OPEN

Posttraumatic Stress Disorder Symptom Clusters in Surrogate Decision Makers of Patients Experiencing Chronic Critical Illness

OBJECTIVES: Symptoms of posttraumatic stress disorder (PTSD) are common among surrogate decision makers of patients with chronic critical illness (CCI). PTSD symptoms can be categorized into clusters including intrusion, avoidance, and hyperarousal, each of which has been associated with distinct outcomes and treatment responses. Our objective was to determine which symptom cluster was predominant among surrogates of patients with CCI.

DESIGN: Secondary analysis of data from a clinical trial of a communication intervention.

SETTING: The original trial was conducted in medical intensive care units at three tertiary-care centers and one community hospital.

PATIENTS: Patients with CCI (\geq 7 d of mechanical ventilation and not expected to die or to be weaned from the ventilator in the subsequent 72 hr) and their surrogates.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Surrogate PTSD symptoms were measured 90 days after onset of patient CCI using the Impact of Events Scale-Revised (IES-R). The IES-R includes a total score (range, 0–88, higher scores indicate severe symptoms) as well as three subscales that assess intrusion, avoid-ance, and hyperarousal (range of intrusion and avoidance scores 0–32 and range of hyperarousal score 0–24). Intrusion symptoms were most severe (mean score, 10.3; 95% CI, 9.3–11.2), followed by avoidance (mean score, 8.0; 95% CI, 7.2–8.8). Hyperarousal symptoms were lowest (mean score, 5.1; 95% CI, 4.5–5.7). In a multivariable linear regression model, we found that surrogates of patients who died had higher odds of intrusion (β , 5.52; p < 0.0001) and avoidance (β , 3.29; p = 0.001) symptoms than surrogates of patients who lived, even after adjusting for baseline symptoms of anxiety and depression. Patient death was not associated with hyperarousal symptoms.

CONCLUSIONS: Intrusive thoughts are the most severe PTSD symptom in surrogates of patients experiencing CCI, with intensified symptoms among surrogates of patients who died. These results have the potential to inform tailored treatment strategies to reduce PTSD symptoms in this population.

KEY WORDS: chronic critical illness; family caregiver; posttraumatic stress disorder symptom clusters; posttraumatic stress disorder; surrogate decision maker

Posttraumatic stress disorder (PTSD) is defined as the somatic, cognitive, affective, and behavioral effects of psychological trauma (1). Although certain forms of trauma such as sexual violence, severe physical injury, and military combat are well-described triggers for PTSD, admission to an ICU is gaining recognition as a traumatic event for both patients and their surrogate decision makers (2–5). Prior studies have shown that up to 80% of surrogates

Agathe Ceppe, MS¹ Bradley N. Gaynes, MD^{2,3} Christopher E. Cox, MD⁴ Laura C. Hanson, MD⁵ Judith E. Nelson, MD^{6,7} Shannon S. Carson, MD¹

Blair Wendlandt, MD¹

Copyright © 2022 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of the Society of Critical Care Medicine. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/CCE.00000000000647

experience significant symptoms of PTSD within the first few days of a loved one's ICU admission, and that 6 months later as many as 35% of surrogates report persistent, significant PTSD symptoms (6, 7). Risk factors for surrogates' PTSD symptoms include patient death as well as their own age and sex, higher levels of anxiety and depression at the time of ICU admission, and perception of inadequate emotional support and communication from healthcare workers in the ICU (8–10). Poor patient outcomes and greater caregiving burden are predictive of higher levels of psychological distress and worse quality of life for family caregivers, who often act as surrogate decision makers (11–15).

Although interventions to reduce surrogate PTSD have the potential to benefit both patients and surrogates, interventions to date have been largely unsuccessful (16–21). One potential reason for this is that these interventions have been targeted to surrogates based on patient condition (such as severity of illness or number of days on the ventilator) rather than tailored for surrogates' own experiences with a loved one's illness and symptom profile.

According to the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition), symptoms of PTSD can be categorized into distinct clusters including intrusive thoughts or reexperiencing of the traumatic event (intrusion), persistent avoidance of stimuli associated with the traumatic event (avoidance), and persistent symptoms of increased arousal such as anger or irritability (hyperarousal) (22). Although individuals with PTSD will generally display symptoms from each cluster, the relative severity of each cluster often differs between individuals (23-25). Research has shown that distinct PTSD symptom clusters can be associated with specific outcomes (26, 27). For example, in a cohort of combat veterans in the U.S. military, avoidant symptoms were associated with higher rates of alcohol abuse than intrusion or hyperarousal symptoms (28). Furthermore, it has been shown that PTSD symptom cluster can inform personalized treatment strategies for PTSD (29). For example, individuals that display intrusion-predominant symptoms may be more responsive to particular classes of pharmacotherapy such as selective serotonin reuptake inhibitors (SSRIs), whereas individuals who display more severe hyperarousal symptoms may be more responsive to cognitive behavioral therapy (30).

