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FROM BATTLEFIELD TO CHRONIC PAIN: RISK FACTORS AFTER COMBAT-RELATED EXTREMITY INJURIES – A MULTICENTER COHORT STUDY

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Abstract

Introduction. Chronic pain is a frequent and disabling consequence of combat-related extremity injuries. However, data on modifiable and non-modifiable risk factors for pain chronification in military trauma populations remain limited.
Aim. To identify risk factors associated with the development of chronic pain after combat-related extremity injuries and to assess the impact of injury characteristics and early treatment strategies on pain outcomes.
Materials and methods. This multicenter observational cohort study included 322 patients with combat-related extremity injuries treated at three tertiary care centers. Demographic, injury-related, and treatment-related variables were prospectively collected. Chronic pain persisting for ≥ 3 months after injury was the primary outcome. Univariate analyses were followed by multivariable logistic regression to identify independent predictors of chronic pain development.
Results. Chronic pain developed in 98 patients (30.4%). In multivariable analysis, peripheral nerve injury (OR 2.78, 95% CI 1.68-4.60), infectious complications (OR 2.14, 95% CI 1.29-3.55), number of surgical procedures (OR 1.29 per procedure, 95% CI 1.14-1.47), and delayed initiation of analgesia (> 6 hours) (OR 1.71, 95% CI 1.05-2.78) were independently associated with chronic pain. Use of regional anesthesia during the acute phase was associated with a reduced risk of chronic pain (OR 0.66, 95% CI 0.43-0.99).
Conclusions. Approximately one-third of patients developed chronic pain following combat-related extremity injuries. Both injury severity and early treatment-related factors contribute to pain chronification. Optimization of early analgesia, prevention of infectious complications, and broader use of regional anesthesia may reduce the long-term burden of chronic pain in military trauma survivors.

Keywords: **combat-related injury, chronic pain, extremity trauma, peripheral nerve injury, regional anesthesia, military medicine, pain chronification, multicenter study**

INTRODUCTION

Advances in battlefield medicine and evacuation systems have significantly improved survival after combat-related injuries [1]. However, an increasing number of survivors develop chronic pain, particularly after extremity trauma, which represents a major long-term clinical, functional, and socio-economic burden [2-4]. Combat-related extremity injuries are characterized by high-energy mechanisms, including blast exposure, fragmentation, and penetrating trauma, frequently combined with nerve damage, vascular injury, infection, and repeated surgical interventions [5]. These factors create a complex biological and psychosocial environment that predisposes patients to pain chronification [6-8]. Despite this, the determinants of chronic pain after military limb trauma remain insufficiently defined. Existing civilian trauma literature has identified several predictors of chronic pain, such as injury severity, nerve involvement, delayed analgesia,

and repeated surgery [9-12]. However, civilian-derived models cannot be directly extrapolated to combat trauma, where injury patterns, treatment timelines, and healthcare pathways differ substantially [13-15]. Importantly, most available studies are single-center, limiting generalizability and external validity [16, 17]. To address these gaps, we conducted a multicenter cohort study aimed at identifying clinical, injury-related, and treatment-related factors associated with the development of chronic pain after combat-related extremity injuries. Understanding these risk factors is essential for early risk stratification, targeted prevention strategies, and the development of evidence-based pain management pathways for military trauma survivors.

AIM

The primary objective of this multicenter cohort study was to identify independent clinical, injury-related, and treatment-related factors associated with the development of chronic pain after combat-related extremity injuries, in order to support early risk stratification and inform preventive and targeted pain management strategies in military trauma care.

MATERIALS AND METHODS

This multicenter cohort study was conducted across several military and civilian tertiary care centers involved in the acute management and rehabilitation of patients with combat-related extremity injuries. Data were collected at Feofaniya Clinical Hospital (Kyiv), Vinnytsia Regional Clinical Hospital (Vinnitsia), and the Superhumans Center (Lviv), which together represent key national referral institutions providing the full continuum of care-from acute trauma management and reconstructive surgery to post-acute rehabilitation of military trauma patients. A total of 322 patients with combat-related extremity injuries were included in the analysis.

Inclusion criteria: patients were aged 18 years or older, sustained a combat-related injury involving one or more extremities, were injured as a result of blast, fragmentation, or gunshot mechanisms, required surgical and/or interventional treatment, survived the acute phase of injury, and had available follow-up data of at least 3 months after injury.

Exclusion criteria: pre-existing chronic pain unrelated to combat trauma, isolated minor soft-tissue injuries without structural damage, severe cognitive impairment precluding reliable pain assessment, incomplete or missing essential clinical data.

