Published in final edited form as:
IJC Metab Endocr. 2016 June ; 11: 1–2. doi:10.1016/j.ijcme.2016.03.002.

Posttraumatic stress disorder symptoms and hypercoagulability during emergency department evaluation for acute coronary syndrome

Vy Thuy Ho,
Columbia University College of Physicians and Surgeons, New York, NY, United States

Daichi Shimbo,
Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, NY, United States

Joan Duer-Hefele,
Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, NY, United States

William Whang,
Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, NY, United States

Melinda Chang, and
Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, NY, United States

Donald Edmondson*
Center for Behavioral Cardiovascular Health, Columbia University Medical Center, New York, NY, United States

Posttraumatic stress disorder is associated with risk for incident and recurrent cardiovascular disease (CVD) and mortality, but the mechanisms for the association are unclear [4]. Recent studies have shown that PTSD is associated with greater coronary artery calcium [1], reduced coronary blood flow [8], and autonomic imbalance [8].

Thrombus formation is critical in the pathogenesis of coronary artery disease, and faster clotting speed as measured by activated partial thromboplastin time (aPTT) has been associated with recurrent cardiovascular events in acute coronary syndrome (ACS) patients [2]. Only two small studies have investigated the association of PTSD with markers of coagulation. One case–control study (N = 14 PTSD) suggested a linear association of PTSD symptoms with clotting factors VII, VIII, XII, fibrinogen, and D-dimer [9]. Another study

*Corresponding author at: Center for Behavioral Cardiovascular Health, Columbia University Medical Center, 622 West 168 Street, PH9-317, New York, NY 10032, United States.

Conflict of interests
The authors have no competing interests to report.

found increased levels of vWF antigen and factor VIII in 30 patients with severe chronic PTSD [6].

In order to determine whether PTSD symptoms are associated with hypercoagulability, a mechanism underlying ACS onset, we tested the association of PTSD symptoms from a prior traumatic event with clotting parameters in 99 patients who presented with an ACS event.

The Reactions to Acute Care in Hospitalization (REACH) study is an ongoing observational cohort study of psychosocial factors and cardiac/mortality risk in cardiac patients being evaluated for ACS. Participants, who later had ACS diagnosis confirmed, underwent testing for aPTT, prothrombin time (PT), and platelet count as part of a cardiac evaluation in the ED. Either during inpatient stay or by telephone a median of 3 days later, participants completed the Life Events Checklist [5] for prior traumatic event burden and the PTSD Checklist-Civilian version (PCL) with reference to the most stressful prior traumatic event. The PCL provides a continuous measure of PTSD symptom severity over 17 items with high diagnostic utility – a cutoff score of 50 is 82% sensitive, 83% specific for PTSD diagnosis via Structured Clinical Interview for DSM disorders [10]. Age, sex, ACS type [Non-ST elevation myocardial infarction (NSTEMI) or unstable angina (UA)], daily aspirin or anticoagulant history, ED aspirin, heparin, or warfarin receipt, Global Registry of Acute Coronary Events (GRACE) score, and Charlson comorbidity index were taken from chart review. Covariates were chosen a priori for variates known to influence aPTT. All participants provided informed consent, and the research was carried out in accordance with the Declaration of Helsinki.

Three linear regression models were tested to determine whether PCL-C scores (log transformed) were associated with hypercoagulability (aPTT and PT) and platelet count with adjustment for the covariates above. We tested for collinearity using the variance inflation factor, no significant collinearity was found.

In 99 participants (Table 1), the cumulative traumatic event burden was 3.3 ± 2.9 events, with a mean PCL score of 27 ± 12 (22% screened positive for pre-existing PTSD at a cutoff of 35). The most common trauma inducing event was the sudden, unexpected death of a close loved one (37%). aPTT and PT in the sample were 30.4 ± 8.3 and 14.4 ± 3.0 s, respectively. In the fully adjusted model, higher PTSD symptoms were associated with lower aPTT values ($\beta = -0.22$, p = .03); which corresponds to 1.5 s of aPTT per 10 points on the PCL. No other variable was statistically significant, but history of anticoagulant use ($\beta =$ 0.17, p = .09), GRACE score ($\beta = 0.26$, p = .09) and heparin receipt in the ED ($\beta = 0.19$, p = .06) were marginally associated with greater aPTT. The full model explained 13% of the variability in aPTT [$F(11,87) = 2.30$, p = .02; $R^2adj = .13$]. PTSD symptoms were not significantly associated with PT values ($\beta = -0.06$, p = .41) or platelet count ($\beta = -0.01$, p = .98). (See Table 2.)

We examined whether PTSD symptoms were associated with hypercoagulability in a cohort of ACS patients during ED evaluation. Although PTSD can occur due to an ACS event, we screened for PTSD symptoms in relation to a traumatic event prior to arriving to the ED. We

found that PTSD symptoms may be associated with reduced aPTT, but not PT or platelet count. The aPTT reflects the activity of the intrinsic and common coagulation pathways, including Factor VIII, IX, X, XI, and XII. Conversely, PT assesses the activity of the extrinsic pathway, particularly Factor VII, a Vitamin K-dependent procoagulant with a short half-life [7]. Therefore, our study suggests that PTSD symptoms may be associated with activation of the intrinsic and common coagulation pathways.

