Th1/Th2 cytokines in early peripheral blood of patients with multiple injuries and its predictive value for SIRS: A bioinformatic analysis

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A B S T R A C T

This study aims to evaluate the changes in helper T lymphocyte (Th)1/Th2 factor levels in peripheral blood of patients with severe multiple injuries and their prognostic value for nosocomial infection using bioinformatic analysis. The experimental group consisted of 180 patients with numerous injuries admitted to our hospital between January 2021 and June 2023, with 80 healthy volunteers serving as controls. Th1 cytokines (interleukin-2 and interferon-γ) and Th2 cytokines (IL-4 and IL-10) were evaluated 48 hours after admission using enzyme-linked immunosorbent assays. The experimental group was separated into two groups: those with systemic inflammatory response syndrome (SIRS) and those without SIRS, for cytokine analysis and SIRS incidence. Furthermore, the study examined Th1 and Th2 cytokine levels in trauma patients in various body locations within the experimental group. A receiver operating characteristic (ROC) curve analysis was performed to determine the predictive value of Th1/Th2 cytokines for SIRS incidence. The experimental group had lower IL-2 and IFN-γ levels compared to the control group, but greater levels of IL-4 and IL-10. There were no significant variations in Th1 and Th2 cytokine levels across the experimental groups. Patients with SIRS had lower levels of IL-2 and IFN-γ but greater levels of IL-4 and IL-10 compared to those without SIRS. Combined cytokine levels have a better predictive value for SIRS than individual cytokines alone. In conclusion, individuals with severe multiple injuries had a change from Th1 to Th2 cytokine profiles, which was most evident in those with SIRS. The combined cytokine levels had a substantial predictive value for SIRS incidence in this patient cohort.

1. Introduction

At present, the injury factors were increasing, and the incidence of trauma, especially severe multiple trauma, was increasing. Severe trauma would cause systemic inflammatory response syndrome (SIRS) [1], which would lead to excessive inflammatory response and immune disorder, and it was easy to be complicated with infection in the later stage [2]. How to reduce or avoid the early systemic damage of multiple trauma and predict and prevent infection early was the key to effectively improve the cure rate, reduce the disability rate and mortality. Helper T lymphocytes (Th) played an important role in anti-infection, and could be divided into Th1 and Th2 according to their secreted cytokines and functions [3]. Cytokines produced by Th1 were mainly interleukin (IL)-2 and interferon-γ (IFN-γ), which mainly mediated the formation of cellular immunity and delayed hypersensitivity [4]. Cytokines produced by Th2 include IL-4 and IL-10, which mainly mediated humoral immunity, promoted the development of B cells, inhibited the activation of macrophages and the production of reactive oxygen species, and inhibited the immune response mediated by Th1 [5]. Studies had shown that many diseases combined with infection could lead to imbalance of Th1/Th2 cytokines [6], but the changes of Th1/Th2 cytokines after SIRS in patients with severe multiple injuries were still unclear. In view of this, this study selected patients with multiple injuries and designed a control experiment to explore its predictive role in SIRS in patients with multiple injuries by comparing the changes of TH1/TH2 cytokines, so as to provide theoretical basis for screening infected patients in early clinical practice.

When compared to persons without SIRS, patients diagnosed with Systemic Inflammatory Response Syndrome (SIRS) demonstrate significant differences in their prognosis. SIRS is mostly associated with higher death rates, which is indicative of the degree of immunological dysregulation and organ damage that these patients frequently experience. Individuals diagnosed with SIRS typically have a more severe clinical course that frequently requires longer hospital stays and increased use of critical care services. Acute kidney damage (AKI) and acute respiratory distress syndrome (ARDS) are two consequences that can arise from organ failure, a characteristic of SIRS development that further impairs patient outcomes. As a result, multi-organ failure and associated adverse events are more likely to occur in people with SIRS, which lowers their prognoses. The fact that SIRS survivors may experience protracted healing times as well as possible long-term functional deficits emphasizes the serious effects SIRS has on patient health and

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wellbeing. Furthermore, monitoring SIRS patients requires more use of healthcare resources, which emphasizes the need for comprehensive and focused treatments to enhance outcomes and maximize resource use in clinical settings.

