Published in final edited form as:

Gen Hosp Psychiatry. 2018 ; 53: 101–107. doi:10.1016/j.genhosppsych.2018.02.007.

Posttraumatic Stress Disorder in Patients Who Rule Out Versus Rule In for Acute Coronary Syndrome

Ian M. Kronish, M.D., M.P.H.¹, Donald Edmondson, Ph.D., M.P.H.¹, Nathalie Moise, M.D., M.S.¹, Bernard P. Chang, M.D., Ph.D.², Ying Wei, Ph.D.³, David Lopez Veneros, M.A.¹, and William Whang, M.D., M.S.¹

¹Center for Behavioral Cardiovascular Health, Columbia University Medical Center, 622 W. 168th St, New York, NY 10032, USA

²Department of Emergency Medicine, Columbia University Medical Center, 622 W. 168th St, New York, NY 10032, USA

³Department of Biostatistics, Mailman School of Public Health, Columbia University, 722 West 168th St, New York, NY, 10032, USA

Abstract

Objective: Many patients who present to the emergency department (ED) with acute coronary syndromes (ACS) develop posttraumatic stress disorder (PTSD) due to the experience. Less is known about risk for PTSD in patients who rule out for ACS. Our objective was to compare the risk of developing PTSD among patients who rule out versus rule in for ACS.

Methods: We enrolled a consecutive sample of 1,000 patients presenting to an emergency department (ED) with symptoms of a probable ACS. We assessed presenting ACS symptoms in the ED. We determined whether presenting symptoms were due to a confirmed ACS or another etiology by chart review. We assessed PTSD by telephone 1 month after discharge using the PTSD Checklist specific for the suspected ACS event (PCL-S). We used logistic regression to determine the association of ruling out versus ruling in for ACS with a positive PTSD screen (PCL-S ≥ 32), adjusting for demographics, comorbidities, depression, trauma history, and pre-existing PTSD.

Results: Approximately two-thirds of patients (68.2%) ruled out for ACS. Compared to confirmed ACS patients, patients who ruled out had similar presenting symptoms, and similar risk of screening positive for PTSD (18.9% versus 16.8%; $p=0.47$; adjusted OR 1.18, 95% CI 0.69–2.00; $p=0.55$).

Corresponding Author: Ian M. Kronish, Center for Behavioral Cardiovascular Health, Columbia University Medical Center, 622 W. 168th Street, PH9-311, New York, NY 10032; Phone: 212-342-1335; Fax: 342-3431; ik2293@cumc.columbia.edu.

Contributors

Study design and concept: I.M.K., D.E., W.W.

Acquisition, analysis, or interpretation of data: I.M.K., D.E., N.M., B.P.C., D.L.V., W.W., Y.W.

Drafting of the manuscript: I.M.K., D.E., N.M., B.P.C., W.W.

Critical revision of the manuscript for important intellectual content: I.M.K., D.E., N.M., B.P.C., D.L.V., W.W.

All authors approved the submitted version.

Conflicts of Interest

None to report.

Conclusions: ED presentation with ACS symptoms was sufficient to trigger a positive PTSD screen whether the etiology was due to a life-threatening ACS or another etiology. Patients who present with ACS symptoms should be considered for interventions to prevent PTSD after hospitalization, regardless of symptom etiology.

Keywords

acute coronary syndrome; posttraumatic stress disorder; emergency department; etiology; trauma; cardiovascular disease

INTRODUCTION

Acute chest pain accounts for nearly 10% of all non-accident related visits to emergency departments (ED) in the US ¹. Of those patients with a confirmed acute coronary syndrome [ACS; myocardial infarction (MI) or unstable angina], the ACS experience can trigger subsequent posttraumatic stress disorder (PTSD) symptoms, in what has been labeled cardiac disease-induced PTSD ². ACS-induced PTSD is common: in a meta-analysis of 24 studies (total n= 2,383), one in eight ACS patients screened positive for PTSD at least one month later ³. ACS survivors who develop elevated PTSD symptoms not only experience emotional distress and functional impairment, but are also at risk for lower adherence to recommended risk-reducing treatments⁴⁻⁶ and have nearly twice the risk of recurrent cardiovascular events and mortality ^{3,4}.

While a number of studies have described the psychological impact of patients who rule in for ACS,⁷ much less is known about the experience of patients who present to the ED with a suspected ACS, but subsequently “rule-out” after diagnostic testing. Of all the patients who present to the ED with ACS-like symptoms (e.g., chest pain, shortness of breath, left arm pain) in the presence of cardiovascular risk factors, less than half are ultimately diagnosed with an ACS such that the patients who rule out represent a substantial patient population ⁸. Most patients who rule out for ACS receive non life-threatening diagnoses for their presenting symptoms, such as musculoskeletal pain or gastroesophageal reflux disorders, while others do not receive any specific diagnosis ⁹.

Prior studies suggest that patients with a non-cardiac etiology for their ACS-like symptoms (i.e., those who rule out) have increased health care utilization and costs, but not increased risk for subsequent cardiovascular events ¹⁰⁻¹². Because of their relatively benign medical prognosis, physicians may see little cause for concern among patients who rule out for ACS. However, from the point of view of the patient, the experience of presenting to the hospital with ACS symptoms may still be traumatic, irrespective of the final diagnosis they receive. PTSD is now commonly understood to be induced by the perception of life threat or serious injury in response to a potentially traumatic event ¹³. Accordingly, patients who rule out for ACS may still be at risk for developing PTSD due to the event, depending on their affective response to the event and the coping resources they have available to recover from the potentially traumatic event.