Previously, Von Kanel et al. found that increased levels of fibrinogen and Factor VIII in patients with PTSD, suggesting subthreshold changes in coagulation [9]. Our findings suggest a detectable change in aPTT during an acutely stressful experience, such as undergoing evaluation for a cardiac event in the ED. As such, patients with PTSD may exhibit a baseline level of subthreshold hypercoagulability, which becomes significant in the setting of subsequent acute stress.

Arbab-Zadeh et al. proposed a “perfect storm” model for understanding the pathophysiology of acute coronary syndrome, wherein a multitude of biological events coalesce to precipitate ACS [3]. When applied to the relationship between PTSD and CVD, the “perfect storm” model captures the complexity of the physiological, psychiatric, and psychosocial factors that play a role in conferring disease. Our analysis suggests that hypercoagulability may be part of the constellation of processes that predispose PTSD patients to ACS onset.

A limitation of this observational cohort study is that aPTT represents the collective behavior of multiple coagulation factors, so the relative influence of individual coagulant proteins in fostering hypercoagulability cannot be determined. However, our findings provide preliminary evidence that the cardiovascular effects of PTSD may be partially explained by hypercoagulability. Additional research using more detailed analysis of clotting factors in large populations can further our understanding of the link between PTSD and cardiovascular risk. Further, serial testing of coagulation parameters may better characterize the extent and magnitude of hypercoagulability in PTSD patients over time.

Acknowledgments

This work was supported by grants R01 HL117832, R01 HL128310 and R01 HL123368 from the National Heart, Lung, and Blood Institute.

References

1. Ahmadi N, Hajsadeghi F, Mirshkarlo HB, Budoff M, Yehuda R, Ebrahimi R. Post-traumatic stress disorder, coronary atherosclerosis, and mortality. Am J Cardiol. 2011; 108:29–33. [PubMed: 21530936]
2. Anand SS, Yusuf S, Pogue J, Ginsberg JS, Hirsh J. Investigators oBotOtASfIS, Relationship of activated partial thromboplastin time to coronary events and bleeding in patients with acute coronary syndromes who receive heparin. Circulation. 2003; 107:2884–2888. [PubMed: 12796128]
3. Arbab-Zadeh A, Nakano M, Virmani R, Fuster V. Acute coronary events. Circulation. 2012; 125:1147–1156. [PubMed: 22392862]
4. Edmondson D, Cohen BE. Posttraumatic stress disorder and cardiovascular disease. Prog Cardiovasc Dis. 2013; 55:548–556. [PubMed: 23621964]
5. Gray M, Litz B, Hsu J, Lombardo T. Psychometric properties of the life events checklist. Assessment. 2004; 11:330. [PubMed: 15486169]

6. Robicsek O, Makhoul B, Klein E, Brenner B, Sarig G. Hypercoagulation in chronic post-traumatic stress disorder. IMAJ-Isr Med Assoc J. 2011; 13:548.
7. Suchman AL, Griner PF. Diagnostic decision: diagnostic uses of the activated partial thromboplastin time and prothrombin time. Ann Intern Med. 1986; 104:810–816. [PubMed: 3706933]
8. Vaccarino V, Goldberg J, Rooks C, Shah AJ, Veledar E, Faber TL, et al. Post-traumatic stress disorder and incidence of coronary heart disease: a twin study. J Am Coll Cardiol. 2013; 62:970–978. [PubMed: 23810885]
9. Von Känel R, Hepp U, Buddeberg C, Keel M, Mica L, Aschbacher K, et al. Altered blood coagulation in patients with posttraumatic stress disorder. Psychosom Med. 2006; 68:598–604. [PubMed: 16868270]
10. Weathers F, Litz B, Herman D, Huska J, Keane T. The PTSD Checklist (PCL): Reliability, Validity, and Diagnostic Utility. 1993

Table 1

Participant characteristics.

	Mean ± SD or % of sample
Age	61 ± 12
Male sex	65%
Non-ST elevation MI	38%
History of daily aspirin use	63%
History of anticoagulant use[a]	7%
Aspirin in ED prior to aPTT	47%
Heparin in ED prior to aPTT	3%
GRACE score [b]	91 ± 28
Charlson comorbidity index[c]	1.9 ± 1.9
Lifetime traumatic events	3.3 ± 2.9
PCL-C score[d]	27 ± 12
aPTT[e]	30.4 ± 8.3
PT	14.4 ± 3.0
Platelet count	228 ± 60

[a]Warfarin or heparin use within 7 days prior to presentation.

[b]Global Registry of Acute Coronary Events score. Higher scores represent greater 6-month risk (e.g., 100–127 predicts a 4.5–11% 6-month mortality risk).

[c]Number of comorbidities weighted by associated mortality risk (<2 predicts <10% risk of 10-year mortality).

[d]PTSD Checklist-Civilian.

[e]Activated partial thromboplastin time.

Table 2

Multiple regression predicting activated partial thromboplastin time (aPTT) from PTSD symptom score, and demographic and clinical covariates.

Variable	B	*SE* (B)	*β*	p
Age	−.01	.10	−.02	.91
Sex	.32	1.69	.02	.85
NSTEMI	2.53	1.68	.15	.14
GRACE cardiac risk score	.08	.05	.26	.09
Charlson Comorbidity score	.48	.49	.11	.33
Cumulative traumatic events	.30	.29	.11	.29
PCL-C PTSD symptoms (log transformed)	−4.82	2.23	−.22	.03
Daily aspirin history	−2.07	1.77	−.12	.25
Anticoagulant history	5.39	3.16	.17	.09
Aspirin in ED	1.37	1.60	.08	.39
Heparin in ED	8.97	4.68	.19	.06