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Research Article

Post-Traumatic Sepsis in an Iranian Polytrauma Cohort: A Prospective Study of Head Injury, Injury Severity, and Central Venous Catheter Use as Independent Predictors in a Resource-Limited Setting

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Abstract

Introduction: Post-traumatic sepsis is a major cause of late mortality and prolonged morbidity following severe trauma. Identifying early clinical factors and potentially modifiable care-related exposures associated with post-traumatic sepsis is important for informing preventive strategies.

Methods: This prospective observational cohort study was conducted at a major teaching hospital. Consecutive adult polytrauma patients (Injury Severity Score [ISS] ≥16) admitted to the intensive care unit were enrolled. The primary outcome was SIRS-defined post-traumatic sepsis, diagnosed >48 hours after admission based on suspected or confirmed infection together with at least two systemic inflammatory response syndrome criteria. Univariate and multivariable logistic regression analyses were done to determine independent predictors.

Results: Out of a total of 197 patients, 21.8% (n=43) developed post-traumatic sepsis. Septic patients had a longer hospital stay (23.9 vs. 9.5 days, p<0.001) as well as the highest mortality (30.2% vs. 6.5%, p<0.001). In multivariable data analysis, three independent predictors were identified which include Head Abbreviated Injury Scale (AIS) (adjusted Odds Ratio [aOR]: 1.10, 95% CI: 1.03 to 1.18), Injury Severity Score (ISS) (aOR: 1.12, 95% CI: 1.04 to 1.20), and implantation of jugular/subclavian central venous catheter (CVC) (aOR: 6.96, 95% CI: 2.39 to 20.27). Predictive models created by employing these variables showed good apparent discrimination for post-traumatic sepsis in the development cohort (AUC: 0.87, 95% CI: 0.80 to 0.94). Survival and TRISS score were identified as significant independent predictors of in-hospital mortality with an adjusted odds ratio of 0.90 (95% CI 0.87-0.94), while transfusion of packed red blood cells had an aOR of 5.85 (95% CI 1.32-25.70).

Conclusion: The severity of head injury, the general grade of injury, and CVC placement are independent determinants of posttraumatic sepsis. Insertion of a jugular or subclavian CVC represents a prominent modifiable risk factor, while early predictive models can help with risk stratification of infection in the ICU.

Keywords: Post-traumatic sepsis; Polytrauma; Central venous catheter; Injury Severity Score; Predictive modeling; Risk factors.

Introduction

Trauma stands as one of the most formidable global health challenges of the modern era, constituting a leading cause of death and long-term disability worldwide, particularly among young adults and individuals under the age of 40[1,2]. It causes a substantial loss of productive life-years and imposes a heavy socioeconomic burden, particularly in low- and middle-income countries where road traffic injuries are

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common[1,2]. While advances in pre-hospital care, damage-control surgery, and trauma systems have significantly increased initial survival rates, the subsequent clinical challenge becomes a prolonged struggle against secondary complications[3,4]. Among these, post-traumatic sepsis is arguably the most devastating, converting a survivable injury into a life-threatening condition that acts as a powerful multiplier of morbidity and mortality[3]. This issue is particularly relevant in Iran, which is currently classified as an upper-middle-income economy by the World Bank[5]. Road-traffic injury remains a major public health burden in the country. A national analysis documented 5,760,835 road-traffic injuries and 472,193 associated deaths between 1997 and 2020, with a mortality rate of 18.4 per 100,000 populations in 2020[6]. Middle-income trauma systems may face shortcomings in their resources for critical care, microbiology, device infection control, and infection control, which may present challenges in the implementation of sepsis-prevention protocols. However, there is a lack of research on the incidence of post-traumatic sepsis and modifiable risk factors for trauma patients in Iranian studies. As defined by the Sepsis-3 definitions, sepsis is caused by a dysregulated host reaction to an infection that leads to organ failure[7]. Nonetheless, using this definition for severely affected patients presents difficulties, since acute organ malfunction can result from the injury itself, hemorrhagic shock, or other medical reasons affecting the person instead of infection[7]. The term "post-traumatic sepsis" is applied in medicine to mean infections that take place after the injury and its urgent treatment, which means that there is a disastrous combination of the harmful injury and any hospital-acquired infections[8,9]. The emergence of this condition changes the process of recovery, increases the time spent in intensive care, leads to higher spending, and raises mortality in the short and long run significantly[9,10]. Various types of immunological damage converge in different clinical scenarios. Serious tissue trauma triggers a huge release of damage-associated molecular patterns (DAMPs) that results in a state of systemic inflammation called systemic inflammatory response syndrome (SIRS), or cytokine storm. This is then often paradoxically followed by a compensatory state that is referred to as compensatory anti-inflammatory response syndrome (CARS), and it leads to immunoparalysis. The biphasic immune deficiency creates a vulnerable period of time: when hyper-inflammation occurs early on, resulting in damage to the organs, and at a later stage, immunoparalysis increases the risk of secondary infections.

For these susceptible individuals, infection may result from or be made worse by other medically needed treatments. Machines such as ventilators, catheters, and central lines can act as a direct route for germs. Other problems associated with medical care, including surgery and blood transfusion, put the body at further risk and increase the chances of developing an infection that is resistant to treatment[13,14]. One of the difficulties in detecting sepsis is that its symptoms resemble the body's normal inflammatory reaction to severe trauma, such as chest pain, unusual white blood counts, and organ failure[15]. Although there have been advancements made over the years, sepsis-related deaths are still quite prevalent. This indicates that non-modifiable risk factors, such as the severity of injuries and how they were sustained, including severe head injuries, still exist because a high level of risk can still be linked to clinical care processes. Important distinctions exist between modifiable factors and those pertaining to processes of care, such as preventing infections from catheters, using sterile procedures, blood transfusion processes, and using antibiotics judiciously. Although there have been advancements made over the years, sepsis-related deaths are still quite prevalent. This indicates that non-modifiable risk factors, such as the severity of injuries and how they were sustained, including severe head injuries, still exist because a high level of risk can still be linked to clinical care processes. Important distinctions exist between modifiable factors and those pertaining to processes of care, such as preventing infections from catheters, using sterile procedures, blood transfusion processes, and using antibiotics judiciously. To this end, we developed an exploratory multivariable predictive model, with a specific focus on evaluating the discriminatory performance of a parsimonious prediction model based on variables available during the early hospitalization period. This data-supported tool aims to provide clinicians with risk stratification capabilities so that intensified preventive measures can be taken before starting a course of treatment for patients at high risk of surviving this disease. This study further generates local evidence specific to an Iranian middle-income setting and attempts to facilitate the adoption of practical infection-prevention protocols in similar trauma centers. In this approach, clinical practice shifts from reactive sepsis management to proactive and evidence-based prevention, thereby reducing the burden on both the

patient and the health care system in terms of costs and quality of life.

Methods

Ethical approval and consent

This prospective observational cohort study was approved by the Ethics Committee and the Thesis Committee of Kerman University of Medical Sciences (Ethics Code: IR.KMU.REC.1396.1211). The study was conducted in accordance with the Declaration of Helsinki. All data were handled anonymously, patient confidentiality was maintained, and records were stored securely. Written informed consent was obtained from all participants or, in cases of incapacitation, from their legally authorized representatives prior to data collection.

