Reevaluating the Association Between Emergency Department Heart Rate and the Development of Posttraumatic Stress Disorder: A Public Health Approach

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Background: *Preliminary investigations in select samples of trauma survivors presenting to acute care settings suggest an association between elevated emergency department heart rate (HR) and the subsequent development of posttraumatic stress disorder (PTSD). Other studies suggest no association, however.*

Method: *In a prospective cohort study of a population-based sample of 161 acutely injured surgical inpatients, HR was assessed at initial presentation to the emergency department. Symptoms of PTSD were assessed with the PTSD Checklist at the time of the surgical inpatient hospitalization and 1, 4–6, and 12 months postinjury.*

Results: *Emergency department HR ≥ 95 beats per minute (BPM) was a significant independent predictor of PTSD symptoms in analyses that adjusted for relevant injury, clinical, and demographic characteristics. This HR cutoff demonstrated modest specificity (range 60%–65%) and sensitivity (range 49%–63%) for the prediction of chronic PTSD.*

Conclusions: *We found an independent association between elevated emergency department HR ≥ 95 BPM and PTSD symptoms in a representative sample of injured acute care inpatients. Future investigations that incorporate clinical epidemiologic methods in the study of acute care biological parameters have the potential to improve the quality of mental health care delivered to injured survivors of individual and mass trauma.*

Key Words: Acute care, disaster mental health, heart rate, PTSD, screening, traumatic injury

Investigations in select samples of trauma survivors initially presenting to acute care settings suggest an association between elevated emergency department heart rate (HR) and the development of posttraumatic stress disorder (PTSD; Bryant et al 2000; Shalev et al 1998), although not all studies have confirmed this (Blanchard et al 2002). This association is thought to reflect a role for immediate postevent adrenergic activity and the subsequent development of PTSD. In animal models, administration of epinephrine after aversive training enhances the consolidation of amygdala-mediated learning and fear conditioning (Gold and McCarthy 1995; McGaugh 1990; McGaugh et al 1984). It has been postulated that an excess of epinephrine at the time of a traumatic life event may lead to an overly strong emotional memory and fear conditioning that underlies the development of PTSD (Pitman 1989). Although these considerations are still preliminary, some clinical investigators have adopted HR cutoffs as screening criteria for the initiation of preventative treatment (Gidron et al 2001; Pitman et al 2002; Vaiva et al 2003).

Because survivors of individual and mass trauma are initially triaged through acute care facilities, these findings have taken on broader significance since the September 11, 2001, terrorist attacks. Within 48 hours after the attack on the World Trade Center, 1,103 trauma survivors were triaged through five New York trauma centers and hospitals (Centers for Disease Control and Prevention 2002). Trauma exposure in civilians and combat veterans, when coupled with physical injury, confers a high risk for the development of PTSD (Green 1993; Helzer et al 1987).

Brief PTSD screening instruments tailored for the acute care setting are now under development (Winston et al 2003). Nonetheless, pragmatically oriented, time-efficient acute care providers have been slow to adopt mental health screening procedures that extend beyond established routine vital sign and physical exam assessments (Danielsson et al 1999; Gentilello et al 1999). These tendencies can only be expected to amplify under mass casualty conditions, leaving initial emergency department HR as potentially the most feasibly implemented early PTSD screen.

We therefore sought to investigate two questions. First, we assessed whether elevated emergency department HR was an independent predictor of PTSD symptom development even after adjusting for relevant acute care demographic, clinical, and injury characteristics. Second, we assessed the utility of using emergency department HR to screen for the development of chronic PTSD. The clinical epidemiologic approach employed by the investigation was designed to optimize the public health relevance of the findings. The investigation recruited a population-based sample of injured acute care inpatients from two trauma centers in the United States. Heart rate measurements were derived from routine emergency department vital sign assessments, and PTSD symptoms were assessed with self-report measures over the course of the year after traumatic injury.

Methods and Materials

This investigation was completed as part of previously described larger studies of symptomatic, functional, and service utilization outcomes among injured trauma survivors (Zatzick et al 2002, 2004).

