RESEARCH ARTICLE

Prevalence and correlation analysis between post-traumatic stress disorder and analgesic use in survivors of ICU in China

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Abstract

Objective: To investigate the prevalence of post-traumatic stress disorder in intensive care unit survivors, and disorder's correlation with analgesia use.

Method: The single-centre retrospective cohort study was conducted at the First Affiliated Hospital of Jinan University, China, and comprised data from February 2021 to January 2022 related to patients of either gender aged ≥18 years who were admitted to the intensive care unit and were successfully transferred out to the general ward. Post-traumatic stress disorder Checklist-Civilian Version scale was used for follow-up within one month of getting transferred out of intensive care. Data was analysed using Empower Stats.

Results: Of the 121 patients with mean age 54.34±18.19 years, 52(43%) were positive for post-traumatic stress disorder; 32(61.5%) males and 20(38.5%) females with mean age 54.48±19.56 years. The remaining 69(57%) patients were negative; 40(58%) males and 29(42%) females with mean age 54.23±17.24 years (p>0.05). The positive rate of re-experiencing symptoms was noted in 68(56.20%) patients. Analgesia usage was positive in 61(50.4%) cases and negative in 60(49.6%) cases. Compared to the non-analgesic group, the risk of post-traumatic stress disorder occurrence in the analgesic group was significantly high (*p*=0.018). The duration of analgesia usage 24-48h was also significant (*p*=0.017).

Conclusions: There was a high prevalence of post-traumatic stress disorder in intensive care unit survivors, which was affected by the use of analgesics in intensive care settings.

Keywords: Post-traumatic stress disorder, PTSD, Analgesics, Intensive care unit. (JPMA 73: 1811; 2023)

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Introduction

Post-traumatic stress disorder (PTSD) is a long-term persistent or delayed mental disorder that develops following trauma exposure directly or indirectly, which is regarded as a chronic and weak mental illness.[1] It is characterised by an overreaction to traumatic situational memory, the involuntary flashback of traumatic memory and impairment of fear regression function, as well as cognitive and learning impairment and nightmare trauma in some cases.[1,2] In other words, PTSD comprises the three aspects of reexperiencing, avoidance/numbing, and hypervigilance symptoms.

With the development of critical care medicine and the progress of medical technology, there is a gradual increase in the survival rate of critically ill patients and the transfer-out rate of patients in the intensive care unit (ICU). Consequently, great concern has been gradually attached to the long-term prognosis and quality of life. However, it is a great challenge for patients to deal with the special environment and treatment of ICU. Patients transferred out of ICU generally have serious physical, psychological and cognitive problems,[3] such as anxiety, depression, pain, insomnia, weakness, fatigue, discomfort, PTSD, etc., requiring the attachment of great importance to their quality of life.[4-8] A meta-analysis revealed that the prevalence of PTSD was 17-34% among patients transferred out of ICU.[5] Another[9] meta-analysis reported PTSD prevalence to be 19.83% in a similar setting, and the predicted prevalence ranged from 3.70% to 43.73%. A large multicentre prospective follow-up study in the United Kingdom found that over 50% of patients who received ICU treatment showed significant symptoms of anxiety, depression or PTSD.[10]

Patients in ICU receive invasive treatment frequently and generally experience pain[11] that is often alleviated by using sedation and analgesics. Multiple studies have been carried out on the association between sedation and PTSD.[11,12] Relevant research has shown that frequent use of opioids in ICU is significantly associated with long-term mental symptoms.[13] Nevertheless, a study found that younger age was the only independent risk factor for PTSD in cardiac arrest survivors, without obvious difference in the use of

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analgesics.[14] At present, there is still an unclear correlation between PTSD occurrence and analgesic use in ICU survivors.

The current study was planned to explore the prevalence of PTSD in patients transferred out of ICU, and the correlation between analgesia use in ICU and PTSD occurrence. It was hypothesised that the use of analgesics in ICU may have an impact on the occurrence of PTSD.

Materials and Methods

The single-centre retrospective cohort study was conducted at the First Affiliated Hospital of Jinan University, China, and comprised data from February 2021 to January 2022 related to patients of either gender aged ≥18 years with no cognitive and psychiatric disorder who were admitted to the ICU for >24h and were successfully transferred out to the general ward.