Study design and patients

The study was conducted at the emergency department and intensive care units (ICUs) of Bahonar Hospital, a major teaching hospital affiliated with Kerman University of Medical Sciences. All eligible patients presenting with multiple trauma during this period were considered for inclusion (census sampling). Consecutive adult patients (aged ≥16 years) presenting with polytrauma, defined as an Injury Severity Score (ISS) ≥16 and an Emergency Severity Index (ESI) of 1 or 2, were screened for enrollment. To isolate the risk factors specifically related to the trauma and subsequent care, patients with the following conditions were excluded: severe pre-existing comorbidities (end-stage renal disease, severe cardiac failure, severe pulmonary disease, diabetes, decompensated cirrhosis), death within the first 48 hours of admission, transfer from another hospital where primary resuscitation was performed, or leaving against medical advice.

All consecutively admitted patients meeting the inclusion criteria and none of the exclusion criteria were enrolled. A flowchart describing patient screening, inclusion and exclusion criteria, follow-up, and final analysis is shown in Figure 1.

Data collection and baseline assessment

At the time of admission, demographic information (age, sex), injury mechanism, and initial vital signs were logged. The severity of the injuries in terms of anatomy was measured using the Abbreviated Injury Scale (AIS), and the total injury severity was quantified using the Injury Severity Score (ISS). Physiological and predictive scores such as the Revised Trauma Score (RTS) and the probability of survival derived from the Trauma and Injury Severity Score (TRISS) were calculated for everybody.

Biomarkers of inflammation and immunity such as C-reactive protein, procalcitonin, and interleukin-6 were excluded from the data collection protocol and measurement process in this study.

Monitoring was done for interventions identified for events such as the placement of CVCs, transfusion of packed red blood cells in the first 24 hours, surgeries like craniotomy, laparotomy, orthopedic surgery, among others, and the use of prophylactic antibiotics. Available information about CVC insertion sites allowed the classification of catheters into jugular/subclavian combined and femoral ones; however, separate tracking of jugular and subclavian sites was not performed. Data on prophylactic antibiotic administration was registered only in terms of yes/no answers. Information about specific antibiotics or antibiotic classes and duration of prophylaxis was omitted from the data collection protocol. Information on CVC insertion and removal dates, needed for evaluation of catheter dwell time, vasopressor usage, and corticosteroid usage, was also unavailable for analysis. Daily monitoring of clinical and laboratory data was conducted by the attending physician and the research team to detect infections, sepsis, other complications, and to record outcomes (discharge or in-hospital death). All data were entered into a standardized data collection form.

Definitions and Outcome Measures

The main endpoint of the study was post-traumatic sepsis, defined as sepsis that occurs due to trauma or its complications and takes place 48 hours after admission. This criterion was used to provide a clear distinction between late infections, occurring in hospital settings, and early inflammatory responses following the injury.

Post-traumatic sepsis was diagnosed by a board-certified critical care specialist, with confirmation by the researcher, based on the presence of a confirmed or suspected infection plus meeting at least two of the four systemic inflammatory response syndrome (SIRS) criteria: (a) temperature >38°C or <36°C; (b) heart rate >90 beats per minute; (c) respiratory rate >20 breaths per minute or arterial $PaCO_2$ < 32 mmHg; (d) White blood cell count > 12,000/μL or < 4,000/μL, or band forms > 10%.

Sepsis-3 defines sepsis as organ dysfunction that can be linked to an infection, which is shown by an increase of

2 points in the Sequential Organ Failure Assessment score. However, the original prospective study did not have the essential information to derive serial measurements of SOFA, have an appropriate baseline score before the infection, and classify new organ dysfunction as due to infection. Therefore, the process of retrospective classification by Sepsis-3 was regarded as not methodologically valid, and all the analyses were performed on the data on SIRS-defined post-traumatic sepsis.

The data were collected on baseline vital parameters (BP, HR, and RR), shock index, injury severity scores (AIS, ISS), physiologic measures (RTS and TRISS-PS), and major clinical measures, which include the placement of central venous catheters, blood transfusion, surgical interventions, antibiotic prophylaxis, etc.

For prediction-model development, CVC exposure was defined as placement of a central venous catheter within the first 24 hours after hospital admission. Thus, all three predictors were defined using information available during the early hospitalization period.

All-cause mortality during the index hospitalization was recorded as the secondary outcome.

Sample size and statistical analysis

The required sample size was calculated based on an anticipated post-traumatic sepsis incidence of 11.85%, as reported in a cohort of patients with severe trauma[16]. Using the single-population proportion formula with a 95% confidence level and an absolute precision of 5%, the minimum required sample size was calculated as 161 patients. After allowing for approximately 10% incomplete or unusable data, the minimum target sample size was increased to 179 patients. Consecutive census enrollment was used, and 197 eligible patients were ultimately included in the analysis, exceeding the calculated minimum sample size. Among these patients, 43 developed post-traumatic sepsis.

Statistical analysis was conducted using SPSS software (version 23.0, IBM Corp.). Continuous variables were presented as mean ± standard deviation or median (interquartile range), and were compared using an independent Student's t-test or Mann-Whitney U test. The categorical variables were presented as frequencies (percentages) and compared utilizing the Chi-squared or Fisher's exact test.

All variables having a p-value of < 0.05 in univariate analysis were included in multivariate logistic regression to determine independent determinants of post-traumatic sepsis (main outcome) and in-hospital death (secondary outcome). The results have been reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI). The model covariates included anatomical scores (ISS, AIS), physiological scores (RTS), the presence of CVC, blood transfusion, surgical procedures, and other relevant variables.

The discriminatory ability of the final logistic regression models was evaluated by generating receiver operating characteristic (ROC) curves and calculating the area under the curve (AUC). A two-tailed p-value < 0.05 was considered statistically significant.

Results

Study population and overall outcomes

After screening the initial total of 279 patients with multiple trauma, 197 patients qualified for the selection criteria and were subsequently included in the cohort group (Figure 1). The average age of patients was 31 years, with the group being predominantly male (162 patients, 82.2%) compared to female (35 patients, 17.8%). The in-hospital mortality rate was 11.7% (23 patients), with the mortality breakdown comprising 18 men and five women.