The primary outcome was the presence of chronic pain, defined as pain persisting for three months or longer after the index injury, localized to the injured extremity or an anatomically related region, and reported by the patient during follow-up assessment. When available, secondary descriptors included pain intensity and neuropathic pain characteristics. Clinical data were collected retrospectively and/or prospectively from institutional trauma registries and medical records using a standardized data collection protocol across all participating centers. Recorded variables included demographic characteristics (age and sex); injury-related factors such as mechanism of injury (blast, fragmentation, or gunshot), injured extremity (upper vs lower limb), laterality (unilateral vs bilateral), presence of fractures, documented peripheral nerve injury, vascular injury, severity of soft-tissue damage, traumatic amputation (yes/no), and infectious complications or wound superinfection; as well as treatment-related variables including time from injury to first analgesic intervention, use of regional anesthesia techniques, opioid administration during the acute phase, duration of continuous analgesic infusions, number of surgical procedures, length of hospital stay, and timing and initiation of rehabilitation. Patients were followed for a minimum of three months after injury. Follow-up information was obtained from outpatient visits, rehabilitation records, or structured clinical assessments at participating centers. The presence or absence of chronic pain was documented during follow-up and entered into the study database.

Statistical analysis

Continuous variables were assessed for normality and are presented as means with standard deviations or medians with interquartile ranges, as appropriate, while categorical variables are reported as absolute numbers and percentages. Comparisons between patients with and without chronic pain were performed using Student's t test or the Mann–Whitney U test for continuous variables and the χ^2 test or Fisher's exact test for categorical variables. Variables associated with chronic pain at a significance level of $p < 0.10$ in univariate analysis were entered into a multivariable logistic regression model to identify independent predictors of chronic pain development, with results presented as odds ratios (ORs) and 95% confidence intervals (CIs). All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant.

RESULTS

A total of 322 patients with combat-related extremity injuries were included in this multicenter cohort study. The median follow-up duration was 6 months (IQR: 4-9). Chronic pain persisting for ≥ 3 months developed in 98 patients (30.4%), while 224 patients (69.6%) did not report chronic pain (Figure 1).

Baseline demographic, injury-related, and treatment-related characteristics stratified by chronic pain status are presented in Table 1.

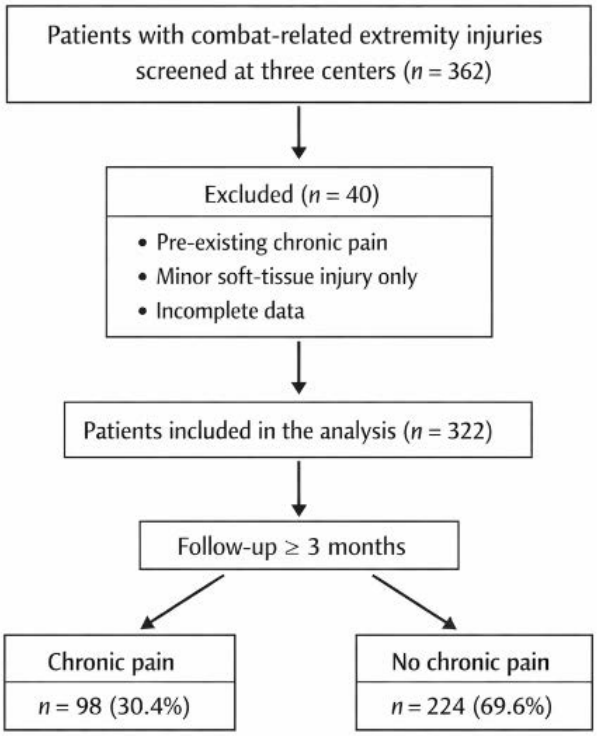

Figure 1. Flow diagram of patient inclusion and outcome assessment in a multicenter cohort study of combat-related extremity injuries (n = 322). Chronic pain developed in 98 patients (30.4%).

Table 1

Baseline Characteristics of Patients with and without Chronic Pain after Combat-Related Extremity Injuries

