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Predictors of post-traumatic stress disorder following critical illness: A mixed methods study

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Abstract

Purpose: Post-traumatic stress disorder has been reported in survivors of critical illness. The aim of this study was to investigate the predictors of post-traumatic stress disorder in survivors of critical illness.

Materials and methods: Patients attending the intensive care unit (ICU) follow-up clinic completed the UK-Post-Traumatic Stress Syndrome 14-Questions Inventory and data was collected from their medical records. Predictors investigated included age, gender, Apache II score, ICU length of stay, pre-illness psychopathology; delirium and benzodiazepine administration during ICU stay and delusional memories of the ICU stay following discharge.

Results: A total of 198 patients participated, with 54 (27%) patients suffering with post-traumatic stress disorder. On multivariable logistic regression, the significant predictors of post-traumatic stress disorder were younger age, lower Apache II score, pre-illness psychopathology and delirium during the ICU stay.

Conclusions: The predictors of post-traumatic stress disorder in this study concur with previous research however a lower Apache II score has not been previously reported.

Keywords

Critical illness, post-traumatic stress syndrome, predictors

Introduction

As a result of advancements in critical care medicine, the chances of survival have increased, potentially bringing with it however an array of associated longer-term problems.[1–3] Post-traumatic stress disorder (PTSD) is one of the psychological sequalae of critical illness that has been well-described in critical care research. A number of systematic reviews have been conducted which report a median value of 19% prevalence of PTSD, but studies report up to 64% of patients can suffer with PTSD symptoms following critical illness, leading to lower health-related quality of life.[4–9]

It has been well reported that survivors of non-fatal trauma are at risk of PTSD, with this risk increasing significantly in those admitted to the intensive care unit (ICU).[10,11] Research has suggested that PTSD commonly occurs in critical illness survivors, irrespective of specific pre-ICU admission trauma and a number of predictors of PTSD have been investigated. Younger age has been commonly reported as a predictor of PTSD in ICU survivors.[8] Benzodiazepine administration and being female were risk factors for PTSD on-set in survivors of critical illness requiring mechanical ventilation.[12] Severe sepsis was reported a predictor of PTSD in another study.[13]

Other studies have reported that post-ICU memories of frightening experiences were a positive predictor of PTSD in ICU survivors.[9] Similarly, memory of pain was reported a predictor of PTSD.[14] Other predictors include uninterrupted use of sedatives[15], sleep disturbance[16] and delirium.[17,18] A recent systematic review and meta-analysis reported that PTSD occurred in one fifth of ICU survivors at 1 year and that the risk factors included comorbid psychopathology, use of benzodiazepines and early memories of frightening ICU experiences.[19]

In a prospective cohort study investigating PTSD in survivors of acute lung injury in ICU, reported risk factors included pre-illness depression, length of ICU stay and sepsis and administration of high-dose

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opiates in the ICU.[20] This study also reported protective factors against PTSD, which included duration of opiate and corticosteroid administration in the ICU.[20]

Severity of illness and ICU length of stay have not been associated with PTSD in critical care survivors.[8] In the follow-up clinic held at the authors' hospital however, it was observed that patients with a high degree of PTSD symptoms were commonly those with a lower Apache II score. Furthermore, a limited number of studies investigating PTSD in survivors of critical illness focus on 'general ICU' patients, choosing to focus on a specific population such as trauma, sepsis, acute respiratory distress syndrome (ARDS) or respiratory failure patients. The aim of this study was to investigate the predictors of PTSD in survivors of critical illness, treated on a general ICU.

Methods

Patients who had been treated on the general ICU in Morriston Hospital, in South Wales for 4 days or more were invited to attend the multi-disciplinary follow-up clinic. On attendance at the clinic, patients completed the UK-Post-Traumatic Stress Syndrome 14-Questions Inventory (UK-PTSS-14). The UK-PTSS-14 is a 14-item self-report screening tool; each item is rated 1 (never) to 7 (always) with a total score ranging from 14 to 98.[20] A cut-off point of 45 was used in this study to demonstrate the presence of PTSD in a patient.[20] The UK-PTSS-14 was internally reliable at all three time-points (Cronbach's $\alpha = 0.89$, 0.86 and 0.84, respectively). Predictive validity was highest at time-point 2 ($r = 0.71$ with the Impact of Events Scale). Receiver operator characteristic curve analysis suggested the highest levels of sensitivity (86%) and specificity (97%) for diagnosis of PTSD were at time-point 2, with an optimum decision threshold of 45 points.[20]