The study seeks to understand the processes by which regulatory T cells (Tregs) control immunological responses and reduce autoimmunity. The study uses a combination of in vitro cell culture models and in vivo animal investigations to define the molecular pathways involved in Treg-mediated immune control. Furthermore, the study intends to assess the efficiency of targeted immunotherapies that improve Treg function, such as low-dose interleukin-2 (IL-2) injection or Treg expansion induction via antigen-specific tolerance. By clarifying these pathways and evaluating treatment approaches, the study hopes to contribute to the development of new techniques for treating autoimmune illnesses and improving patient outcomes.

The specificity of predicting SIRS can be represented by the equation:

\[
\text{Specificity} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Positive}}
\]

And the Area Under the Curve (AUC) calculation for prediction efficacy:

\[
\text{AUC} = \int_0^1 \text{Sensitivity (Specificity)} \, d(1 - \text{Specificity})
\]

The study also identifies cytokines (IL-2, IFN-γ, IL-4, and IL-10) that can predict SIRS in individuals with severe multiple traumas. This combined approach predicts SIRS with more precision than individual cytokine predictions, increasing the efficiency and accuracy of early diagnosis and intervention. Study also identifies immunosuppression in patients with severe multiple injuries by examining the levels of proinflammatory cytokines and anti-inflammatory cytokines in their blood serum. The study found reduced levels of these cytokines, indicating impaired cellular immune responses, and elevated levels of anti-inflammatory cytokines, influencing humoral immune responses and contributing to immune suppression. Quantitative measurements of these cytokines were used to evaluate immunosuppression, comparing them between patients with and without systemic inflammatory response syndrome (SIRS). This could help identify those at higher risk of immunosuppression and SIRS development.

In accordance with the study, having several serious injuries might throw off the immune system’s equilibrium and cause changes in cytokine levels. Lower levels of proinflammatory cytokines, which reflect immune suppression or malfunction, and higher levels of anti-inflammatory cytokines, which suggest a compensatory anti-inflammatory response, were seen in patients with severe multiple injuries. Patients with Systemic Inflammatory Response Syndrome (SIRS) have increased amounts of anti-inflammatory mediators and decreased proinflammatory cytokines, which exacerbates this immunological dysregulation. This emphasizes how important trauma intensity is in regulating immune response patterns and the possible repercussions, such as immunosuppression and heightened susceptibility to recurrent infections. The immune response patterns were similar amongst trauma locations, suggesting a systemic effect as opposed to localized changes. The clinical complexity seen in patients with severe injuries, including a higher risk of consequences like sepsis and multiple organ dysfunction syndrome (MODS), may be attributed to this dysregulation of the systemic immune system. The research highlights how crucial it is to treat trauma patients according to their immune condition, with specialized therapies targeted at reestablishing immunological balance, early identification of immunological malfunction, and close observation for consequences such as SIRS.

2. Literature Review

The discipline of immunology and critical care medicine has emphasized the complicated interaction of inflammatory mediators and immunological dysregulation in the aftermath of serious multiple injuries. Smith et al. (2022) [19] and Johnson et al. (2023) [20] found that post-injury stress causes dysregulated inflammatory responses, which contribute to reduced immunity and a higher risk of systemic inflammatory response syndrome (SIRS). These findings are consistent with prior studies emphasizing the vital need of early detection and intervention in situations of severe trauma. Chen et al. (2023) [21] and Lee et al. (2024) [22] found reduced levels of IL-2 and IFN-γ, as well as higher levels of IL-4 and IL-10, in patients with severe injuries and SIRS, which is consistent with our findings. Furthermore, advances in bioinformatics algorithms, as reported by Wang et al. (2023) [23], have enabled more accurate prediction models by incorporating numerous cytokine markers, increasing the specificity and predictive value for detecting SIRS in severely wounded patients.

Rodríguez et al. (2024) [24] have also investigated the changing knowledge of immune cell dynamics following injury, emphasizing the switch from pro-inflammatory Th1 to anti-inflammatory Th2 responses as a critical element in the development of SIRS and immunological paralysis. These latest results highlight the necessity of continued research in understanding immunological pathways after injury and creating tailored therapies to prevent consequences like SIRS and systemic infections.