Variable	Total cohort (n = 322)	Chronic pain (n = 98)	No chronic pain (n = 224)	p value
Age, years, mean ± SD	36.8 ± 9.4	37.6 ± 9.1	36.4 ± 9.6	0.28
Male sex, n (%)	296 (91.9)	91 (92.9)	205 (91.5)	0.67
Mechanism of injury, n (%)				0.31
– Blast	147 (45.7)	48 (49.0)	99 (44.2)	
– Fragmentation	110 (34.2)	32 (32.7)	78 (34.8)	
– Gunshot	65 (20.1)	18 (18.3)	47 (21.0)	
Lower extremity injury, n (%)	198 (61.5)	63 (64.3)	135 (60.3)	0.49
Bilateral injury, n (%)	56 (17.4)	20 (20.4)	36 (16.1)	0.34
Fracture present, n (%)	229 (71.1)	74 (75.5)	155 (69.2)	0.25
Peripheral nerve injury, n (%)	94 (29.2)	44 (44.9)	50 (22.3)	<0.001
Vascular injury, n (%)	63 (19.6)	26 (26.5)	37 (16.5)	0.018
Traumatic amputation, n (%)	41 (12.7)	15 (15.3)	26 (11.6)	0.35
Infectious complications, n (%)	76 (23.6)	33 (33.7)	43 (19.2)	0.003
Time to first analgesia, h, median (IQR)	4.7 (3.0-7.9)	6.6 (4.1-9.8)	4.3 (2.8-6.9)	0.004
Regional anesthesia, n (%)	118 (36.6)	29 (29.6)	89 (39.7)	0.046
Opioid use (acute phase), n (%)	247 (76.7)	77 (78.6)	170 (75.9)	0.58
Number of surgeries, median (IQR)	3 (2-5)	4 (3-6)	2 (1-4)	<0.001
Length of hospital stay, days, median (IQR)	19 (12-31)	25 (16-38)	16 (10-26)	<0.001
Early rehabilitation (≤14 days), n (%)	189 (58.7)	48 (49.0)	141 (62.9)	0.021

In univariate analysis, patients who developed chronic pain more frequently sustained peripheral nerve injury, vascular injury, and infectious complications, and underwent a higher number of surgical procedures compared with patients without chronic pain. They also experienced a longer delay to first analgesic intervention.

In multivariable logistic regression analysis (Table 2), peripheral nerve injury, infectious complications, number of surgical procedures, and delayed initiation of analgesia remained independently associated with chronic pain development. Use of regional anesthesia during the acute phase was associated with a reduced risk of chronic pain, indicating a potential protective effect.

Table 2

Multivariable Logistic Regression Analysis of Factors Associated with Chronic Pain After Combat-Related Extremity Injuries (n = 322)

Variable	Adjusted OR	95% CI	*p* value
Peripheral nerve injury (yes vs no)	2.78	1.68-4.60	<0.001
Infectious complications (yes vs no)	2.14	1.29-3.55	0.003
Vascular injury (yes vs no)	1.54	0.92-2.57	0.10
Number of surgical procedures (per additional surgery)	1.29	1.14-1.47	<0.001
Delayed analgesia (>6 h) (yes vs no)	1.71	1.05-2.78	0.031
Regional anesthesia (acute phase) (yes vs no)	0.66	0.43-0.99	0.046
Traumatic amputation (yes vs no)	1.32	0.70-2.48	0.39
Fracture present (yes vs no)	1.18	0.72-1.94	0.51
Lower extremity injury (vs upper)	1.09	0.66-1.80	0.73
Age (per year increase)	1.01	0.99-1.03	0.27
Male sex	1.07	0.48-2.41	0.86

DISCUSSION

In this multicenter cohort study of 322 patients with combat-related extremity injuries, approximately 30% developed chronic pain within three months after injury. This finding underscores that chronic pain remains a frequent and clinically relevant consequence of military limb trauma, even in the context of modern trauma care and rehabilitation pathways. The development of chronic pain was independently associated with peripheral nerve injury, infectious complications, repeated surgical interventions, and delayed initiation of analgesia, highlighting the multifactorial nature of pain chronification after combat-related trauma. Importantly, the use of regional anesthesia during the acute phase was associated with a reduced risk of chronic pain, suggesting a potential protective and modifiable treatment-related factor [1-4].

Injury-related factors and pain chronification: Peripheral nerve injury emerged as the strongest independent predictor of chronic pain. This finding is consistent with existing literature demonstrating that nerve damage plays a central role in the transition from acute to chronic pain through mechanisms involving neuropathic sensitization, maladaptive neuroplasticity, and persistent nociceptive input [12-17]. In combat-related extremity trauma, nerve injuries often coexist with high-energy tissue damage, ischemia, and inflammation, further amplifying the risk of long-term pain. Infectious complications were also independently associated with chronic pain development [3-7]. Persistent inflammation, delayed wound healing, and repeated surgical debridement may contribute to prolonged nociceptive signaling and central sensitization. These findings emphasize the importance of early infection prevention, prompt recognition, and aggressive management as part of a comprehensive pain-prevention strategy [8].

Treatment-related factors and modifiable risks: The association between the number of surgical procedures and chronic pain reflects both injury severity and cumulative tissue trauma. Repeated surgical interventions may lead to additional nerve irritation, scar formation, and altered biomechanics, all of which can promote pain persistence. While surgical interventions are often unavoidable in combat trauma, this finding underscores the need for optimized surgical planning and coordinated multidisciplinary care [9-12]. Delayed initiation of effective analgesia was independently associated with an increased risk of chronic pain. This observation aligns with the concept that inadequate early pain control may facilitate central sensitization and long-term pain amplification. In military trauma settings, logistical constraints, prolonged evacuation times, and competing life-saving priorities may contribute to delays in analgesic delivery, reinforcing the importance of early and structured pain management protocols.