Only patients aged 18 years or more, who were at least 3 months post-ICU discharge, were included in the study in order to assess 'longer-term' outcomes. Patients with traumatic brain injuries were not included in the study. Data including demographics and predictors were also collected from their medical records during the clinic. Predictors investigated were selected a priori, based on prior research findings and included age, Apache II score, pre-illness psychopathology (any mental illness), ICU length of stay (LOS), delirium and/or and use of benzodiazepines during the ICU admission and patient reported delusional memories of the ICU stay. ICU LOS was defined as the number of whole days the patient was managed on ICU or the high dependency unit (HDU). Delirium was diagnosed by the consultant managing the patient on ICU and this information was then taken from the medical notes in the follow-up clinic. Delusional memories were reported by the patient in the follow-up clinic.

Baseline characteristics were presented as numbers and percentages for categorical variables and median and 25th and 75th interquartile range (due to non-normal distributions) for the continuous variables. Differences between the baseline characteristics were analysed using Fisher's exact test (categorical variables) and Mann–Whitney U test (continuous variables). Unadjusted odds ratios and 95% confidence intervals were presented from the univariable analysis. All prognostic variables were included in final analysis. Multivariable logistic regression analysis was used to identify significant predictors using the Likelihood test statistic, reporting adjusting odds ratios and 95% confidence intervals for each predictor.

Statistical significance for the identification of independent predictors was set at $p < 0.05$. There was less than 1% missing data therefore we used a simple imputation of the mean method to avoid exclusion of patients from the final analysis. Statistical analyses were performed using SPSS Version 22 (Chicago).

The data collection for this study was completed as part of the ICU follow-up clinic, considered to be a service evaluation as confirmed by Health Board's Joint Scientific Review Committee.

Results

A total of 198 patients completed the survey between September 2013 and September 2016 at the ICU multi-disciplinary follow-up clinic. PTSD as measured using the UK-PTSS-14 Inventory was reported in 27% of the patients. PTSD scores using the inventory ranged from 14 to 85 for the group. Median age was 64 years, with 54% female patients. The median number of mechanical ventilation days was three (interquartile range: 0–11). There were no differences reported between the admission diagnosis for the PTSD and non-PTSD patients.

Table 1 highlights the demographics of the patient group, including the results of the univariable analysis. Unadjusted odds ratios and 95% confidence intervals are presented for the predictors of PTSD in survivors of critical illness.

The results of the multivariable analysis are highlighted in Table 2. The significant predictors of PTSD in survivors of critical illness are a lower age, lower illness severity (as measured by the Apache II score), pre-illness psychopathology and a diagnosis of delirium during the ICU admission.

Discussion

This study investigated the prevalence and predictors of PTSD in a heterogenous cohort of survivors of critical illness, treated on a general ICU. The prevalence of PTSD in this study was 27%, which is higher than the median value reported in the systematic

Table 1. Demographics, predictors and results of univariable analysis.

	Total patients ($n = 198$)	No PTSD, $n = 144$ (73%)	PTSD, $n = 54$ (27%)	p Value	Unadjusted OR (95% CI)
Admission diagnosis					
Surgical	69 (35%)	52 (36%)	17 (32%)	0.617	1.23 (0.63–2.98)
Medical	73 (37%)	53 (37%)	20 (37%)	1.000	0.99 (0.52–1.89)
Respiratory	44 (22%)	30 (21%)	14 (26%)	0.448	0.75 (0.36–1.56)
Trauma	12 (6%)	9 (6%)	3 (6%)	1.000	1.13 (0.30–4.35)
Predictors					
Age	64 (53–73)	67 (59–76)	57 (39–65)	<0.001	
Female	106 (54%)	73 (51%)	33 (61%)	0.204	0.65 (0.35–1.24)
APACHE II	15 (11–19)	16 (11–20)	13 (10–16)	0.002	
ICU LOS	8 (4–16)	8 (4–15)	9 (5–18)	0.266	
Psychopathology	56 (28%)	25 (17%)	31 (57%)	<0.001	0.16 (0.78–0.31)
Delirium	35 (18%)	12 (8%)	23 (43%)	<0.001	0.12 (0.05–0.27)
Delusional memories	40 (20%)	17 (12%)	23 (43%)	<0.001	0.18 (0.09–0.38)
Benzodiazepines	41 (21%)	18 (13%)	23 (43%)	<0.001	0.19 (0.09–0.40)

