auto Profile test (Atherotech, Birmingham, AL), and residual venous blood was used to determine fasting blood sugar using an Ascensia Contour glucometer (Bayer Healthcare, Tarrytown, NY). Using venous blood, the Contour has an acceptable coefficient of variation of 4.2%.20 Accuracy is demonstrated using an error grid analysis with 97.9% of specimens falling within zone A, or ±15% or ±10 mg within the laboratory measurements. Quality control checks were conducted daily.

### Statistical Methods

Data were analyzed using SPSS software (version 16.0; SPSS Inc, Chicago, IL). The \( \chi^2 \) analyses were used to assess differences in the categorical matching factors and to evaluate differences between dichotomous CV risk factor variables. Student \( t \) tests were used to assess differences of continuous variables between cases and controls; univariate conditional logistic regression models were used to determine significance of individual risk factors with the outcome of ACS. Independent variables with \( P < .20 \) were entered into a conditional logistic multivariate model with the outcome of ACS.

### Results

Ninety-three cases and 137 SES, stress, and ethnicity-matched controls were used in the analysis. No statistically significant differences were found between cases and controls on the matched characteristics (Table 1).

Of the 93 cases, 81.7% were diagnosed with acute myocardial infarction (AMI), and 18.3% with unstable angina. The mean age of cases was 44.6 (SD, 7.8) years, with a range of 29 to 60 years, and nearly 3 quarters were enlisted personnel. Both groups had a mean body mass index (BMI) that classified them as overweight. Specifically, 62.4% of cases and 52.6% of controls were overweight, with a BMI between 25 and 29.99 kg/m\(^2\). A BMI of 30 kg/m\(^2\) or higher was recorded in 20.4% of cases and 36.8% of controls. The mean fasting blood sugar was greater than 100 mg/dL in both groups; the range in the healthy controls was 64 to 133 mg/dL, and in the ACS cases, it was 77 to 300 mg/dL. Mean Framingham risk score for the control group was 4.51% (SD, 2.37%).

After controlling for SES, stress, and ethnicity, most major CV risk factors were significantly different between the 2 groups, with the exception of blood sugar and history of dyslipidemia (Table 2). In a univariate conditional logistic regression analysis, all CV risk factors except blood sugar were significant predictors of ACS (Table 3).

In a multivariate analysis, the significance was set at \( P < .05 \). Higher age, higher total cholesterol–HDL cholesterol ratio, and family history of premature CAD remained significant independent predictors of ACS in service personnel deployed in Overseas Contingency Operations.21

### TABLE 1 Comparison of Matching Factors Between Cases and Controls (N = 230)

<table>
<thead>
<tr>
<th>Rank, %</th>
<th>Cases</th>
<th>Controls</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Officer</td>
<td>26</td>
<td>27</td>
<td>NS</td>
</tr>
<tr>
<td>Enlisted</td>
<td>74</td>
<td>73</td>
<td>NS</td>
</tr>
<tr>
<td>Area of operations, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iraq or Afghanistan</td>
<td>83</td>
<td>87</td>
<td>NS</td>
</tr>
<tr>
<td>Other Overseas Contingency</td>
<td>17</td>
<td>13</td>
<td>NS</td>
</tr>
<tr>
<td>Operation location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>79</td>
<td>74</td>
<td>NS</td>
</tr>
<tr>
<td>African American</td>
<td>15</td>
<td>17</td>
<td>NS</td>
</tr>
<tr>
<td>Other</td>
<td>6</td>
<td>9</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviation: NS, not statistically significant.

*Rank = SES surrogate; area of operations = surrogate degree of stress.*
Operations (Table 4). Considered by itself, smoking was associated with ACS (P = .015); however, it did not demonstrate a significant, unique contribution to predict ACS when evaluated along with the other 5 variables in the model. Smoking was tested with each of the individual variables to assess for interactions, and none found. Only when the total cholesterol–HDL cholesterol ratio variable was removed from the model did smoking become significant.

### Discussion

Using a matched case-control design to minimize confounding effects of SES, stress, and ethnicity, variables that remained predictors of ACS in military personnel deployed in support of Overseas Contingency Operations were increased age, family history of premature CAD, and dyslipidemia. Although increased age as a risk factor for CVD was expected, the mean age and age range of the ACS cases were very young. This finding has implications for ongoing health care costs, disability, possible separation from the service, and mortality. The health care costs for ongoing follow-up care as well as the disability assessed after separation from the service can be significant. Furthermore, a unique aspect of the military profession is that the physical health of an individual can potentially affect career progression. Individuals diagnosed with an AMI must successfully complete a 120-day trial of duty to remain on active duty; if unsuccessful, a medical board may convene to determine eligibility for continued service. Finally, although young AMI patients generally have better short-term health outcomes than older AMI patients, evidence suggests they may have higher long-term mortality rates.