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Patients were recruited from the University of California at Davis ($n = 100$) and University of Washington Harborview ($n = 61$) level I trauma centers. Patients were randomly approached for participation as surgical inpatients. The injury, clinical, and demographic characteristics of patients included in the investigations did not differ substantially from the characteristics of the overall population of patients admitted to the trauma centers during the period of investigation (Zatzick et al 2002, 2004). Only patients who were monolingual non-English speaking or so severely injured that they could not participate in the investigation were excluded. Patients were interviewed in the surgical ward and then again 1, 4–6, and 12 months postinjury. Patients included in the study received usual posttraumatic care over the course of the year following their injury.

Ethical Safeguards

All informed consent procedures and trauma registry analyses were approved by the University of California at Davis and the University of Washington institutional review boards prior to the initiation of the investigation. Written informed consent was obtained from all participants after a detailed description of the study. For a comprehensive review of the safety of the recruitment and consent procedure, see (Ruzek and Zatzick 2000). Patient responses to interview items assessing reactions to research participation demonstrated that a substantial majority of subjects tolerated the interview procedure well and felt they could discontinue the protocol at any time (Ruzek and Zatzick 2000).

Assessment of Emergency Department HR

Emergency department HR assessments were derived from the first recorded value for HR in the emergency department medical record. Techniques for the assessment of initial HR for injured patients admitted to the UC Davis Harborview level I trauma center emergency department vary depending on the nature and severity of patient presentations. The majority of Harborview emergency department admission vital sign assessments are conducted using Space Labs Medical (Redmond, Washington) automated vital sign monitors. Only initial HR upon presentation to the emergency department was used in the investigation.

PTSD Assessment

The Post-Traumatic Stress Disorder Checklist, civilian version (PCL), was used to assess PTSD symptoms (Weathers and Ford 1996). A series of investigations have demonstrated the reliability and validity of the PCL across trauma-exposed populations (Asmundson et al 2000; Blanchard et al 1996; Dobie et al 2002; Walker et al 2002; Weathers and Ford 1996). The PCL allows for the ascertainment of a continuous symptom score and a dichotomous algorithm for symptoms consistent with a diagnosis of a DSM-IV diagnosis of PTSD. We used the continuous scale score as the dependent variable in the random regression and ANCOVA analyses that aimed to answer the first research question, is emergency department HR an independent predictor of PTSD symptom development over the course of the year after injury? We used the dichotomous DSM-IV algorithm when calculating the specificity and sensitivity of a HR cutoff for the prediction of chronic PTSD.

Other Clinical, Injury, and Demographic Characteristics

The Center for Epidemiologic Studies Depression Scale (CES-D) was used to assess depressive symptoms in the surgical ward and 1, 4–6, and 12 months postinjury (Radloff 1977). We assessed the number of traumas that predated the index injury event with the trauma history screen developed for the National Comorbidity Survey (Kessler et al 1995). Injury type and severity, medical comorbidities, alcohol and stimulant (i.e., cocaine and amphetamine) intoxication, and opiate administration prior to emergency department admission as well as patient demographic characteristics were derived from trauma registry data. Alcohol, opiate, and stimulant toxicology results were dichotomized as present or absent.

Statistical Analyses

To determine an optimal HR cutoff, we first performed a review of the relevant literature in order to identify an appropriate range of values for consideration in our population of hospitalized injured trauma survivors (Gidron et al 2001; Pitman et al 2002; Vaiva et al 2003). Next, we used ROC curve analysis in combination with visual examination of longitudinal PTSD data to determine an emergency department HR cutoff that optimized the prediction of high levels of PTSD symptoms over the course of the year after injury.

We used mixed-effects random-coefficient regression models to determine whether patients in the high and low emergency department HR groups manifested significantly different patterns of symptom change over time. Post hoc analyses of covariance (ANCOVAs) were used to determine whether emergency department HR grouping was independently associated with differences in PTSD for patients in the two groups cross-sectionally, 4–6 and 12 months after the injury. Age, gender, injury type (intentional vs. unintentional) and injury severity, chronic medical conditions, number of prior traumas, trauma center site, and alcohol, opiate, and stimulant toxicology results were included in all regression and ANCOVA analyses as covariates. Sensitivity and specificity of the HR cutoff was assessed for the 4–6 and 12 month follow-up assessments.