An ICU follow-up team was formed at the study site in 2013 which began to follow up all patients who were transferred out of the ICU, including general condition, feelings and experiences during ICU stay, as well as suggestions and opinions. Health education for nursing management of patients with indwelling catheters and early activities were also included in the follow-up. In December 2020, the team began to supplement the psychological follow-up content. Members of the follow-up team used the PTSD Checklist-Civilian Version (PCL-C) scale[15] to carry out follow-up one month after the patient was transferred out of the ICU. All data was gathered after taking informed consent from the patients.

For the purpose of the current study, relevant data was retrieved from the institutional electronic intensive care system. Data of patients who were unable to complete the questionnaire due to changes in condition, aggravation or emotional excitement, those with communication difficulties and of patients with severe brain injury was excluded.

After approval from the institutional ethics review committee, the sample size was targeted to be 5-10 times the number of 14 variables.

The PCL-C15 is a commonly used PTSD screening tool globally. It is a 17-item symptom checklist, consisting of three dimensions; reexperiencing (items 1-5), avoidance/numbing (items 6-12), and hypervigilance (items 13-17). Each item is scored 1-5, with 1 = no occurrence, 2 = mild, 3 = moderate, 4 = severe, and 5 = extremely severe. The total score is generated by adding up the scores of all the items. At least one item of the dimension must be positive to determine the prevalence of re-experiencing symptom, at least two items for hypervigilance, and at least 3 items must be positive for the confirmation of avoidance/numbing domain. The total score of PCL-C ranged 17-85, and a higher score indicate a higher level of PTSD. Positive PTSD was determined with total score ≥38 points. The Cronbach's alpha (α) coefficient of the scale was 0.83, and validity 0.88.[16]

The data collection form was predesigned and included baseline data, such as gender, age, Glasgow Coma Scale (GCS) score, Critical Care Pain Observation Tool (CPOT) score, Acute Physiology and Chronic Health Evaluation II (APACHE II) score, disease diagnosis, use of mechanical ventilation, sedative use, analgesic use, physical constraints, length of stay in ICU, etc. Analgesics, the drugs that act on the central nervous system (CNS) to selectively relieve pain without affecting consciousness and other sensations, used in the patient population included morphine hydrochloride injection, sufentanil citrate injection, butofino tartrate injection and dezocine injection.

Data was analysed using Empower Stats and R statistical software.[17,18] Data was expressed as frequencies and percentages, mean and standard deviation (SD), and median (interquartile range [IQR]), as appropriate, Chi-square test, independent sample t-test and rank-sum test were used, as appropriate. Multiple regression analysis was performed to identify the correlation between PTSD and analgesia use. The occurrence status of PTSD was taken as the outcome variable, and analgesic use and the duration of analgesic use were used as independent variables. The influence of introducing covariates into the basic model on the regression coefficient was >10%, or $p<0.1$.[19,20] The covariates finally screened included length of stay in ICU, GCS score, CPOT score, sedative use, mechanical ventilation, physical restraint, diagnosis, rescue in ICU, transfer to ICU after the operation, surgery in ICU, and APACHE II score. The crude model had no adjustment for all confounding factors, while covariates of age and gender were adjusted in model I. Besides, adjustments for length of stay in ICU, GCS score, CPOT score, sedative use, mechanical ventilation, physical restraint, diagnosis, rescue in ICU, transfer to ICU after the operation, surgery in ICU, and APACHE II score were performed in Model II. In addition, age, gender, as well as the length of stay in ICU, GCS score, CPOT score, sedative use, mechanical ventilation, physical restraint, diagnosis, rescue in ICU, transfer to ICU after the operation, surgery in ICU, and APACHE II score were adjusted for Model III. $P<0.05$ was taken as statistically significant.

Results

Of the 384 patients treated in the ICU, 198(51.6%) were transferred out to the general ward. Of them, 77(39%) had

to be excluded; 3(4%) could not fill the questionnaire due to changes in their condition, 20(26%) refused to participate, 10(13%) had severe brain organic injury, 15(19.4%) had communication disorders, 17(22%) could not be contacted during the follow-up, and 12(15.5%) had mental diseases. The final sample, as such, stood at 121(61%).