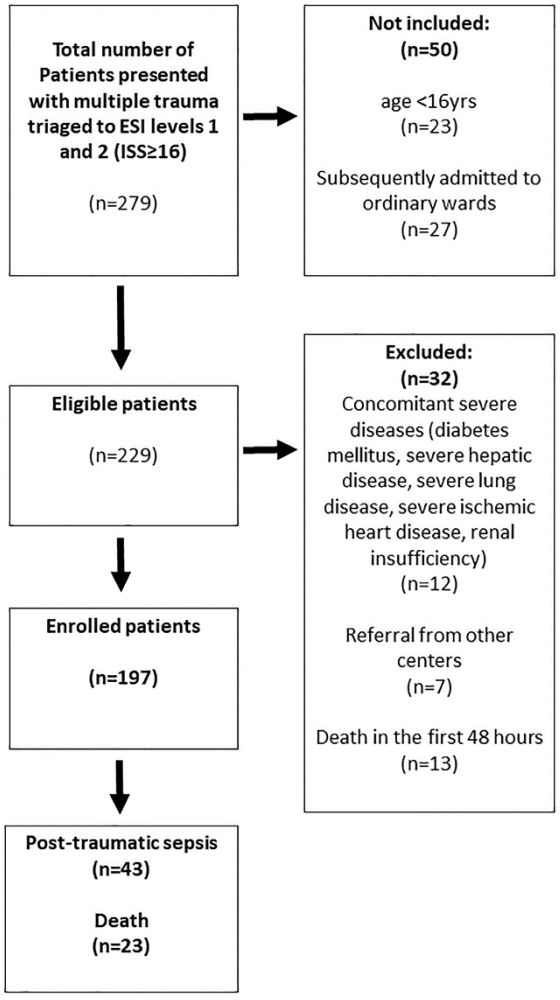


Figure 1. Flow diagram of patient screening, eligibility, enrollment, and study outcomes. A total of 279 patients presenting with multiple trauma, ESI levels 1 or 2, and ISS ≥16 were screened. Fifty patients were not included because they were younger than the prespecified age threshold (n=23) or were subsequently admitted to ordinary wards rather than the ICU (n=27). Among the 229 potentially eligible patients, 32 were excluded because of severe pre-existing disease (n=12), transfer from another center after initial management (n=7), or death within the first 48 hours after admission (n=13). The final cohort comprised 197 patients. During hospitalization, 43 patients developed SIRS-defined post-traumatic sepsis and 23 died. These outcomes were not mutually exclusive; 13 of the 43 patients who developed post-traumatic sepsis died during hospitalization. ESI: Emergency Severity Index, ICU: Intensive Care Unit, ISS: Injury Severity Score, SIRS: Systemic Inflammatory Response Syndrome.

Incidence and timing of post-traumatic sepsis

All sepsis-related results reported below refer to the prespecified SIRS-defined post-traumatic sepsis outcome.

Post-traumatic sepsis was diagnosed in 43 of 197 patients, giving an incidence of 21.8%. Among septic patients, 38 (88.4%) were male, and 5 (11.6%) were female; 13 of the septic patients (30.2%) died during hospitalization. The majority of post-traumatic sepsis cases (31 of 43, 72.1%) were diagnosed within the first four days of admission.

Interventions, supportive care, and microbiology findings

Central venous catheter insertion points were documented as cervical/subclavian in 80 patients (40.6%) of cases, while femoral insertion accounted for just five patients (2.5%). Other than the cervical and subclavian locations, differentiating between the two was not part of this study. Out of the total of 198 patients administered antibiotics, 86 patients (43.7%) received preventive antibiotics; however, the specific agent or class, as well as the duration, were unavailable.

Intubation and ventilatory support were necessary in 99 patients (50.3%). Among this ventilated group, mortality was 19.2% (19 patients), with post-traumatic sepsis at 35.4% (35 patients).

Most patients diagnosed with post-traumatic sepsis had negative microbial cultures. Among positive findings were: 9 had positive blood cultures (20.9%), 2 had positive urine cultures (4.7%), 7 had positive bronchoalveolar lavage (BAL) fluid cultures (16.3%), and 2 had positive cerebrospinal fluid (CSF) cultures (4.7%).

The primary clinical systems identified as the source of sepsis were: respiratory tract in 26 patients; central nervous system in 9; urinary tract in 4; and gastrointestinal tract in 1 patient. Only three patients with positive blood cultures had no identifiable clinical source (Table 1).

Univariate Analysis of Risk Factors

Univariate analysis showed that several continuous variables measured at admission differed significantly between patients who developed post-traumatic sepsis and those who did not. These included head-region AIS, total ISS, RTS, TRISS-based survival probability (PS), Glasgow Coma Scale (GCS), and initial systolic blood pressure (SBP).

For the outcome of mortality, the same factors were significant except for initial SBP, which was replaced by patient age (Table 2).

Urinary catheterization, packed red blood cell transfusion, CVC insertion, and emergency intubation were all significantly associated with the subsequent development of post-traumatic sepsis. For mortality, significant factors were packed red blood cell transfusion and emergency intubation. Neither antibiotic prophylaxis nor surgical procedures showed a significant association with either post-traumatic sepsis or mortality (Table 3). Antibiotic exposure was available only as a binary prophylaxis variable; therefore, associations according to antibiotic agent, class, or duration could not be evaluated. CVC site-specific associations, CVC dwell time, vasopressor use, and systemic corticosteroid use could also not be evaluated because the necessary data were unavailable.

The mean hospital length of stay was significantly longer for septic patients compared to non-septic patients (23.9 vs. 9.5 days, $p < 0.001$). Post-traumatic sepsis was also strongly associated with increased mortality ($p < 0.001$).

Multivariable Logistic Regression Analysis

In logistic regression models, all the variables that were clinically meaningful and had a univariate p-value smaller than 0.05 were included. The independent predictors of post-traumatic sepsis were head AIS, ISS, RTS, Ps, SBP, RespR, GCS, urinary catheter, blood transfusion, CVC, intubation, and craniotomy. Independent predictors of in-hospital mortality included age, head AIS, ISS, RTS, Ps, GCS, blood transfusion, CVC, and intubation (Table 4).

As a result of the multivariable models, the independent predictors for post-traumatic sepsis were Head AIS, ISS, and jugular/subclavian CVC. The independent predictors for in-hospital mortality were blood transfusion and Ps (TRISS).

The Odds Ratios (Table 4) indicated that jugular/subclavian CVC placement was associated with an approximately seven-fold increase in the odds of post-traumatic sepsis (OR = 6.96, 95% CI 2.39–20.27, $p < 0.001$). Furthermore, each unit increase in ISS was associated with an approximately 12% increase in the odds of developing post-traumatic sepsis (OR =1.12, 95% CI 1.04–1.20, $p < 0.001$).

Predictive Performance and ROC Curve Analysis

Receiver Operating Characteristic (ROC) curves were generated to evaluate the discriminative ability of the predictors (Figure 2 for post-traumatic sepsis, Figure 3 for mortality).

For predicting post-traumatic sepsis, the area under the Curve (AUC) was:

- Head AIS: AUC = 0.77 (95% CI 0.68–0.85), with a cut-off point AIS = 3 (sensitivity 95%, specificity 48%),

- ISS: AUC = 0.79 (95% CI 0.70–0.87), cut-off point ISS = 24 (sensitivity 93%, specificity 52%),
- jugular/subclavian CVC Placement: AUC = 0.74 (95% CI 0.65–0.83) (sensitivity 68%, specificity 86%).

The combination of these three variables into a single model yielded an apparent AUC of 0.87 (95% CI 0.80–0.94) for distinguishing patients who developed post-traumatic sepsis from those who did not. This combined model's performance showed statistically significant improvement over jugular/subclavian CVC placement alone (Z-score: 2.5) and head AIS alone (Z-score: 2.0). However, the improvement over the ISS-only model did not reach statistical significance (Z = 1.6).

For in-hospital mortality prediction, ROC analysis revealed:

- TRISS-based survival probability (PS): AUC = 0.83 (95% CI 0.72–0.95), cut-off PS = 66% (sensitivity 97%, specificity 69%),
- Blood Transfusion: AUC = 0.67 (95% CI 0.53–0.82), (sensitivity 46%, specificity 88%).

The combination of these two predictors increased the AUC to 0.89 (95% CI 0.79–0.98). This combined model significantly improved predictive capability compared to blood transfusion alone (Z-score: 2.75), but not compared to Ps (TRISS) alone (Z-score: 0.85).