Results

The mean initial emergency department HR for the sample was 93.8 (SD 17.2). The mean inpatient length of stay was 5.6 days (4.7 days) The mean PCL score for the entire cohort was 36.3 (12.8) in the surgical ward, 39.5 (17.4) 1 month postinjury, 36.5 (16.8) 4–6 months postinjury, and 35.3 (17.1) 12 months postinjury. Patients with emergency department HR $\geq$ 95 beats per minute (BPM) demonstrated elevated mean PCL scores at the 1-, 4- to 6-, and 12-month follow-ups compared with patients with HR $<$ 95 BPM (Figure 1). Patients in the two HR groups did not differ significantly with regard to injury, clinical, and demographic characteristics with the exception of a significantly increased frequency of patients with positive alcohol toxicology results in the HR $\geq$ 95 BPM group (Table 1).

The random regression procedure revealed a significant HR group-by-time interaction effect for PTSD symptoms (estimate = 1.99, standard error = .82, $p = .02$) for the HR of 95 BPM cutoff. An HR cutoff of 95 BPM was independently associated with significantly elevated PTSD symptoms after adjustment for injury, clinical, and demographic characteristics at the 4- to 6-month [$F = 14.4(126,1)$, $p < .01$], and 12-month [$F = 3.8(115,1)$, $p = .05$] postinjury assessments. The HR cutoff of 95 BPM had a specificity of 65% and sensitivity of 63% for the prediction of PTSD symptomatic criteria at 4–6 months and a specificity of 60% and sensitivity of 49% at 12 months postinjury.

The HR cutoff of 95 BPM showed no significant group-by-time interaction effect (estimate = 1.07, standard error = .72, $p = .14$) for the prediction of CES-D scores over the year following injury. Alcohol (estimate = 2.42, standard error = 2.11,

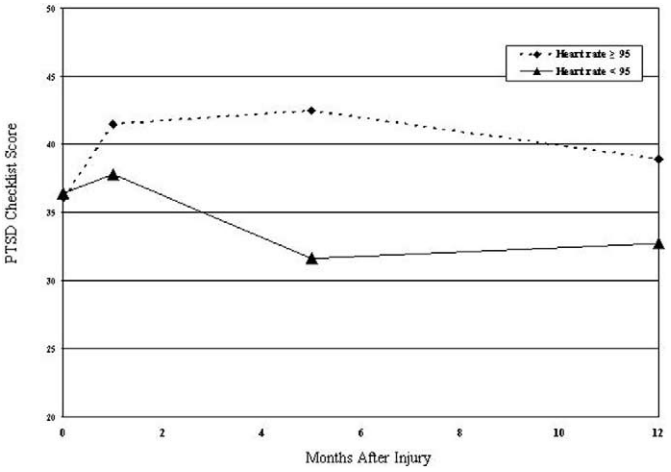

Figure 1. Posttraumatic stress disorder (PTSD) symptoms in patients with emergency department heart rate (HR) ≥ 95 beats per minute (BPM; $n = 76$) and HR < 95 BPM ($n = 85$). Patients' PTSD symptoms were assessed with the PTSD Checklist (PCL; Weathers and Ford 1996). Assessment points include surgical inpatient ward ($n = 161$), 1 month ($n = 141$, 88%), 4–6 months ($n = 127$, 79%), and 12 months postinjury ($n = 116$, 72%). Patients in the HR ≥ 95 group had mean PCL scores of 36.1 in the surgical ward, 41.5 at 1 month, 42.5 at 4–6 months, and 38.9 at 12 months postinjury. Patients in the HR < 95 BPM group had mean PCL scores of 36.4 in the surgical ward, 37.8 at 1 month, 31.6 at 4–6 months, and 32.7 at 12 months postinjury. All PCL mean scores are adjusted for age, gender, injury type, injury severity, chronic medical conditions, number of prior trauma, trauma center site, and alcohol, opiate, and stimulant toxicology results.

$p = .25$) or cocaine (estimate = 4.20, standard error = 2.81, $p = .14$) intoxication at the time of the acute care admission did not significantly contribute to the prediction of PCL scores in the random regression model that included the HR cutoff of 95. Also, random regression analyses that assessed the relationship between emergency department HR cutoffs of 80 BPM (estimate = −.26, standard error = 1.06 , $p = .81$), 85 BPM (estimate = -.34, standard error = .89, $p = .70$), 90 BPM (estimate = −.02, standard error = .83 , $p = .98$), 100 BPM (estimate = 1.46, standard error = .85 , $p = .09$), and continuous emergency department HR (estimate = .02, standard error = .02, $p = .36$) demonstrated no significant group by time interaction effects.