Table-1: General data of intensive care unit (ICU) survivors.

Variables		PTSD		*p*-value
		Negative (n=69) n (%)	**Positive** (n=52) n (%)	
Mean Age (years)		54.23±17.24	54.48 ± 19.56	0.941
Gender	Male	40 (57.97)	32 (61.54)	0.692
	Female	29 (42.03)	20 (38.46)	
Transferred to ICU after the operation	No	50 (72.46)	40 (76.92)	0.578
	Yes	19 (27.54)	12 (23.08)	
Surgery in ICU	No	60 (86.96)	50 (96.15)	0.081
	Yes	9 (13.04)	2 (3.85)	
Mean APACHE II score (points)		18.49±7.59	19.71 ± 7.62	0.384
Length of stay in ICU [days, M (P_{25},P_{75}]		3 (1,4)	2.50 (1.00-5.25)	0.231
GCS score [points, M (P_{25},P_{75})]		15.00 (8.00-15.00)	14.00 (7.00-15.00)	0.385
Sedative use	No	39 (56.52)	32 (61.54)	0.579
	Yes	30 (43.48)	20 (38.46)	
Vasoactive drug use	No	37 (53.62)	29 (55.77)	0.814
	Yes	32 (46.38)	23 (44.23)	
Mechanical ventilation	No	47 (68.12)	38 (73.08)	0.555
	Yes	22 (31.88)	14 (26.92)	
Physical restraint	No	41 (59.42)	29 (55.77)	0.687
	Yes	28 (40.58)	23 (44.23)	
Rescue in ICU	No	69 (100.00)	51 (98.08)	0.247
	Yes	0 (0.00)	1 (1.92)	
Diagnosis	Respiratory system	6 (8.70)	9 (17.31)	0.29
	Circulatory system		10 (14.49)	6(11.54)
	Nervous system		9 (13.04)	5 (9.61)
	Digestive system		24 (34.78)	16 (30.77)
	Endocrine system		6(8.70)	4(7.69)
	Others		14(20.29)	12(23.08)

APACHE: Acute physiology and chronic health evaluation II, GCS: Glasgow coma scale.

Table-2: PTSD symptoms in intensve care unit (ICU) survivors.

Dimensions	Positive cases n (%)
Reexperiencing symptom	68 (56.20)
Avoidance/numbing symptom	43 (35.54)
Hypervigilance symptom	52 (42.98)

PTSD: Post-traumatic stress disorder.

Of these 121 patients with mean age 54.34±18.19 years, 52(43%) were positive for PTSD; 32(61.5%) males and 20(38.5%) females with mean age 54.48±19.56 years. The remaining 69(57%) patients were negative for PTSD; 40(58%) males and 29(42%) females with mean age 54.23±17.24 years (p>0.05) (Table 1).

The mean total PCL-C score was 35.74±12.81. The mean scores of reexperiencing, avoidance/numbing, and hypervigilance were 15.35±4.53, 13.90±5.79 and 10.54±3.71, respectively. The positive rate of re-experiencing was noted in 68(56.20%) patients, followed by hypervigilance 52(42.98%) and avoidance/numbing 43(35.54%) (Table 2).

Analgesia usage was positive in 61(50.4%) cases and negative in 60(49.6%). Compared to the non-analgesic group, the risk of post-traumatic stress disorder occurrence in the analgesic group was significantly high (p=0.018). The duration of analgesia usage 24-48h was also significant (p=0.017) (Table 3).

Discussion

In The current study, the prevalence of PTSD was 43% which was higher than 22% and 24% reported by large-scale, multicentre studies.[10,13] Another study reported 13% prevalence after 3.19±5.37 months of being transferred out of the ICU.[21] The higher incidence in the current study may be related to the suspended ICU visits during the coronavirus disease-2019 (COVID-19) pandemic A study[22] conducted during the pandemic reported PTSD prevalence in the next of kin to be 90.3% and 69.4% during patients' hospitalisation and within 3 months, respectively. In view of the normalisation of COVID-19, attempts should be made for intervention, like video visitation, ICU diary, etc., to reduce the occurrence of mental symptoms in the patients and their families.