Prior studies have examined the association between acute non-cardiac chest pain with negative affect, and found elevated levels of depression, panic disorder, and generalized

anxiety disorder^{9,14–16}. To our knowledge, however, none have examined the extent to which patients who rule out for ACS are at risk for subsequent PTSD. It is important to understand this risk as PTSD symptoms may contribute to increased health care utilization and lower quality of life in the group of patients who rule out for ACS. Further, patients who rule out for ACS that developed elevated PTSD symptoms may benefit from a trauma-informed approach to care. Accordingly, we assessed patients' somatic symptoms and psychological distress during ED evaluation for ACS symptoms, and their PTSD symptoms one month later. We tested whether patients who ruled out for ACS differed in their somatic or psychological distress during ED presentation relative to patients who ruled in for ACS. We also tested whether patients who ruled out for ACS differed in their risk for PTSD one month later relative to those who ruled in.

METHODS

This analysis was conducted among the first 1,000 patients enrolled from November 2013 to February 2016 in the REactions to Acute Care and Hospitalization (REACH) study. REACH is an ongoing prospective observational cohort of a consecutive sample of patients presenting to an urban ED in New York City (Columbia-New York Presbyterian Hospital) with symptoms of suspected ACS. Patients were eligible once they had been given a provisional diagnosis of "probable ACS" by their treating ED physician during the initial evaluation of chest pain in the ED setting. Patients were excluded if they had ST-segment elevations on their electrocardiograms when presenting to the ED as these patients were immediately sent to the cardiac catheterization laboratory upon arrival and were unavailable for consent in the ED. They were also excluded if, in the judgment of the ED physician or research coordinator, they were unable to provide informed consent or complete study questionnaires due to cognitive impairment, need of immediate psychiatric intervention, or terminal illness. Patients were also excluded if they did not speak English or Spanish.

Procedures

While in the ED, patients were interviewed for sociodemographic characteristics, presenting ACS symptoms, and current perceptions of life threat, control, and vulnerability. After being admitted to the hospital, patients were interviewed a second time to assess depressive symptoms, prior exposure to potentially traumatic events, and pre-existing PTSD symptoms unrelated to the index event. These second interviews were conducted by telephone if patients were discharged before the interview could be completed. One month after discharge, patients were contacted by telephone to assess their PTSD symptoms specifically due to the recent suspected ACS. Patients received a \$30 stipend for completing study assessments. Medical history was abstracted from the medical record. All patients provided written informed consent and the Institutional Review Board of Columbia University Medical Center approved the study.

Primary Outcome: PTSD symptoms due to the suspected ACS, assessed 1-month after the index event—PTSD symptoms were assessed by telephone one-month following hospital discharge using the PTSD Checklist for a Specific Stressor (PCL-S), a questionnaire that assesses 17 PTSD symptoms that correspond to the diagnostic criteria in

the Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV.¹⁷ Patients rated the extent to which they were bothered by each symptom in the past month, in relation to “the heart problem, emergency room visit, and hospitalization” during which they enrolled in the study. Responses were rated on a scale from 1 (“Not at all”) to 5 (“Extremely”). Prior research has demonstrated that the PCL is a reliable and valid measure of PTSD.¹⁸ A cutpoint of 32 on the PCL-S has a sensitivity and specificity near 80% for PTSD diagnosis in non-VA primary care populations, and is in the range recommended to screen for PTSD when the prevalence is expected to be less than 15%^{19–21}. Those with a PCL-S score ≥ 32 were categorized as having a positive PTSD screen. A cutpoint of 44 has a specificity of 95% or greater for PTSD in other civilian samples.²² Those with a PCL-S score ≥ 44 were categorized as having probable PTSD. Internal consistency of the PCL-S in the current sample was excellent (Cronbach’s $\alpha=0.92$).

Predictors of PTSD

ACS symptoms at time of index event: Patients reported on the presence (Yes/No) of seven typical ACS symptoms during ED study enrollment, including chest pain or pressure, left arm pain, jaw pain, shortness of breath, nausea, vomiting, and dizziness.

Threat perceptions at time of index event: Perceptions of life threat and personal vulnerability in the ED were assessed at ED study enrollment with 12 items (e.g., “I am afraid,” “I feel helpless,” “I feel vulnerable,” “I worry that I am not in control of my situation”) based on Ozer et al.²³ Responses were rated on a scale of 0, “Not at all” to 4, “Extremely.” Responses were summed to calculate a total perceived threat score with good internal consistency (Cronbach’s $\alpha=.79$). We have used this scale previously^{24,25}

Depressive symptoms, prior to index event: Depressive symptoms during the 2 weeks prior to the index event were assessed during the inpatient follow-up interview using the eight-item Patient Health Questionnaire (PHQ-8), an accurate and reliable tool for assessing depression²⁶. The 8-item PHQ omits a question assessing suicidality as this item is not an accurate suicide screen and can lead to unnecessary referrals for immediate psychiatric evaluations²⁷. The PHQ-8 is otherwise identical to the 9-item version and has similar psychometric properties to the 9-item version²⁷. A PHQ-8 score ≥ 10 has a high sensitivity and specificity for diagnosing depression^{26,28}.

Trauma history, prior to index event: Prior exposure to potentially traumatic events was assessed using the Life Events Checklist (LEC), a 16-item inventory of types of potentially traumatic life events (e.g., natural disaster, motor vehicle accident, sexual assault) that can induce PTSD²⁹. We calculated a total score for exposure to prior traumatic events based on summing the total number of types of potentially traumatic events listed by patients.

PTSD symptoms, prior to index event: PTSD symptoms in the month prior to the suspected ACS event were assessed using the *PTSD Checklist-Civilian (PCL-C)* [¹⁷], with reference to the most stressful event reported on the LEC (above) prior to the presenting ACS symptoms. The PCL-C is identical to the PCL-S except for the index event it references, and has excellent psychometric properties^{18,30,31}.

