Veterans of Combat: Still at Risk when the Battle is Over

Running title: Lampert; Combat and CHD: Still at Risk

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Approximately 2.6 million troops have served or are serving overseas as part of Operation Iraqi Freedom/Operation New Dawn in Iraq, and Operation Enduring Freedom in Afghanistan as of September 2013. \(^1\) There have been 6664 casualties and 51,904 wounded as of February 2014. \(^2\) While definitions of combat experience vary, 30% of veterans with service in Afghanistan and 71-86% of those serving in Iraq have participated in a firefight. \(^3\) The rising mental health problems of returning veterans are well documented, \(^4\) with up to 20% of returning veterans meeting diagnostic criteria for post-traumatic stress disorder (PTSD), \(^5\) and up to 17% meeting criteria for any psychological disorder (depression, anxiety, or PTSD). \(^3\) These mental health problems stem directly from combat with a dose-response relationship--the more firefights the soldiers had experienced, the higher the rate of PTSD and depression. \(^3\)

However, evidence is emerging for a role of combat in exerting not just a psychological, but a physiological toll as well. Prior studies of the long-term physical consequences of combat have shown mixed results. In one prospective longitudinal study enrolling veterans shortly after World War II, those who had experienced combat were more likely to die or report physical decline over a 15-year period. \(^6\) In the Atherosclerotic Risk in Communities (ARIC) study, however, no increase in coronary heart disease (CHD) was seen in combat-exposed veterans compared to those who had not seen combat or to those who not served in the military. \(^7\) Both studies included limited numbers of combat veterans however, and in the ARIC study, combat experience had occurred more than 30 years earlier, in World War II or Korea.

In this issue of *Circulation*, Crum-Cianflone \(^8\) et al use the Millennium Cohort Study, which enrolled over 60,000 military personnel, including active duty, Reserve, and National Guard from all branches of the military, starting in 2001, to provide a definitive answer to the question. All were free of CHD at the onset of the study. Overall about a quarter of the troops...
reported exposure to combat before (N=900) or during (N about 13,000) the study period. Self-reported coronary heart disease (CHD) was evaluated in all, and chart-confirmed diagnoses evaluated in a subset of about a third, who remained on active duty (in whom records were thus accessible). Among the entire cohort, in a model adjusting for only demographic variables, combat exposure increased the odds of self-reported CV disease by 1.8. In the final longitudinal model adjusting for clinical and psychological variables, odds ratio was 1.63. PTSD was associated with CHD in unadjusted analysis, but lost significance after adjustment for depression and anxiety, with which it was moderately associated. Among the continuing active duty participants, results were similar, with combat doubling the likelihood of development of CHD. Addition of PTSD along with other health- and behavior-related variables attenuated the magnitude of the effect of combat, although combat remained highly significantly associated with CHD even after this adjustment. These data have some limitations which do not detract from the validity. Less than a third of those invited to participate agreed, but demographic and military variables were only minimally different, suggesting the results are generalizable. Also, concordance between self-report and chart-diagnosed CHD was only moderate, however, the two types of analyses showed very similar results. The large size and prospective nature of the study as well as longitudinal analyses with control for appropriate covariates strongly support the definitive nature of the results.

The findings raise interesting questions about the pathophysiological links between combat, PTSD, and cardiovascular disease. This study shows combat experience to be more important than PTSD. In other studies however, PTSD prospectively predicted development of clinical CHD as well as perfusion abnormalities in a rigorous twin-design study of Vietnam veterans, and was more predictive of development of coronary disease than combat alone. 10
The truth is likely not either-or/combat-versus-PTSD, but rather, is more complex. The stress of combat has been described from World War I to the present day, with variations in the technology of combat but not the psychological impact.\textsuperscript{11,12} Acutely, psychological stress increases sympathetic\textsuperscript{13} and decreases vagal\textsuperscript{14} activity, and ongoing stressors have longer-term effects on the body\textsuperscript{15} through the wear-and-tear of recurrent sympathetic activation.\textsuperscript{16} These autonomic changes have in turn been linked with inflammation,\textsuperscript{17} well–known to be associated with development of CAD. PTSD perpetuates the physiological stress response through reminiscences of the trauma triggered by external stimuli, and has also been associated with long-term autonomic changes.\textsuperscript{18} For some individuals, the physiological damage wrought by the initial stressor may be enough, for others, the amplification and repetition of this response due to PTSD may mediate some of the effects of the initial combat-related stress, as suggested by the data here showing some attenuation of the combat effect when PTSD is added to the model.

Differences in the relative importance of combat and PTSD between this and prior studies\textsuperscript{10} may also in part be explained by the fact that those studies examined veterans many years after their active service, when the prolonged stress of PTSD may be more important than combat years earlier. Recall bias may also play a role in studies conducted long after the sentinel time-period. Other differences between returning veterans of the current wars compared to previous wars have also been noted, such as the all-volunteer force deployed to Iraq and Afghanistan, compared to prior drafts, and the type of warfare conducted in the regions.\textsuperscript{3}

The role of health-related behaviors is uncertain. While adverse health behaviors such as smoking were more common with combat exposure in the present study\textsuperscript{8}, and with PTSD in the Vietnam veterans twins study above\textsuperscript{9}, in both cases, controlling for these factors did not impact
the significance of combat or PTSD. While there may be some mediating role, health behaviors
do not appear to be a large part of the explanation.

These data suggest that combat experience should be considered a risk factor for CHD.
While past combat experience is not modifiable, like family history, presence of this risk factor
should draw attention to surveillance and treatment of other, modifiable, risk factors such as
hypertension, cholesterol, and smoking. This is particularly important as both hypertension and
hyperlipidemia have been associated with PTSD. While PTSD did not explain the entire
impact of combat on cardiovascular risk, it does appear to have at least some mediating role.

Several modalities for PTSD treatment have been shown to reduce symptoms. The most
effective of these is prolonged exposure, in which patients relive and confront trauma-related
stimuli to extinguish conditioned fear responses. Veterans Administration hospitals are
required to offer either this therapy or cognitive processing therapy. Whether PTSD screening
and treatment will reduce cardiovascular risk is unknown, but treatment of other stressors has
shown cardiovascular benefits. The findings of Crum-Cianflone emphasize the importance of
cardiovascular health as a priority for returning veterans who are at increased risk.

Conflict of Interest Disclosures: None.

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