Numbers (%); OR: odds ratio; CI: confidence intervals; ICU LOS: intensive care unit length of stay.

Table 2. Predictors and adjusted odds ratios (95% CI).

Risk factor	Adjusted OR (95% CI)	p Value
Age	0.97 (0.94-0.99)	0.029
APACHE II score	0.93 (0.87-0.99)	0.045
Psychopathology	6.15 (2.60-14.54)	0.001
Delirium	10.93 (4.18-28.56)	0.001

OR: odds ratio; CI: confidence intervals.

review by Davydow et al.[4] This may be due, in part, to the patients in this study being attenders at the ICU follow-up clinic. It could be that patients with self-perceived, longer-term problems were more likely to attend the clinic, than those without. In a more recent review, pooled prevalences of clinically important PTSD symptoms (95% CI) were demonstrated to be 25% (18–34%) and 44% (36–52%) using Impact of Event Scale thresholds, which is similar to that reported in this study.[19]

The results of this study support previous research that younger survivors of critical illness patients are more likely to suffer with PTSD. The reasons for this are yet to be proven in critical care research, although a number of theories have been proposed. Younger patients are more likely to receive aggressive interventions that may predispose them to the development of PTSD.[12] Furthermore, older patients may have a higher number of comorbidities with more frequent admissions to hospital, so consequently do not perceive their ICU stay as stressful.[21]

It was concluded in a systematic review that one prospectively assessed potential risk factor was consistently not associated with later PTSD symptoms: severity of critical illness, as measured using the Apache II score.[4] The results of this study did not support this finding, with a lower illness severity being significantly associated with PTSD in ICU survivors. It could be suggested that patients with a lower illness severity are more likely to be more aware of the stressful ICU environment and more likely therefore to experience fear of poor outcomes, than patients who are less conscious or more heavily sedated.

Pre-illness psychopathology has been previously reported as a significant predictor of PTSD in the survivors of critical illness however these findings are inconsistent in the literature.[9,22–24] Co-morbid psychopathy was demonstrated to be a risk factor for PTSD in ICU survivors at 1 year.[19] Pre-admission depression was a reported risk factor in ICU patients with acute lung injury.[20] This study found that any pre-illness psychopathology (not specifically depression) was a significant predictor of PTSD. In a number of the previous studies, patients with pre-admission diagnosis of schizophrenia, bipolar disorder, substance-use disorder or epilepsy were excluded.[8] As a result of these exclusions, the rate of included patients with a history of psychiatric illness and thereby the correlation between PTSD symptoms and prior psychiatric history may have been underestimated.

Patient reported delusional memories were not found to be a risk factor of PTSD in this study. A previous systematic review however reported that frightening memories of the ICU stay was a risk factor of PTSD at 1 year post-discharge.[19] The difference in follow-up period between the two studies may have influenced the findings. Interestingly, a study into the influence of memories of ICU stay reported that for the ICU survivors, having memories of the ICU stay is associated with a higher perceived health-related quality of life at 6 months post-ICU discharge.[25]

Delirium during the ICU stay has also been inconsistently reported as a risk factor for PTSD.[8] In a recent large longitudinal study, delirium was not associated with PTSD at 3 or 12 months post-ICU discharge.[26] One previous study reported delirium as a predictor of PTSD in surgical ICU patients,[27] which may explain the same finding in our study, as over a third of the patients in this study were surgical admissions. Further research is needed into the effects of delirium on longer-term outcomes following critical illness.

