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Citation: Castillo, M. I., Cooke, M. L., Macfarlane, B. & Aitken, L. M. (2016). In ICU state anxiety is not associated with posttraumatic stress symptoms over six months after ICU discharge: A prospective study. Australian Critical Care, 29(3), pp. 158-164. doi: 10.1016/j.aucc.2015.09.003

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Link to published version: https://doi.org/10.1016/j.aucc.2015.09.003

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Australian Critical Care xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Australian Critical Care

journal homepage: www.elsevier.com/locate/aucc

Research paper

In ICU state anxiety is not associated with posttraumatic stress symptoms over six months after ICU discharge: A prospective study

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ARTICLE INFORMATION

Article history:
Received 5 June 2015
Received in revised form 24 August 2015
Accepted 30 September 2015
Available online xxx

Keywords:
Intensive care unit
State anxiety
Trait anxiety
Critically ill
Posttraumatic stress symptoms

ABSTRACT

Background: Posttraumatic stress symptoms are common after intensive care treatment. The influence of anxiety during critical illness on the development of posttraumatic stress symptoms needs to be investigated.
Objective: To determine the association between anxiety during critical illness (state and trait components) and posttraumatic stress symptoms over six months after ICU discharge.
Methods: Prospective study including 141 patients admitted ≥24 h to a closed mixed adult ICU in a tertiary hospital. State anxiety was assessed with the Faces Anxiety Scale during ICU stay. Trait anxiety was measured with the State-Trait Anxiety Inventory Form Y-2. Posttraumatic stress symptoms were measured at three and six months after ICU discharge using the Post-Traumatic Stress Symptoms 10-Question Inventory. Clinical and demographical data were also collected. Mixed effect regression models were used to determine if state and trait anxiety were factors significantly associated with posttraumatic stress symptoms over time.
Results: Moderate to severe levels of state anxiety in ICU were reported by 81 (57%) participants. Levels of trait anxiety (median 36 IQR: 29–47) were similar to the Australian population. High levels of posttraumatic stress symptoms occurred at three ($n = 19$, 19%) and six months ($n = 15$, 17%). Factors independently associated with posttraumatic stress symptoms were trait anxiety (2.2; 95% CI, 0.3–4.1; $p = 0.02$), symptoms of anxiety after ICU discharge (0.6; 95% CI, 0.2–1.1; $p = 0.005$), younger age (−1.4; 95% CI, −2.6 to −0.2; $p = 0.02$) and evidence of mental health treatment prior to the ICU admission (5.2; 95% CI, 1.5–8.9; $p = 0.006$).
Conclusions: Posttraumatic stress symptoms occurred in a significant proportion of ICU survivors and were significantly associated with higher levels of trait anxiety, younger age, mental health treatment prior to the ICU admission and more symptoms of anxiety after ICU discharge. Early assessment and interventions directed to reduce state and trait anxiety in ICU survivors may be of benefit.
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1. Introduction

Survivors of critical illness experience compromised psychological health including the development of posttraumatic stress symptoms (PTSS). Consistent predictors of PTSS following treatment in intensive care unit (ICU) include premorbid psychopathology, greater benzodiazepines administration during ICU treatment, post-ICU memories of frightening experiences and psychotic/nightmare experiences during ICU treatment.[1] Younger age

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http://dx.doi.org/10.1016/j.aucc.2015.09.003
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and female gender are less consistent predictors.[1] Although a number of predictors have been identified, the effects of trait and state anxiety during critical illness have not been thoroughly investigated as independent risk factors for the development of PTSS in the ICU survivors. The concept of anxiety has been defined as comprising two components: trait anxiety and state anxiety.[2] Trait anxiety corresponds to the individual personality trait of anxiety; namely, the person's tendency to experience state anxiety. State anxiety corresponds to the emotional (e.g. feelings of fear, worry and apprehension) and physiological (e.g. tachycardia) manifestations of anxiety when faced with a stressful stimuli.[2] One could think of trait anxiety as chronic and state anxiety as acute anxiety.

In the general literature of posttraumatic stress disorder (PTSD), it can be observed that individual differences in personality traits contribute significantly to the development of this condition.[3] Specific personality traits of anxiety and hostility/anger have been associated with PTSD.[4,5] In contrast, personality traits that seem to have a protective effect from PTSD are hardiness and optimism.[6,7]