Among the three symptoms of PTSD in the current study, the positive rate was the highest for reexperiencing (56.20%), followed by hypervigilance (42.98%), and finally the avoidance/numbing symptom (35.54%). The highest

Table-3: Relationship between analgesia use and PTSD.

Variables		PTSD-negative group n (%)	PTSD-positive group n (%)	Crude Model OR (95%CI)	*p*-value	Model I OR (95%CI)	*p*-value	Model II OR (95%CI)	*p*-value	Model III OR (95%CI)	*p*-value
Analgesia use	No	36 (52.17)	24 (46.15)	Reference		Reference		Reference		Reference	
	Yes	33 (47.83)	28 (53.85)	1.27(0.62, 2.62)	0.512	1.29 (0.62, 2.68)	0.494	4.01 (1.27, 12.67)	0.018	4.02(1.27, 12.72)	0.018
Duration of analgesia use	No use	36 (35.17)	24 (46.15)	Reference		Reference		Reference		Reference	
	<24h	10 (14.49)	9 (17.31)	1.35 (0.48, 3.81)	0.571	1.36 (0.48, 3.85)	0.563	4.22 (1.00, 17.71)	0.049	4.12(0.98, 17.38)	0.054
	24-48h	9 (13.04)	9 (17.31)	1.50 (0.52, 4.32)	0.453	1.49 (0.52, 4.30)	0.462	6.24 (1.39, 28.08)	0.017	6.29(1.39, 28.42)	0.017
	>48h	14 (20.29)	10 (19.23)	1.07 (0.41, 2.80)	0.888	1.10 (0.41, 2.94)	0.857	2.49 (0.55, 11.25)	0.237	2.50(0.54, 11.59)	0.242

PTSD: Post-traumatic stress disorder, OR: Odds ratio, CI: Confidence interval.

positive rate of reexperiencing may be attributed to the relatively shorter period of follow-up.

Notably, the study also observed that compared to the non-analgesic group, the risk ratio of PTSD was 4.02 times higher in the analgesic group. Huang et al.[13] showed that the increased use of analgesics in ICU increased the incidence of anxiety and depression, but the difference in the effect on PTSD was not significant. The factor needs to be further explored.

The current study showed that the risk ratio of PTSD occurrence in patients who used analgesics for 24-48h was 6.29 time higher compared to the rest. This supported the idea that analgesic use in ICU is a risk factor for PTSD in ICU survivors, especially in patients who used analgesics for 24-48h. Besides, there was no significant difference in other groups, which may be explained by the insufficient sample size of the study.

As for the reason, analgesics play a role generally through the central nervous system, and PTSD is a post-traumatic mental disorder, both of which exhibit intimate association with the higher nervous centre of patients. A study supported the current findings.[11]

The current study has limitations. It was an observational study that could not determine the causal relationship between analgesic use in ICU and PTSD. The study had a relatively smaller sample size although the study duration was a whole year, resulting in insufficient statistical test efficiency. There was only an understanding of the short-term impact of analgesic use on ICU survivors owing to the limited period of follow-up. The study was conducted during a pandemic, and its impact on the prevalence of PTSD cannot be excluded. Also, the study did not evaluate the impact each of the analgesics used, and, instead, analysed them as a whole. Finally, the occurrence of PTSD is multifactorial, and some influencing factors might be ignored since multiple confounding factors were excluded in the current study. In-depth studies are required to validate the current findings.

Conclusion

There was a high prevalence (of PTSD in ICU survivors, highlighting the significance of attaching importance to the mental and psychological problems of this group of population continuously. Meanwhile, for patients using analgesics, appropriate interventions should be explored to reduce their unfavourable impact on the quality of life of patients transferred out of ICU.