Medical Comorbidity: Medical comorbidity was assessed using the Charlson Comorbidity Index which consists of a combined score of 22 medical conditions weighted by their mortality risk³². We abstracted the medical conditions that are included in the Charlson Index (e.g., congestive heart failure, diabetes mellitus) from the medical record.

ACS symptom etiology (i.e., ruled in versus ruled out for ACS): Adjudicators initially classified patients into one of the following categories: ACS event (either non-ST segment elevation MI or unstable angina) or non-ACS diagnosis. ACS events were defined according to American Heart Association/American College of Cardiology criteria as either acute MI or unstable angina^{33,34}. Patients without a confirmed ACS were then classified as having a non-ACS *cardiac* diagnosis (e.g., congestive heart failure or hypertensive urgency) or one of the following: musculoskeletal pain, gastrointestinal disorder, anxiety-related disorder, drug intoxication (e.g., cocaine), other non-ACS non-cardiac diagnosis (e.g., pulmonary embolism or pneumonia), or a not-otherwise-specified diagnosis. This classification of ACS symptom etiology was independently adjudicated by two board-certified physicians based upon review of the complete medical record. Adjudicators were blinded to PTSD status. Discrepancies were resolved through consensus in the presence of a third physician who was a board-certified cardiologist.

Cohort assembly: Of the first 1639 eligible patients approached, 1000 (61%) consented to participation and were enrolled in the study; no further information was collected about patients who declined study enrollment. Of the first 1,000 patients enrolled, two consented but withdrew before providing any baseline data, and 817 completed the 1-month telephone-administered PTSD assessment. There were no significant differences between patients who did and did not complete the 1-month PTSD assessment with respect to ACS status, gender, race, ethnicity, education, Charlson score, previous cardiovascular and trauma history, and ACS symptoms.

Statistical analysis: We used logistic regression to determine the risk of screening positive for PTSD (PCL-S = 32) associated with non-ACS symptom etiology (i.e., ruling out for ACS) versus a confirmed ACS (i.e., ruling in for ACS), adjusting for covariates. We selected covariates *a priori* based on a prior review of important predictors of PTSD and included age, sex, ethnicity, race, education, partner status, Charlson score, depression, history of coronary artery disease, prior traumatic life events, and PTSD symptoms due to a prior traumatic event³⁵. We conducted a sensitivity analysis using a cutpoint of = 44 on the PCL-S as the outcome. We also conducted an analysis stratified by elevated PTSD symptoms prior to the ACS event (i.e. PCL-C = 32). Finally, we conducted an analysis in which we assessed predictors of a positive PTSD screen separately among patients who ruled in and who ruled out for ACS.

RESULTS

Approximately one-third of patients (31.8%) had a confirmed ACS (unstable angina, 53.8%; MI, 46.2%). The most common non-ACS diagnoses were non-cardiac chest pain due to an unspecified cause (24.0%), musculoskeletal pain (14.5%), other cardiac diagnosis (10.3%),

gastrointestinal disorders (8.9%), other specific non-cardiac disorder (6.1%), anxiety (3.6%), and cocaine intoxication (0.8%). (**Figure**)

Patients who ruled out did not differ from those with a confirmed ACS with respect to ethnicity, race, and education (Table 1). Patients who ruled out were younger ($M=60$, $SD=13$ years versus $M=63$, $SD=13$ years; $p=0.001$), and were less likely to be male (50% versus 65%, $p<0.001$), to have a partner (42% versus 50%; $p=0.02$); to have a prior history of CAD (21% versus 54%, $p<0.001$), and had lower Charlson scores (1.71 SD 2.07 versus 2.20 SD 1.94; $p<0.001$). Patients who ruled out had similar median levels of depressive symptoms ($p=0.24$) and pre-existing PTSD symptoms ($p=0.41$) as those who ruled in. However, those who ruled out were more likely to screen positive for pre-existing PTSD symptoms (i.e., PCL-C 32) than those who ruled in (25.7% vs 19.7%, $p=0.05$). Patients who ruled out and ruled in for ACS underwent diagnostic stress testing at a similar rate (23.6 versus 26.5%; $p=0.32$). In contrast, patients who ruled out for ACS were much less likely to undergo a coronary angiogram (6.2% versus 61.6%; $p<.001$).

Subjective somatic and psychological experience in the ED differed little between patients who ruled out and ruled in for ACS (Table 2). A slightly lower proportion of patients who ruled out reported chest pain or chest pressure (93.4% versus 96.5%; $p=0.04$), but there were no other significant differences in typical ACS symptoms (all $p>0.35$). There were also no significant differences in perceived threat at the time of ED presentation ($p=0.29$).

Overall, 18.1% of patients screened positive for PTSD (PCL-S 32) at one month after discharge from the index hospitalization, and there was no difference in the PTSD rate between patients who ruled out or ruled in unadjusted (18.9% versus 16.8% $p=0.47$) or adjusted models (adjusted OR 1.18, 95% CI 0.69–2.00; $p=0.55$; Table 3). Women were more likely to screen positive for PTSD than men. Depressive symptoms and prior PTSD symptoms were also associated with increased likelihood of a positive screen for PTSD due to the suspected ACS event.

In exploratory analyses that were stratified according to PTSD symptoms from prior to the ACS (PCL-C score 32), patients who ruled out for ACS were at similar risk of developing a positive screen for PTSD 1 month post-discharge compared to patients with confirmed ACS if they had pre-existing PTSD (adjusted OR 1.17, 95% CI 0.29, 4.78; $p=0.83$). However, patients who ruled out for ACS were at much lower risk of a positive screen for PTSD one month after discharge if they did not have elevated PTSD symptoms prior to the suspected ACS event (adjusted OR 0.12, 95% CI 0.03, 0.53; $p=0.006$).