Clinical implications: Taken together, these results suggest that chronic pain after combat-related extremity injuries is driven by a combination of non-modifiable injury characteristics and modifiable treatment-related factors. Identification of high-risk patients – particularly those with nerve injury, infection, or a need for multiple surgical procedures – may allow early targeted interventions [4, 6, 8]. Moreover, optimization of early analgesia and broader implementation of regional anesthesia techniques represent practical avenues for reducing the burden of chronic pain in this population.

CONCLUSIONS

In conclusion, approximately one-third of patients developed chronic pain following combat-related extremity injuries. Peripheral nerve injury, infection, repeated surgical interventions, and delayed analgesia were key risk factors, while regional anesthesia during the acute phase appeared to be protective. These findings highlight opportunities for early risk stratification and preventive pain management strategies aimed at reducing long-term pain-related morbidity in military trauma survivors.

Prospects for further research. The results of this study are aimed at improving the quality of healthcare for

patients with combat trauma, which will subsequently lead to a reduction in costs associated with the development of chronic pain syndrome.

COMPLIANCE WITH ETHICAL REQUIREMENTS

The study was performed in accordance with the Declaration of Helsinki and approved by the local ethics committees (protocol № 02/02.02.2026) of all participating institutions. The study was registered in the Ukrainian Institute of Scientific and Technical Expertise and Information № 0125U003136. Given the observational nature of the study, informed consent procedures were applied in accordance with local regulatory requirements.

Study limitations

The authors of this study consciously acknowledge that the limitations are due to the involvement of only 3 centers. It is necessary to increase the number of centers and patients to objectify and obtain reliable results.

Declaration of the use of generative AI in the preparation of the manuscript

This work did not use artificial intelligence to generate text, analyze data, or create images. All content is prepared by the authors, who bear full responsibility for accuracy, originality, and adherence to ethical standards.

FUNDING AND CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

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Резюме

ВІД ПОЛЯ БОЮ ДО ХРОНІЧНОГО БОЛЮ: ФАКТОРИ РИЗИКУ ПІСЛЯ БОЙОВИХ УШКОДЖЕНЬ КІНЦІВОК – МУЛЬТИЦЕНТРОВЕ КОГОРТНЕ ДОСЛІДЖЕННЯ

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Вступ. Хронічний біль є частим і інвалідизуючим наслідком бойових ушкоджень кінцівок. Водночас дані щодо модифікованих та немодифікованих факторів ризику хронізації болю у пацієнтів із військовою травмою залишаються обмеженими.

Мета. Визначити фактори ризику розвитку хронічного болю після бойових ушкоджень кінцівок та оцінити вплив характеристик травми і ранніх лікувальних стратегій на больові результати.

Матеріали та методи. Проведено мультицентрове обсерваційне когортне дослідження, до якого включено 322 пацієнтів з бойовими ушкодженнями кінцівок, пролікованих у трьох закладах третинного рівня. Проспективно збирали демографічні, травматологічні та лікувальні показники. Первинною кінцевою точкою був хронічний біль, що зберігався ≥ 3 місяців після травми. Проведено однофакторний аналіз з подальшою багатофакторною логістичною регресією для виявлення незалежних предикторів хронізації болю.

Результати. Хронічний біль розвинувся у 98 пацієнтів (30,4%). За даними багатофакторного аналізу незалежними факторами ризику були: ушкодження периферичних нервів (OR 2,78; 95% ДІ 1,68-4,60), інфекційні ускладнення (OR 2,14; 95% ДІ 1,29-3,55), кількість хірургічних втручань (OR 1,29 на одну операцію; 95% ДІ 1,14-1,47) та відтермінування початку аналгезії понад 6 годин (OR 1,71; 95% ДІ 1,05-2,78). Використання регіонарної анестезії у гострій фазі було асоційоване зі зниженим ризиком розвитку хронічного болю (OR 0,66; 95% ДІ 0,43-0,99).

Висновки. Приблизно у третини пацієнтів після бойових ушкоджень кінцівок розвивається хронічний біль. Хронізація болю зумовлюється як тяжкістю травми, так і факторами раннього лікування. Оптимізація ранньої аналгезії, профілактика інфекційних ускладнень та ширше застосування регіонарної анестезії можуть зменшити довгостроковий тягар хронічного болю у постраждалих із військовою травмою.

Ключові слова: **бойова травма, хронічний біль, ушкодження кінцівок, периферичні нерви, регіонарна анестезія, військова медицина, хронізація болю, мультицентрове дослідження**

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