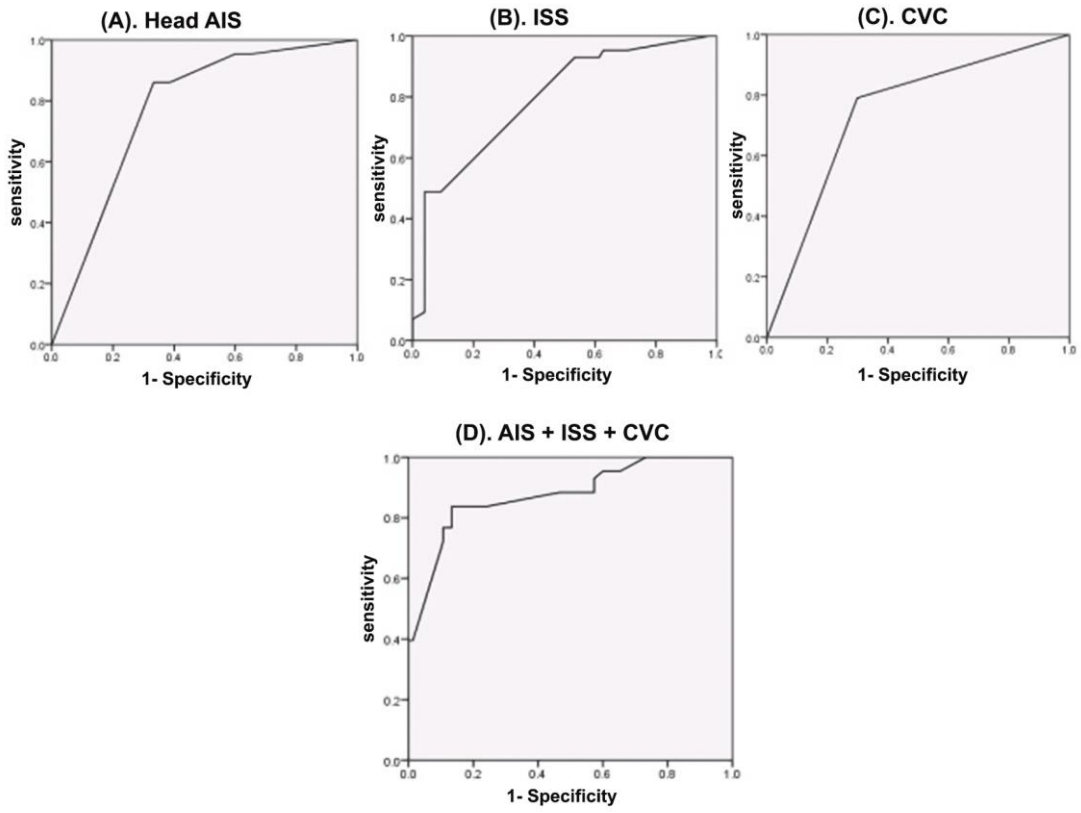


Figure 2. Receiver-operating characteristic curves for prediction of SIRS-defined post-traumatic sepsis in the development cohort. ROC curves were constructed for the 197 enrolled patients, of whom 43 developed SIRS-defined post-traumatic sepsis. Sensitivity is plotted against 1−specificity. (A) Head AIS: AUC 0.77 (95% CI 0.68–0.85); a cutoff value of 3 provided 95% sensitivity and 48% specificity. (B) ISS: AUC 0.79 (95% CI 0.70–0.87); a cutoff value of 24 provided 93% sensitivity and 52% specificity. (C) CVC placement within the first 24 hours: AUC 0.74 (95% CI 0.65–0.83), with 68% sensitivity and 86% specificity. (D) Combined logistic-regression model incorporating head AIS, ISS, and CVC placement: apparent AUC 0.87 (95% CI 0.80–0.94). The combined model demonstrated greater apparent discrimination than CVC placement alone (Z=2.5) and head AIS alone (Z=2.0), whereas its improvement over ISS alone was not statistically significant (Z=1.6). AIS: Abbreviated Injury Scale, AUC: Area Under the Receiver-Operating Characteristic Curve, CI: Confidence Interval, CVC: Central Venous Catheter, ISS: Injury Severity Score, ROC: Receiver-Operating Characteristic, SIRS: Systemic Inflammatory Response Syndrome.

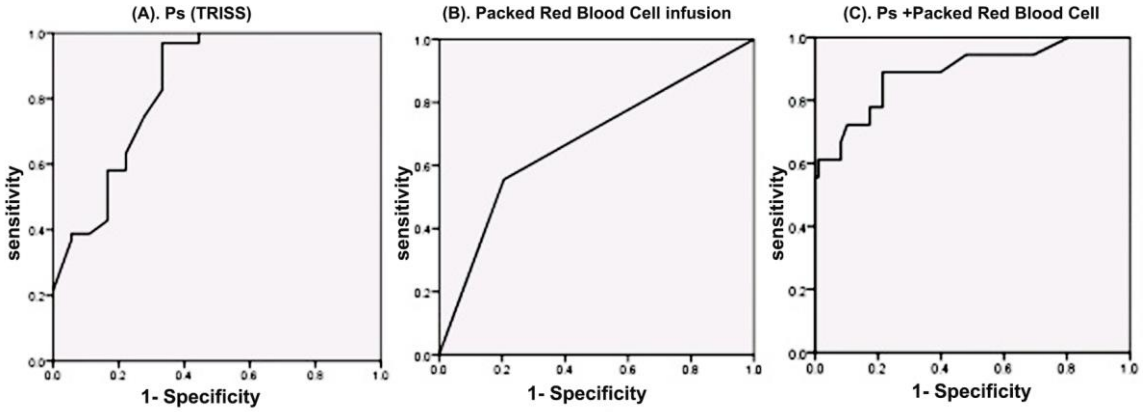


Figure 3. Receiver-operating characteristic curves for prediction of in-hospital mortality in the development cohort. ROC curves were constructed for the 197 enrolled patients, of whom 23 died during the index hospitalization. Sensitivity is plotted against 1−specificity. (A) TRISS-based probability of survival: AUC 0.83 (95% CI 0.72–0.95); a cutoff value of 66% provided 97% sensitivity and 69% specificity. (B) PRBC transfusion within the first 24 hours: AUC 0.67 (95% CI 0.53–0.82), with 46% sensitivity and 88% specificity. (C) Combined logistic-regression model incorporating TRISS-based probability of survival and PRBC transfusion: apparent AUC 0.89 (95% CI 0.79–0.98). The combined model demonstrated greater apparent discrimination than PRBC transfusion alone (Z=2.75), but not than TRISS-based probability of survival alone (Z=0.85). AUC: Area under the Receiver-Operating Characteristic curve, Ps (TRISS): probability of survival by Trauma and Injury Severity Score, PRBC: Packed Red Blood Cells, CI: Confidence Interval.