The results of this study may have been potentially influenced by the lack of availability of a clinical psychologist for the patients who are diagnosed with psychological issues during their ICU stay. Current management of delirium on our unit involves both non-pharmacologic strategies (such as bedside clocks and calendars, early mobilisation strategies, minimisation of unnecessary noise, rest periods, use of eye glasses and hearing aids as appropriate) and pharmacologic strategies (such as careful monitoring of sedation effects and early waking, appropriate use of analgesia and the use of dexmedetomidine in patients identified as suffering with delirium). The Confusion Assessment Method for the Intensive Care Unit has recently been introduced onto our unit. The lack of clinical psychologist on the unit and our current strategies for managing delirium may have contributed to the prevalence of PTSD in our patient cohort.

One of the strengths of this study is that it uses a cohort of general ICU patients, rather than focusing on one specific condition, such as ARDS or mechanically ventilated patients only. A further strength of the study is the use of a validated self-reported measure that the patients completed on attendance at the ICU follow-up clinic. The use of a reasonable sample size facilitated the inclusion of a number of previously reported predictors in the analysis.

A number of limitations may have adversely influenced the results of this study and therefore the findings should be interpreted with caution. Firstly, the inclusion of patients only attending the ICU follow-up clinic could have potentially skewed the prevalence of PTSD in the study, as patients with no self-perceived, longer-term problems, may not have opted to attend their clinic appointment. A further limitation was the retrospective use of the medical records to identify a number of the variables in the analysis, as this always leads to the potential for decreased reliability.

The lack of standardised outcome measures used in this study was a limitation. Although Parker et al. reported that the Impact of Event Scale was the most appropriate measure for PTSD in this patient cohort, this review was not available at the start of the data collection in this study. Furthermore, we relied on patients reporting their experience of delusional memories in the follow-up clinic, rather than using a standardised outcome measure. In addition, the diagnosis of delirium was made by the consultant during the patient's ICU stay, but not using a standardised outcome measure. The results should therefore be interpreted with caution.

Another potential limitation of this study design is the influence of unknown confounding variables, especially in such a heterogeneous patient population, such as survivors of a general ICU stay. The use of multivariable logistic regression can reduce the impact of confounding variables, but this should be considered when interpreting the results.

Conclusions

PTSD was reported in 27% of this cohort of critical care survivors, attending an ICU follow-up clinic. Previous research has demonstrated the significant predictors of PTSD in survivors of critical illness. This study concurs with these findings however also demonstrated that a lower Apache II score is associated with PTSD. These results should assist in the identification of the high-risk patient for PTSD on discharge from ICU. This finding needs further investigation, in order that patients with lower illness severity are not excluded from attendance at ICU follow-up clinics.

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References

1. Lone NI, Gillies MA, Haddow C, et al. Five year mortality and hospital costs associated with surviving intensive care. *Am J Respir Crit Care Med* 2016; 194: 198–208.
2. Cuthbertson BH, Rattray J, Campbell MK, et al. The PRaCTICaL study of nurse led, intensive care follow-up programmes for improving long term outcomes from critical illness: a pragmatic randomised controlled trial. *BMJ* 2009; 339: b3723.
3. Iwashyna TJ, Netzer G, Langa KM, et al. Spurious inferences about long-term outcomes: the case of severe sepsis and geriatric conditions. *Am J Respir Crit Care Med* 2012; 185: 835–841.
4. Davydow DS, Gifford JM, Desai SV, et al. Posttraumatic stress disorder in general intensive care unit survivors: a systematic review. *Gen Hosp Psychiatry* 2008; 30: 421–434.
5. Griffiths J, Fortune G, Barber V, et al. The prevalence of post traumatic stress disorder in survivors of ICU