The relative contribution of each PTSD cluster to overall symptom burden has not previously been

described in medical ICU surrogate decision makers. To better characterize risk for adverse future outcomes and to inform the development of tailored interventions to reduce surrogate distress, we sought to identify the predominance of different PTSD symptom clusters among ICU surrogates. We hypothesized that hyperarousal would be the predominant symptom cluster displayed by ICU surrogate decision makers, with more severe symptoms among surrogates who experienced patient death than those who did not, given that many of the key hyperarousal symptoms (hypervigilance, sleep disturbance, and anger) have previously been described by families of critically ill patients (31, 32).

MATERIALS AND METHODS

We conducted a secondary analysis of data from a randomized trial of a communication intervention for surrogate decision makers of patients experiencing chronic critical illness (CCI) (16). The intervention consisted of a series of palliative care-led meetings with enrolled surrogates that were protocolized to focus primarily on patient prognosis. The intervention was compared with a control group of usual care with family meetings led by ICU clinicians without the protocolized communication template. Adult patients were eligible for inclusion in the original clinical trial if they had received mechanical ventilation for at least 7 days and were unlikely to die or to be liberated in the next 72 hours. Requiring mechanical ventilation for at least 7 days is a widely used criteria for the definition of prolonged mechanical ventilation, which is in turn one of the accepted diagnoses used to define CCI (33, 34). Patients with major trauma, burns, or neuromuscular weakness were excluded, as were patients with prior palliative care consultation or ICU admission during the research hospitalization. For each patient, a primary surrogate decision maker was enrolled as designated by either patient choice or applicable state law. If one or more additional surrogate decision makers were involved, these individuals were enrolled as well. Enrollment generally occurred on or around day 10 of mechanical ventilation, at which time baseline patient and surrogate characteristics were assessed. All enrolled patients and surrogates with complete 90-day follow-up data were included in our secondary analysis.

Surrogate psychological distress symptoms were measured at the time of enrollment using the Hospital

Anxiety and Depression Scale (HADS) Score (35). The HADS consists of two subscales (anxiety and depression), each containing seven items with a score ranging from 0 (lowest level of symptoms) to 3 (highest level of symptoms). A score greater than or equal to 11 on either subscale suggests the presence of anxiety and/or depression disorder(s); scores from 8 to 10 may represent "borderline" symptom levels. Patient level of alertness was measured once at the time of trial enrollment by a trained research coordinator using the Richmond Agitation Sedation Scale (RASS) score (36). For this analysis, the RASS score was categorized as greater than or equal to 0 (awake), -1 to -3 (arousable), and -4 or -5 (unresponsive). Patient chronic comorbidities, including history of cancer, liver disease, end-stage renal disease, and stroke, were obtained via chart abstraction at the time of enrollment. Patient and surrogate outcomes, including patient death and surrogate PTSD symptoms, were then measured 90 days after trial enrollment.

Surrogates' PTSD symptoms were assessed using the Impact of Events Scale-Revised (IES-R), a core outcome measure for assessing PTSD symptoms following ICU admission among patients and their family members (37). The IES-R contains 22 items that measure symptom clusters of intrusion, avoidance, and hyperarousal over the last 7 days (**Fig. 1**) (38, 39). Item scores range from 0 (least distressing) to 4 (most distressing), with a total score ranging from 0 to 88, with the intrusion and avoidance subscores ranging from 0 to 32 each and the hyperarousal score ranging from 0 to 24. The Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 splits the avoidance cluster

IES-R Questionnaire, questions categorized by symptom cluster		
Intrusion		
Any reminder brough back feelings about it		
I had trouble staying asleep		
Other things kept making me think about it		
I thought about it when I didn't mean to		
Pictures about it popped into my mind		
I found myself acting or feeling like I was back at that time		
I had waves of strong feelings about it		
I had dreams about it		
Avoidance		
I avoided letting myself get upset when I thought about it or was reminded of it		
I felt as if it hadn't happened or wasn't real		
I stayed away from reminders of it		
I tried not to think about it		
I was aware that I still had a lot of feelings about it, but I didn't deal with them		
My feelings about it were kind of numb		
I tried to remove it from my memory		
I tried not to talk about it		
Hyperarousal		
I felt irritable and angry		
I was jumpy and easily startled		
I had trouble falling asleep		
I had trouble concentrating		
Reminders of it caused me to have physical reactions, such as sweating, trouble breathing,		
nausea, or a pounding heart		
I felt watchful and on-guard		

Figure 1. Impact of events scale-revised questions categorized by symptom cluster. *Top row*, Questions assessing intrusion symptoms. *Middle row*, Questions assessing avoidance symptoms. *Bottom row*, Questions assessing hyperarousal symptoms.

into separate "avoidance" and "negative alterations in cognition and moods" clusters, between which the IES-R does not distinguish, but this change was made well after the clinical trial began (22).

