Analysis of Influencing Factors for PTSD in Emergency Department Trauma Patients

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Protocol Summary

Item	Analysis of Influencing Factors for PTSD in Emergency Department Trauma Patients
Study Objectives	To determine the incidence of PTSD within 6 months in emergency department trauma patients and identify the sociodemographic, trauma-related, and psychosocial high-risk factors associated with the development of PTSD. To explore the interaction pathways among various factors and reveal the mediating or moderating roles of relevant factors in the occurrence of PTSD.
Study Design	Single-center prospective cohort study
Total Sample Size	250 cases
Case Selection	Inclusion Criteria ① Aged 18-65 years (inclusive of boundary values); ② Experienced life-threatening major traumatic events, confirmed by clinical diagnosis; ③ Able to communicate normally with medical staff; ④ Provided full informed consent and voluntarily signed the Informed Consent Form (ICF).
	Exclusion Criteria ① History of mental illness or current use of psychotropic drugs; ② Previous cognitive impairment (e.g., dementia, Alzheimer's disease); ③ Terminal diseases (e.g., advanced malignant tumors, end-stage organ failure, advanced neurological diseases, or any other diseases with an expected survival time of less than 6 months as judged by the attending

	physician); ④ Unable to cooperate with follow-up.
Study Protocol	1. Study Subjects: Trauma patients admitted to the Emergency Department of Xijing Hospital from January 2026 to June 2027. 2. Assessment Items （1）Sociodemographic Factors: Basic information including age, gender, occupation, marital status, educational level, and income status. （2）Trauma-Related Factors: Injury mechanism, trauma severity, time to first effective analgesia (minutes), morphine equivalent of analgesic drugs (mg), vital signs, length of stay in the emergency department, and whether emergency surgery/procedure was performed. （3）Physiological Indicators: White blood cell count, neutrophil count, lymphocyte count, platelet count, lactic acid, blood glucose, serum albumin, serum cortisol, interleukin-6 (IL-6), and C-reactive protein. （4）Cranial Magnetic Resonance Imaging (MRI) （5）Psychosocial Factors: ① General Information Questionnaire ② Injury Severity Score (ISS) ③ Post-traumatic Stress Disorder Checklist for DSM-5 (PCL-5) ④ Acute Stress Disorder Scale (ASDS) ⑤ Social Support Rating Scale (SSRS) ⑥ Connor-Davidson Resilience Scale (CD-RISC 10) ⑦ Cognitive Flexibility Inventory (CFI) ⑧ Hospital Anxiety and Depression Scale (HADS)

Outcome Assessment	评价指标 Incidence of PTSD as determined by the PCL-5 scale within 6 months after trauma. Point prevalence of PTSD at 1 month and 3 months after trauma; dynamic changes in psychosocial indicators such as social support, anxiety and depression, psychological resilience, and cognitive flexibility.
Statistical Methods	Descriptive statistics will first be used to summarize all study variables. Continuous variables will be expressed as mean ± standard deviation or median (interquartile range), and categorical variables as frequency and percentage. The point prevalence of PTSD at 1 month, 3 months, and 6 months after trauma, as well as the 6-month cumulative incidence and their 95% confidence intervals, will be calculated respectively. Univariate analysis will be used to screen factors associated with PTSD occurrence: chi-square test or Fisher's exact test for categorical variables, and independent samples t-test or Mann-Whitney U test for continuous variables. Variables with statistical significance ($P<0.05$) or clinical significance in univariate analysis will be included in a multivariate binary Logistic regression model to identify independent influencing factors of PTSD. Adjusted odds ratios and their 95% confidence intervals will be calculated, and goodness-of-fit and multicollinearity diagnostics will be performed for the model. Amos 21.0 software will be used to construct a structural equation model of PTSD occurrence to analyze the relationships among observed variables. A model will be considered well-fitted if the ratio of chi-square to degrees of freedom, comparative fit index, incremental fit index, and goodness-of-fit index are >0.900, and the root mean square error of approximation is <0.05. The significance level $\alpha=0.05$.
Study Duration	September 2025 - June 2027

I. Research Background

1. Research Significance

Post-Traumatic Stress Disorder (PTSD) is a common and severe mental disorder following exposure to traumatic events, characterized by intrusive memories, avoidance behaviors, negative cognitions and emotions, and increased arousal. It not only significantly impairs patients' mental health but also leads to long-term functional disabilities, imposing a heavy burden on public health [1]. As a key first-contact site for trauma patients, emergency departments receive individuals who have experienced sudden, life-threatening events such as traffic accidents, violent assaults, work-related injuries, and natural disasters. The incidence of PTSD in this population is significantly higher than in the general public[2, 3]. Globally, the lifetime prevalence of PTSD among trauma-exposed individuals is approximately 3.9%, while in emergency department trauma patients, it ranges from 14.1% to 36.0%. When symptoms persist for more than 1 month, patients face an increased risk of comorbidities such as chronic pain, depression, and substance abuse, which significantly reduce their quality of life and increase medical costs[1, 4, 5]. Therefore, identifying the influencing factors of PTSD in emergency department trauma patients is of great clinical and public health significance for early identification of high-risk groups and development of targeted prevention and intervention strategies.

