

## FACTORS THAT INFLUENCE THE NEGATIVE RESULTS OF TREATMENT OF COMBATANTS' PAIN AFTER MINE-BLAST WOUNDS DURING THE WAR IN UKRAINE

Iurii L. Kuchyn<sup>1</sup>, Henadii I. Posternak<sup>1</sup>, Dmytro O. Govsiev<sup>1</sup>, Rostyslav V. Gybalo<sup>2</sup>

1 – Bogomolets National Medical University, Kyiv, Ukraine

2 – National Military Medical Clinical Center «Main Military Clinical Hospital», Kyiv, Ukraine

### Summary

**Introduction:** In 83.3 % of cases, pain in combatants who sustained mine-blast injuries during the war in Ukraine becomes chronic. Chronic pain leads to a number of negative aspects that affect the quality of life of combatants, and when they return to military service after treatment for professions that require people to act under pressure, it increases the risk not only for them but also for their teammates and the mission. Therefore, the issue of pain chronicity in this category of patients requires further study, and the identification of factors that influence the frequency of chronicity can potentially improve the results of treatment of this category of patients.

**The aim:** to identify factors that influence the negative results of pain treatment in combatants after mine-blast wounds during the war in Ukraine

**Materials and methods:** We analyzed the treatment of 660 combatants with mine-blast wounds. Treatment outcomes were assessed using a visual analog scale (VAS). Groups were compared using the Mann-Whitney test and the chi-square test with a continuity correction. To analyze the association of the risk of a negative treatment outcome with the factor characteristics, we used the method of building univariate and multivariate logistic regression models. The quality of the models was assessed by the area under the ROC curve (AUC). The odds ratio was calculated to quantify the degree of influence of the factor attribute.

**Results:** It was found that the factors of negative results of pain treatment in combatants with mine-blast wounds are: 1) method of pain treatment ( $p < 0.001$ ), OR=0.06 (95 % CI 0.04-0.09); 2) high intensity of pain according to VAS on admission ( $p < 0.001$ ), OR=3.16 (95 % CI 2.52-3.98); 3) anesthetic risk according to ASA ( $p = 0.049$ ) OR=0.67 (0.45-0.99); 4) number of injured anatomical body parts ( $p = 0.015$ ), OR=1.17 (95 % CI 1.03-1.32); 5) a combination of indicators: method of pain treatment, patient age and number of injured anatomical body parts AUC=0.82 (95 % CI 0.79-0.85).

**Conclusions:** Our study demonstrates that if combatants with mine-blast wounds use a method of pain treatment that does not provide reliable control over the intensity of pain, then during evacuation to a medical facility, such pain becomes high-intensity pain. In addition, the conditions of the injury (combat conditions) and the injury itself cause a significant anesthetic risk according to the ASA. Such patients are associated with a higher risk of chronic pain. In the future, in-depth studies are needed to demonstrate the effectiveness or benefits of combining pain management with regional anesthesia methods. High-quality pain control during the medical evacuation of wounded from the battlefield to a medical facility could potentially improve the treatment outcomes of these combatants and reduce the incidence of pain chronicity.

**Key words:** pain treatment, mine-blast wounds, war, chronic pain, stages of treatment, combatants

### INTRODUCTION

In combatants with mine-blast injuries sustained during the war in Ukraine, pain becomes chronic in 83.3 %

of cases on average [1], and in combatants with gunshot wounds – in 75 % of cases [2]. Pain management is an integral part of treatment in the care of combat wounded [1]. Studies show that more wounded in war require

analgesics for pain management than life-saving measures [3]. The earlier the treatment of pain is started, the better the results of treatment of post-traumatic stress disorder [4]. Over the past 20 years of the large-scale War on Terror [5], pain management on the battlefield has changed significantly. However, new research shows that ineffective pain treatment is associated with sleep disturbances in combatants [6]. There are studies that indicate that the results of pain treatment in combatants are associated with post-traumatic stress disorder (PTSD) [7]. Taking into account the data on the frequency of pain chronicity, an opinion is formed that this problem can develop into a more global one and become of national importance.