Table 1. Patient Characteristics and Clinical Data (197 included polytrauma patients)

Quantitative Variables with Non-Normal Distribution	Median (IQR) [min, max]	Quantitative Variables with Normal Distribution	mean ± SD [min, max]	Qualitative Variables	No. (%)
Chest AIS	0 (2) [0,4]	BE (mEq/L)	-5.8 ± 3.9 [–21, 5.6]	Urinary Catheter	149 (75.6)
Abdomen AIS	0 (0) [0,5]	PR (beats/min)	93.9 ± 25 [47, 160]	PRBC Infusion	43 (21.8)
Head AIS	4 (3) [0,5]	Hb (g/dL)	12.2 ± 2.3 [7.3, 18.5]	Jugular/Subclavian CVC	80 (40.6)
ISS	25 (5) [16,66]			Femoral CVC	5 (2.5)
RTS	6.90 (1.88) [4.09,8.30]			Intubation	99 (50.3)
Ps (TRISS) (%)	92.7 (11.0) [10.7,98.9]			Laparotomy	10 (5.1)
SBP (mmHg)	120 (23) [65,180]			Orthopedic Surgery	42 (21.3)
RR	16 (4) [7,29]			Craniotomy	55 (27.9)
GCS	12 (7) [3,15]			Prophylactic Antibiotics	86 (43.7)

Data are presented as counts (%) or as means and SD for parametric variables and medians (IQR) for non-parametric variables. No. represents the number of patients with the specified characteristic. The CVC insertion site was recorded as jugular/subclavian combined or femoral; jugular and subclavian insertion sites were not available separately. Antibiotic exposure represents receipt of prophylactic antibiotics only. AIS: Abbreviated Injury Scale, ISS: Injury Severity Score, RTS: Revised Trauma Score, Ps (TRISS): Probability of Survival by Trauma and Injury Severity Score, SBP: Systolic Blood Pressure, GCS: Glasgow Coma Scale, BE: Base Excess, PR: Pulse Rate, Hb: Hemoglobin, CVC: Central Venous Catheter, PRBC: Packed Red Blood Cells.

Table 2. Univariate analysis of Quantitative variables

Quantitative variables	post-traumatic sepsis		P value	Mortality		P value
	No (154)	Yes (43)		No (174)	Yes (23)	
Age, years, median (Q1–Q3)	31 (22–42)	30 (21–40)	0.60	30 (21–40)	37 (25–50)	0.02
Chest AIS, median (Q1–Q3)	0.0 (0.0–3.0)	0.0 (0.0–3.0)	0.56	0.0 (0.0–3.0)	0.0 (0.0–3.5)	0.31
Abdomen AIS, median (Q1–Q3)	0.0 (0.0–2.0)	0.0 (0.0–0.0)	0.32	0.0 (0.0–2.0)	0.0 (0.0–0.0)	0.26
Head AIS, median (Q1–Q3)	3 (2–5)	5 (4–5)	<0.001	4 (2–5)	5 (4–5)	0.01
ISS, median (Q1–Q3)	24 (21–27)	31 (27–38)	<0.001	25 (21–28)	32 (26–40)	<0.05
RTS, median (Q1–Q3)	7.84 (6.90–7.84)	5.97 (4.09–6.90)	<0.001	6.90 (6.38–7.84)	5.03 (4.09–5.97)	0.001
Ps (TRISS), %, median (Q1–Q3)	94.8 (90.0–97.8)	82.5 (62.0–91.5)	<0.001	94.4 (89.0–97.8)	72.0 (45.0–86.0)	<0.001
SBP, mmHg, median (Q1–Q3)	118 (105–130)	130 (115–140)	0.01	120 (105–130)	125 (105–140)	0.34
RR, breaths/min, median (Q1–Q3)	16 (14–18)	15 (13–18)	0.06	16 (14–18)	17 (14–20)	0.26
GCS, median (Q1–Q3)	13 (9–15)	8 (4–13)	<0.001	13 (9–15)	5 (3–9)	<0.001
BE (mEq/L) [mean ± SD]	−5.6 ± 3.8	−6.1 ± 4.1	0.50	−5.8 ± 3.6	−5.7 ± 5.6	0.74
PR [mean ± SD]	92.3 ± 24.9	96.7 ± 25.7	0.36	93.6 ± 25.5	95.4 ± 24.0	0.78
Hb (g/dL) [mean ± SD]	12.1 ± 2.5	12.3 ± 2.1	0.79	12.2 ± 2.3	12.4 ± 2.4	0.93

Non-normally distributed and ordinal variables are presented as median (Q1–Q3), and normally distributed variables are presented as mean ± standard deviation. Comparisons were performed using the Mann–Whitney U test or independent-samples Student's t-test, as appropriate. P values <0.05 were considered statistically significant. AIS: Abbreviated Injury Scale, ISS: Injury Severity Score, RTS: Revised Trauma Score, Ps (TRISS): probability of survival calculated using the Trauma and Injury Severity Score, SBP: systolic blood pressure, RR: respiratory rate, GCS: Glasgow Coma Scale, BE: base excess, PR: pulse rate, Hb: hemoglobin, Q1: first quartile, Q3: third quartile, SD: standard deviation.

Table 3. Univariate analysis of Qualitative variables

Qualitative variables		post-traumatic sepsis		P value	Mortality		P value
		no	yes		no	yes	
Gender	male	124	38	0.40	144	18	0.47
	female	30	5		30	5	
Urinary catheter	no	46	2	0.002	45	3	0.52
	yes	108	41		129	20	
PRBC infusion	no	130	24	0.001	143	11	0.001
	yes	24	19		31	12	
CVC placement (jugular/subclavian)	no	108	9	<0.001	106	11	0.21
	yes	46	34		68	12	
ED intubation	no	90	8	<0.001	94	4	0.001
	yes	64	35		80	19	
Laparotomy	no	146	41	0.81	161	22	0.97
	yes	8	2		9	1	
Orthopedic surgery	no	122	33	0.75	134	21	0.26
	yes	32	10		40	2	
Craniotomy	no	116	26	0.07	122	16	0.77
	yes	38	17		48	7	
Prophylactic antibiotics	no	88	23	0.69	96	15	0.62
	yes	66	20		78	8	

Comparisons were performed using the Chi-square and Fisher's exact test. P values <0.05 were considered statistically significant. ED intubation: Endotracheal intubation, CVC: Central Venous Catheter, PRBC: Packed Red Blood Cells.

Table 4. Logistic regression model for SIRS-defined post-traumatic sepsis and mortality

Outcome	Predictor	S.E.	P value	OR (95% CI)	Cox & Snell R^2	Nagelkerke R^2
post-traumatic sepsis	Head AIS	0.03	0.002	1.10 (1.03–1.18)	0.40	0.55
	ISS	0.03	<0.001	1.12 (1.04–1.20)		
	Jugular/subclavian CVC placement	0.57	<0.001	6.96 (2.39–20.27)		
Mortality	Ps (TRISS)	0.02	<0.001	0.90 (0.87–0.94)	0.32	0.57
	PRBC infusion	0.75	0.02	5.85 (1.32–25.7)		

Associations were evaluated using univariate logistic regression followed by multivariable logistic regression. The P value reflects the independent association between each predictor and the outcome after adjustment. AIS: Abbreviated Injury Scale, ISS: Injury Severity Score, Ps (TRISS): probability of survival by Trauma and Injury Severity Score, CVC: Central Venous Catheter, PRBC: Packed Red Blood Cells, OR: Odds Ratio, CI: Confidence Interval.