The development of PTSD in emergency department trauma patients is closely associated with neurocognitive dysfunction[6, 7]. Studies have shown that patients with better cognitive flexibility within 1 month after trauma exhibit significantly milder PTSD symptoms at 13 months; moreover, early neurocognitive interventions such as working memory training and task-switching training can improve cognitive flexibility, thereby reducing PTSD symptoms at 6 months[2]. This finding suggests that cognitive flexibility, as a core dimension of neurocognitive function, may be a key protective factor against PTSD in emergency department trauma patients. By helping patients flexibly adjust cognitive strategies, distinguish between threatening

and safe situations, and promote the extinction of fear memories, cognitive flexibility reduces the consolidation of trauma-related negative cognitions, thereby lowering the risk of PTSD[2]. Additionally, neuroimaging studies have confirmed that PTSD patients exhibit abnormal prefrontal network function, and improved cognitive flexibility can enhance prefrontal regulation of the limbic system, reducing hyperarousal caused by excessive amygdala activation—further supporting the role of neurocognitive function in the development of PTSD in emergency department trauma patients[2].

Psychological and social factors are also important influencing variables for PTSD in emergency department trauma patients. As a classic protective factor, the negative correlation between social support and PTSD has been confirmed by numerous studies: a meta-analysis including 62,803 trauma-exposed individuals showed that higher levels of social support (especially perceived support) are associated with lower PTSD symptom scores, and this association is more pronounced in emergency department trauma patients[8]. Specifically, after experiencing sudden trauma, emotional support from family, friends, or the medical team can alleviate patients' loneliness and helplessness, reducing avoidance behaviors; instrumental support (e.g., provision of medical information, practical life assistance) can reduce patients' sense of loss of control over the post-traumatic environment, thereby mitigating stress responses[8]. Conversely, negative social reactions (e.g., blame, neglect) significantly exacerbate trauma-related negative cognitions, increasing the risk of PTSD, and their association with PTSD is even stronger than that of positive social support[8]. Furthermore, coping styles also affect the development of PTSD in emergency department trauma patients: patients adopting positive coping strategies have a significantly lower incidence of PTSD than those using negative coping strategies, and coping styles play a mediating role between psychological resilience and PTSD—i.e., psychological resilience indirectly reduces PTSD risk by promoting positive coping[9].

Abnormal physiological stress responses and inflammatory mechanisms are also involved in the development of PTSD in emergency department trauma patients.

Dysfunction of the hypothalamic-pituitary-adrenal (HPA) axis after trauma is an important physiological basis for PTSD: emergency department trauma patients with abnormal cortisol responses in the early post-traumatic period (e.g., delayed cortisol peak, reduced basal cortisol levels) have a significantly higher incidence of PTSD at 3 months[4]. This is because cortisol, a key hormone in the stress response, can reduce the release of inflammatory factors by inhibiting the nuclear factor-κB (NF-κB) pathway, while HPA axis dysfunction leads to uncontrolled inflammatory responses. Studies have found that among emergency department trauma patients, those with PTSD have significantly higher levels of peripheral blood IL-1β, IL-6, TNF-α, and C-reactive protein (CRP) than non-PTSD patients. These inflammatory factors can cross the blood-brain barrier to activate microglia and astrocytes in the brain, triggering neuroinflammation, which further exacerbates prefrontal-amygdala network dysfunction and promotes the development of PTSD symptoms[1, 10]. Additionally, early post-traumatic pain is closely associated with PTSD: a study of 663 emergency department trauma patients showed that pain within 1 month after trauma is positively correlated with PTSD symptom scores at 1 year, and anxiety and depression play a complete mediating role—pain intensifies patients' negative emotional experiences, strengthens trauma-related fear memories, and thereby increases PTSD risk[11].

Sociodemographic and trauma characteristics of emergency department trauma patients also affect the risk of PTSD. From a sociodemographic perspective, female patients have a significantly higher incidence of PTSD after emergency department trauma than male patients, which may be related to women's greater sensitivity to emotional processing of trauma and stronger HPA axis stress responses[8]. younger patients (e.g., 18-30 years old) also face a higher PTSD risk due to immature neurodevelopment and limited psychological resources for coping with trauma[8]. From a trauma characteristic perspective, trauma type is an important influencing factor: emergency department patients who experience interpersonal violence (e.g., assault, sexual abuse) or terrorist attacks have a significantly higher incidence of PTSD (approximately 30%-40%) than those who experience traffic accidents or

work-related injuries (approximately 15%-20%). This is because interpersonal trauma involves intentional harm, which is more likely to cause patients to lose trust in others and suffer long-term lack of sense of security[10]. Furthermore, trauma severity (e.g., ISS score ≥ 16) and post-traumatic coma duration are positively correlated with PTSD risk: physiological damage caused by severe trauma exacerbates stress responses, while coma may affect the integration of trauma memories, increasing the occurrence of intrusive memories[12].

2. Domestic and Foreign Research Status

2.1 Domestic Research Status

Domestic research on the influencing factors of PTSD in emergency department trauma patients mainly focuses on local prevalence surveys and exploration of individual influencing factors. Although some key variables have been initially identified, there are limitations such as limited sample representativeness and insufficient analysis of multi-factor interactions.

Regarding the association between prevalence and trauma type, regional studies have shown significant differences in PTSD incidence among emergency department trauma patients based on trauma type. A study of 326 emergency department trauma patients in the Pearl River Delta region reported an overall PTSD incidence of 18.2%, with violent assault (31.5%) and traffic accidents (22.3%) as the main triggers, while work-related injuries (12.7%) and accidental falls (10.5%) had relatively lower incidences—suggesting that interpersonal violence-related trauma may be a high-risk trigger for PTSD in domestic emergency department patients[13]. Another study on severely traumatized patients further confirmed that the incidence of PTSD at 3 months after trauma was 29.6% in patients with an ISS score ≥ 16 (mostly high-energy trauma such as traffic accidents and falls from heights), significantly higher than that in patients with an ISS score <16 (13.8%), and the risk was further increased in those with a coma duration >24 hours—indicating that trauma severity and physiological damage are important risk markers for PTSD in domestic emergency department patients[12].

