

## THE ROLE OF WOUND MICROBIOTA IN SHAPING THE QUALITY OF LIFE OF PATIENTS WITH COMBAT-RELATED LIMB INJURIES

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**Introduction.** Limb injuries resulting from combat-related trauma, including amputations, burns, and blast injuries, significantly impact patients' physical and psychological well-being. However, the influence of injury location (upper vs. lower limb) and wound microbiological characteristics on recovery outcomes remains understudied.

**Objective.** To evaluate the impact of wound infection, trauma character and its location in physical and mental health outcomes of patients with upper and lower limb injuries.

**Methods.** A total of 68 male patients aged 25–60 years with traumatic limb injuries were divided into two groups based on injury location: upper limb (Group 1, n=31) and lower limb (Group 2, n=37). Demographic data, trauma type, and wound microbial contamination were recorded. The SF-36 questionnaire was used to assess physical and mental health. Statistical analysis included group comparisons and multivariate regression to identify predictors of SF-36 scores.

**Results.** No statistically significant differences were found between the groups in terms of age, trauma type, or SF-36 scores ( $p > 0.05$ ). However, patients with lower limb injuries demonstrated a trend toward lower physical functioning scores. Group 2 showed slightly higher mean scores on mental health subscales. Multivariate regression revealed that the presence of polymicrobial wound infection was significantly associated with lower physical functioning scores ( $p = 0.0025$ ), independent of trauma type or injury location.

**Conclusions.** While the anatomical site of injury did not significantly affect SF-36 outcomes, the presence of mixed wound infections was a significant negative predictor of physical functioning. These findings highlight the need for integrated trauma care that includes accurate infection control to support functional recovery.

**Keywords:** SF-36, trauma, limb injury, wound infection, physical functioning, mental health, rehabilitation.

## РОЛЬ РАНОВОЇ МІКРОБІОТИ У ФОРМУВАННІ ЯКОСТІ ЖИТТЯ ПАЦІЄНТІВ З БОЙОВИМИ ПОРАНЕННЯМИ КІНЦІВОК

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**Вступ.** Травми кінцівок, отримані внаслідок бойових дій, включаючи ампутації, опіки та вибухові травми, суттєво впливають на фізичне та психологічне благополуччя пацієнтів. Однак вплив місця травми (верхня та нижня кінцівка) та мікробіологічних характеристик рани на результати одужання залишається недостатньо вивченим.

**Мета.** Оцінити вплив інфікування рани, характеру травми та її локалізації на фізичне та психічне здоров'я пацієнтів з травмами верхніх і нижніх кінцівок.

**Методи.** Загалом 68 пацієнтів чоловічої статі віком 25-60 років з травматичними травмами кінцівок були розділені на дві групи залежно від місця травми: верхня кінцівка (Група 1, n=31) та нижня кінцівка (Група 2, n=37). Були записані демографічні дані, тип травми та мікробне забруднення рани. Для оцінки фізичного та психічного здоров'я використовувався опитувальник SF-36. Статистичний аналіз включає порівняння груп та багатовимірну регресію для визначення предикторів балів SF-36.

**Результати.** Не було виявлено статистично значущих відмінностей між групами за віком, типом травми або балами за шкалою SF-36 ( $p > 0,05$ ). Однак у пацієнтів з травмами нижніх кінцівок спостерігалася тенденція до нижчих балів фізичного функціонування. Група 2 показала дещо вищі середні бали за субшкалами психічного здоров'я. Багатовимірні регресія показала, що наявність полімікробної ранової інфекції була суттєво пов'язана з нижчими балами фізичного функціонування ( $p = 0,0025$ ), незалежно від типу травми чи місця пошкодження.

**Висновки.** Хоча анатомічне місце пошкодження суттєво не впливало на результати SF-36, наявність змішаних ранових інфекцій була значним негативним предиктором фізичного функціонування.

Ці результати підкреслюють необхідність комплексної допомоги при травмах, яка включає агресивний контроль інфекцій для підтримки функціонального відновлення.

**Ключові слова:** SF-36, травма, травма кінцівок, ранова інфекція, фізичне функціонування, психічне здоров'я, реабілітація.

**Introduction.** Traumatic limb injuries resulting from combat operations include amputations, burns, and blast injuries, and have a significant impact on the physical and psychological state of patients [1,2]. Thus, according to the results of the study in Iraq and Afghanistan, a significant proportion of soldiers received severe limb injuries, about 82%. The proportion of amputations during this period was 4%. However, with more frequent encounters with improvised explosive devices during foot patrols, the number of amputations has increased significantly [3].