In an exploratory analysis that assessed predictors of PTSD in patients who ruled in versus ruled out for ACS separately, we found that the significant predictors ($p<.05$) of a positive screen for PTSD at 1-month differed between the two groups. Among patients who ruled in, significant predictors included younger age, female sex, lower education, and depressive symptoms. In contrast, among patients who ruled out, significant predictors were Charlson comorbidity score, depressive symptoms, and PTSD symptoms due to a prior traumatic event.

Finally, in the sensitivity analysis using a higher screening threshold for PTSD (PCL-S 44), there was again no significant difference between patients who ruled out versus rule in for ACS in the unadjusted comparison (9.1% versus 7.8%; $p=0.50$). In fully adjusted analyses, however, patients who ruled out for ACS were less likely to have probable PTSD (adjusted OR 0.42, 95% CI 0.19, 0.91; $p=0.03$).

DISCUSSION

We found that nearly one in five patients presenting to the ED with ACS symptoms screened positive for PTSD at 1 month post-discharge. This finding was comparable to the 16% prevalence of PTSD found in a recent meta-analysis among studies in which ACS-induced PTSD symptoms were assessed using a screening instrument, and was comparable to the prevalence of PTSD after a sexual assault or the unexpected death of a loved one^{3,36}. Furthermore, patients who ruled out for a true ACS were no less likely to screen positive for PTSD than patients with a confirmed ACS diagnosis. This supports the notion that risk for PTSD is dependent on the subjective experience of the ACS event, and not on whether the symptoms are due to a true acute coronary event. In a systematic review of 10 studies assessing psychological symptoms in patients with acute non-cardiac chest pain, patients with non-cardiac reasons for chest pain had increased levels of anxiety and depressive symptoms compared to patients with cardiac etiologies to their symptoms¹⁴. Our study extends these findings by demonstrating that patients who rule out for ACS, the majority of whom have a non-cardiac etiology for their symptoms, are also at risk of PTSD.

One possible explanation for why patients who ruled out for ACS were at equally increased risk for screening positive for PTSD is that these patients had a similar burden of typical cardiac symptoms, and may have been insufficiently reassured that they did not have a cardiac etiology to their symptoms. This may have contributed to a misperception that they had an internal somatic threat that put them at ongoing risk for a recurrent cardiovascular event or mortality, a factor that is theorized to underlie cardiac disease-induced PTSD^{2,37}. Two-thirds of patients who ruled out did not undergo cardiac stress testing or angiography. Further, prior studies suggest that many patients presenting with ACS symptoms are confused as to whether or not they had an ACS. For example, in a study of US Medicare beneficiaries, less than 50% of patients who self-reported an MI had a claim for an MI or unstable angina submitted in the corresponding time period³⁸. Thus, it may indeed be that a substantial proportion of patients who are ruled out still hold fears that they had a cardiac problem and erroneously believe that they are at elevated risk for a recurrence. Nevertheless, education about the non-cardiac etiology of the symptoms, alone, is unlikely to be sufficient to prevent PTSD symptoms from arising in patients who rule out for ACS as once the affective response to a potentially traumatic event is initiated, more intensive psychological or pharmacological interventions are typically needed to prevent or reduce PTSD symptoms³⁹⁻⁴¹.

Another potential explanation for the similar rates of a positive screen for PTSD among patients who rule out versus have a confirmed ACS is that the experience of presenting to a crowded, hectic ED may be part of the reason for subsequent PTSD symptoms. We have previously shown that the crowdedness of the ED independently predicts subsequent PTSD

symptoms in true ACS patients⁴². Patients who are ruled out for ACS are vulnerable to the same exposure to the stressful ED environment as patients with a confirmed ACS.

Patients with non-cardiac etiologies for acute chest pain symptoms have been found to have high levels of underlying psychological stress in terms of anxiety and depressive symptoms.⁹ Depression, in particular, has been found to potentiate the development of PTSD symptoms both in cardiac and non-cardiac populations, and this was confirmed as a predictor of a positive screen for PTSD in our sample⁴³. We added to this literature by showing that approximately 25% of patients who ruled out for ACS screened positive for PTSD prior to the current suspected ACS event (i.e., due to a prior traumatic event), a proportion with elevated pre-existing PTSD symptoms that was higher in those who ruled out than ruled in.

When predictors of a positive PTSD screen were comprehensively compared among those who did and did not rule out for ACS, we found that there were differences between the two groups. Among those who ruled in for ACS, younger age, female sex, and low education were important demographic predictors of PTSD as is found in other populations of trauma exposed individuals⁴⁴. However, these demographic characteristics were not significantly associated with PTSD in those who ruled out. In contrast, Charlson comorbidity score and PTSD symptoms due to a prior traumatic event were associated with a positive screen for PTSD in those who ruled out, but not those who ruled in for PTSD. This suggests that while the prevalence of PTSD is similar in those who rule in and rule out, the pathways that lead to elevated PTSD symptoms may differ in patients who rule in versus rule out. Depressive symptoms predicted a positive PTSD screen in both those who ruled in and ruled out for ACS.

Patients who ruled out for ACS were at similar risk of developing a positive PTSD screen as those who ruled in for ACS if they had elevated PTSD symptoms (PCL-C 32) from before the suspected ACS event. In contrast, patients who ruled out for ACS appeared to be less likely to develop a positive PTSD screen if they did not have prior PTSD symptoms. Thus, underlying psychological vulnerabilities appeared to have contributed to the surprisingly high prevalence of elevated PTSD symptoms in patients who ruled out for ACS.