In the ICU context, the exploration of the role of personality in the development of PTSS is at the early stages. There is beginning evidence regarding two relevant personality traits: trait optimism and trait anxiety. Trait optimism was found to be an independent predictor of reduced PTSS after ICU treatment in a study exploring adverse emotional outcomes after ICU.[8] Trait anxiety was moderately correlated (rho = 0.49, $p = 0.007$) with intrusion symptoms (one of the four distinct diagnostic clusters of PTSD described in the DSM-V)[9] at eight weeks after ICU discharge.[10] However, this finding needs further consideration and statistical approaches such multivariate analysis to determine unique contributions and rule out the influence of confounding factors. In addition, it is unclear if this association would persist over a longer period of time. The state component of anxiety during critical illness has also been proposed as a possible risk factor for the development of PTSS during recovery.[11] Further, state anxiety and PTSS have been found to co-occur frequently during recovery.[12]

The distinction between PTSS and the fully activated disorder (PTSD) needs to be made. Unlike PTSS, PTSD is a psychiatric diagnosis that impairs patients' ability to function. In this study, PTSS correspond to patients' self-report of posttraumatic stress symptoms at 3 and 6 months after ICU discharge using a validated questionnaire without the clinical diagnosis (i.e. PTSD) performed by a physician. Another term conceptually related to this topic is acute stress symptoms, which refers to PTSS experienced shortly (less than 1 month) after the exposure to the traumatic event.[13]

In this study, we hypothesised that anxiety during critical illness would be associated with the development of PTSS over six months after ICU discharge. Data about social support, cognitive functioning, optimism, symptoms of anxiety and depression after the ICU experience and medications such as corticosteroids, opioids and beta-blockers were also collected because they appear in the literature as possible risk factors for adverse emotional outcomes.[8,14–19] As such, the purpose of this research was to determine the association between anxiety during critical illness (state and trait components) and posttraumatic stress symptoms over six months after ICU discharge in survivors of intensive care treatment.

2. Methods

2.1. Settings

This prospective study was carried out at one mixed medical/surgical/trauma adult ICU in a tertiary hospital located in Brisbane, Australia. There were approximately 1130 admissions to this ICU during the six-month enrolment period (September 2012 to February 2013). This 25-bed closed ICU had a registered nurse-patient ratio of 1:1. The Griffith University (NRS/35/12/HREC) and Princess Alexandra Hospital Ethics Committees (HREC/12/QPAH/173) approved this research, informed written consent was obtained from all participants, and the study protocol was published elsewhere.[20] A summary of the methods is provided below and in Table 1.

2.2. Patients

Adult patients (≥18 years of age) who stayed in ICU for ≥24 h, were able to communicate verbally or non-verbally at the time of enrolment and each subsequent day of data collection; understand English; and, open their eyes spontaneously or in response to voice were invited to participate in this study. We performed power analysis a priori using multiple regression test (fixed model, R^2 increase); power of 80%; significance level of $\alpha = 0.05$; a maximum of seven variables; and, medium size effect (0.15). This was based on previous research reporting a strong association between trait anxiety and PTSS (Spearman's correlation rank 0.49) and reflecting a medium effect size.[10,21] An in-hospital mortality rate of 10% and a dropout of 30% at six months were projected.[20,22] A sample size of 104 participants was estimated for this study.

2.3. Data collection

As soon as patients agreed to participate in this study, the principal investigator or the ICU research nurse commenced the state anxiety assessments in ICU using the Faces Anxiety Scale (FAS). Patients reported on their levels of state anxiety twice a day (morning 8–11 am and afternoon 4–7 pm) up to 30 days. Clinical data collected twice a day at the moment of state anxiety assessment included: Delirium status (The Confusion Assessment Method for the ICU: CAM-ICU), airway status (tracheostomy, endotracheal tube), mechanical ventilation status (invasive, non-invasive, non-ventilation), oxygen saturation, pain score (Critical-Care Pain Observation Tool: CPOT) and sedation (total dose of sedatives and analgesics as well as total hours of continuous infusion of sedoanalgesia).[23,24] ICU diagnosis, Acute Physiology and Chronic Health Evaluation (APACHE) III, mental health history, gender and age were also collected from medical records.

Marital status, level of education, employment status, evidence of mental health treatment prior to the ICU admission, current smoking habits as well as pre-ICU medications (opioids, beta-blockers and corticosteroids) were obtained through a demographic questionnaire administered when patients were in the hospital wards. Patients who answered "Yes" to either of the following two question were considered to have evidence of mental health treatment prior to the ICU admission: (1) Have you ever visited a general practitioner (GP) or a mental health professional for symptoms of psychological distress or emotional problems? (2) Were you taking benzodiazepines, anxiolytics or antidepressants medications within the 12 months prior to the ICU admission? A similar approach has been used previously.[25] Trait anxiety was assessed using the Trait component of the State-Trait Anxiety Inventory (STAI) for adults Form Y-2.[2]

In the hospital wards, patients confirmed their wish to participate in this project by giving written informed consent and completing the questionnaires. The principal investigator or the ICU research nurse assisted the patients (when needed due to physical impairment) with the surveys in hospital wards.