Also, other researchers report that during combat-related events, 51.7 % of cases have ASR, which is associated with a positive screening result for PTSD [8]. The problem of pain chronicization in combatants with mine-blast wounds requires in-depth study and identification of new factors that can improve the results of treatment of this category of patients. In 82.1 % of combatants who sustained gunshot wounds during combat operations, PTSD is resistant to treatment, which is associated with chronic pain [7, 12]. Our study aims to identify new factors that influence the negative results of treatment of combatants' pain after mine-blast wounds sustained during the war in Ukraine.

### THE AIM OF THE ARTICLE

To identify factors that influence the negative results of pain treatment in combatants after mine-blast wounds during the war in Ukraine

### MATERIALS AND METHODS

The study was retrospective and conducted at the National Military Medical Clinical Center «Main Military Clinical Hospital» in Kyiv. The data from the medical records of combatants who participated in the Anti-Terrorist Operation/Joint Forces Operation in Eastern Ukraine (ATO/JFO) from 2014 to 2021, as well as from 24.02.2022 to 24.05.2022 during the full-scale Russian invasion of Ukraine and the defense of the capital city of Kyiv, were analyzed. Those combatants who participated in the ATO/JFO from the moment of injury were evacuated to the following stages of treatment (stages of treatment are those medical facilities where the wounded are provided with medical care; for example, surgical operations, pain management, intensive care). After being injured (from the battlefield), the patient is first evacuated to a hospital with at least 1 anesthesiologist, 1 surgeon, 1 anesthesia nurse, 1 operating room nurse and the possibility of minimal examination – this is called a medical and nursing team, it is located as close as possible to the contact line (theater of operations). Here, the wounded soldier's life is saved, his general condition is stabilized and then he is evacuated to a military mobile hospital, then to a military medical clinical

center (a larger military hospital with powerful medical and diagnostic capabilities), and after treatment is completed, the wounded soldier undergoes rehabilitation. During the defense of Kyiv, all wounded combatants were evacuated immediately to the National military medical clinical center «Main military clinical hospital» after being wounded.

Tactics for treating pain in combatants who have completed all stages of treatment: at the stage of a medical and nursing brigade – on request or as a routine pain management (injectable narcotic analgesic +/- non-steroidal anti-inflammatory drugs); at the stage of a military mobile hospital – on request or as a routine pain management (injectable narcotic analgesic +/- non-steroidal anti-inflammatory drugs +/- epidural catheter); at the stage of a military medical clinical center – at the request of the patient or planned pain relief (transdermal fentanyl patch or injectable narcotic analgesic +/- non-steroidal anti-inflammatory drugs +/- adjuvants +/- epidural catheter +/- regional blocks).

The tactics of pain treatment for combatants who were evacuated immediately, at the stage of treatment at the National Military Medical Clinical Center «Main Military Clinical Hospital» – planned pain relief: fentanyl patch, transdermal or injectable narcotic analgesic + NSAIDs + adjuvants + epidural catheter +/- or regional blocks; during the rehabilitation phase – at the patient's request (if necessary) non-steroidal anti-inflammatory drugs +/- adjuvants +/- regional blocks.

Anesthetic support for surgical operations was provided in the form of general or regional anesthesia. Some combatants undergoing regional anesthesia received sedation. For sedation, a constant infusion of 1 % propofol was used at a rate of 1-4 mg/kg/h depending on the Bispectral Index (60-70 for regional anesthesia and 40-60 for general anesthesia). Analgesia during surgery was provided by 0.005 % fentanyl: during induction – 3-10 mcg/kg or 0.05-0.2 mcg/kg/min, and for maintenance of analgesia – 2-10 mcg/kg/h by periodic bolus injection of 25-100 mcg or by continuous infusion. Regional anesthesia was performed under ultrasound control (Mindray DP-30 device with a 5-10 MHz linear transducer). The needle was brought to the nerve roots and 20-30 ml of 0.5 % bupivacaine solution was injected. Postoperative pain relief was provided according to the local clinical protocol: paracetamol +/- non-steroidal anti-inflammatory drugs +/- opioids, repeated peripheral blocks, or injection of 0.25 % bupivacaine solution into the catheter for prolonged regional anesthesia.