When using the threshold of PTSD symptoms indicative of probable PTSD, we found that in adjusted models, those who ruled out were less likely to develop probable PTSD than those who ruled in. This contrasted with the finding that there was no difference in the risk of a positive PTSD screen between the two groups. This suggests a need for future studies that complement PTSD questionnaire assessments with psychiatric interviews after suspected ACS events to compare the extent to which those who rule in and rule out are at risk for a clinical diagnosis of PTSD.

There were several strengths of our analyses. We enrolled a sizable cohort of racially and ethnically diverse patients from an ED that serves a vulnerable urban population. We also had robust measures of PTSD and other psychological factors. There were also some limitations. Although our recruitment and follow-up rate was high for a study that enrolled patients from the hectic ED environment, a significant number of patients did not complete follow-up at 1 month. Additionally, patients were enrolled from a single urban ED with a

large proportion of Hispanic patients. These factors limit the generalizability of the findings. PTSD was assessed using the measure from DSM-IV rather than DSM-5, and a psychiatric interview was not used to diagnose PTSD. Nevertheless, elevated PTSD symptoms irrespective of a psychiatric diagnosis appear to confer increased cardiovascular risk.^{3,45} A psychiatric interview was also not used at the index event and this could have led to under-recognition of psychiatric disorders such as panic disorder or PTSD as being the etiology of presenting symptoms in patients who ruled out for ACS. Finally, we did not assess patients' understanding of their ACS symptoms, and hence, cannot determine whether patients with elevated PTSD symptoms understood that they did not have an ACS.

Conclusions

A substantial proportion of patients presenting to the ED with ACS symptoms developed a positive screen for PTSD, irrespective of whether they ruled out or had a true ACS. Prior studies have shown that PTSD may have an adverse impact on adherence to medical treatments^{46–48} and quality of life.⁴⁹ PTSD has also been shown to increase risk for both incident⁴⁵ and recurrent CVD risk³. Future studies should test whether PTSD subsequent to a suspected but unconfirmed ACS confers similarly increased cardiac risk and unnecessary use of health care services. Future studies should also assess patients' understanding of the reasons for their presenting ACS symptoms after discharge, and the extent of agreement with the understanding of medical professionals. In the meantime, as it is known that PTSD has a negative impact on quality of life, future studies should assess whether psychoeducation or other psychological therapies can prevent the onset of PTSD, and whether distinct strategies are needed for patients who rule out for ACS, particularly in light of the finding of differences in predictors of PTSD depending on ACS status^{9,50,51}. Education about the non-cardiac etiology of symptoms may be particularly helpful in patients who rule-out for ACS. However, more intensive psychological therapies grounded in cognitive behavioral therapy, or even pharmacologic approaches, may be needed to prevent or reduce PTSD symptoms in such patients.

Acknowledgments

Funding

This project was supported by the National Heart, Lung, and Blood Institute (grants R01-HL117832, R01-HL128497, R01-HL123368, and R01-HL 128310). Dr. Kronish received additional support from the National Center for Advancing Clinical Translational Sciences (UL1-TR001873).

References

- [1]. Bhuiya F, Pitts S, McCaig L. Emergency department visits for chest pain and abdominal pain: United States, 1999–2008 Hyattsville, 2010.
- [2]. Vilchinsky N, Ginzburg K, Fait K, Foa EB. Cardiac-disease-induced PTSD (CDI-PTSD): A systematic review. *Clin Psychol Rev* 2017;55:92–106. [PubMed: 28575815]
- [3]. Edmondson D, Richardson S, Falzon L, Davidson KW, Mills MA, Neria Y. Posttraumatic Stress Disorder Prevalence and Risk of Recurrence in Acute Coronary Syndrome Patients: A Meta-analytic Review. *PLoS One* 2012;7:e38915. [PubMed: 22745687]
- [4]. Kronish IM, Edmondson D, Li Y, Cohen BE. Post-traumatic stress disorder and medication adherence: Results from the Mind Your Heart Study. *J Psychiatr Res* 2012;46:1595–9. [PubMed: 22809686]