All instruments used in this study: The Posttraumatic Stress Symptoms 10-Question Inventory (PTSS-10); trait component of the State-Trait Anxiety Inventory (STAI) for Adults Form Y-2; Hospital Anxiety and Depression Scale (HADS); Faces Anxiety Scale (FAS); Multidimensional Scale of Perceived Social Support (MSPSS); Life Orientation Test-Revised (LOT-R); and, Cognitive Functioning Scale

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Table 1
Study constructs, instruments and data collection schedule.

Construct	Instrument	Number of items	Possible score	Measurement time points	Comments
State anxiety	Faces Anxiety Scale (FAS)	1	1–5	During ICU stay Twice a day (morning 8–11 and afternoon 4–7)	5 faces representing different levels of anxiety ranging from no anxiety to extreme anxiety.
Trait anxiety	Trait component of the State-Trait Anxiety Inventory (STAI) for Adults Form Y-2	20	For each item, a rating score between 1 and 4 is possible. Total score 20–80	Hospital wards within three weeks after ICU discharge.	Higher scores indicate greater levels of trait anxiety.
Trait optimism	Life Orientation Test-Revised (LOT-R)	10	For each item, a rating score between 0 and 4 is possible. Total score 0–24	Hospital wards within three weeks after ICU discharge.	6 items concerning general expectations relative to positive or negative consequences. 4 filler items not used in the scoring. Higher scores indicate greater optimism.
Symptoms of anxiety and depression	Hospital Anxiety and Depression Scale (HADS)	Depression: 7 items Anxiety: 7 items Total: 14 items	For each item, a rating score between 0 and 3 is possible. Total score 0–21	Hospital wards within three weeks after ICU discharge and three-month follow-up	The total score for each subscale can be classified into four categories: normal (0–7), mild (8–10), moderate (11–14) and severe (15–21)
Perceived social support	Multidimensional Scale of Perceived Social Support (MSPSS)	12	For each item a rating score between 1 (very strongly disagree) and 7 (very strongly agree) is possible. Total score 1–7	Three-month follow-up	Three subscales: family, friends and significant other. Higher scores indicated higher levels of perceived social support.
Self-perceived cognitive functioning	Cognitive Functioning Scale Medical Outcome Study 6-Item (MOS COG)	6	Each item is scored from 1 (all the time) to 6 (none of the time). Summing the individual item scores and transforming the resulting score to a 0–100 scale calculate the total score.	Hospital wards within three weeks after ICU discharge. Three-month follow-up	Self-reported cognitive functioning including areas of memory, attention and reasoning. Higher scores indicate better cognitive functioning.
Post-traumatic stress symptoms	Post-Traumatic Stress Symptoms 10-Question Inventory (PTSS-10)	Part A: 4 memories Part B: 10 symptoms	Part A: for each memory, a Yes (presence of memory) or No (absence of memory) answer can be selected. Part B: for each symptom, a rating score between 1 (never) and 7 (always) were possible. Total score 10–70	Three and six-month follow-ups	Two-parts instrument: Part A consists of four traumatic memories of their ICU stay (memories of nightmares, severe anxiety or panic; severe pain; and feelings of suffocation); Part B, the presence and intensity of 10 post-traumatic symptoms are assessed. Total score can be classified into two categories: high probability of PTSD (total score ≥35 points) and low probability of PTSD (<35 points)

Medical Outcome Study 6-Item (MOS COG) were chosen because they are self-reported, well validated, easy to understand, take a few minutes to complete, and with the exception of Cognitive Functioning Scale Medical Outcome Study 6-Item (MOS COG), have all been used in ICU research.[2,26–31] A description of these instruments as well as the time point measurements is presented in Table 1.

At three and six-month follow-up, participants were mailed the surveys after a phone call to remind them about their involvement in this study. Most patients returned the surveys in the reply paid envelope provided, twelve participants read their answers to the researcher over the phone, and two patients preferred to use Only one participant left unanswered questions in the HADS, which did not allow its inclusion into the analysis.

2.4. Data analysis

All data were cleaned and checked for missing and invalid values. Descriptive characteristics are presented using means and standard deviations (SDs) or medians and interquartile ranges (IQRs) for continuous variables and percentages for categorical variables.

All variables were assessed using linear mixed models to identify those with a potential longitudinal relationship with PTSS. Those variables that were significant at an alpha level of $p < 0.2$ were then checked against one another for multicollinearity using Spearman correlations and Chi-square, then entered into the model based on level of significance.

