UDC: 616.89-008.441.3-06:616.89-008.1]-037-057.36
DOI: https://doi.org/10.32345/USMYJ.3(164).2026.66-72

PROGNOSTIC VALUE OF ALCOHOL USE DISORDERS IN COMBATANTS WITH POST-TRAUMATIC STRESS DISORDER FOR THE SEVERITY OF COGNITIVE DYSFUNCTION

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ABSTRACT

Introduction. Literature data on the impact of alcohol use disorders (AUD) on cognitive function in combatants with post-traumatic stress disorder (PTSD) remain inconclusive, which underscores the rationale and relevance of the present study.

Aim. To assess the prognostic value of alcohol use disorders in combatants with post-traumatic stress disorder in relation to the severity of cognitive dysfunction.

Materials and methods. The study analyzed the results of examinations of 274 inpatients with PTSD, all of whom were male combatants aged 20-56 years. Depending on the presence of AUD, the patients were divided into two groups: those with isolated PTSD and those with PTSD comorbid with AUD. PTSD was diagnosed according to Order No. 121 of the Ministry of Health of Ukraine dated February 23, 2016. AUD was assessed using the CAGE, AUDIT, and CIWA-Ar tests, while cognitive function was evaluated using the MMSE, MoCA, SAGE, Clock Drawing Test, and 10-Word Recall Test. The results were statistically analyzed and presented as (M±m). Prognostic value was determined using multivariable logistic regression analysis.

Results. Alcohol use disorders in combatants were associated with an increased frequency of difficulties with concentration and feelings of loneliness, fluctuations in blood pressure, episodes of dizziness, and flashbacks. In combatants with PTSD, AUD was a prognostic marker of difficulty concentrating, increasing its likelihood by 9.76-fold ($p<0.0001$), and of feelings of loneliness, increasing the likelihood by 1.69-fold ($p=0.057$). The comorbidity of PTSD and AUD increased the likelihood of dementia according to the MMSE by 7.24-fold ($p=0.001$), cognitive dysfunction according to the SAGE by 3.30-fold ($p=0.0002$), and impairment on the Clock Drawing Test by 2.04-fold ($p=0.015$), as well as increasing the likelihood of medium and low memory performance by 33.45-fold ($p<0.0001$).

Conclusions. Alcohol use disorders in combatants with post-traumatic stress disorder are a marker of cognitive dysfunction and are associated with an increased likelihood and severity of cognitive impairment.

Keywords: alcohol use disorder, post-traumatic stress disorder, cognitive dysfunction, combatants, psychological testing.

INTRODUCTION

Post-traumatic stress disorder (PTSD) is an important public health problem affecting both military combatants and the civilian population [1], particularly in the context of full-scale warfare and regular shelling of civilian areas. PTSD is defined as an acute or chronic mental disorder or neurosis resulting from exposure to severe psychologically traumatic events, including military operations involving graphic scenes of death and mutilation, terrorist attacks, major accidents, fires and natural disasters, as well as scenes of sexual, physical, and psychological violence, most often involving violent death, that an individual has experienced or witnessed [2].

Cognitive impairment is an important predisposing factor and, at the same time, a consequence of PTSD. It affects cognitive processes in the brain, thereby impairing the individual's ability to interact rationally with their environment. A meta-analysis of 21 studies involving 1,977 military personnel demonstrated increased attention to threat-related stimuli, which, on the one hand, may enhance safety and, on the other, is associated with PTSD [3]. Military personnel with PTSD also tended to describe memories in an overly general manner, exhibited altered perception,

demonstrated impaired interpretation, and more frequently provided negative responses to ambiguous statements [3]. For combatants, previous traumatic brain injuries and blast-related injuries are also important, as these conditions may independently cause cognitive impairment, including alterations in social functioning, the emergence of intrusive thoughts, and impaired ability to recognize the emotions of others and regulate one's own emotions [4]. In combatants with coexisting cognitive dysfunction (CD) and PTSD, a sixfold higher rate of suicide has been reported compared with individuals diagnosed with only one of these conditions [5]. Among veterans with PTSD, cognitive impairments have been documented for decades following traumatic events and military service [6].

The complex of emotional and somatic reactions experienced by combatants creates a background for the development of addictive behavior. This is particularly relevant to alcohol use disorders (AUD) [7, 8]. PTSD and AUD have synergistic clinical manifestations, and their comorbidity is associated with insufficient treatment efficacy [9]. However, the available literature remains inconclusive [10], which underscores the rationale and relevance of the present study.