- [5]. Kronish IM, Edmondson D, Goldfinger JZ, Fei K and Horowitz CR. Posttraumatic Stress Disorder and Adherence to Medications in Survivors of Strokes and Transient Ischemic Attacks. *Stroke* 2012;43:2192–7. [PubMed: 22618380]
- [6]. Husain SA, Edmondson D, Kautz M, Umland R, Kronish IM. Posttraumatic stress disorder due to acute cardiac events and aversive cognitions towards cardiovascular medications. *J Behav Med* 2017 12 4 [Epub ahead of print].
- [7]. Cohen BE, Edmondson D, Kronish IM. State of the Art Review: Depression, Stress, Anxiety, and Cardiovascular Disease. *Am J Hypertens* 2015;28:1295–302. [PubMed: 25911639]
- [8]. Goodacre S, Cross E, Arnold J, Angelini K, Capewell S, Nicholl J. The health care burden of acute chest pain. *Heart* 2005;91:229–30. [PubMed: 15657244]
- [9]. Chambers JB, Marks EM, Hunter MS. The head says yes but the heart says no: what is non-cardiac chest pain and how is it managed? *Heart* 2015;101:1240–9. [PubMed: 25882503]
- [10]. Fagring AJ, Lappas G, Kjellgren KI, Welin C, Manhem K, Rosengren A. Twenty-year trends in incidence and 1-year mortality in Swedish patients hospitalised with non-AMI chest pain. Data from 1987–2006 from the Swedish hospital and death registries. *Heart* 2010;96:1043–9. [PubMed: 20483906]
- [11]. Tenkorang JN, Fox KF, Collier TJ, Wood DA. A rapid access cardiology service for chest pain, heart failure and arrhythmias accurately diagnoses cardiac disease and identifies patients at high risk: a prospective cohort study. *Heart* 2006;92:1084–90. [PubMed: 16387821]
- [12]. Eslick GD, Talley NJ. Non-cardiac chest pain: predictors of health care seeking, the types of health care professional consulted, work absenteeism and interruption of daily activities. *Aliment Pharmacol Ther* 2004;20:909–15. [PubMed: 15479363]
- [13]. Laubmeier KK, Zakowski SG. The role of objective versus perceived life threat in the psychological adjustment to cancer. *Psychol Health* 2004;19:425–437.
- [14]. Webster R, Norman P, Goodacre S, Thompson A. The prevalence and correlates of psychological outcomes in patients with acute non-cardiac chest pain: a systematic review. *Emerg Med J* 2012;29:267–73. [PubMed: 22034535]
- [15]. Serlie AW, Erdman RA, Passchier J, Trijsburg RW, ten Cate FJ. Psychological aspects of non-cardiac chest pain. *Psychother Psychosom* 1995;64:62–73. [PubMed: 8559955]
- [16]. Campbell KA, Madva EN, Villegas AC, Beale EE, Beach SR, Wasfy JH, et al. Non-cardiac Chest Pain: A Review for the Consultation-Liaison Psychiatrist. *Psychosomatics* 2017;58:252–265. [PubMed: 28196622]
- [17]. Weathers F, Litz B, Herman D, Huska J, Keane T. The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility. Annual Convention Of The International Society For Traumatic Stress Studies, San Antonio, TX 1993.
- [18]. Blanchard E, Jones-Alexander J, Buckley T, Forneris C. Psychometric properties of the PTSD Checklist (PCL). *Behav Res Ther* 1996;34:669–73. [PubMed: 8870294]
- [19]. Walker EA, Newman E, Dobie DJ, Ciechanowski P, Katon W. Validation of the PTSD checklist in an HMO sample of women. *Gen Hosp Psychiatry* 2002;24:375–80. [PubMed: 12490338]
- [20]. Yeager DE, Magruder KM, Knapp RG, Nicholas JS, Frueh BC. Performance characteristics of the posttraumatic stress disorder checklist and SPAN in Veterans Affairs primary care settings. *Gen Hosp Psychiatry* 2007;29:294–301. [PubMed: 17591505]
- [21]. National Center for PTSD. Using the PTSD Checklist for DSM-IV (PCL) National Center for PTSD Washington, D.C.: U.S. Department of Veterans Affairs, 2012.
- [22]. Jordan HT, Stellman SD, Morabia A, Miller-Archie SA, Alper H, Laskaris Z, et al. Cardiovascular Disease Hospitalizations in Relation to Exposure to the September 11, 2001 World Trade Center Disaster and Posttraumatic Stress Disorder. *J Am Heart Assoc* 2013;2: e000431 [PubMed: 24157650]
- [23]. Ozer EJ, Best SR, Lipsey TL, Weiss DS. Predictors of posttraumatic stress disorder and symptoms in adults: a meta-analysis. *Psychol Bull* 2003;129:52–73. [PubMed: 12555794]
- [24]. Wiedemar L, Schmid JP, Muller J, Wittmann L, Schnyder U, Saner H, et al. Prevalence and predictors of posttraumatic stress disorder in patients with acute myocardial infarction. *Heart Lung* 2008;37:113–21. [PubMed: 18371504]

- [25]. Sumner JA, Kronish IM, Pietrzak RH, Shimbo D, Shaffer JA, Parsons FE, et al. Dimensional structure and correlates of posttraumatic stress symptoms following suspected acute coronary syndrome. *J Affect Disord* 2015;186:178–85. [PubMed: 26241667]
- [26]. Kroenke K, Strine TW, Spitzer RL, Williams JB, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. *J Affect Disord* 2009;114:163–73. [PubMed: 18752852]
- [27]. Razykov I, Ziegelstein RC, Whooley MA, Thombs BD. The PHQ-9 versus the PHQ-8--is item 9 useful for assessing suicide risk in coronary artery disease patients? Data from the Heart and Soul Study. *J Psychosom Res* 2012;73:163–8. [PubMed: 22850254]
- [28]. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–13. [PubMed: 11556941]
- [29]. Gray M, Litz B, Hsu J, Lombardo T. Psychometric properties of the life events checklist. *Assessment* 2004;11:330–41. [PubMed: 15486169]
- [30]. Bliese P, Wright K, Adler A, Cabrera O, Castro C, Hoge C. Validating the primary care posttraumatic stress disorder screen and the posttraumatic stress disorder checklist with soldiers returning from combat. *J Consult Clin Psychol* 2008;76:272–81. [PubMed: 18377123]
- [31]. Walker E, Newman E, Dobie D, Ciechanowski P, Katon W. Validation of the PTSD checklist in an HMO sample of women* 1. *Gen Hosp Psychiatry* 2002;24:375–80. [PubMed: 12490338]
- [32]. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83. [PubMed: 3558716]
- [33]. Cannon CP, Battler A, Brindis RG, Cox JL, Ellis SG, Every NR, et al. American College of Cardiology key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes. A report of the American College of Cardiology Task Force on Clinical Data Standards (Acute Coronary Syndromes Writing Committee). *J Am Coll Cardiol* 2001;38:2114–30. [PubMed: 11738323]
- [34]. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. *J Am Coll Cardiol* 2012;60:1581–98. [PubMed: 22958960]
- [35]. Ozer EJ, Weiss DS. Who develops posttraumatic stress disorder? *Current Directions in Psychol Sci* 2004;13:169–72.
- [36]. Kessler RC, Aguilar-Gaxiola S, Alonso J, Benjet C, Bromet EJ, Cardoso G, et al. Trauma and PTSD in the WHO World Mental Health Surveys. *Eur J Psychotraumatol* 2017;8:1353383. [PubMed: 29075426]
- [37]. Edmondson DE. An Enduring Somatic Threat Model of Posttraumatic Stress Disorder Due to Acute Life-Threatening Medical Events. *Soc Personal Psychol Compass* 2014;8:118–34. [PubMed: 24920956]
- [38]. Yasaitis LC, Berkman LF, Chandra A. Comparison of self-reported and Medicare claims-identified acute myocardial infarction. *Circulation* 2015;131:1477–85; discussion 1485. [PubMed: 25747935]
- [39]. Forneris CA, Gartlehner G, Brownley KA, Gaynes BN, Sonis J, Coker-Schwimmer E, et al. Interventions to prevent post-traumatic stress disorder: a systematic review. *Am J Prev Med* 2013;44:635–50. [PubMed: 23683982]
- [40]. Cusack K, Jonas DE, Forneris CA, Wines C, Sonis J, Middleton JC, et al. Psychological treatments for adults with posttraumatic stress disorder: A systematic review and meta-analysis. *Clin Psychol Rev* 2016;43:128–41. [PubMed: 26574151]
- [41]. Hoskins M, Pearce J, Bethell A, Dankova L, Barbui C, Tol WA, et al. Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis. *Br J Psychiatry* 2015;206:93–100. [PubMed: 25644881]
- [42]. Edmondson D, Shimbo D, Ye S, Wyer P, Davidson KW. The association of emergency department crowding during treatment for acute coronary syndrome with subsequent posttraumatic stress disorder symptoms. *JAMA Intern Med* 2013;173:472–4. [PubMed: 23400256]