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Repeated measures analysis using mixed models with a random intercept per subject was performed to determine variables independently and significantly associated with PTSS over a six-month period. Significance level of 5% and the Akaike Information Criteria (AIC) were used to identify a robust and parsimonious model. Model diagnostics included assessment of influential observations, multicollinearity amongst variables and residual checks. Stata version 13 (StataCorp, College Station, TX) was used for statistical analysis.[32]

3. Results

One hundred and forty one patients provided data while in ICU between September 2012 and February 2013, 120 completed the follow-up in the hospital wards, 101 completed three-month follow-up and 92 six-month follow-up (Fig. 1). Patients were aged 54 (SD ± 15) years and 70% male. The majority (61%) was in a relationship and working (57%). Forty-five (37%) patients reported some evidence of mental health treatment prior to critical illness. The median score for the trait component of the STAI Form-Y was 36 (IQR: 29–47) and the mean score for the LOT-R (trait optimism) was 15 (SD ± 4). Patients stayed in ICU for about 4 (IQR: 3–7) days and 15 (IQR: 10–28) days in hospital. Most patients required invasive mechanical ventilation (82%) for 52 (IQR: 13–148) hours; and, 81 (57%) patients reported moderate to severe levels of state anxiety (FAS 3–5). Participants were only able to report on their levels of state anxiety half of their ICU days because they were: unconscious during the first 24 h in ICU; their clinical condition deteriorated; or, they required deeper sedation. Most patients received propofol (84%), fentanyl (79%), midazolam (35%) and morphine (18%). Other clinical and demographic characteristics are presented in Table 2.

There were no significant differences in gender, length of ICU stay, length of hospital stay and APACHE III score between those who completed the study ($n = 92$) and those who were lost to follow-up at six months ($n = 49$). Patients lost to follow-up were significantly younger (mean 49 SD ± 17 vs. 57 SD ± 14, $p = 0.008$) and reported significantly higher levels of state anxiety (median 3.0 IQR: 1.7–3.5 vs. 2.0 IQR: 1.2–3.0, $p = 0.029$) and trait anxiety (median 46 IQR: 35–52 vs. 35 IQR: 28–42, $p = 0.001$) at baseline than those who completed the study.

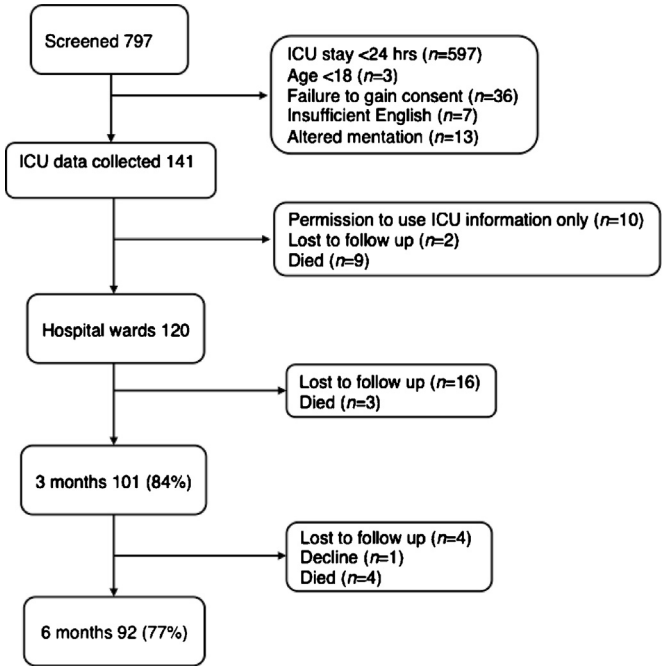

Fig. 1. Participant flow through study.

Table 2
Clinical and demographic characteristics.

	$n = 120$ (%)
Employment status pre-ICU	
Full time work	49 (41)
Part time/casual	19 (16)
Retired	25 (21)
Student/other	4 (3)
Disability benefit	18 (15)
Unemployed	5 (4)
Level of education pre-ICU	
Primary/secondary school (years 8–10)	47 (39)
Secondary school (years 11–12)	26 (22)
Trade/vocational/diploma	26 (22)
University	21 (17)
Smoking status pre-ICU	
Yes	33 (28)
No	87 (72)
Corticoids pre-ICU	
Yes	15 (12)
No	105 (88)
Opioids pre-ICU	
Yes	16 (13)
No	104 (87)
Benzos/anxiolytics/antidepressants pre-ICU	
Yes	24 (20)
No	96 (80)
Beta-blockers pre-ICU	
Yes	25 (21)
No	95 (79)
	$n = 141$ (%)
Reason for ICU admission	
Surgical	30 (21)
Medical	69 (49)
Cardiothoracic surgery	18 (13)
Trauma	24 (17)
	$n = 141$ Median (IQR)
APACHE III score	58 (43–74)
Length of sedation and analgesia in ICU (h)	
Propofol ($n = 116$)	23 (7–83)
Fentanyl ($n = 80$)	46 (15–94)
Midazolam ($n = 47$)	36 (15–109)
Morphine ($n = 26$)	30 (15–85)
Ketamine ($n = 8$)	40 (9–80)
Total dosage of sedatives and analgesics in ICU (mg)	
Propofol ($n = 119$)	2960 (750–11290)
Fentanyl ($n = 111$)	4 (1–7)
Midazolam ($n = 49$)	101 (17–218)
Morphine ($n = 37$)	48 (9–161)
Ketamine ($n = 8$)	260 (36–350)
Hydrocortisone ($n = 10$)	450 (325–588)
Oxycodone ($n = 38$)	10 (5–65)
Paracetamol ($n = 120$)	7500 (4000–14750)

APACHE: Acute Physiology and Chronic Health Evaluation System.