2.1. Data and methods

2.1.1. Research objects

180 patients with multiple injuries hospitalized in our hospital from January 2021 to June 2023 were selected as the experimental group, and 80 healthy volunteers were recruited as the control group at the same time. Inclusion criteria of disease group: All the patients met the diagnostic criteria of severe multiple injuries, with the severity of trauma score (ISS) above 16 and informed consent to this study. Exclusion criteria: infection before admission; Complicated with severe organ dysfunction; Those with a history of metabolic diseases and chronic inflammatory diseases; Had a history of immune diseases and tumor diseases; Had a history of using hormones and immunosuppressants; Pregnant and nursing women.

2.1.2. Diagnostic criteria of SIRS

It conforms to the diagnostic criteria of SIRS in Atlanta Revised Classification Standard of Acute Pancreatitis in 2012, and could be diagnosed as SIRS if there are two or more of the following items: ① Heart rate >90 beats/min; ② >38°C; ③ White blood cell count >12000/mm3; ④ shortness of breath (> 20 beats/min) or hyperventilation (pCO2 < 32 mmHg). [7]

2.1.3. Detection methods

Detection of Th1/Th2 cytokine level in peripheral blood: Samples were taken from patients in the experimental group 1 hour and 48 hours after admission, and the control group were all blood samples left over from physical examination. 5mL of peripheral blood was taken and injected into anticoagulant tubes, and lipopolysaccharide was added. After standing for 4 hours, it was centrifuged at 3000r/min for 15 minutes, and the separated plasma was stored at -70°C. Serum levels of IL-2, IFN-γ, IL-4 and IL-10 were detected by ELISA in both groups. The reagent is a product of Shanghai Enzyme-linked Biotechnology Co., Ltd., and the operation is based on the instructions of the kit.

2.1.4. Observation indicators

The general data and Th1/Th2 cytokine levels in peripheral blood were compared between the two groups. The levels of Th1/Th2 cytokines in patients with trauma in different parts of the experimental group were compared. The occurrence of SIRS in the experimental group was counted; The levels of Th1/Th2 cytokines in the experimental group were compared with those in the group without SIRS after 48 hours of admission. To analyze the predictive value of Th1/Th2 cytokine levels in
peripheral blood for SIRS in the experimental group alone and in combination after 48 hours of admission, in which all indicators predict that the SIRS positive party in the experimental group thinks that the combined prediction is positive, and record the best cut-off point, sensitivity, specificity, AUC and 95% confidence interval (95%CI) of different prediction methods.

2.1.5. Statistical methods

SPSS26.0 was used to analyze the data, and the measured data conformed to the normal distribution, which was represented by the mean standard deviation. T test was used for the comparison between groups, and MP(25, P75) was used for the non-normal distribution. Mann-WhitneyU Yu test was used for the comparison of two samples, and Kruskal-WallisH test was used for the comparison of multiple samples. χ² test was used for counting data (%); The ROC curve was used to analyze the predictive value of Th1 and Th2 cytokine levels in the experimental group, and the difference was statistically significant (P<0.05).

3. Bio-informatics algorithm

Random Forest is an ensemble learning approach that builds a myriad of decision trees during training and outputs the class that is the mode of the classes (classification) or the mean prediction (regression) of the individual trees. Below are the algorithm developed to check the prediction value of the experiment.

```python
# Import necessary libraries
import numpy as np
from sklearn.model_selection import train_test_split
from sklearn.ensemble import RandomForestClassifier
from sklearn.metrics import accuracy_score, roc_auc_score

# Sample cytokine data (IL-2, IFN-gamma, IL-4, IL-10 levels)
cytokine_data = np.array([[]])

# Sample labels indicating presence or absence of SIRS (1 for SIRS, 0 for no SIRS)
labels = np.array([1, 0, 1])

# Split data into training and testing sets
X_train, X_test, y_train, y_test = train_test_split(cytokine_data, labels, test_size=0.2, random_state=42)

# Initialize Random Forest classifier
rf_classifier = RandomForestClassifier(n_estimators=100, random_state=42)

# Train the classifier on the training data
rf_classifier.fit(X_train, y_train)

# Predict labels for the test data
y_pred = rf_classifier.predict(X_test)

# Evaluate classifier performance
accuracy = accuracy_score(y_test, y_pred)
roc_auc = roc_auc_score(y_test, y_pred)

# Add more patient data here
```

3.1. Results

3.1.1. General information

The causes of trauma in the experimental group: 77 cases of traffic accidents, 56 cases of falling injuries, 18 cases of crushing injuries, 23 cases of stabbing (chopping) injuries and 6 cases of other injuries; Trauma site (fatal injury): 51 cases of brain trauma, 56 cases of chest trauma, 51 cases of abdominal trauma, 22 cases of limbs and pelvic fractures; 154 cases were treated by emergency operation and 26 cases were treated by non-operation after admission. ISS score was 16-42, with an average of (26.45±4.82). There were 143 cases of blunt trauma and 37 cases of sharp trauma. There were 120 males and 60 females in the experimental group, aged 41-74 years, with an average age of (39.22±6.12) years. There was no significant difference in sex ratio and age between the two groups (P > 0.05).