- [43]. Edmondson D, Kronish IM, Wasson LT, Giglio JF, Davidson KW, Whang W. A test of the diathesis-stress model in the emergency department: who develops PTSD after an acute coronary syndrome? *J Psychiatr Res* 2014;53:8–13. [PubMed: 24612925]
- [44]. Koenen KC, Ratanatharathorn A, Ng L, McLaughlin KA, Bromet EJ, Stein DJ, et al. Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med* 2017;47:2260–74. [PubMed: 28385165]
- [45]. Kronish IM, Lin JJ, Cohen BE, Voils CI, Edmondson D. Posttraumatic stress disorder and medication nonadherence in patients with uncontrolled hypertension. *JAMA Intern Med* 2014;174:468–70. [PubMed: 24296721]
- [46]. Shemesh E, Rudnick A, Kaluski E, Milovanov O, Salah A, Alon D, et al. A prospective study of posttraumatic stress symptoms and nonadherence in survivors of a myocardial infarction (MI). *Gen Hosp Psychiatry* 2001;23:215–22. [PubMed: 11543848]
- [47]. Shemesh E, Yehuda R, Milo O, Dinur I, Rudnick A, Vered Z, et al. Posttraumatic stress, nonadherence, and adverse outcome in survivors of a myocardial infarction. *Psychosom Med* 2004;66:521–6. [PubMed: 15272097]
- [48]. Fagring AJ, Kjellgren KI, Rosengren A, Lissner L, Manhem K, Welin C. Depression, anxiety, stress, social interaction and health-related quality of life in men and women with unexplained chest pain. *BMC Public Health* 2008;8:165. [PubMed: 18489751]
- [49]. Edmondson D, Kronish IM, Shaffer JA, Falzon L, Burg MM. Posttraumatic stress disorder and risk for coronary heart disease: a meta-analytic review. *Am Heart J* 2013;166:806–14. [PubMed: 24176435]
- [50]. Sheps DS, Creed F, Clouse RE. Chest pain in patients with cardiac and noncardiac disease. *Psychosom Med* 2004;66:861–7. [PubMed: 15564350]
- [51]. Meister R, Princip M, Schmid JP, Schnyder U, Barth J, Znoj H, et al. Myocardial Infarction-Stress PRevention INtervention (MI-SPRINT) to reduce the incidence of posttraumatic stress after acute myocardial infarction through trauma-focused psychological counseling: study protocol for a randomized controlled trial. *Trials* 2013;14:329. [PubMed: 24119487]

Key Messages**What is already known about this subject?**

One in eight patients who rule in for an ACS develops post-traumatic stress disorder (PTSD) induced by the cardiac event. Patients who develop PTSD are at increased risk for medication nonadherence and recurrent cardiovascular events. The impact of ruling out for an ACS on subsequent PTSD was previously unknown.

What does this study add?

We learned that there were minimal differences in the somatic symptoms experienced by patients who ruled out and ruled in for ACS. Further, we learned that patients who ruled out for ACS were equally likely to develop elevated PTSD symptoms.

How might this impact on clinical practice?

Clinicians should explore the psychological impact of presentation to the emergency department with suspected ACS in patients who rule out, and should assess for symptoms of PTSD at follow-up visits. Efforts to educate patients who rule out for ACS about the meaning of their symptoms may be useful for reducing the psychological impact of being ruled out for ACS.

Figure 1.

Reasons for Symptoms Among Patients Presenting to the Emergency Department with Suspected Acute Coronary Syndrome (N=1,000)

Legend: Confirmed ACS, symptoms due to a confirmed acute coronary syndrome; Non-ACS NOS, symptoms due to a non-specified reason; MSK, symptoms due to a musculoskeletal disorder; Non-ACS Cardiac, symptoms due to a cardiac disorder other than ACS; GI, symptoms due to a gastrointestinal disorder; Other, symptoms due to a specific cause other than those listed; Anxiety, symptoms due to anxiety; Cocaine, symptoms due to cocaine ingestion

Table 1.