At the third-month follow-up, 19 (19%) patients scored ≥35 (high levels of PTSS) on the PTSS-10. Of these 19 patients, 14 (74%) reported at least one traumatic memory of their ICU admission. Of the 15 (17%) patients who reported high levels of PTSS (>35 on PTSS-10) at the sixth-month follow-up, 14 reported at least one traumatic memory. Traumatic memories of pain, difficulty breathing and anxiety were significantly associated with higher scores on PTSS-10 at six months follow-up (Table 3). The association of social support, cognitive functioning, and anxiety and depression symptoms with PTSS at six months after ICU discharge are presented in Supplementary material 1.

Numerous factors were associated with PTSS-10 score on univariate analyses (Supplementary material 2). When simultaneously entered into a mixed effect model trait anxiety, symptoms of anxiety after ICU (HADS), age and mental health history remained

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Table 3
Relationship between traumatic memories and post-traumatic stress symptoms at six months after ICU discharge ($n = 90$).

Group	PTSS-10 score (Median IQR)	Number (%) of participants who reported memories on Part A PTSS-10			
		Memories of pain	Memories of difficulty breathing	Memories of nightmares	Memories of anxiety
All patients	22 (15–31)	30 (33)	39 (43)	34 (38)	34 (38)
Symptomatic for PTSS	47 (44–55)	9 (60)	12 (80)	8 (53)	11 (73)
Asymptomatic for PTSS	18 (14–27)	21 (28)	27 (36)	26 (35)	23 (31)
Difference between symptomatic and asymptomatic patients		$X^2 = 4.410$; $p = 0.036$	$X^2 = 8.145$; $p = 0.004$	$X^2 = 1.144$; $p = 0.285$	$X^2 = 7.951$; $p = 0.005$

PTSS-10: Post-Traumatic Stress Symptoms 10-Question Inventory.
Symptomatic for PTSS = PTSS-10 score ≥35.
Asymptomatic for PTSS = PTSS-10 score <35.

significantly ($p < 0.05$) associated with PTSS score over six months after ICU discharge (Table 4). State anxiety during ICU stay (FAS) no longer had a significant association to PTSS after ICU discharge in the full model.

4. Discussion

The presence of PTSS in survivors of critical illness has been well documented.[1,8] Our study confirms these findings, with PTSS prevalence of 19% at three-month and 17% at six-month follow-up. We investigated factors potentially related to PTSS after ICU, with the primary focus on anxiety (state and trait) during critical illness. Numerous factors were significantly associated with PTSS in the univariate analyses. Using multivariate analysis only trait anxiety, symptoms of state anxiety after ICU discharge (HADS), younger age and evidence of mental health treatment prior to the ICU admission remained significantly associated with PTSS over six months after ICU discharge.

In this cohort, the levels of trait anxiety were similar to those found in the general Australian population.[33] Mixed effects analysis showed that personality trait of anxiety contributed significantly to the development of PTSS in the ICU survivor. This finding is in line with the general literature on PTSD.[5] It also confirms previous reports suggesting this association in the ICU survivors.[10]

The assessment of trait anxiety prior to hospital discharge could help clinicians to identify patients at higher risk of developing PTSS during recovery. There is growing evidence supporting that trait personalities can be modified with interventions such as cognitive behavioural therapy, educational programmes, cognitive training intervention and combination of psychological interventions and medications, to mention but a few.[34–37] However, these have not been tested in the critically ill population.

The assessment of state anxiety was performed at multiple time points and using two instruments. The FAS was used in ICU and HADS (anxiety subscale) in hospital wards and at three-month follow-up. We treated state anxiety as measured by the FAS as a different variable from the state anxiety measured by the HADS and not as repeated measure of the same variable because we wanted to test if state anxiety in ICU alone had a long term effect on PTSS. Only symptoms of state anxiety measured with the HADS were significantly associated with PTSS over time.

Table 4
Linear Mixed Model: factors associated with post-traumatic stress symptoms over six months after ICU discharge ($n = 120$).