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References

1. Friedman MJ. Finalizing PTSD in DSM-5: getting here from there and where to go next. J Trauma Stress 2013; 26: 548-56.
2. Auxéméry Y. Post-traumatic psychiatric disorders: PTSD is not the only diagnosis. Presse Med 2018; 47: 423-30.
3. Desai SV, Law TJ, Needham DM. Long-term complications of critical care. Crit Care Med 2011; 39: 371-9.
4. Needham DM, Davidson J, Cohen H, Hopkins RO, Weinert C, Wunsch H, et al. Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. Crit Care Med 2012; 40: 502-9.
5. Nikayin S, Rabiee A, Hashem MD, Huang M, Bienvenu OJ, Turnbull AE, et al. Anxiety symptoms in survivors of critical illness: a systematic review and meta-analysis. Gen Hosp Psychiatry 2016; 43: 23-9.
6. Parker AM, Sricharoenchai T, Raparla S, Schneck KW, Bienvenu OJ, Needham DM. Posttraumatic stress disorder in critical illness survivors: a meta analysis. Crit Care Med 2015; 43: 1121-9.
7. Rabiee A, Nikayin S, Hashem MD, Huang M, Dinglas VD, Bienvenu OJ, et al. Depressive symptoms after critical illness: a systematic review and meta-analysis. Crit Care Med 2016; 44: 1744-53.
8. Miyamoto K, Shibata M, Shima N, Nakashima T, Ogawa A, Anai S, et al. Subjective symptoms and their association with psychiatric symptoms 3 months after ICU discharge: sub-analysis of a single-center prospective observational study. Ir J Med Sci 2022; 191: 355-7.
9. Righy C, Rosa RG, de Silva RTA, Kochhann R, Migliavaca CB, Robinson CC, et al. Prevalence of post-traumatic stress disorder symptoms in adult critical care survivors: a systematic review and meta-analysis. Crit Care 2019; 23: 213.
10. Hatch R, Young D, Barber V, Griffiths J, Harrison DA, Watkinson P. Anxiety, depression and post traumatic stress disorder after critical illness: a UK-wide prospective cohort study. Crit Care 2018; 22: 310.
11. Pota V, Coppolino F, Barbarisi A, Passavanti MB, Aurilio C, Sansone P, et al. Pain in intensive care: a narrative review. Pain Ther 2022; 11: 359-67.
12. Morrissey M, Collier E. Literature review of post-traumatic stress disorder in the critical care population. J Clin Nurs 2016; 25: 1501-14.
13. Huang M, Parker AM, Bienvenu OJ, Dinglas VD, Colantuoni E, Hopkins RO, et al. Psychiatric symptoms in acute respiratory distress syndrome survivors: a 1-year national multicenter study. Crit Care Med 2016; 44: 954-65.
14. Gamper G, Willeit M, Sterz F, Herkner H, Zoufaly A, Hornik K, et al. Life after death: posttraumatic stress disorder in survivors of cardiac arrest--prevalence, associated factors, and the influence of sedation and analgesia. Crit Care Med 2004; 32: 378-83.
15. Ruggiero KJ, Del BK, Scotti JR, Rabalais AE. Psychometric properties of the PTSD Checklist-Civilian Version. J Trauma Stress 2003; 16: 495-502.
16. Chen Y. The application study of nursing intervention based on solution focused approach in the resilience and post-traumatic stress disorder for patients with acute myocardial infarction. Univ South China 2021; 23. [not found]
17. X&Y Solutions. EmpowerStats[Online] [Cited 2023 June 01]. Available from: http://www.empowerstats.com.
18. X&Y Solutions. The R Project for Statistical Computing. [Online] [Cited 2023 June 01]. Available from: URL: http://www.R-project.org.
19. Jaddoe VW, de Jonge LL, Hofman A, Franco OH, Steegers EA, Gaillard R. First trimester fetal growth restriction and cardiovascular risk factors in school age children: population based cohort study. BMJ 2014; 348: g14.

20. Yan J, Pan Y, He Y, Wang R, Shao W, Dong S. The effects of serum iron level without anemia on long-term prognosis of patients with coronary heart disease complicated with chronic heart failure: a retrospective cohort study. Heart Vessels 2020; 35: 1419-28.
21. Askari HSM, Arab M, Karzari Z, Razban F. Post-traumatic stress disorder in critical illness survivors and its relation to memories of ICU. Nurs Crit Care 2021; 26: 102-8.
22. Zante B, Erne K, Grossenbacher J, Camenisch SA, Schefold JC, Jeitziner MM. Symptoms of post-traumatic stress disorder (PTSD) in next of kin during suspension of ICU visits during the COVID-19 pandemic: a prospective observational study. BMC Psychiatry 2021; 21: 477.