In all combatants, before surgery, anesthetic risk was assessed according to the American Society of Anesthesiologists (ASA) scale at the time of admission to all stages of treatment [9]. To determine the intensity of pain, the visual analog scale (VAS) was used, which is a pain rating scale first used by Hayes and Patterson in 1921, with scoring criteria from 0 to 10 points: 0 – no

pain; 1-3 – mild pain; 4-6 – moderate pain; 7-10 – severe pain [10]. The intensity of pain was studied: 1) before and after anesthesia – at the stage of a medical and nursing team, military mobile hospital, military medical clinical center; 2) at the stage of a medical and nursing team – for 2 days; 3) at the stage of a military mobile hospital – for 5 days 4) at the stage of a military medical clinical center – within 7 days, and for combatants who were evacuated immediately to the National military medical clinical center «Main military clinical hospital» within 14 days, and then during discharge from inpatient treatment in 1, 3, 6, 12 months and rehabilitation.

The research was carried out within the framework of the accordance with the protocol on bioethical examination No. 158 of May 23, 2022, issued by the Commission on biotic expertise and research ethics of the O. Bogomolets National medical university, Ministry of Health of Ukraine. All study data were reflected in the patient's medical history. They are stored in the archives of the National military medical clinical center «Main military clinical hospital», Kyiv, 18 Hospitalna Street, Ukraine. The analysis of the research results was carried out in the EZR v.1.35 package (R statistical software version 3.4.3, R Foundation for Statistical Computing, Vienna, Austria).

All methods were carried out in accordance with relevant guidelines and regulations Declarations of Helsinki. Informed consent was obtained from all subjects and/or their legal guardian(s). All study participants provided informed consent to participate in accordance with the protocol on bioethical examination No. 158 of May 23, 2022, issued by the Commission on biotic expertise and research ethics of the O. Bogomolets National medical university, Ministry of Health of Ukraine.

The study protocol was approved for research by the Commission on biotic expertise and research ethics of the O. Bogomolets National medical university, Ministry of Health of Ukraine.

The study is a fragment of the research topic of the department of surgery, anesthesiology and intensive care of the institute of postgraduate education of the O. Bogomolets National medical university «Development and improvement of new technologies in diagnostics and surgical interventions in patients with combined surgical pathology» (No. 0117U00263 of the state registration of the research project).

The results of the study were analyzed using the EZR v.1.35 package (R statistical software version 3.4.3, R Foundation for Statistical Computing, Vienna, Austria) [11]. The Shapiro-Wilk test was used to test the distribution of quantitative indicators for normality. The law of distribution differed from the normal one, the median value (Me) and interquartile range (QI-QIII) were given to present quantitative indicators, and the comparison of indicators in the two groups was performed

using the Mann-Whitney test. To analyze the dynamics of indicators, the Friedman criterion for linked samples was used, and the posterior comparison was performed using the Bonferroni correction. For qualitative indicators, the absolute frequency of the trait and the relative frequency (%) are presented, and the chi-square test with the correction for continuity was used to compare the two groups. In all cases, the critical significance level was set at 0.05. To analyze the association of the risk of not achieving the treatment effect with the factor characteristics, we used the method of building univariate and multivariate logistic regression models. The quality of the models was assessed by the area under the ROC curve (AUC) [12], and the 95 % probability interval (CI) of the indicator was calculated. To quantify the degree of influence of the factor trait, the odds ratio (OR) and its 95 % CI were calculated (direct selection at the alpha level of 5 %).