AIM

To assess the prognostic value of alcohol use disorders in combatants with post-traumatic stress disorder in relation to the severity of cognitive dysfunction.

MATERIALS AND METHODS

The study analyzed the results of examinations of 274 inpatients with PTSD who underwent standard diagnostic assessment and treatment. All patients were male combatants aged 20-56 years. Depending on the presence of AUD, the patients were divided into two groups: Group 1 (G1; n=150; mean age 31.0±2.6 years) with isolated PTSD and Group 2 (G2; n=124; mean age 27.5±4.0 years; p>0.05) with PTSD comorbid with AUD. The study was conducted in accordance with the Declaration of Helsinki of the World Medical Association, with informed consent obtained from all participants, under the supervision of the Bioethics Committee of Danylo Halytsky Lviv National Medical University (protocols No. 10 dated December 16, 2019, and No. 1 dated January 20, 2025).

PTSD was diagnosed in accordance with Order No. 121 of the Ministry of Health of Ukraine dated February 23, 2016. To identify AUD and assess its severity, an interview was conducted to encourage patients to provide candid and reliable information. With the participants' consent, combatants were additionally assessed using validated questionnaires: the CAGE Questionnaire, AUDIT (*Alcohol Use Disorders Identification Test*), MAST (*Michigan Alcoholism Screening Test*), and CIWA-Ar (*Clinical Institute Withdrawal Assessment for Alcohol–Revised*). Cognitive impairment was objectively assessed using neuropsychological methods [11], including the Mini-Mental State Examination (MMSE) [12], Montreal Cognitive Assessment (MoCA) [13], SAGE (*Self-Administered Gerocognitive Examination*) [14], Clock Drawing Test, and 10-Word Recall Test [13].

The results were statistically analyzed and tested for normality of distribution, which was consistent with a Gaussian distribution; therefore, parametric statistical methods were used. The data are presented as (M ± m). Comparisons of the obtained results and assessment of the significance of the observed differences were performed using Student's t-test. Prognostic value was determined using multivariable logistic regression analysis [15]. Odds ratios (OR), 95% confidence intervals (95% CI), statistical significance (p), and the Z-statistic were calculated. For statistically significant prognostic markers, sensitivity (the proportion of true-positive results) and specificity (the proportion of true-negative results) were determined and expressed as percentages. A p value < 0.05 was considered statistically significant.

RESULTS

PTSD in combatants was characterized by the most frequent manifestations of avoidance symptoms (84–89%), intrusive behavior and hyperarousal (45–51%), and emotional numbing and detachment (21–37%), regardless of comorbidity with alcohol use disorders (AUD). Compared with isolated PTSD, comorbid PTSD and AUD was characterized by a higher frequency of autonomic reactions manifested by dizziness accompanied by nausea (42.74% vs. 31.33%), a craving for alcohol to relieve tension and reduce the intensity of distressing experiences (95.16% vs. 22.66%), and impaired concentration (87.90% vs. 42.66%), along with less frequent mood changes (73.33% vs. 87.33%).

The severity of the leading PTSD symptoms in combatants with isolated PTSD and PTSD comorbid with AUD is presented in Fig. 1. In patients with PTSD, the presence of AUD was associated with greater difficulties in concentration, increased feelings of loneliness, fluctuations in blood pressure, more frequent episodes of dizziness, and flashbacks.

Screening assessment of cognitive function was primarily aimed at determining the nature and severity of PTSD itself. The course of PTSD in the presence of AUD was characterized by significantly more frequent difficulties with attention and feelings