Factors	Coefficient (95% CI)	p-Value
(Intercept)	17.4 (7.0, 27.7)	0.001
Time (6 months)	2.0 (−0.5, 4.5)	0.112
Symptoms of anxiety (per unit) (score range 0–21)	0.6 (0.2,1.1)	0.005
Trait anxiety (per 10 units) (score range 20–80)	2.2 (0.3, 4.1)	0.023
Age (per 10 units) (age range 18–84)	−1.4 (−2.6, −0.2)	0.024
Evidence of mental health treatment		
No	Reference	
Yes	5.2 (1.5, 8.9)	0.006

Akaike Information Criterion/Bayesian Information Criterion for model = 1394/1423.

Younger survivors were more likely than older survivors to have high levels of PTSS. The association between younger age and PTSS has been reported previously as well as possible explanations for this relationship.[38] Older patients might not consider critical illness as a traumatic experience since they might have been exposed to chronic diseases and previous hospitalisations. In addition, more elderly patients might not receive as aggressive ICU treatment as younger ones, interventions that may predispose them to PTSS.[39] Evidence of mental health treatment prior to the ICU admission was also associated with PTSS. Pre-ICU psychopathology was considered to be a consistent predictor of PTSD after ICU in a systematic literature review.[1] It is also a consistent predictor in the general literature of PTSD.[3]

No intra-ICU factor such as sedation, mechanical ventilation and ICU diagnosis were significantly associated with PTSS over time. In the literature of PTSS after ICU, greater benzodiazepines administration during ICU treatment is considered to be a consistent predictor of PTSS.[1] In our research, we did not find this association. This inconsistency may be explained by the current sedation practices, where light sedation with a more interactive patient is the goal in contrast to a deeply sedated patient in past years.[40]

Findings of this study suggest that the strategies addressing PTSS after ICU should be focused on the assessment and management of state and trait anxiety during and after critical illness. Patients' trait anxiety levels could be assessed in ICU or prior to hospital discharge to identify patients at higher risk, and individuals could be helped through interventions such as cognitive bias modification therapy and cognitive behavioural therapy to reduce trait anxiety and therefore the risk of PTSS. However, while these interventions have been shown to be effective in other populations, they need to be tested in the ICU survivor population to determine benefit and ensure no harm.[41] In addition, future research should investigate a broader spectrum of personality traits (e.g. openness, conscientiousness, extroversion and agreeableness) as predictors of emotional well-being in survivors of critical illness since contemporaneous work suggest that personality traits are potentially modifiable factors.[42] While in-ICU state anxiety was not an explanatory variable for PTSS over time, it was strongly associated with trait anxiety at the multivariable analysis of the ICARe study.[43] Thus, intra-ICU assessment and management of state anxiety might have positive effects in reducing trait anxiety and subsequent PTSS.

Limitations of this study include the assessment of PTSS using a questionnaire instead of formal diagnosis of PTSD through clinical interview. There is a possibility that the incidence of PTSS might have been underestimated if patients experiencing avoidance behaviours were lost to follow-up. In addition, we did not

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assess if patients sought mental health assistance after ICU; therefore, it is unknown if patients on mental health treatment during recovery experienced a decrease in PTSS. Further, acute stress reactions were not assessed as a potential risk factor for PTSS. This current study might have benefited from this assessment since recent research suggests that acute stress reactions are a contributing factor for PTSD.[13,44]

The final sample size obtained at six-month follow up (92 participants) was smaller than estimated (difference 12 participants from the a priori estimated sample size = 104). However, the a priori estimated number of variables ($n = 7$) was greater than the number of variables that remained in the final model ($n = 5$ including time). We acknowledge that the final sample size of 92 participants at 6 months follow-up might have not provided sufficient power for the modelling process of the outcomes of posttraumatic stress symptoms. Results of this current single-centre study are limited to general ICU patients with length of stay greater than 24 h. Recruitment from multiple study sites might have resulted in a more diverse cohort of patients with the potential to improve generalizability of our results.

Patients lost to follow-up were significantly younger and reported significantly higher levels of state anxiety and trait anxiety than those who completed the study. However, these three factors were still significantly associated with PTSS over time. While evidence of mental health treatment prior to the ICU was a factor significantly associated with PTSS over six months after ICU discharge, the manner in which this variable was operationalised lacks of specificity.

5. Conclusion

This study confirms that PTSS occur in an important proportion of survivors of ICU and were significantly associated with higher levels of trait anxiety, younger age, mental health treatment prior to the ICU admission and more symptoms of anxiety after ICU discharge. Early assessment and interventions directed to reduce state and trait anxiety in the ICU patient and survivor might reduce the risk of PTSS after critical illness. While in-ICU state anxiety was not a predictive variable for PTSS over time in this sample, its management during ICU treatment might contribute to reduce trait anxiety and subsequent PTSS.

Conflict of interest

The authors declare that they have no conflicts of interest.