## RESULTS AND DISCUSSION

Our study is based on the clinical experience of treating 660 combatants for mine-blast wounds sustained during the hostilities in Ukraine while performing combat missions. The control group included 280 combatants from 2014 to 2021 who participated in the ATO/JFO in eastern Ukraine and underwent all stages of treatment, and the experimental group included 380 combatants who sustained mine-blast wounds from 24.02.2022 to 24.05.2022. 05.2022 during russia's full-scale invasion of Ukraine and the defense of Kyiv, they were evacuated to the National military medical clinical center «Main military clinical hospital» for treatment, where they received different tactics of pain treatment. Tables 1 and 2 present the general characteristics of the groups and the median Me and interquartile range (QI-QIII). Table 1 shows the general characteristics of the groups, and the frequency of different types of anesthesia and ASA risks in the studied combatants is shown in Table 2.

To analyze the risk of pain chronicity (VAS>0 after 3 months), the method of constructing and analyzing univariate and multivariate logistic regression models was used [13-16]. The results of treatment of 658 combatants with mine-blast wounds (258 patients in the control group and 380 patients in the experimental group) were used in the analysis. If the VAS score was >0 after three months, it was considered that the positive effect was not achieved (resultant variable Y=1, there were 346 combatants); if the VAS score was 0 after three months, the positive effect was considered achieved (resultant variable Y=0, there were 312 combatants). The analysis was conducted for 11 risk factors: group, age, height of the combatant, weight, number of surgical operations, types of anesthesia, number of wounded anatomical areas of the body, anesthetic risk according to ASA, average duration of anesthesia, average duration of surgical operations, VAS on admission to the hospital. Table 3 shows the results of the analysis.

Table 1

**General characteristics of combatants who sustained mine-blast wounds and were included in the study**

Variable	Control group (n=280)	Group experimental (n=380)	P
Age (years)	30 (26-41)	32 (26-39)	0.81
Height (cm)	178 (175-182)	178.5 (176-182)	0.536
Weight (kg)	80 (74.5-86)	79.5 (75-84)	0.227
Number of surgical operations	5 (4-7)	5 (4-7)	0.535
Number of wounded anatomical parts of the body	1 (1-3)	2 (1-3)	0.016
Average duration of anesthesia (min.)	125 (110-150)	125 (110-150)	0.809
Average duration of surgery (min.)	115 (100-130)	115 (105-130)	0.17
VAS on admission to the hospital (points)	8 (8-9)	7 (7-7)	<0.001

Notes: The comparison was based on the Mann-Whitney test.

Table 2

**Incidence of different types of anesthesia and risks according to ASA in the studied combatants (abs. (%))**

Variable		Group control (n=280)	Group experimental (n=380)	P
Anesthesia types	General anesthesia	105 (37.5)	154 (40.5)	0.626
	Regional anesthesia	81 (28.9)	111 (29.2)	
	Regional anesthesia and sedation	94 (33.6)	115 (30.3)	
ASA	2	4 (1.4)	0 (0.0)	0.038
	3	233 (83.2)	309 (81.3)	
	4	43 (15.4)	71 (18.7)	

Notes: The comparison was based on the chi-square test, adjusted for continuity.

Table 3

**Coefficients of univariate logistic regression models for predicting the risk of chronic pain in combatants with mine-blast wounds**

Factor variable		Coefficient, b±m	P	OR (95 % CI)
Group	Control		Reference	
	Experimental	-2.79±0.21	<0.001	0.06 (0.04-0.09)
Anesthesia types	General anesthesia		Reference	
	Regional anesthesia	0.12±0.19	0.519	—
	Regional anesthesia and sedation	-0.06±0.19	0.760	—
Age		-0.014±0.00	0.106	—
Height		-0.019±0.015	0.197	—
Weight		0.009±0.010	0.360	—
Number of wounded anatomical parts of the body		0.039±0.051	0.452	—
Number of surgical operations		-0.035±0.043	0.415	—
ASA		-0.40±0.20	0.049	0.67 (0.45-0.99)
Average duration of anesthesia, per 100 minutes.		-0.16±0.12	0.175	—
Average duration of surgical operations, per 100 minutes.		-0.16±0.12	0.177	—
VAS age on admission to the hospital		1.15±0.12	<0.001	3.16 (2.52-3.98)

The univariate analysis revealed a decrease ( $p<0.001$ ) in the risk of pain chronicity with the proposed method of treatment in the experimental group, OR=0.06 (95 % CI 0.04-0.09) compared with the control group. It was found that there is an increase in the risk of chronic pain ( $p=0.049$ ) with an increase in anesthetic risk according to ASA. With a higher VAS score on admission to the hospital, the risk of pain chronicity increases ( $p<0.001$ ), OR=3.16 (95 % CI 2.52-3.98) for each VAS score.