Chronic postoperative pain is a serious public health problem with significant medical and economic consequences. Its development is often associated with an imbalance between nociceptive and antinociceptive systems. Activation of the latter is necessary for pain relief after surgery, and their dysfunction is considered one of the key mechanisms for the transition of acute pain to chronic pain [4-6].

Chronic pain is also a common complaint among military veterans, leading to lower quality of life, functional disability, and psychological symptoms. Over the years, survival rates for serious combat injuries have increased as medical care in combat environments has improved. However, the number of people with post-traumatic infections, especially those involving the extremities, has increased. Post-traumatic infections of limb wounds often lead to reoperations and late amputations [7, 8].

To investigate the molecular mechanisms of ineffective healing, RNA sequencing was performed on wound biopsies classified by colonization and healing outcome. The analysis revealed that colonized wounds that healed activated the adaptive immune response, while ineffectively healed wounds did not. Wounds that failed to heal exhibited inflammatory and immune abnormalities, but the mechanisms differed depending on colonization. The data obtained suggest different biological pathways for ineffective healing, which may help improve approaches to the treatment of combat wounds [9, 10].

The literature describes the results of research increased physical functioning was associated with higher quality of life, while decreased physical functioning was more

common among respondents who screened positive for posttraumatic stress disorder (PTSD) or depression. When stratified by mental status, the association between physical functioning and amputation status was statistically significant only among participants who screened negative for PTSD or depression. In addition, respondents with bilateral amputees reported significantly lower physical functioning scores compared to those with unilateral amputees [11, 12].

Other results describe that service members with combat injuries subsequently have a stable level of activity and participation, as well as quality of life, because they use adaptive mechanisms [13].

In most studies, chronic pain is usually assessed in terms of its intensity. However, recent scientific evidence suggests that pain intensity is less correlated with functional outcomes than is the so-called pain barrier. Pain barrier differs from intensity in that it measures the extent to which pain interferes with a person's participation in various areas of life—physical, cognitive, emotional, and recreational [14].

To evaluate the impact of wound infection, trauma character and its location in physical and mental health outcomes of patients with upper and lower limb injuries.

#### **Materials and Methods.**

This observational study included 68 males who sustained combat-related injuries to the limbs, such as amputations, burns, or blast injuries. All patients were treated in a single clinical center during the same therapeutic period, 3-6 weeks after injury. To analyze the impact of injury location on recovery and health-related quality of life, the participants were divided into two groups based on the site of injury: Group 1 consisted of patients with upper limb injuries (n = 31), and Group 2 included those with lower limb injuries (n = 37).

Eligibility criteria for inclusion in the study were: male gender, age between 25 and 60 years, and the presence of a single-site traumatic injury either to an upper or lower extremity with prolonged time healing wounds (more than 1 month) Patients with polytrauma, systemic chronic illnesses, or a documented history of psychiatric disorders were excluded to minimize confounding factors. All patients provided informed consent for participation.

*Study design*

Each participant underwent a comprehensive clinical assessment, which included demographic data collection (age, gender), characterization of the trauma (type and location), and microbiological evaluation of the wound. For microbiological assessment, standard wound swabs were collected and cultured to identify bacterial isolates and determine the degree of microbial contamination, expressed as colony-forming units per milliliter (CFU/ml). Both monomicrobial and polymicrobial infections were recorded.

Functional and quality-of-life outcomes were assessed using the SF-36 (Short Form-36) Health Survey, a validated instrument that measures health status across eight subscales grouped into two major components: the Physical Health Component and the Mental Health Component.

*Statistical analysis*

We used standard software. Descriptive statistics (mean values and standard deviations) were used to summarize demographic and clinical variables. Group comparisons for continuous

variables were conducted using independent-sample t-tests or non-parametric equivalents depending on the data distribution. The significance level was set at  $p < 0.05$ . Additionally, multivariate linear regression analysis was performed to assess the influence of independent variables – including trauma type, injury location, infection type, and microbial load – on SF-36 subscale scores, particularly focusing on the Physical Functioning domain.