Authors' contributions

MIC made a substantial contribution to the design of the study, enrolment of patients, collection of data, data analyses, interpretation of data and wrote the manuscript. LA and MC were responsible for the design of the study and made a substantial contribution to the interpretation of data and writing of the manuscript. BM conducted the mixed model analysis and assisted with data interpretation and writing of the manuscript. MIC, LA, MC and BM revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

Acknowledgements

We thank the Intensive Care Foundation and the Australian College of Critical Care Nurses for supporting this research. We thank Dr. Robert Ware for advising on statistical analyses. We also thank the ICU Research Nurses Lena James and Kelly Perkins for their assistance with data collection.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.aucc.2015.09.003.

References

1. Davydow DS, Gifford JM, Desai SV, Needham DM, Bienvenu OJ. Posttraumatic stress disorder in general intensive care unit survivors: a systematic review. *Gen Hosp Psychiatry* 2008;**30**:421–34.
2. Spielberger CD. *Manual for the State-Trait Anxiety Inventory (Form Y)*. Palo Alto, CA: Mind Garden; 1983.
3. Jaksic N, Brajkovic L, Ivezic E, Topic R, Jakovljevic M. The role of personality traits in posttraumatic stress disorder (PTSD). *Psychiatr Danub* 2012;**24**:256–66.
4. Ouimette P, Cronkite R, Prins A, Moos RH. Posttraumatic stress disorder, anger and hostility, and physical health status. *J Nerv Mental Dis* 2004;**192**:563–6.
5. Ristvedt SL, Trinkaus KM. Trait anxiety as an independent predictor of poor health-related quality of life and post-traumatic stress symptoms in rectal cancer. *Br J Health Psychol* 2009;**14**:701–15.
6. Bartone PT. Hardiness protects against war-related stress in Army Reserve forces. *Consult Psychol J: Pract Res* 1999;**51**:72–82.
7. Thomas JL, Britt TW, Odle-Dusseau H, Bliese PD. Dispositional optimism buffers combat veterans from the negative effects of warzone stress on mental health symptoms and work impairment. *J Clin Psychol* 2011;**67**:866–80.
8. Myhren H, Ekeberg O, Tøien K, Karlsson S, Stokland O. Posttraumatic stress, anxiety and depression symptoms in patients during the first year post intensive care unit discharge. *Crit Care* 2010;**14**:R14-R.
9. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5th ed. Washington, DC: Author; 2013.
10. Jones C, Griffiths RD, Humphris G, Skirrow PM. Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. *Crit Care Med* 2001;**29**:573–80.
11. Nelson BJ, Weinert CR, Bury CL, Marinelli WA, Gross CR. Intensive care unit drug use and subsequent quality of life in acute lung injury patients. *Crit Care Med* 2000;**28**:3626–30.
12. Bienvenu OJ, Colantuoni E, Mendez-Tellez PA, Shanholtz C, Dennison-Himmelfarb CR, Pronovost PJ, et al. Cooccurrence of and remission from general anxiety, depression, and posttraumatic stress disorder symptoms after acute lung injury: a 2-year longitudinal study. *Crit Care Med* 2015;**43**:642–53.
13. Davydow DS, Zatzick D, Hough CL, Katon WJ. In-hospital acute stress symptoms are associated with impairment in cognition 1 year after intensive care unit admission. *Ann Am Thorac Soc* 2013;**10**:450–7.
14. Deja M, Denke C, Weber-Carstens S, Schroder J, Pille CE, Hokema F, et al. Social support during intensive care unit stay might improve mental impairment and consequently health-related quality of life in survivors of severe acute respiratory distress syndrome. *Crit Care* 2006;**10**:R147.
15. Hopkins RO, Weaver LK, Collingridge D, Parkinson RB, Chan KJ, Orme Jr JF. Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2005;**171**:340–7.
16. Schelling G, Briegel J, Roozendaal B, Stoll C, Rothenhäusler HB, Kapfhammer HP. The effect of stress doses of hydrocortisone during septic shock on posttraumatic stress disorder in survivors. *Biol Psychiatry* 2001;**50**:978–85.
17. Bryant RA, Creamer M, O'Donnell M, Silove D, McFarlane AC. A study of the protective function of acute morphine administration on subsequent posttraumatic stress disorder. *Biol Psychiatry* 2009;**65**:438–40.
18. Fletcher S, Creamer M, Forbes D. Preventing post traumatic stress disorder: are drugs the answer? *Aust N Z J Psychiatry* 2010;**44**:1064–71.
19. Castillo MI, Cooke ML, Macfarlane B, Aitken LM. Trait anxiety, but not state anxiety during critical illness was associated with anxiety and depression over six months after ICU. *Crit Care Med* 2015 [forthcoming].
20. Castillo MI, Aitken LM, Cooke ML. Study protocol: Intensive care anxiety and emotional recovery (Icare)—a prospective study. *Aust Crit Care* 2013;**26**:142–7.
21. Pallant J. *SPSS survival manual: a step by step guide to data analysis using IBM SPSS*. 5th ed. Crows Nest, NSW: Allen & Unwin; 2013.
22. Faul F, Erdfelder E, Buchner A, Lang A-G. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods* 2009;**41**:1149–60.
23. Ely EW, Margolin R, Francis J, May L, Truman B, Dittus R, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med* 2001;**29**:1370–9.
24. Gelinas C, Fillion L, Puntillo KA, Viens C, Fortier M. Validation of the critical-care pain observation tool in adult patients. *Am J Crit Care* 2006;**15**:420–7.
25. Cuthbertson B, Hull A, Strachan M, Scott J. Post-traumatic stress disorder after critical illness requiring general intensive care. *Intensive Care Med* 2004;**30**:450–5.
26. Stoll C, Kapfhammer HP, Rothenhausler HB, Haller M, Briegel J, Schmidt M, 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.