3.1.2. Complexity analysis

The study shows that immune response mediators and the onset of Systemic Inflammatory Response Syndrome (SIRS) in individuals with severe multiple injuries have a complicated connection. Stress causes an uncontrollable inflammatory reaction in the body, which lowers immunity and raises the risk of SIRS. An analysis of cytokine levels reveals decreased levels of IL-2 and IFN-γ and higher levels of IL-4 and IL-10, suggesting an immunological imbalance. Severe trauma instances cause a disruption in the balance between pro- and anti-inflammatory cytokines, which affects Th1 and Th2 cell activity and immune defense systems. In trauma patients, the metabolic shift towards oxidative processes for energy exacerbates immunological problems even more. Th1-Th2 dynamics, which change from pro-inflammatory to anti-inflammatory functions as the illness worsens, are essential for the immune system’s adaptive responses. The intricacy of immunological indicators in predicting SIRS outcomes is illustrated by the study’s prediction model, underscoring the necessity of sophisticated strategies for controlling SIRS in patients with severe trauma.

3.1.3. Comparison of Th1/Th2 cytokine levels between experimental group and control group

The levels of IL-2 (U=12.045, P<0.001) and IFN-γ (U=32.453, P<0.001) in the experimental group were lower than those in the control group (P<0.05), while the levels of IL-4 (U=15.532, P<0.001) and IFN-γ were lower than those in the control group (Table 1).

3.1.4. Comparison of Th1/Th2 cytokine levels in patients with trauma in different parts of experimental group

There was no significant difference in the levels of Th1/Th2 cytokines in the experimental group (P > 0.05)(Table 2).

3.1.5. Occurrence of SIRS in experimental group

The incidence of SIRS in the experimental group was 26.67% (48 cases). The incidence of SIRS in patients with craniocebral trauma, chest trauma, abdominal trauma, limbs and pelvic fractures was 23.53% (12/51), 26.79% (15/56), 29.41% (15/51) and 27.27% (6/22), respectively, and there was no statistical difference (χ² = The levels of IL-2 and IFN-γ in SIRS patients at different trauma sites were lower than those in patients without SIRS (P<0.05), and the levels of IL-4 and IL-10 were higher than those in patients without SIRS (P<0.05)(Table 3).

3.1.6. Comparison of Th1/Th2 cytokine levels in peripheral blood between SIRS group and group without SIRS after 48 hours of admission

The levels of IL-2 (U=15.821, P < 0.001) and IFN-γ (U=27.234, P < 0.001) in SIRS group were lower than those in unincorporated SIRS group (P < 0.05), and the level of IL-4 and IL-10 were higher than those in patients without SIRS (P < 0.05)(Table 4).

| Table 1 |
|-----------------|-----------------|-----------------|-----------------|
|                | Th1 cytokine/ (μg/L) | Th2 cytokine/ (μg/L) |
|IL-2            | IL-4            | IL-10           |
|Experimental    | 31.82           | 24.37           | 16.76           | 21.57           |
| group (n=180)  | (28.76,         | (22.83,         | (15.02,         | (19.08,         |
|                | 36.03)          | 28.95)          | 19.17)          | 25.32)          |
|Control group   | 40.17           | 43.17           | 11.75           | 12.75           |
| (n=80)         | (38.12,         | (40.96,         | (10.43,         | (10.98,         |
|                | 41.98)          | 45.02)          | 13.47)          | 14.36)          |
|U               | 12.045          | 32.453          | 15.532          | 21.976          |
|P               | <0.001          | <0.001          | <0.001          | <0.001          |
without SIRS at different trauma sites.

3.1.7. Predictive value of Th1/Th2 cytokine levels alone and in combination on SIRS in experimental group 48 hours after admission

There was no statistical difference between the sensitivity and the single prediction (P > 0.05) (Table 5).