To identify a set of indicators associated with the risk of pain chronicity, significant features were selected (using the method of stepwise rejection/inclusion of features, with

an inclusion threshold of  $p<0.075$  and a rejection threshold of  $p>0.15$ ) in a multivariate logistic regression model. During the selection process, three characteristics were identified: group, age, and number of injured anatomical parts of the body. A three-factor logistic regression model for predicting the risk of pain chronicity was built on the selected features, the model is adequate ( $\chi^2=249$  at  $p<0.001$ ).

Figure 1 shows the curve of operating characteristics for predicting the risk of chronic pain according to the model in combatants with mine-blast wounds. The area under the receiver operating characteristic curve, AUC=0.82 (95 % CI



0.79-0.85), indicating the presence of pain chronicity with these factor characteristics.

Table 4 shows the results of multivariate analysis in combatants with mine-blast wounds.

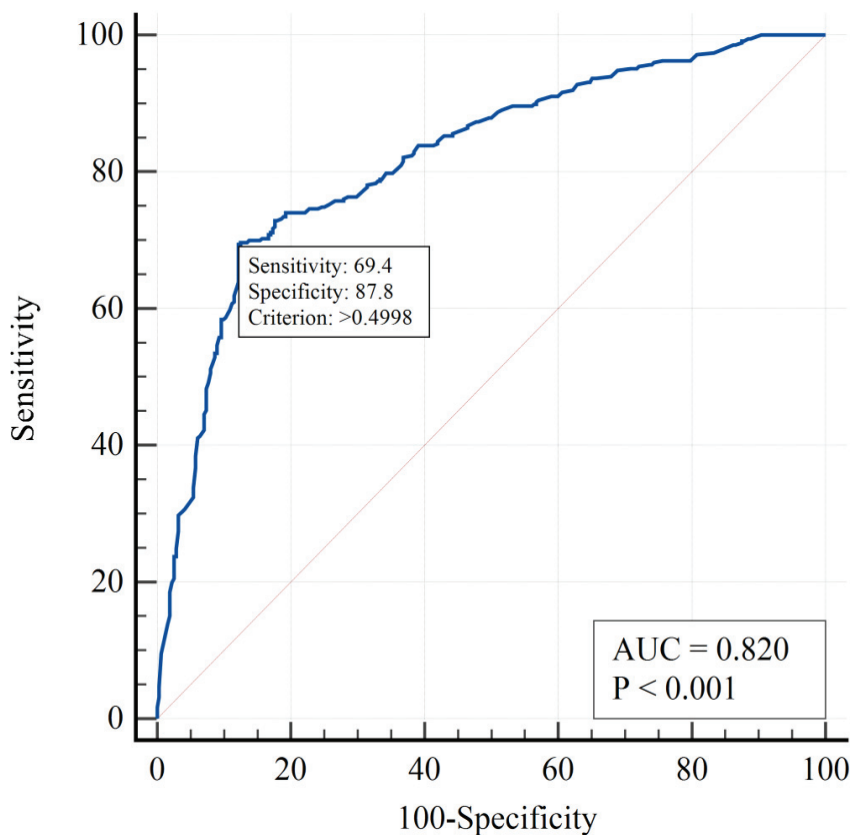


Fig. 1. Receiver operating characteristic curve of the three-factor model for predicting the risk of chronic pain in combatants with mine-blast wounds. The critical threshold, sensitivity and specificity of the model at the selected threshold are shown.