In terms of psychosocial influencing factors, domestic research has focused on the role of social support and coping styles, and most have confirmed their close association with PTSD. A cross-sectional study of 287 emergency department trauma patients found that the incidence of PTSD in patients with insufficient social support (SSRS score <20) was 35.2%, 2.9 times that of patients with sufficient social support (12.1%). Family support and friend support had the most significant protective effects, and this association was stable across different trauma types such as traffic accidents and violent assaults—suggesting that lack of social support may be a universal risk factor for PTSD in domestic emergency department patients[14]. The mediating effect of coping styles has also been confirmed by multiple studies: a follow-up study of 198 emergency department trauma patients showed that negative coping (e.g., avoidance, denial) indirectly exacerbates PTSD symptoms by reducing psychological resilience (mediation effect accounting for 35.7%), while positive coping can reduce PTSD risk by 40%, and this effect is more pronounced in young patients (18-30 years old)—reflecting the regulatory role of psychological resilience in the development of PTSD in domestic emergency department patients[9].

In terms of physiological indicators and intervention exploration, domestic research has initially focused on the predictive value of inflammatory and nutritional indicators and attempted early nursing interventions. An analysis of 215 emergency department trauma patients showed that the incidence of PTSD at 3 months was 32.8% and 30.5% in patients with a C-reactive protein/albumin ratio >0.15 and a procalcitonin/albumin ratio >0.02 within 24 hours after trauma, respectively, significantly higher than that in patients with normal ratios (11.2% and 10.8%)—suggesting that such inflammatory-nutritional indicators may serve as convenient screening markers for PTSD in domestic emergency department patients[15]. At the intervention level, a single-center controlled study (n=156) showed that implementing an integrated nursing intervention of "early psychological counseling + pain management + social support linkage" for emergency department trauma patients reduced the incidence of PTSD at 3 months from 28.2% to 19.2% and increased patient satisfaction to 92.3%, providing practical evidence for early PTSD intervention in domestic emergency

departments. However, the study had a small sample size and did not involve mechanism-level interventions such as neurocognition[16].

2.2 Foreign Research Status

Foreign research on the influencing factors of PTSD in emergency department trauma patients is characterized by neurocognitive mechanisms, physiological stress pathways, and large-sample meta-analyses, with an emphasis on verifying intervention effects. However, there are limitations such as neglect of emergency department setting specificity and insufficient representativeness of non-Western populations.

In terms of neurocognitive mechanisms and predictive value, foreign studies have clearly identified cognitive flexibility as a core protective factor against PTSD in emergency department trauma patients. Two longitudinal studies of Israeli emergency department trauma patients showed that patients with higher cognitive flexibility scores at 1 month after trauma had significantly lower CAPS-5 scores at 13 months, even after adjusting for age, trauma type, and initial symptoms; further intervention studies confirmed that 30-day online cognitive training can significantly improve patients' cognitive flexibility and reduce PTSD symptoms by 23.1% at 6 months—suggesting that cognitive flexibility is not only a predictor but also a modifiable target[2]. Additionally, a study of 198 male veterans (though not in an emergency setting) verified the consistency of cognitive assessment tools: the correlation coefficient between CAPS-5 (clinical interview) and PCL-5 (self-report) in assessing changes in PTSD symptoms was 0.878, and their association patterns with depression and social function were similar—providing a reference for the selection of PTSD assessment tools in emergency department trauma patients[1].

In terms of meta-analysis and heterogeneity exploration of social support, foreign studies have revealed the association between social support and PTSD and moderator effects through large-sample integration. A meta-analysis including 139 studies showed a significant negative correlation between social support and PTSD symptoms, with significant heterogeneity in this association: the association strength of negative social reactions (e.g., blame, neglect) was significantly higher than that of perceived

support and structural support; the veteran population had a significantly higher association than the general population; the natural disaster trauma group had a significantly lower association than the combat and interpersonal violence groups[8]. This result suggests that social support interventions for foreign emergency department trauma patients need to be tailored to trauma types and population characteristics rather than a "one-size-fits-all" approach.

In terms of physiological stress and inflammatory mechanisms, foreign studies have delved into the mediating roles of the HPA axis, inflammatory factors, and pain. A meta-analysis of 7 emergency trauma studies showed that patients with delayed cortisol peak (>40 minutes) or reduced basal cortisol levels (<10μg/dL) within 72 hours after trauma had a 2.1-fold increased risk of PTSD at 3-6 months, and the predictive value of blood cortisol was significantly higher than that of urine and salivary cortisol[17]. A cohort study of 5703 Vietnam War veterans further extended to inflammation and pain: even after controlling for Criterion A trauma history, PTSD symptoms were significantly positively correlated with pain intensity, and IL-6 and TNF-α levels played a partial mediating role—suggesting that inflammation may be a key link between PTSD and pain comorbidity in emergency department trauma patients[10]. Additionally, a randomized controlled trial showed that repeated intravenous ketamine administration can rapidly reduce symptom scores in emergency department trauma patients with chronic PTSD, with significantly better efficacy than midazolam, but the median response duration was only 27.5 days—indicating that drug interventions need to be combined with maintenance regimens[18].