Table 5. Comparison of the present model with selected published models for predicting sepsis after trauma

Study/model	Population and design	Predictors	No. of predictors	Validation method	Reported AUC	Principal comparison with the present model
Present study	Prospective, single-center cohort of 197 adult polytrauma patients with ISS ≥16	Head AIS, ISS, and CVC placement	3	No internal resampling or external validation	Apparent AUC: 0.87 (95% CI 0.80–0.94)	Parsimonious and clinically interpretable, but requires internal and external validation
Traumatic Sepsis Score, Lu et al.[37]	Prospective cohort of 684 trauma patients divided into training and validation cohorts	ISS, GCS, temperature, heart rate, albumin, INR, and CRP	7	Training-validation split	Training: 0.799; validation: 0.790	Requires additional clinical and laboratory variables but was assessed in a separate validation cohort
XGB model, Liu et al.[38]	Retrospective ICU cohorts of patients with traumatic brain injury from the MIMIC-IV and eICU databases	Mechanical ventilation, SAPS II, vasopressor use, blood transfusion at admission, diabetes, and post-stroke sequelae	6	Internal and external validation	Internal: 0.807; external: 0.762	Externally evaluated but restricted to patients with TBI and more computationally complex
LightGBM model, Sun et al.[17]	Multicenter cohort of 961 patients with major trauma	Twelve demographic, physiological, injury-related, and laboratory variables	12	Internal and external validation	Internal: 0.913; external: 0.886	Stronger validation and similar or higher discrimination, but substantially more complex
Logistic-regression model, Fu et al.[8]	Retrospective cohort of 722 trauma patients	Ten clinical, laboratory, injury-related, and hospital-course variables	10	No internal resampling or external validation	Apparent AUROC: 0.998	Higher apparent discrimination but includes downstream hospital-course variables and is susceptible to optimistic performance

AUC values across studies are presented for descriptive comparison only and should not be interpreted as formal evidence of superiority because the studies differed in patient populations, sepsis definitions, predictor-measurement windows, case mix, model-development strategies, and validation methods. AIS: Abbreviated Injury Scale, AUC: Area under the receiver operating characteristic curve, CRP: C-reactive protein, CVC: Central Venous Catheter, GCS: Glasgow Coma Scale, INR: International Normalized Ratio, ISS: Injury Severity Score, SAPS II: Simplified Acute Physiology Score II, TBI: Traumatic Brain Injury, XGB: Extreme Gradient Boosting.

Discussion

Post-traumatic sepsis is regarded as one of the important and therefore preventable causes of post-trauma late death and prolonged critical illness[8]. Over the last few years, while advances made in pre-hospital treatment, damage control resuscitation, and urgent surgical intervention have improved early survival rates, the outcome does not look improved from a long-term perspective. This is of utmost importance to younger people who have the potential to recover completely[3,4,15]. Ever since, the burden has been more significant in low-and middle-income countries (LMICs), where the majority of trauma-related deaths occur. In such conditions, high severity of injury, limited resources, and lack of adherence to infection prevention methods all combined raise the chance of developing post-traumatic sepsis[18]. The nature of post-traumatic sepsis has been described by the Sepsis-3 framework, wherein the sequence of events begins with a hyperinflammatory response followed by an immunosuppressive reaction[19,20].

In this paper, we presented a consecutive prospective observational study that included 197 polytrauma adult cases with an Injury Severity Score (ISS) of at least 16 and an Emergency Severity Index (ESI) level 1 or 2, performed in a hospital specializing in trauma treatment. Cases of post-traumatic sepsis are defined as sepsis initiated in the hospital more than 48 hours after admission that was diagnosed according to SIRS criteria. These were observed in 43 patients. Most patients diagnosed had four days of hospitalization. Severely septic patients had longer ICU and hospital stays, higher mortality (5-fold), and in-hospital mortality was reported to be 30.2%. These findings are broadly consistent with more recent cohorts of patients with severe trauma, in which post-injury sepsis rates of approximately 22%–26% have been reported. However, estimates vary according to patient selection, injury severity, surveillance practices, and the sepsis definition applied[3,8]. The early increase in sepsis diagnosis (72.1% in the first four days of diagnosis) proves the limited time available for therapeutic interventions to take effect and questions the concept of sepsis as a mere late complication. This finding corresponds with studies focused on immune profiling. Studies show that injuries lead to suppression of the myeloid response and to the impairment of immune activity within hours of injury, resulting in increased chances of hospital-acquired infections. Having sepsis after an injury leads to hospitalization for a longer period (23.9 days compared to 9.5 days) and a higher death rate (meaning sepsis acts as a catalyst for fatal outcomes). The finding is consistent with global statistics that determine sepsis as one of the major causes of late deaths in trauma critical care. The most frequent reasons for sepsis were

infections of the respiratory tract, and the high incidence of culture-negative cases highlighted the diagnostic challenges associated with trauma.

Defining Sepsis can be a true challenge in patients who suffer substantial injuries. While Sepsis–3 highlights organ dysfunction related to infectious processes, the applicability of this definition in patients with trauma should be approached cautiously. SOFA score may already show some abnormalities due to inflicted brain injury, thoracic injury, hypovolemic shock, sedation, ventilation, transfusion, and administration of pressors. Hence, making a difference between organ dysfunction as a result of trauma and progressive organ dysfunction due to infection becomes very complicated. On the contrary, SIRS criteria may demonstrate some signs of SIRS in response to injury without any indications of infection-related organ dysfunction. Trauma-specific investigations have demonstrated substantial disagreement among approaches used to classify post-traumatic sepsis. In particular, Sepsis-3 has been shown to identify fewer trauma patients than the older SIRS-based definition while identifying a population more strongly associated with adverse outcomes[7,20,24]. These differences indicate that the incidence, prognostic associations, and predictive performance reported in studies of post-traumatic sepsis may vary according to the definition used and the temporal method by which organ dysfunction is attributed to infection.

In addition, multivariable logistic regression identified three independent predictors of post-traumatic sepsis: the severity of head injury (head AIS), the overall injury burden (ISS), and the placement of a central venous catheter (CVC). This reinforces the complex interplay between the initial first hit of trauma and subsequent second hits from clinical interventions. The identification of head injury severity as an independent predictor corroborates a substantial body of evidence. Severe traumatic brain injury (TBI) induces profound systemic immunodysregulation, often characterized by an early excessive inflammatory response followed by protracted immunosuppression or CNS injury-induced immunodepression. This involves dysregulated autonomic output and neuroendocrine pathways that impair the function of innate and adaptive immune cells[25,26]. The current finding that a Head AIS $\geq$3 provided high sensitivity (95%) for sepsis risk underscores that even moderate-to-severe brain injury should trigger heightened vigilance for infectious complications. Similarly, the overall injury burden, quantified by the ISS, was a strong independent predictor, with each 1-unit increase in the ISS associated with a 12% increase in the odds of sepsis (aOR 1.12). This relationship is biologically plausible, as greater tissue injury may result in greater DAMP release, which enhances the overall inflammatory response and contributes to follow-up trauma-related immune dysfunction and risk of subsequent infections[9,11].

A significant observation was the prominent independent association between the occurrence of CVC and septic shock, with a modified odds ratio of 6.96. However, this association cannot imply a cause-and-effect relationship since CVC may serve as a sign of patients with other risks of infection or various conditions needing intensive treatment. The observation conforms to the findings of earlier registry analyses. For instance, a 2024 study of the Trauma Quality Improvement Program (TQIP) database revealed that the OR for catheter-related bloodstream infection and the subsequent development of septic shock was 5.52[27].