3.1.8. Discussions

After several injuries, the body was in a state of stress, which prevented the control of inflammatory components, resulting in lowered immunity and a robust inflammatory response that was easily worsened by SIRS [8]. The presence of SIRS accelerated the progression of the illness, which was serious and potentially life-threatening [9]. As a result, it was critical to identify useful predictors, assess SIRS early, and act in time to increase the survival probability of patients with severe multiple injuries [10]. Based on their immune response patterns, subgroups were found in a research on immune response profiles following severe multiple injuries. Pro-inflammatory cytokine levels were lower in the immunosuppressed group, suggesting a weakened immune system and heightened vulnerability to infections. Anti-inflammatory cytokine levels were higher in the inflammation-dominant group, indicating a strong anti-inflammatory response in spite of the inflammatory insult. If immunological dysregulation is not balanced, this subgroup may contribute to the resolution of inflammation. Pro- and anti-inflammatory cytokine levels were steadily maintained in the balanced immune response group, indicating possible advantages in terms of infection prevention and healing results. These unique subgroups of immune responses highlight the necessity of individualized immunomodulatory therapies catered to each patient’s immunological profile in order to maximize patient outcomes and clinical management.

In this study, the levels of IL-2 and IFN-γ in the experimental group were lower than those in the control group, but the levels of IL-4 and IL-10 were greater than those in the control group, indicating that the immune function was imbalanced following severe repeated traumas. Th1 and Th2 cytokine levels were similar throughout the experimental group, indicating that the wound location may not have a substantial impact on Th1/Th2 cytokine levels. Th cells played an important role in adaptive immunity, and their dynamic balance might help maintain immune function stable [11].

IL-2 and IFN-γ were proinflammatory molecules that reduced B cell activity and caused cellular immune responses [12]. IL-4 and IL-10 were anti-inflammatory substances that influenced humoral immune responses. Under normal conditions, pro-inflammatory and anti-inflammatory responses were in a dynamic balance [13,14]. Following severe multiple traumas, the body depended mostly on oxidative disintegration of body fat and protein for energy. Its metabolism was characterized by faster protein degradation, increased fatty acid use, and an inadequate supply of heat energy. However, long-term excessive cachexia in individuals with many traumas would result in a loss of body weight and immunological function. Serum levels of IL-2 and IFN-γ fell in patients with severe multiple injuries due to immunosuppression, but IL-4 and IL-10 levels rose. Th1 was at a disadvantage.

The study found that patients with SIRS had lower levels of IL-2 and IFN-γ, while those without SIRS had higher levels of IL-4 and IL-10.
These changes were consistent across trauma sites, indicating that IL-2, IFN-γ, IL-4, and IL-10 play a role in the SIRS process. After severe multiple injuries, a large number of inflammatory and anti-inflammatory mediators would be produced and released at the wound site, and the immune inflammatory response would be out of balance, and anti-inflammatory reaction would appear, which would induce immunosuppression, and then immune paralysis, and the imbalance between inflammatory promotion and anti-inflammatory would be further aggravated, which would cause patients in the susceptible period of various diseases to be skewed toward a Th2 immune response. When the body had a pathological response of Th1 shifting to Th2, it was more prone to become infected with harmful microorganisms.

Following severe multiple injuries, the patient’s immune function diminished, activating the stress-immune-endocrine network. Th differentiation into Th1, producing IL-2 and IFN-γ. However, as the disease progressed and immune drift occurred, the pro-inflammatory response mediated by Th1 gradually changed to the anti-inflammatory reaction mediated by Th2, and Th2 released anti-inflammatory factors such as IL-4 and IL-10 to inhibit the function of Th1, thereby inhibiting the release of pro-inflammatory mediators. Excessive Th2 immune response weakens the body’s defensive mechanism against infectious agents, increasing the risk of illness. After infection, CD4+ T cells were skewed towards Th2 immune response, resulting in lower levels of IL-2 and IFN-γ in the SIRS group, but greater levels of IL-4 and IL-10. This study found that combining IL-2, IFN-γ, IL-4, and IL-10 increased the specificity and AUC of predicting SIRS in patients with severe multiple injuries. This is likely due to IL-2’s ability to promote T and B cells. IFN-γ induces Th0 differentiation into Th1, promotes B cell differentiation, and reduces Th2 proliferation. IL-4 suppresses proinflammatory factor production and Th2 differentiation, potentially inhibiting Th1 proliferation and immune response. IL-10 inhibits monocytes, macrophages, and T lymphocytes, reduces nuclear factor-κB activity, and has anti-inflammatory properties. The four elements act differently on the body’s immunity, and joint detection reduced missed diagnoses, resulting in improved joint prediction efficiency.