For analyses, descriptive statistics were first performed using means and 95% confidence intervals for continuous variables and percentages for categorical variables. We determined the mean total IES-R score as well as symptoms cluster scores at 90 days. To assess whether the risk for each symptom cluster differed between surrogates of patients who died and surrogates of patients who survived, we performed three separate multiple linear regression models, each with patient death by 90 days as the exposure and surrogate PTSD symptom cluster score as the outcome. Covariates were selected based on prior literature and mechanistic plausibility using a directed acyclic graph, which is the recommended method for guiding studies of causal inference in critical care research (40, 41). The selected covariates were patient age, surrogate symptoms of anxiety and depression at time of trial enrollment, patient history of cancer, patient history of chronic liver disease, and patient level of arousal as measured by the RASS score (directed acyclic graph shown in Supplemental Figure 1, http://links. lww.com/CCX/A938). The model was adjusted for multiple respondents, using a mixed model, considering the patients as a random factor. All tests were two-sided, with a significance level of 0.05. Analysis was performed using Statistical Analysis System 9.4 (SAS Institute, Cary, NC). This work was approved by the University of North Carolina Institutional Review Board (10-1692).

RESULTS

Complete 3-month follow-up data were present for 224 patients and their 306 surrogate decision makers (84% surrogate retention rate). Patients were 49% (n = 109) female, a mean age of 59 years (95% CI, 56.4–60.7 yr), and were enrolled on mean day 10 (sD, 3.4) of mechanical ventilation. Surrogates were primarily female (n = 218 [71%]) and middle-aged (mean age, 51 yr [95% CI, 49.3–52.4 yr]). Mean surrogate HADS score at the time of enrollment was 16.0 (95% CI, 15.1–16.9), indicating moderate distress. Mean total hospital length of stay was 47.7 days. By 90 days, n = 94 patients (43%) had died and nearly one-third of those alive (n = 39 [31%]) resided in a medical facility; death and other patient outcomes did not differ between intervention and control groups in the original clinical

TABLE 1.Characteristics of Surrogate DecisionMakers

Characteristic	Surrogate Decision Makers (n = 306)
Age, mean (95% Cl), yr	51 (49.3–52.4)
Female sex, n (%)	218 (71)
Ethnicity, <i>n</i> (%) Hispanic or Latino	38 (12)
Not Hispanic or Latino	267 (88)
Race, n (%)	207 (00)
Black	72 (24)
Caucasian	193 (63)
Other	41 (13)
Marital status	
Married/live with partner	207 (68)
Separated/divorced	38 (12)
Single/widowed	61 (20)
Education	
Advanced degree	53 (17)
College graduate	82 (27)
Some college	84 (28)
High school or less	86 (28)
Employment	
Disabled from employment	30 (10)
Employed/student	168 (55)
Homemaker	22 (7)
Retired	58 (19) 27 (9)
Unemployed Relationship	27 (9)
Child	109 (36)
Parent	41 (13)
Sibling	37 (12)
Spouse/partner	100 (33)
Other	19 (6)
Previous diagnosis of depression	103 (28)
Previous diagnosis of anxiety	80 (22)
Number of decision makers per patient	t
1	152 (50)
≥ 2	154 (50)
Hospital Anxiety and Depression Scale score at baseline, mean (95% Cl)	
Total	16 (15.1–16.9)
Anxiety subscale	10 (9–10.1)
Depression subscale	7 (6–7)

trial. Surrogate and patient characteristics are shown in **Tables 1** and **2**.

TABLE 2. Characteristics of Patients

Characteristic	Patients (<i>n</i> = 224)
Age, mean (95% CI), yr	59 (56.4–60.7)
Female sex, n (%)	109 (49)
Race, <i>n</i> (%)	
Black	53 (24)
Caucasian	138 (63)
Unavailable	17 (8)
Other	10 (5)
Insurance, n (%)	
Medicare	107 (48)
Medicaid	20 (9)
Commercial	76 (34)
None	21 (9)
Language	
English	197 (90)
Spanish	12 (6)
Other	9 (4)
Activities of daily living score, mean (95% Cl) ^a	5 (4.6–5.2)
Instrumental activities of daily living score, mean (95% CI) ^b	16 (14.8–16.9)
History of liver disease, n (%)	29 (13)
History of cancer, n (%)	53 (24)
History of stroke, n (%)	20 (9)
History of end-stage renal disease, n (%)	9 (4)
Presence of advance directive at enrollment, n (%)	31 (14)
1-yr mortality as predicted by ProVent score, mean % (95% Cl)	62 (58.6–64.8)
Richmond Agitation Sedation Scale at enrollment, n (%)	
−5 or −4 (unresponsive)	95 (44)
-3 to -1 (arousable)	81 (38)
\geq 0 (awake)	38 (18)
Acute renal failure requiring renal replacement therapy, n (%)	48 (19)
Tracheostomy, n (%)	139 (54)
Duration of mechanical ventilation after randomization, mean (95% CI), d	20.2 (15.1–25.2)
Hospital length of stay, mean (95% Cl), d	47.7 (42.1–53.3)
Health status by level of care at 90 d	
Died	94 (43)
Readmitted to an acute care hospital	10 (5)
Long-term acute care hospital	9 (4)
Skilled nursing facility	14 (6)
Acute rehabilitation facility	6 (3)
Living at home	86 (39)

^aThe range is 0 (dependent) to 6 (independent) in six activities.