The entry points for the germs that attack there are known as central lines. In the last 30 years of literature about critical care, it has been shown that the danger of contamination increases by 11.5% for each extra day that the catheter is in the bloodstream. The majority of hospital-acquired infections (from central venous catheterization (CVC)) originate from the lines[28,29]. In their multi-center study, Zhong et al. showed that immediate CVC was related to higher mortality rates of individuals on the areas after they had been suspected of having catheter-associated infections[30]. The unusually high odds ratios (OR) in our research may represent the effect that regional factors, how long the catheter was placed, and site insertion may have on the results (31, 32According to the research, TRISS-based survival prediction and early packed red blood cell transfusion were both found to be independent predictors of mortality in the hospital. The findings on the link between transfusion within the first 24 hours and increased mortality confirm numerous recent trauma studies. Transfusion is allowed and vital to saving lives in hemorrhagic shock. Still, it involves immunomodulatory risks due to TRIM, which may result in higher chances of infection and organ failure in some cases. It is striking that both massive transfusion

and emergency surgical procedures did not carry independent associations with sepsis in the last model, even though strong univariate signals were seen. This could reflect the effective application of damage-control resuscitation principles and restrictive transfusion thresholds at the study center; both are part of the global changes, promulgated by trials such as PROPPR and PAMPer. There was no independent association in the final multivariable model of either prophylactic antibiotics or substantive operations-apart from laparotomy or orthopedic surgery-with sepsis. In this way, it suggests that after taking into account the seriousness of injuries and important medical treatments done, their own influence may not be visible enough, implying that their risk is blended with the overall body's condition and that more invasive help is needed.

The model used for making predictions based on the head AIS, ISS, and CVC showed significant discrimination for post-traumatic sepsis in the discovery cohort. The AUC score of the model was 0.87. The model may be beneficial because it was not complicated and the clinical interpretation of the results obtained was straightforward. The model had only three predictors and did not use biomarkers of inflammation, a huge laboratory test, ongoing continuous electronic data extraction, or advanced machine-learning tools. After validation, this model can be used in practice with a regular electronic device, for instance, a calculator or spreadsheet, without the need for other data to be obtained.

Nonetheless, the term simplicity should not be seen as an indication of supremacy over the existing models. Head AIS and ISS need precise injury documentation and personnel experienced in anatomical trauma scoring; CVC status should be available on time. In addition, the model was created and tested in the same single-center cohort, which raises questions about its practicality, calibration, clinical usefulness, and applicability. Several previously published models have evaluated the risk of sepsis after trauma, although their populations, predictors, outcome definitions, and validation approaches differ substantially. Lu et al. developed the seven-variable Traumatic Sepsis Score using ISS, GCS, temperature, heart rate, albumin, international normalized ratio, and C-reactive protein. The model achieved AUCs of 0.799 in the training cohort and 0.790 in the validation cohort[37]. In a TBI-specific machine-learning study, Liu et al. reported that an Extreme Gradient Boosting model based on six clinical variables achieved an AUC of 0.807 during internal validation and 0.762 during external validation[38]. More recently, Sun et al. developed a multicenter artificial-intelligence model for patients with major trauma. Their selected LightGBM model achieved AUCs of 0.913 during internal validation and 0.886 during external validation, although it required a larger set of clinical and laboratory inputs[17]. Fu et al. reported an apparent AUROC of 0.998 for a ten-variable post-traumatic sepsis model; however, that model included variables arising during the subsequent hospital course and did not undergo internal resampling or external validation[8]. The principal characteristics and reported performance of these models are compared with those of the present model in Table 5. The apparent AUC of 0.87 in the present study is numerically higher than the discrimination reported for some conventional trauma-sepsis scores. It lies within the broad range reported for more complex machine-learning models[8,17,37,38]. Nonetheless, these numerical disparities do not indicate superiority because the different models were developed from different populations using different definitions of sepsis, predictor measurement periods, populations, and validation strategies. In addition, since the model was developed and validated in the same population as its design, the AUC of the present model is merely a measure of apparent performance and may be overly optimistic. In this respect, the main significance of the current model is its simplicity, comprehensibility, and ease of evaluation in low-resource environments.

In light of previous statements, these results have a number of clinical implications and support proper assessment of a tiered CVC stewardship pathway in a limited-resource trauma ICU. A risk assessment approach that includes head AIS, ISS, and early CVC placement may be useful in discerning those patients who might be at higher risk for post-traumatic sepsis and thus deserve closer surveillance and preventative measures, once validated on independent populations. Notably, the model should not become a part of clinical use until appropriately validated both internally and externally. Also, the strong association of CVC insertion and post-traumatic sepsis again highlights the need for careful catheter stewardship. The indication for catheter placement should be carefully documented and should also consider whether peripheral or less invasive vascular access would suffice for the anticipated treatment. If central access needs to be obtained, the number of lumens should be kept to the minimum required, femoral access should be avoided in adults

when clinically feasible and taking into account the risks of infection as well as mechanical complications, and the time in place of the catheter should be reduced to a minimum. Strict aseptic insertion techniques and consistent adherence to catheter-insertion and maintenance bundles are essential[29,40,41]. A standardized documentation form should be used to document the date of insertion, insertion site, its indication, the operator, and whether the procedure was performed in an emergency setting or was elective. The procedure for inserting the central venous catheter should be performed by a competent and trained person who complies with the hand hygiene rules, uses maximal sterile barriers, follows the insertion checklist, and cleans the skin using an alcoholic chlorhexidine solution. If chlorhexidine is not available, a suitable iodophor or 70% alcohol can be used, depending on local policies. Trained nurses or staff responsible for infection control should be given responsibility to stop carrying out a non-emergency procedure in case of violation of aseptic techniques. Because trauma resuscitation may require catheter placement under emergency conditions in which full aseptic technique cannot be ensured, such catheters should be clearly identified and replaced as soon as clinically feasible and within 48 hours[31].

A standardized documentation form should be used to document the date of insertion, insertion site, its indication, the operator, and whether the procedure was performed in an emergency setting or was elective. The procedure for inserting the central venous catheter should be performed by a competent and trained person who complies with the hand hygiene rules, makes use of maximal sterile barriers, follows the insertion checklist, and cleans the skin using an alcoholic chlorhexidine solution. If chlorhexidine is not available, a suitable iodophor or 70% alcohol can be used, depending on local policies. Trained nurses or staff responsible for infection control should be given the responsibility to stop carrying out a non-emergency procedure in case of a violation of aseptic techniques.

In resource-constrained hospitals, implementation could initially focus on low-cost, high-priority measures, including standardized indications, competency-based staff training, preassembled insertion kits, bedside checklists, daily assessment of catheter necessity, prompt removal of unnecessary lines, and regular audit and feedback. Relevant performance indicators include the CVC-utilization ratio, total catheter-days, compliance with insertion and maintenance bundles, and CLABSI incidence per 1,000 catheter-days. Evidence from intensive-care hospitals in the low-and middle-income economies indicates that these multimodal programs combining standard practices, education, supervision, and performance feedback may put in place the long-awaited reductions in CLABSI rates[42,43]. The use of more expensive techniques like antimicrobial catheters, dressings that have chlorhexidine incorporated into them, port protectors that are antiseptic, specialized vascular access groups, and improved electronic monitoring may only be considered after the implementation of the complete set of measures is successful. Even after all this has been done, rates of infection are still above the limits imposed by local standards[31]. It was impossible to conduct a formal analysis of cost-effectiveness because the study did not prospectively collect the catheter-implementation-specific costs, full catheter-day data, CLABSI-attributable expenditures, health-related quality-of-life outcomes, or costs associated with additional ICU and hospital days.