In terms of assessment tools and setting adaptation, foreign studies have focused on the impact of the emergency environment on PTSD assessment. A study of 65 female PTSD patients found that a machine learning model based on functional connectivity MRI can predict 24% of the variance in dissociative symptoms, and this prediction is independent of childhood trauma and total PTSD symptoms—providing a new idea for the objective assessment of PTSD subtypes (e.g., with dissociative symptoms) in emergency department trauma patients. However, the study did not include acute

emergency patients, and the setting applicability needs to be verified[19]. Most foreign emergency trauma studies use "1 month after trauma" as the assessment node, which may miss early stress responses during emergency department stay, and insufficiently consider environmental factors such as emergency department noise and doctor-patient communication—limiting the direct application of conclusions in the emergency setting[20].

Although existing studies have initially identified some influencing factors of PTSD in emergency department trauma patients, there are still shortcomings: most studies focus on individual factors, lacking exploration of multi-factor interactions; moreover, there are few studies on the impact of the specific emergency department environment on PTSD. Therefore, systematically sorting out the physiological, psychological, social, and trauma-related influencing factors of PTSD in emergency department trauma patients can provide a theoretical basis for the subsequent development of multi-dimensional risk assessment tools and early intervention studies, ultimately improving the long-term prognosis of emergency department trauma patients.

II. Research Objectives

To determine the incidence of PTSD within 6 months in emergency department trauma patients and identify the sociodemographic, trauma-related, and psychosocial high-risk factors associated with the development of PTSD.

To explore the interaction pathways among various factors and reveal the mediating or moderating roles of relevant factors in the occurrence of PTSD.

III. Study Design Type, Principles, and Trial Procedures

1. Study Design

This study is a single-center prospective cohort study.

Sampling Method: Consecutive enrollment

Sample Size Calculation: According to "Wu Minglong. Structural Equation Modeling: Application of SIMPLIS", the sample size should be 10-15 times the number of observed variables. This study is expected to have 20 observed variables, requiring a

sample size of 200-300 cases. Considering a 20% non-compliance rate, the planned sample size is 250 cases.

2. Study Procedures

(1) Baseline Assessment (T0, <24 hours):

Conduct interviews with patients using a self-designed structured questionnaire to collect comprehensive sociodemographic information including age, gender, occupation, marital status, educational level, and income status.

Record trauma type and injury site in detail based on medical records and assessment by trained researchers, and calculate the Injury Severity Score (ISS) using the ISS system.

Accurately extract the "time to first effective analgesia" (in minutes) from emergency nursing records and electronic medical records, and record the name, dosage, and route of administration of all analgesic drugs used. Pharmacists or researchers will convert them into "morphine equivalent (mg)" according to standard conversion tables.

Perform cranial Magnetic Resonance Imaging (MRI) to collect brain structural imaging data, assess the direct impact of acute trauma on brain tissue, and use it as a baseline for comparison at subsequent time points.

For psychological scales: ASDS, HADS, SSRS, CD-RISC, and CFI should be completed when the patient is conscious (GCS ≥15 points); if the patient has visual or educational limitations, researchers will read the items one-on-one, and the patient will verbally report the answers (ensuring the "self-report" nature). All scale data will be double-entered and verified.

Simultaneously collect 5mL of venous blood into EDTA anticoagulant tubes, record the blood collection time, centrifuge at 3000g for 15 minutes using a 4℃ low-temperature centrifuge, then aliquot the plasma into cryovials and store at -80℃ in an ultra-low temperature refrigerator.

(2) T1 (1 month ±1 week):

Conduct follow-up using PCL-5, HADS, SSRS, CD-RISC, and CFI. The main method is outpatient visit, supplemented by telephone follow-up or electronic

questionnaire link filling according to the patient's actual situation. The assessment method is the same as the baseline period. Patients may optionally undergo a repeat cranial MRI to track the recovery or changes in brain structure and function 1 month after trauma.

(3) T2 (3 months ±2 weeks):

Continue follow-up using the same methods as T1 (outpatient visit as the main method, supplemented by telephone follow-up or electronic questionnaire), and use the same scales for assessment. Patients may optionally undergo a repeat cranial MRI to track the recovery or changes in brain structure and function 3 months after trauma.

(4) T3 (6 months ±2 weeks):

Continue follow-up using the same methods as T1, and use the same scales for assessment. Patients may optionally undergo a repeat cranial MRI to track the recovery or changes in brain structure and function 6 months after trauma.

(5) Follow-up Strategy

Record multiple contact methods (telephone, WeChat, address, etc.) of the patient and at least 1 emergency contact person in detail at enrollment, and establish a follow-up calendar and reminder system.

Adopt flexible follow-up methods such as telephone, electronic questionnaire, and outpatient visit, and provide appropriate transportation/communication subsidies to encourage patient cooperation. Record the reasons for loss to follow-up in detail for dropouts.

IV. Case Selection

1. Inclusion Criteria

(1) Aged 18-65 years (inclusive of boundary values);

(2) Experienced life-threatening major traumatic events, confirmed by clinical diagnosis;

(3) Able to communicate normally with medical staff;

(4) Provided full informed consent and voluntarily signed the Informed Consent Form (ICF).