^bThe range is 8 (dependent) to 31 (independent) in eight activities.

The mean total IES-R score at 90 days for surrogates was 23.3 (95% CI, 21.3-25.4). A total of 91 (30%) of 306 surrogates had an IES-R score greater than or equal to 33, suggestive of a probable diagnosis of PTSD. The intrusion PTSD cluster had the highest mean subscale score (10.3; 95% CI, 9.3–11.2), followed by avoidance (8.0; 95% CI, 7.2-8.8) and hyperarousal (5.1; 95% CI, 4.5-5.7). Compared with surrogates whose loved one survived, we found that surrogates of patients who died had higher mean intrusion (13.2 vs 8.3; p < 0.0001) and avoidance (9.8 vs 6.8, p = 0.0009) subscale scores. Hyperarousal symptoms were similarly low for both groups (5.7 vs 4.7; p = 0.13) (Fig. 2). Differences in intrusion and avoidance symptoms persisted even after adjusting for the clinically important covariates shown in Table 3. Surrogates of patients who died also had higher odds of experiencing both intrusion symptoms (beta coefficient, 5.52; p <0.0001) and avoidance symptoms (beta coefficient, 3.29; p = 0.001) at 90 days (Table 3).

DISCUSSION

We found that 30% of surrogate decision makers of patients with CCI experienced symptoms suggestive of a diagnosis of PTSD and that intrusion and avoidance

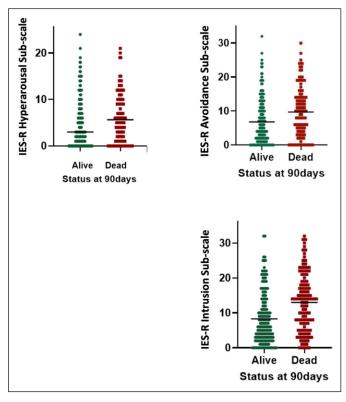


Figure 2. Mean IES-R score by patient status at 90 d. *Green*, Patient alive at 90 d. *Red*, Patient deceased at 90 d.

symptoms of PTSD were more severe than hyperarousal symptoms. We also found that surrogates who experienced the death of a family member reported higher levels of intrusion and avoidance symptoms than surrogates who did not experience a family member's death. These findings were contrary to our hypothesis that hyperarousal symptoms would be most severe and provide insight into the future of traumainformed care for this population.

The finding that one in three surrogate decision makers experience PTSD symptoms has compelling implications for clinical care, since critical care teams treat patients but have no formal role in diagnosing and treating conditions that are being experienced by family members. With future research, investigators may discover ways of supporting these decision makers during CCI that mitigate subsequent PTSD symptoms. Alternatively, healthcare systems and reimbursement policy may require reforms to support outreach and psychological services triggered by the role of surrogate decision maker for someone with CCI.

Considered to be the "classic" symptoms of PTSD(30), intrusion symptoms involve reexperiencing of the traumatic event and can include recurrent and involuntary memories, nightmares, flashbacks, intense or prolonged psychological distress in response to reminders of the traumatic event, or intense physiological reactions to reminders of the event (22). In other surrogate populations, intrusion symptoms are theorized to be driven by frequent encounters with and reminders of a particular traumatic event (42). Because patients experiencing CCI experience long hospital stays, persistently high severity of illness, and frequent encounters with the healthcare system following hospital discharge, their surrogate decision makers may be especially prone to reexperiencing and intrusive thoughts (43, 44). Furthermore, development of intrusion symptoms has been associated with a particularly strong fear response to a traumatic event (45, 46). Fear is a common emotional response described by surrogate decision makers following a patient's ICU stay (32, 47), with uncertainty about the future, seeing a loved one become severely ill, and the potential for major life change as a result of the ICU stay all as items that are particularly fear-inducing (47). Although the predominance of PTSD symptom clusters among surrogate decision makers of patients experiencing CCI