Discussion

We found that in hospitalized injury survivors, elevated emergency department HR ≥ 95 was an independent predictor of PTSD symptom development over the course of the year after injury. The prospective design, representative sampling procedure, and adjustment for multiple acute care confounds corroborate and extend the finding of an association between elevated emergency department HR and the development of PTSD described in the prior reports by Shalev et al (1998) and (Bryant et al 2000). The (Shalev et al 1998) investigation employed a prospective design in a select sample of 91 injured trauma survivors who were discharged from the emergency department within 12 hours and did not require inpatient injury admissions. Shalev et al excluded 105 patients who had incurred severe head or other injuries or had current or lifetime substance abuse. Heart rate was routinely recorded by a registered nurse in the emergency department and then by expert research staff 1 week, 1 month, and 4 months after the injury. Expert clinicians diagnosed PTSD at each assessment point using the Clinician Administered PTSD Scale (Blake et al 1990). Emergency department HR correlated significantly with chronic PTSD symptoms 4 months after the injury and in multivariate models added significantly to the prediction of 4-month PTSD. Bryant et al (2000) employed a prospective design and standardized expert clinician assessments of HR and acute stress disorder (ASD)/PTSD (Composite International Diagnostic Interview; World Health Organization 1997) to assess the relationship between HR and the development of chronic PTSD 6 months postinjury. Bryant et al consecutively sampled hospitalized injury survivors, and systematically excluded patients who were prescribed beta-blockers, hypertensive medication, or narcotic analgesia within 4 weeks after the trauma. Heart rate was assessed on the day of hospital discharge and added significantly to the prediction of PTSD 6 months after the injury admission. Taken together these three prospective investigations provide support for an association between elevated sympathetic arousal and the development of enduring PTSD symptoms in acutely traumatized patients, despite variations in HR and PTSD assessments, participant injury severity, study inclusion and exclusion criteria, and timing and duration of follow-up.

The results of these investigations stand in contrast to the study by Blanchard et al (2002) that found a significant negative association between emergency department HR and increasing PTSD symptom levels. Blanchard et al enrolled 76 treatment-seeking motor vehicle crash survivors who had been admitted to multiple emergency departments and were recruited through advertisements and local media coverage. The investigation used routine emergency department HR assessments recorded in medical records. Participants underwent expert clinician diagnostic assessments (CAPS; Blake et al 1990) approximately 13 months after the initial trauma; during this assessment, a retrospective assessment of PTSD 1 month after the crash was also performed.

In our investigation, we observed that the HR cutoff of 95 BPM was not a significant predictor of the development of depressive symptoms despite the fact that major depressive disorder (MDD) has been associated with elevated HR in a number of investigations (Carney et al 1999; Moser et al 1998). Similarly, Shalev et al (1998) found that emergency department HR significantly predicted 4-month PTSD and anxiety but not

Table 1. Demographic, Injury, and Clinical Characteristics of Patients with Emergency Department HR <95 or ≥95 BPM.

	HR <95 BPM ($n = 85$)	HR ≥95 BPM ($n = 76$)	Statistical Test $\chi^2(1)$ or $t(159)$
% Sample from UC Davis	57.6	67.1	1.15
% Male	63.5	69.7	.44
% Caucasian	57.6	53.3	.15
% Married	32.9	21.1	2.29
Age, Mean (SD)	38.0 (15.4)	34.3 (12.6)	1.66
% Unintentional Injury	77.6	67.1	1.75
% Cocaine or Amphetamine Positive	10.6	17.1	.94
% Alcohol Toxicology Positive	28.2	46.1	4.75[a]
% Opiate Positive	17.6	9.2	1.76
% With One or More Chronic Diseases	14.1	17.1	.09
ISS Score, Mean (SD)	8.4 (5.8)	10.4 (8.4)	1.72
Number of Prior Traumas, Mean (SD)	3.5 (2.2)	3.8 (2.1)	.66

[a] $p < .05$.

depressive symptoms. This is consistent with the possibility that autonomic nervous system perturbations develop as a consequence of MDD, whereas for PTSD increased autonomic activity contributes to the pathogenesis of the disorder (Carney et al 1999; Gold and McCarthy 1995; McGaugh 1990; McGaugh et al 1984; Moser et al 1998).