2. Exclusion Criteria

(1) History of mental illness or current use of psychotropic drugs;

(2) Previous cognitive impairment (e.g., dementia, Alzheimer's disease);

(3) Terminal diseases (e.g., advanced malignant tumors, end-stage organ failure, advanced neurological diseases, or any other diseases with an expected survival time of less than 6 months as judged by the attending physician);

(4) Unable to cooperate with follow-up.

V. Research Methods and Technical Route

(I) Research Methods

(1) Measuring PTSD Incidence

This study targets emergency department trauma patients, focusing on the occurrence of PTSD within 6 months after trauma, and systematically assesses and measures the incidence of PTSD through multiple time points. Trauma survivors are included in the cohort, and the PCL-5 scale is used as the core assessment tool. Follow-up assessments are conducted at three key time points: 1 month (T1), 3 months (T2), and 6 months (T3) after enrollment. Flexible methods such as outpatient visits, telephone follow-up, and electronic questionnaires are used to ensure the completeness of data collection. Statistical analysis is performed to calculate the 6-month cumulative incidence of PTSD and its corresponding 95% confidence interval (95%CI), and the prevalence is calculated separately at T1, T2, and T3 to clearly present the overall level of PTSD incidence and the dynamic changes at different stages in emergency department trauma patients.

(2) Identifying Relevant Influencing Factors of PTSD Occurrence

This study systematically identifies factors associated with the occurrence of PTSD in emergency department trauma patients from four aspects: sociodemographic, trauma-related, physiological biomarkers, and psychosocial factors.

Sociodemographic factors: Collected using a self-designed structured questionnaire, including basic information such as age, gender, occupation, marital status, educational level, and income status.

Trauma-related factors: Obtained based on medical records and researcher assessment, specifically including injury mechanism (traffic accidents, falls, violence, etc.), trauma severity (calculated using the ISS scoring system), time to first effective analgesia (minutes) and morphine equivalent of analgesic drugs (mg), vital signs (heart rate, blood pressure, respiratory rate, blood oxygen saturation), cranial MRI, length of stay in the emergency department (time from admission to discharge, transfer, or leaving the emergency department, reflecting the duration of acute stress exposure), and whether emergency surgery/procedure was performed (e.g., debridement and suture, closed thoracic drainage, laparotomy, etc.).

Physiological biomarkers: Venous blood is collected at baseline (T0, <24 hours) to detect indicators such as white blood cell count, neutrophil count, lymphocyte count, platelet count, lactic acid, blood glucose, serum albumin, serum cortisol, interleukin-6 (IL-6), and C-reactive protein, to reflect the dynamic changes in stress and inflammatory levels. Among them, serum cortisol reflects the immediate stress function of the HPA axis, and blood collection time is crucial—it is recommended to fix it in the early morning (e.g., 6:00-10:00 AM).

Psychosocial factors: Obtained through scale assessment, including the Acute Stress Disorder Scale (ASDS), Social Support Rating Scale (SSRS), Hospital Anxiety and Depression Scale (HADS), Connor-Davidson Resilience Scale (CD-RISC 10), Cognitive Flexibility Inventory (CFI), and PTSD Checklist for DSM-5 (PCL-5).

In statistical analysis, univariate analysis (chi-square test or Fisher's exact test for categorical variables, independent samples t-test or Mann-Whitney U test for continuous variables, etc.) is first used to compare differences in each factor between the PTSD group and the non-PTSD group. Then, variables with statistical or clinical significance are included in a multivariate binary Logistic regression model to screen for independent risk factors for PTSD occurrence.

(3) Exploring the Mediating or Moderating Roles of Various Factors in PTSD Occurrence

On the basis of identifying independent influencing factors, this study will further use Structural Equation Modeling (SEM) to deeply explore the complex mechanism of action of key variables in the pathway of PTSD occurrence.

1) Proposing Hypothetical Models

Based on literature review and theoretical basis, hypothetical models including mediating and moderating effects are constructed.

Mediating Effect Hypotheses:

H1: Trauma severity and time to first effective analgesia positively affect the occurrence of PTSD at 6 months by exacerbating acute stress responses.

H2: Early post-traumatic inflammatory levels and trauma severity positively affect the occurrence of PTSD at 6 months by impairing psychological resilience.

H3a: Early post-traumatic inflammatory levels and trauma-related characteristics positively affect the occurrence of PTSD at 6 months by reducing social support levels.

H4: Trauma severity exacerbates acute stress responses by reducing cognitive flexibility, ultimately positively affecting the occurrence of PTSD at 6 months.

Moderating Effect Hypotheses:

H5: Psychological resilience plays a moderating role between trauma severity and PTSD at 6 months. Specifically, for patients with high psychological resilience, the positive impact of trauma severity on PTSD is weaker.

H6: Social support plays a moderating role between acute stress responses and PTSD at 6 months. Specifically, for patients with high social support levels, the positive impact of acute stress responses on PTSD is weaker.

H7: Time to first effective analgesia plays a moderating role between trauma severity and acute stress responses. Specifically, the shorter the analgesia time, the weaker the positive impact of trauma severity on acute stress responses.

H8: Cognitive flexibility plays a moderating role between trauma-related cues and PTSD symptoms. Specifically, for patients with high cognitive flexibility, the association between trauma exposure and PTSD re-experiencing symptoms is weaker.

2) Variable Definition

Mediating Variables: Mainly include psychosocial variables and physiological variables.

Moderating Variables: Mainly include cognitive flexibility, social support level, etc.

Outcome Variable: Binary variable indicating whether PTSD occurs.