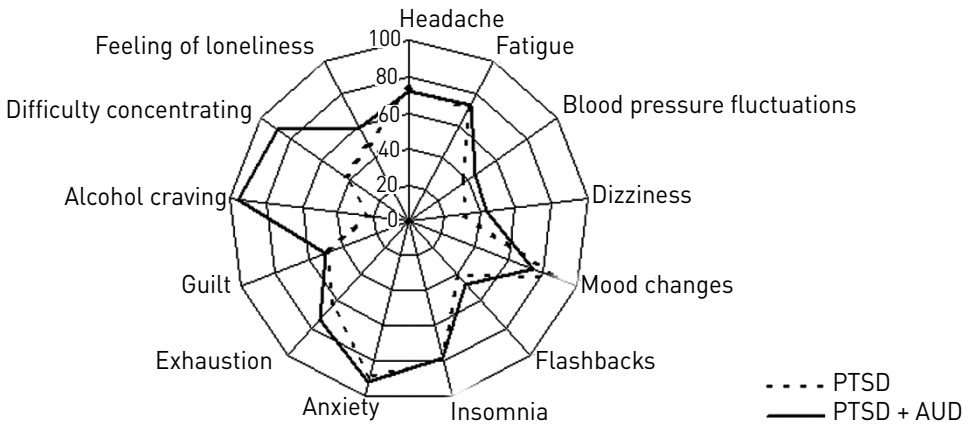

Fig. 1. Frequency and severity of PTSD symptoms in combatants with isolated PTSD and PTSD comorbid with AUD

of loneliness (Table 1). Thus, difficulty concentrating was observed 9.76 times more frequently in patients with comorbid PTSD and AUD, with a high level of statistical significance (95% CI=5.20-18.32; p<0.0001). The sensitivity of this indicator was relatively high (87.90%), whereas its specificity was somewhat lower (57.33%). The PTSD symptom of feeling of loneliness approached statistical significance, being 1.69 times more frequent in patients with comorbid PTSD and AUD (95% CI=0.90-2.57; p=0.0575), with similar sensitivity and specificity values (Tables 1 and 2).

Multivariable odds analysis of the psychometric characteristics of cognitive function revealed statistically significant differences between isolated PTSD and PTSD comorbid with AUD according to the MMSE and SAGE scales, memory performance

Table 1. Probabilistic analysis of cognitive dysfunction (CD) for differentiating PTSD with alcohol use disorders from isolated PTSD

Diagnostic indicator	G2	G1	OR	95 % CI		Z-statistic	p
	Present	Absent		from	to		
Cognitive syndrome as a manifestation of PTSD							
Difficulty concentrating	109	86	9.76	5.20	18.32	7.097	<0.0001
Feeling of loneliness	73	79	1.59	0.99	2.57	1.899	0.0575
Cognitive function							
MMSE, dementia	119	35	7.24	2.74	19.14	3.995	0.001
MoCA, severe cognitive dysfunction + dementia	75	70	1.34	0.83	2.16	1.187	0.2351
MoCA, dementia	4	148	2.47	0.44	13.69	1.032	0.3020
SAGE, marked cognitive dysfunction	31	138	3.30	1.87	7.85	3.676	0.0002
Medium and low memory performance	90	139	33.45	16.12	69.39	9.427	<0.0001
Clock Drawing Test, moderate and severe cognitive dysfunction	38	123	2.01	1.14	3.54	2.427	0.0152

Table 2. Sensitivity and specificity of significant odds-based indicators for differentiating combatants with PTSD and comorbid alcohol use disorders from those with isolated PTSD

Indicator	Sensitivity	Specificity
Cognitive manifestations in PTSD assessment: difficulty concentrating	87.90 %	57.33 %
Cognitive manifestations in PTSD assessment: feeling of loneliness	58.87 %	52.67 %
MMSE, dementia of any severity	95.97 %	23.33 %
SAGE, marked cognitive dysfunction	25.00 %	92.00 %
Medium and low memory performance	72.58 %	92.67 %
Moderate and severe cognitive dysfunction according to the Clock Drawing Test	30.65 %	82.00 %

tests, and the Clock Drawing Test. Thus, in the presence of comorbid PTSD and AUD, the likelihood of dementia of any severity according to the MMSE increased 7.24-fold (95% CI=2.74-19.14; p=0.001), with very high sensitivity (95.97%) and moderate specificity (23.33%). Indeed, combatants with comorbid PTSD, AUD, and dementia of any severity according to the MMSE (18.33±0.12 points; n=105) differed from individuals in the same group with moderate cognitive impairment (24.33±0.14 points; n=19; p<0.05) by significantly lower cognitive function according to the MoCA (20.82±0.37 vs. 23.62±0.67 points; p<0.05) and higher fasting glucose levels (6.79±0.06 vs. 6.18±0.09 mmol/L; p<0.01). It may be assumed that impaired carbohydrate metabolism is accompanied by peripheral insulin resistance, which may also develop in brain tissue and contribute to cognitive dysfunction.