The study was conducted in accordance with ethical standards and approved by the relevant institutional review board

**Results.** After dividing the study participants into two observation groups, their demographic characteristics, including age, gender, and nature of the injury, were analyzed. The results of the statistical analysis revealed no significant difference between the groups in terms of age distribution ( $p > 0.05$ ), indicating that the groups were comparable in this indicator. Further analysis of demographic data allowed us to assess the homogeneity of the groups and their suitability for comparing clinical outcomes. (Table 1)

Table 1

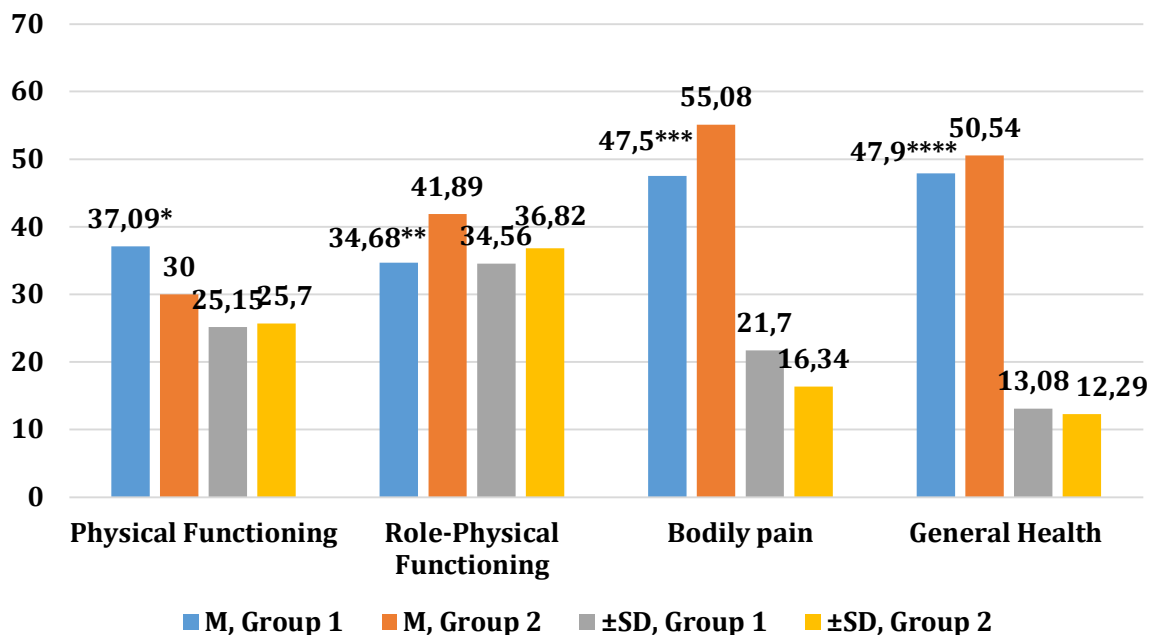
**Demographic Characteristics of Participants**

Variable	Group 1	Group 2
Number of patients	31	37
Age (mean ± SD)	35.94 (±9,4)	33.9 (±9,8)
Gender (male)	31(100%)	37 (100%)
Character of trauma (n)		
Blast injury	13	12
Burns	8	12
Amputations	10	13

The diagram illustrates the difference in mean scores for the Physical Health Component of the SF-36 between participants with injuries to the upper limb and those with injuries to the lower limb. According to the figure, individuals with upper limb injuries demonstrated higher mean physical health scores compared to those with lower limb injuries, suggesting that lower limb trauma may have a more pronounced negative impact on perceived physical functioning. This difference may reflect to tendency of greater mobility limitations associated with leg injuries, which directly influence daily physical activity. Although no statistical difference was achieved in the mean values of the SF 36 scales in the compared groups ( $p > 0.05$ ). (Figure 1)

In addition, we compared the four subscales of the Mental Health component of the SF-36 between the two groups of participants. Overall, Group 2 showed higher mean values for all SF-36 subscales examined with generally lower or comparable variability, indicating a trend towards more consistently positive self-rated health in this group, although statistical significance of the difference in the scores between the groups was not established, ( $p > 0.05$ ).

In the first group (n = 31), a combination of several types of pathogens was isolated among 13 patients in the samples taken for study, and in the second group (n=37), among 16 patients. (Figure 3).