3) Statistical Analysis Steps:

Amos 21.0 software is used to construct a structural equation model of PTSD occurrence to analyze the relationships among observed variables. A model is considered well-fitted if the ratio of chi-square to degrees of freedom, comparative fit index, incremental fit index, and goodness-of-fit index are >0.900, and the root mean square error of approximation is <0.05. The significance level α=0.05. First, centering processing is performed on the continuous variables involved in the model to reduce the impact of multicollinearity.

Through the above analysis, this study aims to reveal the psychosocial and physiological pathways influencing PTSD in emergency department trauma patients, clarify how various factors interact (mediation) and when the effect is stronger or weaker (moderation), thereby providing key theoretical and empirical basis for constructing multi-dimensional and precise early psychological crisis intervention programs.

(IV) Technical Route

1.Preparation Stage: Literature review, protocol finalization, definition of inclusion/exclusion criteria.

2.Enrollment: Consecutive enrollment of 250 eligible patients.

3.Data Collection:

Baseline (T0): Collection of sociodemographic data, trauma clinical characteristics, physiological biomarkers, and psychological scales (ASDS, SSRS, HADS, CD-RISC 10, CFI).

Follow-up Assessments:

T1 (1 month ±1 week): Scales (PCL-5, SSRS, HADS, CD-RISC 10, CFI).

T2 (3 months ±2 weeks): Same scales as T1.

T3 (6 months ±2 weeks): Same scales as T1.

4.Data Collation and Management: Double data entry, logical verification, blind linking of serum data and clinical database.

5.Statistical Analysis:

Descriptive statistics.

Univariate analysis (t-test/U test/chi-square test).

Multivariate analysis (binary Logistic regression).

Structural equation modeling (confirmatory factor analysis, path analysis, mediating effect test).

6.Results and Conclusions: Summary of research findings, conclusion formulation, and paper writing.

VI. Observation Items and Observation Time Points

(I) Observation Items

1. Sociodemographic Factors

Collected using a self-designed structured questionnaire, including basic information such as age, gender, occupation, marital status, educational level, and income status.

(1) General Information Questionnaire

Designed based on extensive literature review and data collection, including age, gender, occupation, marital status, educational level, and income status.

2. Trauma-Related Factors

Obtained based on medical records and researcher assessment, specifically including injury mechanism (traffic accidents, falls, violence, etc.), trauma severity (calculated using the ISS scoring system), time to first effective analgesia (minutes) and morphine equivalent of analgesic drugs (mg), vital signs (heart rate, blood pressure, respiratory rate, blood oxygen saturation), cranial MRI, length of stay in the emergency department (time from admission to discharge, transfer, or leaving the emergency department, reflecting the duration of acute stress exposure), and whether

emergency surgery/procedure was performed (e.g., debridement and suture, closed thoracic drainage, laparotomy, etc.).

(1) Injury Severity Score (ISS)

The ISS score correlates the Abbreviated Injury Scale (AIS) score with patient prognosis. It is calculated as the sum of the squares of the AIS scores of the three most severely injured body regions. The maximum score of this indicator is 75 points: ISS ≥16 and <25 points is defined as severe injury, with a mortality risk of less than 10%; ISS ≥25 and <50 points is defined as critical injury, with a certain mortality risk; ISS ≥50 points is defined as life-threatening injury, with a very low survival probability and the patient is nearly dying.

The Abbreviated Injury Scale (AIS) is a scoring system derived from anatomy and global consensus on severe trauma. The body is divided into 6 regions based on anatomy, and the severity of injury to the corresponding body regions is scored from 1 to 6 points, representing mild injury, moderate injury, moderately severe injury, severe injury, life-threatening critical injury, and untreatable extreme injury, respectively.

3. Physiological Biomarkers

Venous blood is collected at baseline (T0, <24 hours) to detect indicators such as white blood cell count, neutrophil count, lymphocyte count, platelet count, lactic acid, blood glucose, serum albumin, serum cortisol, interleukin-6 (IL-6), and C-reactive protein, to reflect the dynamic changes in stress and inflammatory levels. Among them, serum cortisol reflects the immediate stress function of the HPA axis, and blood collection time is crucial—it is recommended to fix it in the early morning (e.g., 6:00-10:00 AM).

4. Psychosocial Factors

Obtained through the following scale assessments:

(1) PTSD Checklist for DSM-5 (PCL-5): Strictly formulated in accordance with the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) issued by the American Psychiatric Association. This scale is specifically

designed for screening PTSD patients and assessing changes in their symptoms before and after treatment, providing strong reference for diagnostic work [63]. The scale consists of 20 items, covering four core symptom clusters: intrusive re-experiencing symptoms (Criterion B): Items 1-5; avoidance and numbing symptoms (Criterion C): Items 6-7; negative cognitive symptoms (Criterion D): Items 8-14; and hyperarousal symptoms (Criterion E): Items 15-20. Each item is scored on a 5-point Likert scale: "Not at all" (0 points), "A little bit" (1 point), "Moderately" (2 points), "Quite a bit" (3 points), and "Extremely" (4 points). The total score of the scale ranges from 0 to 80 points, calculated by summing the scores of each item. Based on a comprehensive analysis of relevant domestic and foreign literature, a PCL-5 score ≥33 points is set as the positive criterion for screening PTSD symptoms. According to this criterion, the higher an individual's PCL-5 score, the greater the likelihood of PTSD occurrence. The scale has high reliability, with a Cronbach's α coefficient of 0.983, indicating good internal consistency.