Patient Sociodemographic and Medical Characteristics at Presentation to the Emergency Department According to Final Acute Coronary Syndrome Status

Characteristic	Overall (N=998)	Confirmed ACS (N=317; 31.8%)	Ruled Out for ACS (N=681; 68.2%)	P-value
Age, mean (SD), years	60.81 (13.17)	62.74(12.56)	59.91 (13.35)	0.001
Female	455 (45.6%)	115 (36.2%)	340 (49.9%)	<0.001
Hispanic	544 (56.7%)	163 (53.8%)	379 (57.9%)	0.24
Black	233 (23.3%)	62 (19.5%)	171 (25.1%)	0.05
High school diploma or less	515 (51.6%)	164 (49.1%)	319 (46.8%)	0.15
Has a partner	444 (44.5%)	158 (49.8%)	286 (42.0%)	0.02
Charlson score, mean (SD)	1.87 (2.04)	2.20 (1.94)	1.71 (2.07)	<0.001
History of CAD	315 (31.6%)	172 (54.2%)	143 (21.0 %)	<0.001
ACS Evaluation				
Cardiac stress test	256 (25.6%)	75 (23.6%)	181 (26.5%)	0.32
Coronary angiogram	238 (23.8%)	196 (61.6%)	42 (6.2%)	<0.001

Data are presented as N (%) unless otherwise specified.

Denominator does not always equal to 1,000 as data were missing for some characteristics; data on 1% or fewer patients are missing for these variables.

Abbreviations: CAD, coronary artery disease; ACS, acute coronary syndrome

Table 2.

Somatic and Psychological Characteristics of Patients Presenting to the Emergency Department with Probable Acute Coronary Syndrome Symptoms

	Confirmed ACS (N=317; 31.8%)	Ruled Out for ACS (N=681; 68.2%)	P-value
<i>At emergency department presentation (N=1,000)</i>			
Somatic ACS symptoms			
Chest pain or pressure, N (%)	306 (96.5%)	632 (93.4%)	0.04
Arm pain, N (%)	109 (34.4%)	240 (35.5%)	0.74
Jaw pain, N (%)	42 (13.2%)	79 (11.7%)	0.48
Shortness of breath, N (%)	177 (55.8%)	397 (58.6%)	0.40
Nausea, N (%)	77 (24.3%)	171 (25.3%)	0.74
Vomiting, N (%)	23 (7.3%)	49 (7.2%)	0.99
Dizziness, N (%)	115 (36.3%)	265 (39.1%)	0.39
Psychological symptoms			
Threat perceptions due to current ACS symptoms, median (IQR)	11.03 (4.14)	10.92 (4.50)	0.29
Number of types of potentially traumatic life events, median (IQR)	2.86 (2.65)	2.71 (3.11)	0.02
Depressive symptoms (PHQ-8 score), median (IQR)	6.18 (5.68)	6.66 (6.03)	0.24
PTSD symptoms due to prior trauma, median (IQR)	24.89 (12.15)	25.72 (13.53)	0.41
<i>At 1 month after discharge (N=817)</i>			
PTSD symptoms due to probable ACS experience (PCL-S), mean (SD)	24.72 (11.08)	24.79 (11.33)	0.93
Elevated PTSD symptoms (PCL-S 32), N(%)	46 (16.8%)	102 (18.9%)	0.47
Probable PTSD (PCL-S 44), N(%)	25 (9.1%)	42 (7.8%)	0.50

Abbreviations: ACS, acute coronary syndrome; PHQ, Patient Health Questionnaire-8 item; PTSD, posttraumatic stress disorder; PCL-S, PTSD Checklist due to a specific stressor

Table 3.

Odds of Developing a Positive PTSD Screen 1 Month After Discharge in Patients Who Ruled Out for Acute Coronary Syndrome Versus Patients with a Confirmed Acute Coronary Syndrome (N=817)

Characteristic	Positive PTSD Screen at 1 Month (PCL-S 32) Odds Ratio, 95% CI	P- value	Positive PTSD Screen at 1 Month (PCL-S 32) Odds Ratio, 95% CI	P-value
Ruled Out for ACS Confirmed ACS	1.02 (0.97, 1.08) 1 (Ref)	0.47	0.85 (0.50, 1.44) 1 (Ref)	0.55
Age	-	-	0.99 (0.97, 1.01)	0.27
Male	-	-	0.60 (0.35, 0.99)	0.05
Hispanic	-	-	0.64 (0.35, 1.16)	0.14
Black	-	-	0.83 (0.44, 1.56)	0.56
Less than high school diploma	-	-	0.92 (0.55, 1.53)	0.74
Have a partner	-	-	0.96 (0.57, 1.61)	0.88
Charlson score	-	-	1.00 (0.95, 1.07)	0.90
History of CAD	-	-	1.37 (0.77, 2.41)	0.29
Depressive symptoms (PHQ-8 score)	-	-	1.11 (1.07, 1.16)	<0.001
Cumulative traumatic life events (Life Events Checklist)	-	-	1.04 (0.95, 1.14)	0.37
PTSD symptoms due to prior traumatic event (PCL-C)	-	-	1.04 (1.02, 1.06)	<0.001

Abbreviations: ACS, acute coronary syndrome; CAD, coronary artery disease; PTSD, posttraumatic stress disorder; PCL-S, PTSD Checklist due to a specific stressor (i.e., the ACS symptoms that brought patient to the emergency department); PCL-C, PTSD Checklist-Civilian version