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27. Zigmond A, Snaith R. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361–70.
28. McKinley S, Stein-Parbury J, Chehelnabi A, Lovas J. Assessment of anxiety in intensive care patients by using the Faces Anxiety Scale. *Am J Crit Care* 2004;**13**:146–52.
29. Zimet G, Dahlem N, Zimet S, Farley G. The multidimensional scale of perceived social support. *J Pers Assess* 1988;**52**:30–41.
30. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. *J Pers Soc Psychol* 1994;**67**:1063–78.
31. Stewart A, Ware J. *Measuring functioning and well-being. The medical outcomes study approach*. Durham and London: Duke University Press; 1992.
32. StataCorp. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP; 2013.
33. Crawford J, Cayley C, Lovibond PF, Wilson PH, Hartley C. Percentile norms and accompanying interval estimates from an Australian general adult population sample for self-report mood scales (BAI, BDI, CRSD, CES-D, DASS, DASS-21, STAI-X, STAI-Y, SRDS, and SRAS). *Aust Psychol* 2011;**46**:3–14.
34. Clark DM, Clark DM, Ehlers A, McManus F, Hackmann A. Cognitive therapy versus fluoxetine in generalized social phobia: a randomized placebo-controlled trial. *J Consult Clin Psychol* 2003;**71**:1058–67.
35. Krasner MS, Epstein RM, Beckman H, Suchman AL, Chapman B, Mooney CJ, et al. Association of an educational program in mindful communication with burnout, empathy, and attitudes among primary care physicians. *JAMA* 2009;**302**:1284–93.
36. Jackson JJ, Hill PL, Payne BR, Roberts BW, Stine-Morrow EA. Can an old dog learn (and want to experience) new tricks? Cognitive training increases openness to experience in older adults. *Psychol Aging* 2012;**27**:286–92.
37. Tang TZ, DeRubeis RJ, Hollon SD, Amsterdam J, Shelton R, Schalet B. Personality change during depression treatment: a placebo-controlled trial. *Arch Gen Psychiatry* 2009;**66**:1322–30.
38. Girard TD, Shintani AK, Jackson JC, Gordon SM, Pun BT, Henderson MS, 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.
39. Hamel MB, Teno JM, Goldman L, Lynn J, Davis RB, Galanos AN, et al. Patient age and decisions to withhold life-sustaining treatments from seriously ill, hospitalized adults SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment. *Ann Intern Med* 1999;**130**:116–25.
40. Elliott D, Aitken LM, Bucknall TK, Seppelt IM, Webb SA, Weisbrodt L, et al. Patient comfort in the intensive care unit: a multicentre, binational point prevalence study of analgesia, sedation and delirium management. *Crit Care Resusc* 2013;**15**:213–9.
41. Brosan L, Hoppitt L, Shelfer L, Sillence A, Mackintosh B. Cognitive bias modification for attention and interpretation reduces trait and state anxiety in anxious patients referred to an out-patient service: results from a pilot study. *J Behav Ther Exp Psychiatry* 2011;**42**:258–64.
42. Magidson JF, Roberts BW, Collado-Rodriguez A, Lejuez CW. Theory-driven intervention for changing personality: expectancy value theory, behavioral activation, and conscientiousness. *Dev Psychol* 2014;**50**:1442–50.
43. Castillo MI [dissertation] *The relationship between anxiety during critical illness and adverse emotional outcomes*. Brisbane: Griffith University; 2015, 343 p.
44. Karnatovskaia LV, Johnson MM, Benzo RP, Gajic O. The spectrum of psychocognitive morbidity in the critically ill: a review of the literature and call for improvement. *J Crit Care* 2015;**30**:130–7.

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