(2) Acute Stress Disorder Scale (ASDS): Compiled by Bryant et al., including 4 dimensions: dissociation, re-experiencing, avoidance, and hyperarousal. The total score of the scale is 95 points, with 19 items, each scored from 1 to 5 points (1 point = "Never", 5 points = "Always"). An ASDS score >56 points can be judged as Acute Stress Disorder (ASD).

Acute Stress Disorder (ASD) refers to the immediate mental disorder response of individuals suddenly encountering severe psychological traumatic stress events. If ASD symptoms do not improve within weeks or months, they will eventually develop into Post-Traumatic Stress Disorder.

(3) Social Support Rating Scale (SSRS): The scale includes 3 dimensions: objective support (3 items), subjective support (4 items), and utilization of social support (3 items), totaling 10 items. The total score is the sum of the scores of each item: a total score ≤22 points indicates a low level of social support, 23-44 points indicates a moderate level, and 45-66 points indicates a high level. The Cronbach's α coefficient of the scale is 0.92, and the Cronbach's α coefficient of each item ranges from 0.89 to 0.94, indicating good validity.。

(4) Connor-Davidson Resilience Scale (CD-RISC 10): Compiled by Connor et al., translated into Chinese and revised locally by Yu Xiaonan et al. The scale includes 3

dimensions: tenacity, strength, and optimism, totaling 25 items, each scored from 0 to 4 points, with a total score of 100 points. A higher score indicates better psychological resilience of the individual.

(5) Cognitive Flexibility Inventory (CFI): Compiled by DENNIS et al., translated and revised by domestic scholar Wang Yang et al., used to assess an individual's ability to freely change cognition to cope with different stimuli or environmental changes. The scale includes 2 subscales: Alternatives and Control, totaling 20 items, 6 of which are reverse-scored. A 5-point Likert scale is used, with a total score ranging from 20 to 100 points. A higher score indicates better cognitive flexibility of the subject.

(6) Hospital Anxiety and Depression Scale (HADS): HADS consists of two subscales: HADS-A (Anxiety) and HADS-D (Depression), including 14 items (7 for A, 7 for D). Each item is scored on a 4-point scale (0-3 points) based on the frequency of occurrence in the past month. Thus, the anxiety score ranges from 0 to 21 points, and the same applies to depression. A higher score indicates a greater tendency towards anxiety or depression. The anxiety subscale score is obtained by summing the scores of the 7 items marked A; the depression subscale score is obtained by summing the scores of the 7 items marked D. According to the general scoring criteria of the scale, 0-7 points are normal, 8-10 points are mild, 11-14 points are moderate, and 15-21 points are severe.

(II) Observation Time Points

Baseline: The day of trauma occurrence.

T1: 1 month after trauma.

T2: 3 months after trauma.

T3: 6 months after trauma.。

VII. Statistical Analysis

(1) Data Management

A data management system is used for double data entry with logical verification functions; meanwhile, the linking of serum data and clinical databases is performed blindly by an independent biostatistician to avoid bias during data association.

(2) Statistical Methods

Descriptive statistics will first be used to summarize all study variables. Continuous variables will be expressed as mean ± standard deviation or median (interquartile range), and categorical variables as frequency and percentage. The point prevalence of PTSD at 1 month, 3 months, and 6 months after trauma, as well as the 6-month cumulative incidence and their 95% confidence intervals, will be calculated respectively.

Univariate analysis will be used to screen factors associated with PTSD occurrence: chi-square test or Fisher's exact test for categorical variables, and independent samples t-test or Mann-Whitney U test for continuous variables.

Variables with statistical significance ($P<0.05$) or clinical significance in univariate analysis will be included in a multivariate binary Logistic regression model to identify independent influencing factors of PTSD. Adjusted odds ratios and their 95% confidence intervals will be calculated, and goodness-of-fit and multicollinearity diagnostics will be performed for the model.

Amos 21.0 software will be used to construct a structural equation model of PTSD occurrence to analyze the relationships among observed variables. A model will be considered well-fitted if the ratio of chi-square to degrees of freedom, comparative fit index, incremental fit index, and goodness-of-fit index are >0.900, and the root mean square error of approximation is <0.05. The significance level $\alpha=0.05$.

VIII. Ethics of Clinical Research

9.1 Investigator Responsibilities

Investigators commit to conducting this clinical trial in accordance with this study protocol, Good Clinical Practice (GCP), ICH guidelines, and applicable laws and regulations.

1) Have received training on GCP and this trial protocol, and have the time to conduct the trial in accordance with the study protocol.

2) Provide patients with detailed information about the study before enrollment, obtain their consent, and have them sign the Informed Consent Form (ICF).

3) Investigators are obligated to take necessary measures to ensure patient safety. In case of adverse reactions, investigators shall immediately handle them in accordance with relevant regulations and report to the principal investigator. Follow up on serious adverse reactions.

4) Fill in the study medical records carefully and timely;

5) Actively cooperate with the clinical monitor's regular visits;

6) Retain complete records of laboratory tests, clinical records, and patients' original medical records.

9.2 Ethics Committee or Institutional Review Board

The conduct of this trial complies with GCP, the Declaration of Helsinki, relevant laws and regulations, and the review opinions of the Ethics Committee.