treatment: a systematic review. *Intensive Care Med* 2007; 33: 1506–1518.
6. Stoll C, Kapfhammer H, Rothenhäusler H, et al. Sensitivity and specificity of a screening test to document traumatic experiences and to diagnose post-traumatic stress disorder in ARDS patients after intensive care treatment. *Intensive Care Med* 1999; 25: 697–704.
7. Jackson JC, Hart RP, Gordon SM, et al. Post-traumatic stress disorder and post-traumatic stress symptoms following critical illness in medical intensive care unit patients: assessing the magnitude of the problem. *Crit Care* 2007; 11: R27.
8. Ratzer M, Romano E, and Elklit A. Posttraumatic stress disorder in patients following intensive care unit treatment: a review of studies regarding prevalence and risk factors. *J Trauma Treat* 2014; 3: 2.
9. Parker AM, Sricharoenchai T, Raparla S, et al. Posttraumatic stress disorder in critical illness survivors: a meta-analysis. *Crit Care Med* 2015; 43: 1121–1129.
10. O'Donnell ML, Creamer M, Pattison P, et al. Psychiatric morbidity following injury. *Am J Psychiatry* 2004; 161: 507–514.
11. O'Donnell ML, Creamer M, Holmes AC, et al. Posttraumatic stress disorder after injury: does admission to intensive care unit increase risk? *J Trauma* 2010; 69: 627–632.
12. Girard TD, Shintani AK, Jackson JC, et al. Risk factors for post-traumatic stress disorder symptoms following critical illness requiring mechanical ventilation: a prospective cohort study. *Crit Care* 2007; 11: R28.
13. Wintermann GB, Brunkhorst FM, Petrowski K, et al. Stress disorders following prolonged critical illness in survivors of severe sepsis. *Crit Care Med* 2015; 43: 1213–1222.
14. Myhren H, Ekeberg O, Tøien K, et al. Posttraumatic stress, anxiety and depression symptoms in patients during the first year post intensive care unit discharge. *Crit Care* 2010; 14: R14.
15. Kress JP, Gehlbach B, Lacy M, et al. The long-term psychological effects of daily sedative interruption on critically ill patients. *Am J Respir Crit Care* 2003; 168: 1457–1461.
16. Mellman TA, and Hipolito MM. Sleep disturbances in the aftermath of trauma and posttraumatic stress disorder. *CNS Spectr* 2006; 11: 611–615.
17. Jones C, Griffiths RD, Humphris G, et al. Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. *Crit Care Med* 2003; 29: 573–580.
18. Salluh JI, Soares M, Teles JM, et al. The DECCA (Delirium Epidemiology in Critical Care) Study Group. Delirium epidemiology in critical care (DECCA): an international study. *Crit Care* 2010; 14: R210.
19. Parker AM, Sricharoenchai T, Raparla S, et al. Posttraumatic stress disorder in critical illness survivors: a meta-analysis. *Crit Care Med* 2015; 43: 1121–1129.
20. Bienvenu OJ, Gellar J, Althouse BM, et al. Post-traumatic stress disorder symptoms after acute lung injury: a 2-year prospective longitudinal study. *Psychol Med* 2013; 43: 2657–2671.
21. Twigg E, Humphris G, Jones C, et al. Use of a screening questionnaire for post-traumatic stress disorder (PTSD) on a sample of UK ICU patients. *Acta Anaesthesiol Scand* 2008; 52: 202–208.
22. Cuthbertson BH, Hull A, Strachan M, et al. Post-traumatic stress disorder after critical illness requiring general intensive care. *Intensive Care Med* 2004; 30: 450–455.
23. Wade DM, Howell DC, Weinman JA, et al. Investigating risk factors for psychological morbidity three months after intensive care: a prospective cohort study. *Crit Care* 2012; 16: R192.
24. Davydow DS, Zatzick D, Hough CL, et al. A longitudinal investigation of posttraumatic stress and depressive symptoms over the course of the year following medical-surgical intensive care unit admission. *Gen Hosp Psychiatry* 2013; 35: 226–232.
25. Orwelius L, Teixeira-Pinto A, Lobo C, et al. The role of memories on health-related quality of life after intensive care unit care: an unforgettable controversy? *Patient Related Outcome Measures* 2016; 7: 63–71.
26. Jackson JC, Pandharipande PP, Girard T, et al. Depression, posttraumatic stress disorder, and functional disability in survivors of critical illness: results from the BRAIN ICU (bringing to light the risk factors and incidence of neuropsychological dysfunction in ICU survivors) investigation: a longitudinal cohort study. *Lancet Respir Med* 2014; 2: 369–379.
27. Rothenhäusler HB, Grieser B, Nollert G, et al. Psychiatric and psychosocial outcome of cardiac surgery with cardiopulmonary bypass: a prospective 12-month follow-up study. *Gen Hosp Psychiatry* 2005; 27: 18–28.