TABLE 3.Results of Multivariable Modeling^a

Variable Name	Coefficient (95% CI) ^b	p
Avoidance subscale		
Patient death	3.29 (1.39–5.20)	0.001
Patient age	-0.07 (-0.13 to -0.01)	0.034
Patient history of cancer	-1.68 (-3.71 to 0.36)	0.10
Patient history of liver disease	1.07 (-1.70 to 3.83)	0.44
HADS	0.24 (0.14–0.35)	< 0.0001
RASS score		
−5 or −4 (unresponsive)	-2.57 (-5.41 to 0.26)	0.02
−3 to −1 (arousable)	-2.61 (-4.48 to -0.75)	
\geq 0 (awake)	-	
ProVent 14 Score	-0.008 (-0.06 to 0.04)	0.76
Intrusion subscale		
Patient death	5.52 (3.36-7.68)	< 0.001
Patient age	-0.06 (-0.14 to 0.02)	0.12
Patient history of cancer	-2.63 (-4.93 to -0.34)	0.03
Patient history of liver disease	-0.66 (-3.70 to 2.38)	0.67
HADS	0.47 (0.36–0.57)	< 0.0001
RASS score		
−5 or −4 (unresponsive)	-0.39 (-3.54 to 2.77)	0.57
-3 to -1 (arousable)	-1.13 (-3.25 to 0.99)	
\geq 0 (awake)	-	
ProVent 14 Score	0.01 (-0.05 to 0.07)	0.72
Hyperarousal Subscale		
Patient death	0.94 (-0.68 to 2.57)	0.25
Patient age	0.02 (-0.03 to 0.07)	0.39
Patient history of cancer	-1.55 (-3.27 to 0.17)	0.08
Patient history of liver disease	0.18 (-2.04 to 2.40)	0.87
HADS	0.28 (0.20–0.35)	< 0.0001
RASS score		
−5 or −4 (unresponsive)	-1.10 (-3.47 to 1.27)	0.62
-3 to -1 (arousable)	-0.49 (-2.08 to 1.10)	
\geq 0 (awake)	-	
ProVent 14 Score	-0.01 (-0.05 to 0.02)	0.49

HADS = Surrogate baseline anxiety and depression, RASS = Richmond Agitation Sedation Scale.

^aAll models were adjusted for multiple respondents.

^bFor continuous variables, the coefficient represents mean change in IES-R score per one-unit increase. For categorical variables, the coefficient represents mean difference in IES-R score compared with the reference group. Dashes denote reference group.

has not previously been described, such clusters have been described in surrogates of those with an acute critical illness and provide findings consistent with ours. One study conducted among surrogate decision makers of patients admitted to a neurointensive care unit with acute brain injury found that intrusion symptoms were most prominent among surrogates, and that lower patient Glasgow Coma Scale score at the time of admission was associated with increased symptoms across all three clusters (48).

Intrusion symptoms can be especially detrimental to psychological well-being, mood adjustment, and coping (2, 49, 50), offering a potential clue as to why the development of effective emotional support strategies has been challenging in these populations (51, 52). Our finding that surrogate decision makers experience high levels of intrusion symptoms can be used to inform future support interventions that are more specifically targeted to this cluster type. (30). Group-based interventions can play a role in the reduction of intrusion symptoms (53), which is promising for the growing field of peer support interventions for ICU recovery (54). Additionally, group-based interventions to reduce PTSD can be effectively delivered via telehealth, offering potential for use throughout the COVID-19 pandemic and for surrogates with limited capacity for in-person treatment due to patient care responsibilities or other obligations (55, 56). If pharmacotherapy is required, SSRIs are recommended as first-line treatment for individuals with intrusion-predominant symptoms (30).

Additionally, we found that although mean symptom cluster scores were higher among surrogates of patients who experienced patient death than surrogates who did not, the pattern of PTSD cluster predominance (highest mean intrusion symptoms and lowest mean hyperarousal symptoms) was the same between the two groups. Many experts suggest that the predominant PTSD symptom cluster can be used to inform treatment approach even in individuals who have "subthreshold" PTSD symptoms or symptoms that do not exceed the threshold for a formal diagnosis of PTSD (30, 57). As such, our finding that indicates that there is potential for a single-treatment approach could provide benefit for both groups.

Although the mean score for avoidance symptoms was slightly lower than that for intrusion symptoms in our cohort at 90 days, this finding still merits attention as avoidance symptoms are associated with many negative effects including reduced self-confidence, self-efficacy, and quality of life (58). This is notable as reductions in family self-efficacyhavebeen associated with worse patienthealth outcomes, such as increased emergency department visits, in other disease processes such as dementia (15). Avoidant symptoms are associated with a desire to avoid triggers that remind the affected individual of the initial trauma, which ultimately leads to inadequate processing of trauma and hinders recovery (49). Furthermore, prior studies have shown that avoidance and intrusion symptoms can become more strongly intercorrelated over time, potentially posing even greater long-term risk to surrogates of CCI patients (2). In terms of treatment approach, cognitive behavioral therapy holds promise for reduction in these symptoms especially among individuals with severe PTSD symptoms prior to treatment (53, 59). Finally, although hyperarousal symptoms such as anger or irritability are often easier for clinicians to identify, they were less severe in the population we studied. This further reinforces the need for use of validated instruments to screen for surrogates who are at high risk for distress as opposed to relying solely on clinician judgment or intuition. Prior research indicates that high PTSD symptoms within the first 48 hours of patient ICU admission are predictive of high PTSD symptoms 6 months later for surrogate decision makers (60). Administration of the IES-R to all ICU surrogates upon patient ICU admission, with attention toward not only total score but predominant symptom cluster, could facilitate early identification of high-risk surrogates and subsequent guidance toward tailored treatment.