Table 4

**Coefficients of the three-factor logistic regression model for predicting the risk of chronic pain in combatants with mine-blast wounds.**

Factor variable		Coefficient, b±m	P	OR (95 % CI)
Group	Control		Reference	
	Experimental	-2.89±0.22	<0.001	0.06 (0.04-0.08)
Age		-0.022±0.011	0.053	0.98 (0.96-1.00)
Number of wounded anatomical parts of the body		0.16±0.06	0.015	1.17 (1.03-1.32)

Thus, the multivariate analysis revealed that, when standardized by the number of injured anatomical parts of the body and age, the use of pain management tactics used in combatants with mine-blast wounds during treatment at the National military medical clinical center «Main military clinical hospital» reduces ( $p<0.001$ ) the risk of chronic pain, OR=0.06 (95 % CI 0.04-0.08) compared to the control group. There was also an increase in the risk of chronic pain ( $p=0.015$ ) with an increase in the number of wounded anatomical parts of the body, OR=1.17 (95 % CI 1.03-1.32) for each additional injury.

In the available literature, the results of treatment of pain and its chronicity in combatants with minefield

injuries are scarce or partially limited. Some studies have shown that group psychotherapy has a positive effect on the treatment of PTSD in patients with combat trauma [17], and there is also evidence of a genetic predisposition to PTSD in Vietnam War veterans [18]. However, there are practically no studies that identify factors that may indicate the causes of chronic pain in this category of patients. There are no studies that demonstrate that early treatment of pain after trauma improves long-term outcomes, and that poorly treated pain can contribute to poorer PTSD treatment and outcomes [5]. An analysis of the treatment of soldiers with chronic pain who participated in the wars in Iraq and Afghanistan shows

a problem in the military health care system related to the transfer to other stages of treatment: 1) alcohol and drugs; 2) suicidal thoughts; 3) intentional self-harm; 4) mortality from all of these causes, and multimodal chronic pain management, including opioids, can reduce the risk of serious adverse outcomes associated with chronic pain and opioid use [19]. Another study indicates that life-saving interventions are a hallmark of combatant care, reducing mortality and morbidity, and analgesia is another important treatment that has been shown to improve outcomes and reduce long-term complications [20].

Military doctors in Ukraine have gained unique experience. The problem of treating and pain chronicity in combatants after injuries is gaining more and more attention from the scientific community. Our study found that such factors as the method of pain treatment, high pain intensity according to the VAS on admission to the hospital, and the number of injured anatomical parts of the body have an impact on the frequency of chronic pain in combatants with mine-blast wounds sustained during combat missions. These data must be taken into account when providing care to patients in this category. However, the impact of acute stress reaction and post-traumatic stress disorders in combatants with wounds during the war on the transformation of acute pain into chronic pain remains unexplored, because the results obtained involuntarily suggest that the onset of transformation and formation of chronic pain occurs much earlier, perhaps even at the time of injury.

## CONCLUSIONS

The analysis of the results of pain treatment in 660 combatants with mine-blast wounds in combat conditions while performing combat missions during the war in Ukraine showed that the method of pain treatment, high

pain intensity according to VAS on admission to the hospital and high anesthetic risk according to ASA are important for pain chronicity and are associated with a higher risk of pain chronicity.

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The authors declare that that is no conflict of interests. The article is self-funded.

## COMPLIANCE WITH ETHICAL REQUIREMENTS

The study was held within the bioethics expertise protocol No.158 of May 23, 2022 issued by the Commission on Biotic Expertise and Research Ethics of O.Bogomolets National medical university, Ministry of Health of Ukraine.

I confirm that all methods have been performed in accordance with the relevant guidelines and standards by including a statement in the Methods section.

All study participants provided informed consent to participate in accordance with the protocol on bioethical examination No. 158 of May 23, 2022, issued by the Commission on Biotic Expertise and Research Ethics of the O.Bogomolets National Medical University, Ministry of Health of Ukraine.

**Authors' contributions.** Kuchyn Iu.L. – concept, design of the study. Posternak H. I. – collection, processing of materials, design of figures. Govsiev D. O., Gybalo R. V. – analysis of the data, writing the text.