Although the Framingham risk score for the control group is now greater than 20% or high risk, they are part of a population that is generally considered low risk because of the relatively young age of military personnel. As expected, the mean Framingham risk score for the control group was less than 10% or low risk. Low Framingham risk scores are not unique to the military population, and similar findings are identified among young AMI cohorts. One limitation of the Framingham risk score is that it does not include family history in the algorithm, and given its independent association with ACS in this study, this is an important clinical consideration when evaluating CV risk in young military personnel. Evidence exists that family history of cardiac disease independently predicts

### Abbreviations

- CAD: coronary artery disease
- CI: confidence interval
- HDL: high-density lipoprotein
CV events\textsuperscript{26} and may act synergistically with traditional risk factors in CAD.\textsuperscript{27} In young men, family history is particularly important; young AMI patients have higher rates of premature CAD in family members when compared with older AMI patients.\textsuperscript{28,29} Moreover, the risk factor profile of AMI patients with and without a family history of premature CAD is different. Patients with a family history are male and younger and have a greater prevalence of smoking and dyslipidemia when compared with patients without a family history of premature CAD.\textsuperscript{30}

The Army regulation that previously governed the mandatory 5-year physical examination required assessment of only total cholesterol until age 39 years; complete lipid panels were required only in service members 40 years and older. It is conceivable that a major CV risk factor is missed with the total cholesterol evaluation because “normal” levels less than 200 mg/dL could result from low HDL cholesterol and may contribute to elevated total cholesterol–HDL cholesterol ratio. Dyslipidemia warrants counseling at a minimum, and depending on other risk factors, pharmacological management. The current physical health assessment guidelines require complete lipid panels at age 35 years in men and 40 years in women; however, these guidelines are inconsistent with the American Heart Association\textsuperscript{31} and National Cholesterol Education Program/Adult Treatment Panel III\textsuperscript{32} that recommend complete lipid panels every 5 years beginning at age 20 years.

Half of the entire sample had no evidence of previous lipid testing in their records. Although the omissions may be a result of the transient nature of the military population, the unavailability of reservist’s civilian medical records may overestimate this percentage. With the military’s dependence on reservists to maintain the current deployment schedule, however, it is imperative for military health care providers to know the current lipid panel of activated reservists. The independent association of total cholesterol–HDL cholesterol ratio with ACS is consistent with findings in large prospective studies.\textsuperscript{33,34} Indeed, higher ratios are associated with physiological changes associated with increased risk for ACS including hyperinsulinemia; small, dense LDL particles; intermediate-density lipoproteins; and elevated apolipoprotein B, the structurally important component of very-low-density lipoproteins.\textsuperscript{34} Early screening is essential, and health care providers must assess the lipid profiles of service members irrespective of age to determine accurately their CV risk profile during their annual physical health assessment and, most importantly, prior to an overseas deployment. Implementation of aggressive lipid reduction measures with appropriate treatment and follow-up is important for individuals with dyslipidemia.

The lack of association of smoking to CV events in this sample was unexpected. Although smokers deployed in support of Overseas Contingency Operations were twice as likely to have ACS, the effect was not large enough to be statistically significant. Smoking is unequivocally associated with increases in CVD; moreover, smoking is sometimes noted as the only CV risk factor associated with AMI in young patients.\textsuperscript{35} In civilian cohorts of young patients with AMI, however, rates of smoking are reported at 74% or higher\textsuperscript{21,36} considerably greater than the reported prevalence in our cases of 45%. Although a larger sample size would likely detect differences between the groups, the insignificant findings also indirectly highlight the high rates of smoking in the control group. Irrespective of case or control group, however, the smoking rate in this sample of military personnel exceeded the overall prevalence in the civilian population (22.1%).\textsuperscript{37} Implementation of convenient, accessible smoking cessation programs is essential and should be offered at each health care visit, including predeployment, postdeployment, and at the mandatory 90-day redeployment assessment.

Parenthetically, evidence suggests that not all smokers are at equal risk for the development of an atherogenic lipid profile or ACS. Insulin-resistant smokers have greater small, dense LDL particles; very-low-density lipoprotein cholesterol; and triglycerides than do insulin-sensitive smokers.\textsuperscript{38} Furthermore, in the Copenhagen Male Study,\textsuperscript{39} there were no differences in the incidence of ACS between nonsmokers with low HDL cholesterol–high triglyceride dyslipidemia and smokers with high HDL cholesterol–low triglyceride pattern.