Strengths of our study include the relatively unexplored research question among a broad range of medical and surgical critical care conditions, large sample size, and the high 90-day retention/data capture rate (84% of surrogates with complete 90-d follow-up information). In addition, we were able to control for baseline anxiety and depression symptoms in our analyses using the HADS instrument. Last, our study population was drawn from both large academic medical centers and a smaller community center across multiple geographic regions, thus increasing generalizability of our findings.

Our study also has limitations. First, following the initiation of the clinical trial from which our data were derived, the DSM was revised to expand the requisite symptom clusters for the diagnosis of PTSD to include emotional numbing—a cluster not assessed by the ICU outcomes core measure IES-R—in addition to intrusion, avoidance, and hyperarousal. Second, it is possible that surrogates lost to follow up from the original trial and thus underrepresented in our analyses were more highly distressed and, in particular, more likely to have suffered

from avoidant symptoms. Third, participants were enrolled into the original clinical trial based on designation as the patient's surrogate decision maker. Many of them were family caregivers, but it is not known whether findings are generalizable to family caregivers who are not also responsible for surrogate decision making. Finally, this study was conducted among surrogate decision makers of patients experiencing CCI and may not be representative of PTSD symptoms in other populations of surrogate decision makers including surrogates for patients experiencing only acute critical illness.

CONCLUSIONS

We found that intrusive thoughts are the most severe type of PTSD symptom among surrogate decision makers of patients with CCI, with more severe symptoms among surrogates of patients who died. These findings may be important in informing the development of personalized treatment strategies designed to reduce psychological distress among ICU surrogate decision makers.

- 1 Division of Pulmonary Diseases and Critical Care Medicine, Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC.
- 2 Department of Psychiatry, UNC School of Medicine, University of North Carolina, Chapel Hill, NC.
- 3 Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC.
- 4 Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine, Duke University, Durham, NC.
- 5 Division of Geriatric Medicine and Palliative Care Program, Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC.
- 6 Departments of Medicine, Anesthesia, and Critical Care, Memorial Sloan Kettering Cancer Center, New York, NY.
- 7 Weill Cornell Medical College, Cornell University, New York, NY.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (http://journals.lww.com/ccejournal).

Supported, in part, by R01-NR012413, T32HL007106-41, KL2TR002490, and R01-AG058915.

The work for this study was performed at The University of North Carolina at Chapel Hill.

The authors have disclosed that they do not have any potential conflicts of interest.

For information regarding this article, E-mail: blair.wendlandt@ unchealth.unc.edu

REFERENCES

- van der Kolk BA, Pelcovitz D, Roth S, et al: Dissociation, somatization, and affect dysregulation: The complexity of adaptation of trauma. *Am J Psychiatry* 1996; 153:83–93
- 2. Segal A, Wald I, Lubin G, et al: Changes in the dynamic network structure of PTSD symptoms pre-to-post combat. *Psychol Med* 2020; 50:746–753
- Resnick HS, Kilpatrick DG, Dansky BS, et al: Prevalence of civilian trauma and posttraumatic stress disorder in a representative national sample of women. *J Consult Clin Psychol* 1993; 61:984–991
- deRoon-Cassini TA, Mancini AD, Rusch MD, et al: Psychopathology and resilience following traumatic injury: A latent growth mixture model analysis. *Rehabil Psychol* 2010; 55:1-11
- Jutte JE, Erb CT, Jackson JC: Physical, cognitive, and psychological disability following critical illness: What is the risk? *Semin Respir Crit Care Med* 2015; 36:943–958
- 6. Paparrigopoulos T, Melissaki A, Efthymiou A, et al: Short-term psychological impact on family members of intensive care unit patients. *J Psychosom Res* 2006; 61:719–722
- Anderson WG, Arnold RM, Angus DC, et al: Posttraumatic stress and complicated grief in family members of patients in the intensive care unit. J Gen Intern Med 2008; 23:1871–1876
- Johnson CC, Suchyta MR, Darowski ES, et al: Psychological sequelae in family caregivers of critically iii intensive care unit patients. A systematic review. *Ann Am Thorac Soc* 2019; 16:894–909
- Wendlandt B, Ceppe A, Choudhury S, et al: Risk factors for post-traumatic stress disorder symptoms in surrogate decision-makers of patients with chronic critical illness. *Ann Am Thorac Soc* 2018; 15:1451–1458
- Wendlandt B, Ceppe A, Choudhury S, et al: Modifiable elements of ICU supportive care and communication are associated with surrogates' PTSD symptoms. *Intensive Care Med* 2019; 45:619–626
- Ankuda CK, Maust DT, Kabeto MU, et al: Association between spousal caregiver well-being and care recipient healthcare expenditures. J Am Geriatr Soc 2017; 65:2220–2226
- Douglas SL, Daly BJ, Kelley CG, et al: Impact of a disease management program upon caregivers of chronically critically ill patients. *Chest* 2005; 128:3925–3936
- Azoulay E, Pochard F, Kentish-Barnes N, et al; FAMIREA Study Group: Risk of post-traumatic stress symptoms in family members of intensive care unit patients. *Am J Respir Crit Care Med* 2005; 171:987–994
- Schulz R, Beach SR, Friedman EM: Caregiving factors as predictors of care recipient mortality. *Am J Geriatr Psychiatry* 2021; 29:295–303
- Guterman EL, Allen IE, Josephson SA, et al: Association between caregiver depression and emergency department use among patients with dementia. JAMA Neurol 2019; 76:1166-1173
- Carson SS, Cox CE, Wallenstein S, et al: Effect of palliative care-led meetings for families of patients with chronic critical illness: A randomized clinical trial. *JAMA* 2016; 316:51-62