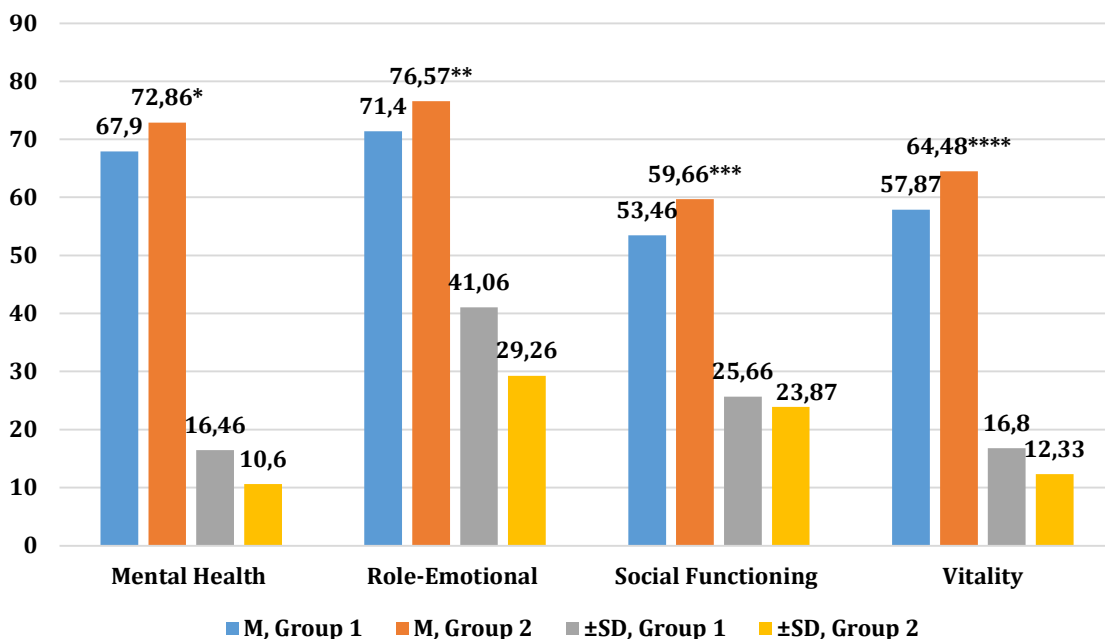
**Figure 1.** Comparison of mean values of the physical health component of the SF-36 in groups of study participants depending on the lesion site (arm/leg)

\* - No statistically significant difference in the mean values of the scale between group 1 and group 2 was achieved, (p > 0.05).

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\*\*\*\* - No statistically significant difference in the mean values of the scale between group 1 and group 2 was achieved, (p > 0.05).



**Figure 2.** Comparison of mean values of the psychological health component of the SF-36 in groups of study participants depending on the lesion site (arm/leg)

\* - No statistically significant difference in the mean values of the scale between group 1 and group 2 was achieved, (p > 0.05).

\*\* - No statistically significant difference in the mean values of the scale between group 1 and group 2 was achieved, (p > 0.05).

\*\*\* -No statistically significant difference in the mean values of the scale between group 1 and group 2 was achieved, (p > 0.05).

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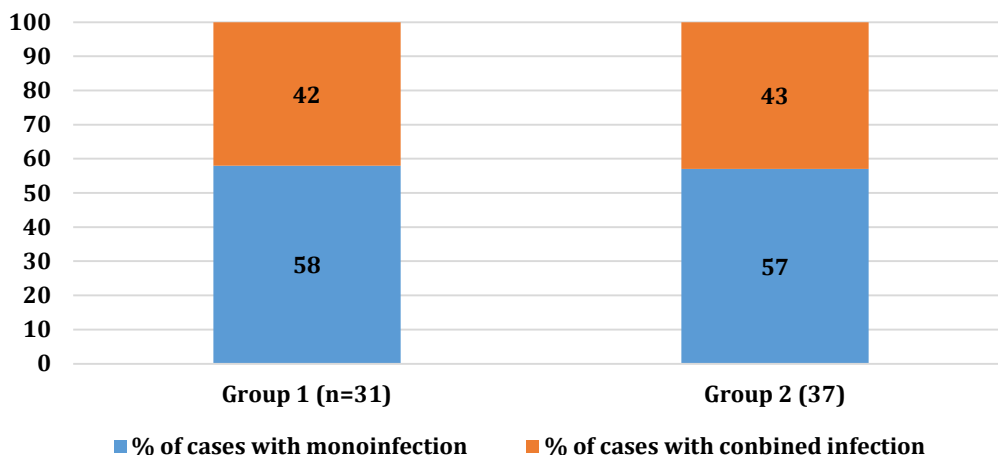


Figure 3. Quantitative characterization of isolated pathogens in the studied groups.