An individual’s medical history of hypertension did not independently predict ACS in this study. Indeed, hypertension is a major risk factor for CVD, and the lifetime risk of CVD in hypertensive individuals at age 50 years is 46.4%.\textsuperscript{40} The findings are consistent with other studies that found no differences in history of hypertension between young AMI patients and healthy controls.\textsuperscript{41,42} Moreover, the risk factor profile of the young AMI patient may be different; the prevalence of hypertension is consistently lower in young AMI patients when compared with older AMI patients.\textsuperscript{29,36,43}

Although BMI was significant in the univariate analysis and trended toward significance in the multivariate analysis, it is important to address the inverse association that not only is counterintuitive but also stands in contrast to a large population study with data supporting increased CV death with increased BMI.\textsuperscript{44} The physical demands of the military require individuals to be physically fit, and the higher BMI in the healthy control group may be attributable to the nature of a physically conditioned population rather
than abdominal adiposity. Despite this premise, however, investigators found that in a young cohort of physically active construction workers, a BMI of greater than 25 kg/m² was associated with increased CV mortality.\textsuperscript{45} It is unclear whether the use of BMI to appraise health risks is valid in the military population; other correlates of obesity, such as measurements of body fat or waist circumference, warrant further exploration in this population. This should not diminish the fact that both groups are overweight or that nearly one-third of the entire sample was classified as obese with a BMI of 30 kg/m² or greater. Obese young men have significant atherosclerotic disease with vessel stenosis.\textsuperscript{46}

Finally, although no differences were noted between groups with respect to fasting blood glucose, the mean of both groups was greater than 100 mg/dL, meeting criteria for impaired fasting glucose. Individuals with impaired fasting glucose are not necessarily insulin resistant, however; Kim and Reaven\textsuperscript{47} identified insulin resistance in 57% of individuals with impaired fasting glucose. They also had characteristics associated with greater CV risk, including higher BMI, triglycerides, systolic and diastolic blood pressure, and lower HDL cholesterol when compared with individuals with normal glucose tolerance.

The case-control design as described in this study is useful to study infrequent outcomes or disease processes that develop over extended periods. It was optimal to study ACS in deployed military personnel because ACS is relatively rare in the military, and CVD is a pathophysiological process that develops over many years, making cross-sectional and longitudinal studies inappropriate in this low-risk population. Strengths of this study included careful matching of rank and area of operation, surrogate measures of SES and stress, and ethnicity, minimizing the confounding effects of these variables. Moreover, use of record review for the cases minimized recall bias, a flaw cited often in case-control study designs.

In summary, while controlling for the confounding effects of SES, stress, and ethnicity, the major CV risk factors of age, family history of premature CAD, and a high total cholesterol–HDL cholesterol ratio remained independent predictors of ACS in deployed military personnel. As a population, military service members have “low-risk” Framingham risk scores, and investigation of biomarkers that add greater predictive ability to the Framingham risk score is warranted. The military is presently engaged in a conflict with no foreseeable end, and preserving the health of military members is critical to maintain the current operational tempo. Seasoned enlisted personnel and officers are irreplaceable; the time and cost to produce these national assets are formidable. There is great emphasis on psychological surveillance programs, when service members return home; however, improvement in CV preventive medicine surveillance programs is crucial to identify and treat service personnel with multiple CV risk factors. The US military makes every effort to ensure service personnel are capable of undertaking complex missions through extensive training and use of proper, functional equipment. Similar standards must be applied to ensure the cardiac fitness of every service member, especially prior to a deployment in support of Overseas Contingency Operations.

**Limitations**

Ideally, in case-control studies, participants in the control group are randomly selected. Because this study required current clinical and laboratory measurements after deployment, random selection was not feasible. The retrospective nature of data collection in the case group after experiencing ACS is a limitation. Because of the unique location of deployed personnel, lipid panels were not obtained in our sample in the critical 24-hour window of ACS presentation. Although problematic, the lack of timely laboratory results is somewhat mitigated by the stability of the total cholesterol–HDL cholesterol ratio.\textsuperscript{48,49} Known inaccuracies of self-report of smoking history\textsuperscript{50} or family history of CAD\textsuperscript{51} may underestimate their true prevalence.

Direct comparisons of laboratory values obtained using different methods of measurement also pose potential weaknesses in this study. All controls had direct measurements of their lipid panels versus cases, where the calculated LDL cholesterol was reported prior to October 2005. To improve precision and accuracy, the laboratory conducting lipid panels for the cases changed their protocol to direct measurement of LDL cholesterol in October 2005 (personal electronic communication with Aziz Qabar, March 4, 2008).

Assessment of blood sugar using whole venous blood and a portable glucometer may have produced inaccurate measurements. The Ascensia Contour meets the American Diabetic Association recommendations
of 5% coefficient of variation, but exceeds the recommenda-
tions for total variability of less than 10%. Further research is
needed to determine whether the results reflect changes in an individual’s insulin sensi-
tivity, inadequate fasting, or the accuracy of the glucometer. Finally, comparison of blood sugar in which the fasting state of the cases is unknown may not be valid.

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