- 17. Cox CE, Hough CL, Carson SS, et al: Effects of a telephoneand web-based coping skills training program compared to an education program for survivors of critical illness and their family members: A randomized clinical trial. *Am J Respir Crit Care Med* 2017
- Cox CE, White DB, Hough CL, et al: Effects of a personalized web-based decision aid for surrogate decision makers of patients with prolonged mechanical ventilation: A randomized clinical trial. *Ann Intern Med* 2019; 170:285–297
- 19. White DB, Angus DC, Shields AM, et al; PARTNER Investigators: A randomized trial of a family-support intervention in intensive care units. *N Engl J Med* 2018; 378:2365–2375
- Curtis JR, Treece PD, Nielsen EL, et al: Randomized trial of communication facilitators to reduce family distress and intensity of end-of-life care. *Am J Respir Crit Care Med* 2016; 193:154–162
- Schoeman T, Sundararajan K, Micik S, et al: The impact on new-onset stress and PTSD in relatives of critically ill patients explored by diaries study (the "INSPIRED" study). *Aust Crit Care* 2018; 31:382–389
- 22. Diagnostic and statistical manual of mental disorders: DSM-5[™]. Fifth Edition. Arlington, VA, American Psychiatric Publishing; 2013
- Henigsberg N, Folnegović-Smalc V, Moro L: Stressor characteristics and post-traumatic stress disorder symptom dimensions in war victims. *Croat Med J* 2001; 42:543–550
- 24. Campbell SB, Trachik B, Goldberg S, et al: Identifying PTSD symptom typologies: A latent class analysis. *Psychiatry Res* 2020; 285:112779
- 25. Timmer-Murillo SC, Hunt JC, Geier T, et al: Identification of risk for posttraumatic stress disorder symptom clusters early after trauma. *J Health Psychol* 2021; 26:2794–2800
- 26. Forbes D, Nickerson A, Bryant RA, et al: The impact of post-traumatic stress disorder symptomatology on quality of life: The sentinel experience of anger, hypervigilance and restricted affect. *Aust N Z J Psychiatry* 2019; 53:336–349
- 27. Morabito DM, Boffa JW, Bedford CE, et al: Hyperarousal symptoms and perceived burdensomeness interact to predict suicidal ideation among trauma-exposed individuals. *J Psychiatr Res* 2020; 130:218–223
- 28. Livingston NA, Farmer SL, Mahoney CT, et al: The role of PTSD symptom clusters and criterion in predicting future high-risk drug and alcohol use among returning veteran men and women. *Psychol Serv* 2021 Apr 12. [online ahead of print]
- 29. Cloitre M: The "one size fits all" approach to trauma treatment: Should we be satisfied? *Eur J Psychotraumatol* 2015; 6:27344
- Norrholm SD, Jovanovic T: Tailoring therapeutic strategies for treating posttraumatic stress disorder symptom clusters. *Neuropsychiatr Dis Treat* 2010; 6:517–532
- Schneeberger A, Brandstetter S, Bein T, et al: Stressors and strains of next of kin of patients with ARDS in intensive care: A qualitative interview study using a stress-strain approach. *Intensive Crit Care Nurs* 2020; 57:102783
- 32. Harlan EA, Miller J, Costa DK, et al: Emotional experiences and coping strategies of family members of critically ill patients. *Chest* 2020; 158:1464–1472
- Kahn JM, Le T, Angus DC, et al; ProVent Study Group Investigators: The epidemiology of chronic critical illness in the United States*. *Crit Care Med* 2015; 43:282–287