In contrast, according to multivariable logistic regression analysis, the SAGE test demonstrated low sensitivity (25.00%) and very high specificity (95.97%) (Table 2). The combination of PTSD and AUD increased the likelihood of marked cognitive dysfunction (≤14 points) by 3.30-fold (95% CI=1.87-7.85; p=0.0002) (Table 1). Indeed, normal SAGE scores were not observed at all among combatants with comorbid PTSD and AUD, while 25% of those examined had marked cognitive dysfunction (13.45±0.12 points).

The combination of PTSD and AUD also proved to be a prognostic marker of medium and low memory performance on the 10-Word Recall Test, with the likelihood increasing 33.45-fold compared with patients with isolated PTSD (95% CI=6.12-69.39; p<0.0001), with a sensitivity of 72.58% and specificity of 92.67% (Tables 1 and 2). High memory performance (8-10 points) was not observed in any combatant with PTSD and AUD, whereas medium and low memory performance (≤4.0 points) was diagnosed in 60.48% of those examined.

Alcohol use disorders also significantly increased the likelihood of moderate and severe impairment of cognitive and executive functions according to the Clock Drawing Test by 2.04-fold (95% CI=1.14-3.54; p=0.0152), with a sensitivity of 30.65% and specificity of 82.00% (Tables 1 and 2). Indeed, among patients with comorbid PTSD and AUD, a normal Clock Drawing Test score (9-10 points) was observed in only 3.22%.

DISCUSSIONS

Alcohol use disorders among combatants represent a significant problem [16], and their prevalence is expected to increase further among Ukrainian combatants [17]. We found that AUD in combatants increased the frequency of difficulties with concentration and feelings of loneliness, fluctuations in blood pressure, episodes of dizziness, and flashbacks, which, according to the literature, were also frequently associated with sleep disturbances [18]. According to our findings, AUD were significant prognostic markers of dementia according to the MMSE, cognitive dysfunction according to the SAGE and Clock Drawing Test, as well as medium and low memory performance. No studies assessing the prognostic value of the impact of AUD on cognitive function in combatants with PTSD were identified in the available literature. Therefore, the patterns described above may serve both as tools for the precise diagnosis of AUD in the presence of substantially poorer cognitive performance among combatants with PTSD and, conversely, for the identification of cognitive dysfunction [11] and the risk of dementia in cases of comorbid PTSD and AUD.

The literature has reported an n-shaped association between glycated hemoglobin levels and MMSE and MoCA test results in patients with AUD, indicating the need to monitor glucose levels in such patients [19]. We confirmed these findings: combatants with comorbid PTSD, AUD, and dementia according to the MMSE differed from those with moderate cognitive impairment by significantly higher levels of hyperglycemia. This allowed us to hypothesize that impaired carbohydrate metabolism causes peripheral insulin resistance and may also induce insulin resistance in brain tissue, thereby contributing to deterioration of cognitive function.

The multivariable logistic regression analysis we performed complemented the available literature by demonstrating that AUD increased the risks of snoring by 1.14-fold (95% CI=1.07-1.22), having an evening chronotype of sleep onset by 1.28-fold (95% CI=1.20–1.37), and experiencing difficulty waking in the morning by 1.24-fold (95% CI=1.13-1.36); all p<0.001 [20].

CONCLUSIONS

Alcohol use disorders in combatants increased the frequency of difficulties with concentration and feelings of loneliness, fluctuations in blood pressure, episodes of dizziness, and flashbacks. In combatants with PTSD, AUD was a prognostic marker of difficulty concentrating, increasing its likelihood by 9.76-fold (p<0.0001), and of feelings of loneliness, increasing its likelihood by 1.69-fold (p=0.057). The comorbidity of PTSD and AUD increased the likelihood of dementia according to the MMSE by 7.24-fold (p=0.001), cognitive dysfunction according to the SAGE by 3.30-fold (p=0.0002) and the Clock Drawing Test by 2.04-fold (p=0.015), and medium and low memory performance by 33.45-fold (p<0.0001).

Article Declarations

Prospects for further research. Further research should focus on assessing the prognostic value of alcohol use disorders in relation to the development and severity of anxiety and depressive symptoms in combatants, particularly in the context of comorbid post-traumatic stress disorder.