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## Резюме

### ФАКТОРИ, ЩО ВПЛИВАЮТЬ НА НЕГАТИВНІ РЕЗУЛЬТАТИ ЛІКУВАННЯ БОЛЮ В УЧАСНИКІВ БОЙОВИХ ДІЙ ПІСЛЯ МІННО-ВИБУХОВИХ ПОРАНЕНЬ ПІД ЧАС ВІЙНИ В УКРАЇНІ

Юрій Л. Кучин<sup>1</sup>, Геннадій І. Постернак<sup>1</sup>, Дмитро О. Говсєєв<sup>1</sup>, Ростислав В. Гибало<sup>2</sup>

1 – Національний медичний університет імені О.О. Богомольця, м. Київ, Україна

2 – Національний військово-медичний клінічний центр «Головний військовий клінічний госпіталь», м. Київ, Україна

**Вступ.** Біль у комбатантів, які отримали мінно-вибухові поранення під час бойових дій в Україні у 83.3 % випадках стає хронічним. Хронічний біль призводить до цілого ряду негативних аспектів, які впливають на якість життя комбатантів, а при поверненні, після лікування, на військову службу для професій, які вимагають від людей діяти під тиском, підвищує ризик не лише для нього, але для товаришів по команді та місії. Отже, питання хронізації болю у даної категорії пацієнтів потребує подальшого вивчення, а виявлення факторів, які мають вплив на частоту хронізації може, потенційно, покращити результати лікування даної категорії пацієнтів.

**Мета.** Виявити фактори, що впливають на негативні результати лікування болю в учасників бойових дій після мінно-вибухових поранень під час війни в Україні

**Матеріали та методи.** Проаналізовано лікування 660 комбатантів з мінно-вибуховими пораненнями. Результати лікування оцінювали за візуальною аналоговою шкалою (VAS). Порівняння груп проводилося за критерієм Манна-Уїтні і критерієм хі-квадрат з урахуванням поправки на неперервність. Для аналізу зв'язку ризиків отримання негативного результату лікування з факторними ознаками було використано метод побудови однофакторних та багатофакторних моделей логістичної регресії. Якість моделей оцінювалася за площею під ROC-кривою (AUC – Area under the ROC curve). Для кількісної оцінки ступеню впливу факторної ознаки розраховувався показник відношення шансів.

**Результати.** Виявлено, що факторами негативних результатів лікування болю у комбатантів з мінно-вибуховими пораненнями є: 1) метод лікування болю ( $p < 0.001$ ), ВШ=0.06 (95 % ВІ 0.04-0.09); 2) висока інтенсивність болю за ВАШ при поступленні ( $p < 0.001$ ), ВШ=3.16 (95 % ВІ 2.52-3.98); 3) анестезіологічний ризик за ASA ( $p = 0.049$ ) ВШ=0.67 (0.45-0.99); 4) кількість поранених анатомічних ділянок тіла ( $p = 0.015$ ), ВШ=1.17 (95 % ВІ 1.03-1.32); 5) сукупність показників: метод лікування болю, вік пацієнта та кількість поранених анатомічних ділянок тіла AUC= 0.82 (95 % ВІ 0.79-0.85).

**Висновки.** Наше дослідження демонструє, що якщо у комбатантів після мінно-вибухових поранень використовувати метод лікування болю, який не забезпечує надійний контроль над інтенсивністю болю, то під час евакуації до лікувального закладу такий біль стає боєм високої інтенсивності. Також умови поранення (умови бойових дій) та, безпосередньо, саме поранення обумовлює значний анестезіологічний ризик за ASA. Такі пацієнти асоціюються з більшим ризиком хронізації болю. Надалі необхідні поглиблені дослідження, які б змогли продемонструвати ефективність чи переваги застосування поєднання методів лікування болю з регіонарними методами знеболення. Якісний контроль над боєм під час медичної евакуації поранених з поля болю до лікувального закладу потенційно можуть покращити результати лікування таких комбатантів та знизити частоту хронізації болю.

**Ключові слова:** лікування болю, мінно-вибухові поранення, війна, хронічний біль, етапи лікування, комбатанти