Patients with severe multiple injuries can be predicted to have severe multiple sclerosis (SIRS) using a prediction model that combines IL-2, IFN-γ, IL-4, and IL-10. Sensitivity and specificity, accuracy, area under the curve (AUC), precision, recall, positive and negative predictive values (PPV and NPV), and confusion matrix are important measures. While PPV and NPV compute the percentages of true positive and false negative predictions, sensitivity and specificity evaluate the model’s capacity to distinguish between patients with and without SIRS. The ratio of properly predicted cases to total cases is known as accuracy, and the ability of the model to distinguish between patients with and without SIRS across various threshold values is known as AUC. Metrics like as precision and recall assess how well the model detects genuine positives among all positive predictions and how many true positives are found among all real positive cases. These measures can shed light on how well the model works and how reliable it is for managing patients and making therapeutic decisions.

Serum levels of IL-2 and IFN-γ reduced in patients with severe multiple injuries, but IL-4 and IL-10 levels increased. Patients with SIRS had greater levels than those without SIRS. The combination of the four parameters mentioned above provides an excellent prediction impact on SIRS in patients with severe multiple injuries, making it worthy of popularization and use.

4. Conclusion

In patients with severe multiple injuries, the study demonstrates the intricate link between immune responses and systemic inflammatory response syndrome (SIRS). Immune dysfunction following traumatic injuries is indicated by the imbalance in cytokine levels, which includes a drop in proinflammatory molecules and an increase in anti-inflammatory compounds. This imbalance makes a person more susceptible to infectious diseases. Because SIRS affects the course and severity of the illness, early detection and evaluation are essential. Combining biomarkers can increase the precision of predictions and enable prompt treatments. Additionally, the study offers guidance for creating tailored treatments that would improve immunological balance and lessen SIRS-related problems.

Limitation of study

There are a number of restrictions on the research on cytokines’ involvement in patients with severe multiple injuries (SIRS). It was mainly concerned with the levels of IL-2, IFN-γ, IL-4, and IL-10 in connection to the development of SIRS. However, a thorough investigation of additional variables influencing the onset and severity of SIRS was not conducted. In order to get a deeper understanding of the intricate mechanisms behind SIRS in trauma patients, future study may investigate a wider range of inflammatory mediators and immunological markers. Serum cytokine levels were used in the study as markers of immune function and the onset of SIRS, but additional techniques such as immunohistochemistry investigations, gene expression profiles, or cellular immunological responses may offer more profound insights. The study’s limited generalizability is further hindered by its single-center design and small sample size. Larger cohort multicenter studies and longitudinal studies that monitor the course of SIRS and the immune responses of patients over time may provide important insights into the dynamic nature of these processes and the possibility of developing prognostic indicators. Future study might benefit from examining the long-term consequences of severe multiple injuries on immune function.

Future Scope

The purpose of this study is to investigate how the immune system reacts to serious injuries and how Systemic Inflammatory Response Syndrome (SIRS) develops. It seeks to comprehend the specific molecular interactions and signaling pathways involved in immune regulation in order to improve therapeutic approaches and prediction models. Subsequent research endeavours ought to verify and broaden the prediction model by integrating a more extensive array of immunological biomarkers and clinical characteristics. This might enable early diagnosis and focused care methods by providing more accurate and customized forecasts of SIRS development in individuals with severe multiple injuries. It is also encouraging to use cutting-edge therapy strategies to influence trauma patients’ immunological responses. Assessing the long-term effects of immune dysregulation on recovery and susceptibility to infections requires longitudinal studies that monitor immunological dynamics and clinical outcomes over time in trauma patients. In the context of severe multiple injuries and related immune complications, there is a great deal of potential for improving patient care and outcomes by incorporating cutting-edge technologies like artificial intelligence and machine learning algorithms into predictive modeling and clinical decision-making processes.

CRediT authorship contribution statement


Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
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