Study limitations. This study has several limitations. First, the study included only male combatants receiving inpatient treatment, which may limit the generalizability of the findings to female military personnel, veterans, outpatients, and other populations with PTSD. Second, the study was conducted in a single clinical setting and therefore may not fully reflect the characteristics of combatants treated in other institutions or regions. Third, cognitive function was assessed primarily using screening neuropsychological tools rather than an extensive standardized neuropsychological battery. In addition, the observational design does not allow causal relationships to be established between alcohol use disorders and cognitive impairment. Potential confounding factors, including previous traumatic brain injury, duration and severity of PTSD and alcohol use, pharmacological treatment, sleep disturbances, and other psychiatric or somatic comorbidities, may also have influenced cognitive performance and were not comprehensively controlled in the present analysis. Therefore, the identified associations should be interpreted as prognostic relationships rather than evidence of direct causality.

Primary data and materials. The author of the manuscript certifies that the work uses the results of his own clinical studies, which were systematized and analyzed by the author. Primary data include summary patient outcomes, protocols, and derived quantitative characteristics. All materials are preserved and can be provided upon reasonable request to the author, taking into account the requirements of confidentiality and ethical norms.

Research ethics. The author of the manuscript certifies that the study was conducted using data from primary medical records and included clinical observations of patients. Materials related to examination and scientific research and treatment of patients comply with the norms of bioethics, as evidenced by the conclusion of the commission on bioethics of Danylo Halytsky Lviv National Medical University (protocol No. 1 dated January 20, 2025).

Conflict of interest. The author declares that there is no conflict of interest related to the conduct of this study, its results, or their publication.

Declaration of AI use. No artificial intelligence tools were used in the design, conduct, analysis, interpretation, or preparation of this manuscript.

Funding. This study received no external financial support and was conducted using the author's own funds.

Author Contributions (CRediT taxonomy)

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ПРОГНОСТИЧНА ЦІННІСТЬ РОЗЛАДІВ ВЖИВАННЯ АЛКОГОЛЮ У КОМБАТАНТІВ З ПОСТТРАВМАТИЧНИМ СТРЕСОВИМ РОЗЛАДОМ ЩОДО ВИРАЖЕНОСТІ КОГНІТИВНОЇ ДИСФУНКЦІЇ

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РЕЗЮМЕ

Вступ. Дані літератури щодо впливу розладів вживання алкоголю (РВА) на когнітивну функцію у комбатантів з посттравматичними стресовими розладами (ПТСР) дотепер не є одностайними, що зумовило доцільність та актуальність нашого дослідження.

Мета. Оцінити прогностичну цінність розладів вживання алкоголю у комбатантів з посттравматичним стресовим розладом щодо вираженості когнітивної дисфункції.

Матеріали та методи. Проаналізовано результати обстеження 274 стаціонарних пацієнтів з ПТСР, усі чоловіки, учасники бойових дій, віком 20-56 років, які залежно від РВА поділені на дві групи: з ізольованим ПТСР та з ПТСР, поєднаним з РВА. Діагностика ПТСР проведена за наказом МОЗ України від 23.02.2016 №121, РВА – за тестами CAGE, AUDIT та CIWA-Ar, когнітивної функції – за тестами MMSE, MoCA, SAGE, малюванням годинника та запам'ятовуванням 10 слів. Результати опрацьовані статистично, подані як (M±m). Прогностична цінність визначена за мультиваріантним логістично-регресивним аналізом.

Результати. Розлади вживання алкоголю у комбатантів збільшували частоту затруднень концентрації і відчуття самотності, коливань артеріального тиску, епізодів запаморочення та флешбеків. РВА у комбатантів з ПТСР були прогностичним маркером утруднення концентрації уваги у 9,76 раза (p<0,0001) та відчуття самотності в 1,69 раза (p=0,057). Поєднання ПТСР з РВА призводило до зростання ймовірності деменції за MMSE у 7,24 раза (p=0,001), когнітивної дисфункції за SAGE у 3,30 раза (p=0,0002) і тестом малювання годинника у 2,04 раза (p=0,015) та до середньої та низької продуктивності пам'яті у 33,45 раза (p<0,0001).
Висновки. Розлади вживання алкоголю у комбатантів з посттравматичним стресовим розладом є маркером когнітивної дисфункції, що збільшують її ймовірність та важкість.

Ключові слова: розлад вживання алкоголю, посттравматичний стресовий розлад, когнітивна дисфункція комбатант, психологічне тестування

Received: June 02, 2026
Accepted: August 14, 2026
Published online: September 16, 2026