This and prior acute care investigations document that a substantial proportion of injured patients initially triaged in the acute care setting are intoxicated with alcohol, stimulants, or other substances at the time of the injury (Dunn et al 2003; Schermer and Wisner 1999; Soderstrom et al 1997). Although a previous pilot investigation suggested a possible protective effect of alcohol intoxication at the time of injury (Mellman et al 1998), we found no protective or deleterious effect of alcohol intoxication on the development of PTSD. Similarly, we did not identify a significant protective or deleterious effect of stimulant intoxication, despite a previous population-based investigation that found stimulant intoxication at the time of the acute care admission was independently associated with the development of elevated PTSD symptom levels during the year after injury (Zatzick et al 2002).

A number of potential compounds have been recommended as early intervention agents for the secondary prevention of PTSD (Friedman 2002) including antiadrenergic agents. Encouraging pilot trials of propranolol for select samples of injured emergency department attendees (Pitman et al 2002) and injured acute care inpatients (Vaiva et al 2003) have been published. We previously suggested that the development of secondary prevention strategies for PTSD could capitalize on medication regimes already being routinely delivered in acute care settings (Zatzick and Roy-Byrne 2003). Our investigation documents that approximately 10% of injured patients receive opiate pain medication from acute care providers and are opiate toxicology positive at the time of injury admission. Trauma registry data suggests that a majority of injured surgical inpatients receive opiate pain medications and a substantial number also continue to require opiate analgesics in the days and weeks postinjury (Zatzick and Roy-Byrne 2003). Opiates have been identified as potent anxiolytics in animal models (Golub and Kaaekuahiwi 1995) and pain responses appear to be regulated in part by centrally mediated catecholamine metabolism (Vastag 2003; Zubieta et al 2003). Preliminary studies suggest that adequate levels of opiate pain control are associated with the development of lower PTSD symptom levels in child burn injury survivors (Saxe et al 2001). Thus, newer agents such as GABA P and pregabalin with combined analgesic and anxiolytic properties may also hold promise as early preventive agents for acutely injured trauma survivors (Feltner et al 2003; Nemeroff 2003; Sabatowski et al 2004; Spira and Beran 2003).

There are a number of important considerations in interpreting the results of this investigation. First, in accord with the public health approach, the investigation relied on a single naturalistic measurement of HR routinely obtained in the emergency department. Also, the investigation employed self-report assessments of symptom severity rather than structured clinical interviews to assess PTSD. Although potentially enhancing the generalizability of study results, these assessments are vulnerable to inaccuracy and may in part be responsible for the variability of findings across acute care studies. Finally, we did not adjust in our regression models for the experience of intense fear, helplessness, or horror at the time of the injury (DSM-IV A2 PTSD criteria; American Psychiatric Association 1994). In our experience, patients frequently present to the emergency department either unconscious (e.g., head injury) or obtunded (e.g., alcohol intoxication). Retrospective reports of peritraumatic distress appear to be strongly influenced by current posttraumatic symptom levels (Marshall and Schell 2002). Thus, accurate assessments of early symptomatic distress may be difficult to attain for acute care patients, particularly in high-volume mass trauma scenarios.

These observations are what led to our investigative focus on the feasibility of using a readily available, objective measure, such as emergency department HR, as an early screen for PTSD symptom development after traumatic injury. Injured trauma survivors triaged through acute care in the immediate aftermath of a mass attack represent a high-risk subgroup of patients who are rapidly transported to central points of contact within the health care system (MacKenzie et al 2003; Ursano 2002; Zatzick 2003). It is premature to recommend a specific HR cutoff as a proxy for PTSD screening after individual or mass trauma. We observed only modest sensitivity and specificity for the HR cutoff of 95 BPM in the prediction of chronic PTSD. In particular, use of a screen with sensitivities between 49% and 63% risks screening out a substantial proportion of patients who will go on to develop PTSD. Previous acute care reports have enhanced the predictive value of initial emergency department HR by combining HR cutoffs with other clinical characteristics to develop PTSD screening algorithms (Bryant et al 2000; Winston et al 2003). Future population-based investigations could test the HR cutoff of 95 BPM derived in our study as a screening tool alone and in combination with other demographic, injury, and clinical characteristics readily available for injured acute care inpatients. Subsequent investigations that incorporate clinical epidemiological methods in the study of acute care biological parameters, have the potential to improve the quality of mental health care delivered to injured survivors of individual and mass trauma.

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