The next stage of our study was to assess whether each SF-36 scale separately, as a dependent variable, depends on such independent factors as the nature of the injury, injury to the upper or lower limb, and the characteristics of microbial contamination of the wound, namely the number of different bacterial isolates isolated and their microbial load. As a result, statistical

significance was obtained only in the case of multiregression analysis of the Physical Functioning scale from the studied independent variables (p < 0,05). When comparing other scales of the SF-36 questionnaire, no statistically significant dependence on the studied factors was obtained. (Table 2)

Table 2

**Multiregressive analysis of the values the Physical Functioning cluster dependence on the studied factors**

Independent variables	Coefficient	Std. Error	r <sub>partial</sub>	t	P
Wound mono-infection and combined infection	-19.3170	6.0917	-0.3993	-3.171	<b>0.0025</b>
Trauma character	-6.0055	6.9740	-0.1175	-0.861	0.3930
Upper or lower limb injury	-6.1784	5.9751	-0.1406	-1.034	0.3058
CFU/ml	15.1109	8.7190	0.2316	1.733	0.0889
Constant - 33.8352					
F-ratio - 3.9656; P=0.007; R <sup>2</sup> 0.2304					

**Discussion.** The study aimed to explore the impact of limb injury location (upper vs. lower) on patients' perceived physical and mental health, as measured by the SF-36, and to identify whether wound microbiology and trauma characteristics influenced functional outcomes.

The demographic characteristics of the groups were well balanced, with no statistically significant differences in age or trauma type distribution, ensuring comparability of the cohorts.

In a similar study *Atar et al. (2022)*, compared with uninjured patients, combat-wounded soldiers were younger, had more severe injuries, and were more likely to require surgery

and rehabilitation. Their long-term well-being, as well as social and cognitive functioning, were lower. At the same time, amputees had better physical well-being and less pain than those who were limb-sparing. Combat injuries to the lower extremities can cause permanent functional loss, but many wounded soldiers demonstrate high levels of adaptation and participation in society [15]. One more study *Schafer et al. (2024)* showed that quality of life and loneliness are closely linked to mental and physical health, which is especially relevant for veterans. A study using data from the Military Health and Wellbeing Project (n=1.469) examined the relationship between five domains of quality of life (general quality of life, physical

health, psychological health, social relationships, and environment) and levels of loneliness among U.S. veterans. Results showed that all domains of quality of life were negatively associated with loneliness ( $r < -0.45$ ,  $p < 0.001$ ), i.e., as loneliness increased, quality of life indicators decreased. Linear regression revealed that the strongest predictors of low levels of loneliness were the quality of social relationships ( $\beta = -0.385$ ), psychological functioning ( $\beta = -0.196$ ), and physical health ( $\beta = -0.133$ ) [16].

In our previous studies, we have already studied various characteristics of the composition of the wound microbiota on the severity of pain and mental health. According to the results superinfection was characterized as independent predictor of pain severity ( $\beta = 1.31$ ;  $p = 0.001$ ) and was associated with higher pain intensity ( $p < 0.01$ ) [17, 18].

Although patients with upper limb injuries tended to report slightly better physical functioning scores than those with lower limb injuries, these differences did not reach statistical significance. This trend may reflect the more severe limitations in mobility and independence typically associated with lower limb trauma, especially in a military or active lifestyle context. These findings align with prior literature indicating that lower extremity injuries often have more profound consequences on mobility, work reintegration, and social participation.

Surprisingly, participants with lower limb injuries (Group 2) exhibited marginally higher scores on all mental health subscales, although again without statistical significance. This may reflect various psychosocial coping strategies, differences in pain perception, rehabilitation experience, or access to psychological support – factors not directly assessed in this study.

Importantly, the multivariate regression analysis revealed that the presence of wound monoinfection vs. mixed infection had a statistically significant negative impact on the Physical Functioning subscale of the SF-36 ( $p = 0.0025$ ), independent of trauma type or injury location. This suggests that bacterial wound contamination – especially polymicrobial – may be an underrecognized factor contributing to delayed recovery and worse self-perceived health status. This finding highlights the importance of early and targeted infection control in traumatic wound management.

#### Conclusions:

These findings suggest that while anatomical injury location plays a role in recovery trajectories, wound microbiology may be an equally or more important factor in determining perceived health and quality of life post-injury. The presence of mixed microbial contamination had a significant negative association with Physical Functioning scores, underlining the role of infection control in optimizing rehabilitation outcomes.

**Prospects for further research:** Future studies should further explore the impact of wound microbiology on physical recovery and quality of life, including the role of polymicrobial infections. Psychosocial factors that may explain the unexpectedly higher mental health scores in patients with lower extremity injuries should also be investigated. Larger samples and possibly qualitative methods (interviews, surveys) are needed to more accurately assess the impact of injury location. Combining infection data with an individualized rehabilitation plan may improve treatment outcomes.

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