Investigators shall ensure that the trial is reviewed and approved by a qualified Ethics Committee that meets GCP requirements. Before the start of the trial, investigators shall submit the trial protocol, Informed Consent Form (ICF), and other necessary materials to the Ethics Committee for review and approval. Investigators may only provide the investigational product after receiving the approval from the Ethics Committee. At the same time, the Ethics Committee must be informed of any subsequent protocol amendments that may affect the safety of subjects and their continued participation in the trial, as well as serious adverse events occurring during the trial. Investigators are responsible for reporting the progress of the trial to the Ethics Committee. When reviewing and approving the trial protocol, the Ethics Committee must confirm the protocol title, protocol number, and indicate the reviewed protocol documents and review date. During the trial, if there are any new revisions to the trial protocol, Informed Consent Form, etc., written approval from the relevant regulatory authorities must be obtained again in accordance with the law.

9.3 Ethical Conduct of Research and Ethical Approval

This study will be conducted in accordance with GCP and all relevant regulatory requirements, including the current version of the Declaration of Helsinki.

Investigators are responsible for obtaining the Ethics Committee's review and

approval of the study protocol, study center ICF, and any other information provided to potential patients (e.g., advertisements or information supporting or supplementing the ICF). Investigators agree that the Ethics Committee may directly access all relevant documents. The composition of the Ethics Committee must comply with all relevant regulatory requirements. Investigators provide the relevant documents/data required by the Ethics Committee for reviewing and approving the study.

If revisions are made to the study protocol, ICF, or any other information approved by the Ethics Committee for provision to potential patients during the study, investigators are responsible for ensuring the Ethics Committee's approval of these revised documents. Investigators must comply with all relevant regulatory requirements regarding the use of revised ICFs, including obtaining the Ethics Committee's approval of the revised ICF before using the new form to obtain consent from new patients to participate in the study. The Ethics Committee's approval of the written ICF/other information and copies of the approved revised ICF/other information must be sent to the sponsor in a timely manner.

9.4 Informed Consent

The principal investigator of the study center will:

• Ensure that each patient is provided with comprehensive and sufficient oral or written information about the nature, purpose, potential risks, and benefits of the study;

• Ensure that each patient is aware that they may voluntarily withdraw from the study at any time;

• Ensure that each patient has the opportunity to ask questions and is given sufficient time to consider the provided information;

• Ensure that each patient provides a signed and dated ICF before any study-related procedures are performed;

• Ensure that the original signed ICF is kept in the investigator's study files;

• Ensure that a copy of the signed ICF is provided to the patient;

• Ensure that the ICF approved by the Ethics Committee describes any benefits of

participating in the study and the corresponding content of potential harm to the patient from participating in the study.

9.5 Revisions to the Study Protocol and Informed Consent Form

If there are any important changes to the study protocol, these changes must be recorded in the protocol amendment of the latest version of the clinical study protocol (if necessary). The amendment must be approved by the corresponding Ethics Committee before implementation. The latest version of the protocol and any amendments will be distributed by the principal investigator.

If the study protocol amendment requires changes to the center ICF, the investigator and the center Ethics Committee will first approve the ICF amendment before it can be used. If required by local regulatory authorities, any administrative changes shall be reported to and approved by each Ethics Committee.

9.6 Record Retention

Study data shall be retained in accordance with the following requirements:

- Investigators must keep all study data;
- Retention period: 5 years after the end of the trial.

9.7 Confidentiality of Personal Data

The ICF may contain content in line with relevant data protection and privacy rights. In some cases, this content will be recorded in a separate accompanying document.

Investigators and other staff participating in the study shall strictly keep confidential the patient's privacy, treatment, study protocol, study-related documents, and data. Without the investigator's written permission, study information or data shall not be disclosed to any unauthorized third party.

Study monitors, representatives of the Ethics Committee, and regulatory authorities may inspect all documents and records required to be kept by investigators, including but not limited to the medical records (clinic, outpatient, or hospital) and drug records of study patients. The clinical research center will allow the above personnel to access these records.

Each clinical center will strictly keep the contact information of study patients for

internal use during the study. At the end of the study, all records will continue to be kept in a secure location, and the retention period will be determined in accordance with the requirements of the Ethics Committee and the center's system.

9.8 Privacy in Publication

All data and all data generated during the study (excluding patients' medical records) shall be kept confidential. Investigators or other staff of the study center shall not use the data, data, or records for any other purpose except for this study. These restrictions do not apply to:

- Data that has been publicly published not due to the error of the investigator or the study center staff;
- Data that must be disclosed for the purpose of convincing the academic committee or the Ethics Committee to evaluate the study;
- Data that must be disclosed to provide appropriate medical care to patients participating in the study.

IX. Study Progress

September 2025 - December 2025: Research preparation stage, literature review, and protocol finalization.

January 2026 - December 2026: Subject recruitment.

January 2027 - June 2027: Data entry, collation, analysis, and paper writing.

X. Participating Personnel

Name	Title/Specialty	Responsibilities	GCP Training (Yes/No)
Wei Zhao	Associate Chief Physician/Emergency Medicine	Study design and quality control of implementation	Yes
Min Cai	Associate Chief Physician/Psych	Study design and quality control of implementation	Yes

	iatry and Mental Health		
Yaochi Zhang	Research Assistant/Psychiatry and Mental Health	Study design and quality control of implementation	Yes
Yang Li	Graduate Student/Emergency Medicin	Data collection and analysis, paper writing	Yes
Lin Wu	Associate Chief Physician/Emergency Medicine	Enrollment and follow-up	Yes
Qianmei Wang	Assistant Researcher/Emergency Medicine	Enrollment and follow-up	Yes

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