- Carson SS, Cox CE, Holmes GM, et al: The changing epidemiology of mechanical ventilation: A population-based study. J Intensive Care Med 2006; 21:173–182
- 35. Zigmond AS, Snaith RP: The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67:361–370
- Han JH, Vasilevskis EE, Shintani A, et al: Impaired arousal at initial presentation predicts 6-month mortality: An analysis of 1084 acutely ill older patients. *J Hosp Med* 2014; 9:772-778
- Creamer M, Bell R, Failla S: Psychometric properties of the impact of event scale - revised. *Behav Res Ther* 2003; 41:1489–1496
- Needham DM, Sepulveda KA, Dinglas VD, et al: Core outcome measures for clinical research in acute respiratory failure survivors. An international modified Delphi consensus study. *Am J Respir Crit Care Med* 2017; 196:1122–1130
- 39. Bell CC: DSM-IV: Diagnostic and statistical manual of mental disorders. *JAMA* 1994; 272:828–829
- 40. Lederer DJ, Bell SC, Branson RD, et al: Control of confounding and reporting of results in causal inference studies. Guidance for authors from editors of respiratory, sleep, and critical care journals. *Ann Am Thorac Soc* 2019; 16:22–28
- Suttorp MM, Siegerink B, Jager KJ, et al: Graphical presentation of confounding in directed acyclic graphs. *Nephrol Dial Transplant* 2015; 30:1418–1423
- Cella DF, Perry SW, Kulchycky S, et al: Stress and coping in relatives of burn patients: A longitudinal study. *Psychiatr Serv* 1988; 39:159–166
- Unroe M, Kahn JM, Carson SS, et al: One-year trajectories of care and resource utilization for recipients of prolonged mechanical ventilation: A cohort study. *Ann Intern Med* 2010; 153:167–175
- Cox CE, Carson SS: Medical and economic implications of prolonged mechanical ventilation and expedited post-acute care. Semin Respir Crit Care Med 2012; 33:357–361
- Levin-Aspenson HF, Watson D, Ellickson-Larew S, et al: Beyond distress and fear: Differential psychopathology correlates of PTSD symptom clusters. J Affect Disord 2021; 284:9–17
- Davis M: The role of the amygdala in fear-potentiated startle: Implications for animal models of anxiety. *Trends Pharmacol Sci* 1992; 13:35–41
- 47. McAdam JL, Dracup KA, White DB, et al: Symptom experiences of family members of intensive care unit patients at high risk for dying. *Crit Care Med* 2010; 38:1078–1085
- Pielmaier L, Walder B, Rebetez MM, et al: Post-traumatic stress symptoms in relatives in the first weeks after severe traumatic brain injury. *Brain Inj* 2011; 25:259–265
- 49. Oliveri S, Arnaboldi P, Pizzoli SFM, et al: PTSD symptom clusters associated with short- and long-term adjustment in early diagnosed breast cancer patients. *Ecancermedicalscience* 2019; 13:917
- 50. Weiss NH, Contractor AA, Raudales AM, et al: Extending our understanding of the association between posttraumatic stress disorder and positive emotion dysregulation: A network analysis approach. *J Anxiety Disord* 2020; 71:102198
- 51. LaBuzetta JN, Rosand J, Vranceanu AM: Review: Postintensive care syndrome: Unique challenges in the neurointensive care unit. *Neurocrit Care* 2019; 31:534–545

- 52. Cherak SJ, Rosgen BK, Amarbayan M, et al: Mental health interventions to improve psychological outcomes in informal caregivers of critically ill patients: A systematic review and meta-analysis. *Crit Care Med* 2021; 49:1414–1426
- 53. Beck JG, Clapp JD, Unger W, et al: Moderators of PTSD symptom change in group cognitive behavioral therapy and group present centered therapy. *J Anxiety Disord* 2021; 80:102386
- 54. Haines KJ, Holdsworth C, Cranwell K, et al: Development of a peer support model using experience-based co-design to improve critical care recovery. *Crit Care Explor* 2019; 1:e0006
- 55. Morland LA, Wells SY, Glassman LH, et al: Advances in PTSD treatment delivery: Review of findings and clinical considerations for the use of telehealth interventions for PTSD. Curr Treat Options Psychiatry 2020:1–21
- 56. Jones C, Miguel-Cruz A, Smith-MacDonald L, et al: Virtual trauma-focused therapy for military members, veterans, and

public safety personnel with posttraumatic stress injury: Systematic scoping review. *JMIR Mhealth Uhealth* 2020; 8:e22079

- 57. Shea MT, Vujanovic AA, Mansfield AK, et al: Posttraumatic stress disorder symptoms and functional impairment among OEF and OIF National Guard and Reserve veterans. *J Trauma Stress* 2010; 23:100–107
- Kube T, Berg M, Kleim B, et al: Rethinking post-traumatic stress disorder – a predictive processing perspective. *Neurosci Biobehav Rev* 2020; 113:448–460
- 59. Bryant RA, Moulds ML, Nixon RV: Cognitive behaviour therapy of acute stress disorder: A four-year follow-up. *Behav Res Ther* 2003; 41:489–494
- 60. Wendlandt B, Chen YT, Lin FC, et al: Posttraumatic stress disorder symptom trajectories in ICU family caregivers. *Crit Care Explor* 2021; 3:e0409