Qualitative evaluation shows that the basic stewardship methods, such as identification documentation, hand hygiene, maximum sterile barrier precautions, checklist application, review of necessity on a daily basis, disinfecting the hub, and removing the catheter in due course, would not cost much more in resources. These expenditures may be offset by the decrease in microbiological investigations, broad-spectrum antibiotic consumption, catheter exchanges, bloodstream infection treatment, and increased length of ICU and hospital stay. Antiseptic barrier caps might contribute to reduction of CLABSI and therefore cut costs connected with infections. Still, previously published estimates vary a great deal, thus making them unsuitable for today's Iranian trauma context due to different processes and costs involved, such as the initial rate of infection, costs of equipment, staff, and other factors. In that case, the tiered system may be the best option, wherein one applies cheap primary practices and saves expensive technologies only for units with high infection rates, even with adherence to the bundle applied.

Future implementation studies should compare usual care with a tiered CVC-stewardship program from the hospital perspective. These types of research must account for the expenses associated with training and delivery, staff hours, CVC usage and catheter-days; adherence to bundles, terminations for CLABSI and post-trauma sepsis, consumption of antibacterial agents, replacement of the catheter, and the lengths of hospital stay and ICU stay. As the current study is observational, it cannot conclude that the placement of CVC has caused post-trauma sepsis or that the suggested pathway could be called an evidence-based approach, providing the possibility for implementing a trial for its efficacy, feasibility, safety, and cost-effectiveness assessment. For in-hospital mortality, the combination of TRISS-based probability of survival and blood-transfusion history demonstrated good apparent discrimination in the development cohort, with an AUC of 0.89. This model may have prognostic value, but it also requires internal and external validation before clinical application.

Strengths and limitations

Some notable strengths of the study are its design and the use of consecutive patients combined with the simultaneous assessment of the anatomical injury severity score (ISS), the physiological status, and the potentially modifiable exposures related to the treatment. In spite of that, it has some weaknesses that should be taken into account.

To start with, this was a pilot single-center study with a very small sample size of just 43 patients with post-traumatic sepsis. The small number of events compromised the accuracy of the estimates, did not allow for assessment of rare combinations, and increased the chances of the overfitting effect. The significance of this matter is related to the necessity of those predictors to be chosen based on a priori statistical significance in each variable separately. In addition, the model that contains three variables was developed and validated in the same cohort without implementing any internal bootstrapping, cross-validation, or external validation. The fact that the AUC does not show the real predictive power of the model in different cohorts, since it only demonstrates the so-called apparent discrimination degree, is well known. The paper also evaluates the model's calibration and clinical utility as a result.

The reported associations should not be viewed as causal. While CVC placement was strongly associated with post-traumatic sepsis, an indication of confounding by indication may exist. Patients whose medical conditions necessitated greater attention may, therefore, have undergone CVC placement and ended up developing infections in turn. The adjustment for head AIS and ISS may not have fully controlled for differences in physiological derangements, intensity of care, or other unmeasured factors against other confounders.

Detailed catheter-related characteristics—including separate jugular and subclavian insertion sites, emergency or elective insertion circumstances, number of insertion attempts, insertion and removal dates, dwell time, maintenance practices, and confirmed catheter-related bloodstream infection—were not comprehensively available for analysis. Available insertion-site information was limited to jugular/subclavian combined or femoral placement. Other potentially important treatment-related variables were also unavailable. Antibiotic exposure was recorded only as receipt or nonreceipt of prophylaxis, without information regarding antibiotic type, class, indication, timing, or duration. Vasopressor use and systemic corticosteroid administration were not included in the original prospective data-collection protocol. Therefore, the independent associations of these treatment- and catheter-related variables with post-traumatic sepsis could not be evaluated, and residual confounding remains possible. The placement of a central venous catheter must serve as an early indicator of potential risk; however, it is not to be considered a certain factor in the sepsis pathogenesis.

Furthermore, despite this model consisting of only three routinely used predictors, the practical applicability of the model in resource-limited settings has not been investigated. Proper calculation of head AIS and ISS requires full documentation of injuries as well as trained healthcare workers. In addition, the value of CVC status relies on the availability of this factor at the time of prediction.

Third, post-traumatic sepsis was defined using suspected or confirmed infection together with SIRS criteria rather than the contemporary Sepsis-3 definition. SIRS has limited specificity after severe trauma because tissue injury, hemorrhage, surgery, transfusion, mechanical ventilation, and other interventions can produce inflammatory and physiological abnormalities without infection-associated organ dysfunction. The SIRS-based

definition may therefore have overestimated the incidence of post-traumatic sepsis and influenced the observed relationships between injury severity and the outcome, as well as the apparent performance of the prediction model.

On the other hand, it should be noted that retrospective use of Sepsis-3 was considered to be methodologically flawed. In the trauma group of patients, SOFA-inferred organ dysfunction could be induced by damage to the brain, injuries to the chest cavity, hemorrhagic shock, sedation, mechanical ventilation, vasopressor administration, blood transfusion, or any surgical intervention rather than infection. There were no complete serial SOFA assessments, precise pre-infection baseline, or time attribution of organ dysfunction to infection. For this reason, the numerical frequency of the phenomena, its predictors, and performance indicators should be regarded as typical for SIRS-defined post-traumatic sepsis. It cannot be easily compared to the outcomes of the research using Sepsis-3.

Also, it should be mentioned that inflammatory and immune system biomarkers like C-reactive protein, procalcitonin, and interleukin-6 have not been collected prospectively at the defined times, so it was impossible to gather independent prognostic value of the biomarkers in addition to the standard prognosis provided by doctors.

The need to exclude subjects with certain relevant pre-existing illnesses and those dying within a day and a half reduces the generalizability to the general population of polytrauma patients, besides having the potential to lead to survivor-selection bias. Furthermore, a rather high sepsis incidence rate compared to some studies based on registries might be a consequence of a high injury load of this cohort, in addition to daily pre-planned monitoring of patients, utilization of the SIRS definition, and healthcare-related specifics of this study.

All of these drawbacks lead to various ways in which subsequent studies might be carried out. It is of primary importance that multicenter studies are carried out in a forward-looking direction and among a variety of trauma patients to confirm that the predictive model based on 3 factors that uses Sepsis-3 criteria is reliable. It is particularly important to use fixed, regular measurements of inflammatory and immune markers, which are CRP, procalcitonin, and interleukin-6. Finally, it is crucial to conduct studies aimed at finding out how the CVC management process impacts the reduction of sepsis. Ultimately, integrating these clinical predictive models and biomarker data with emerging real-time artificial intelligence tools could further refine early identification of at-risk patients and facilitate timely preventive interventions.

Conclusion

The methodical examination presented in this article shows that severity of brain injury, level of trauma experienced, and subclavian/jugular vein catheterization are separate predictors of the development of post-injury sepsis. Results demonstrate a strong association between the use of this technique and its potential as one of the risk factors during therapy.

Having incorporated head AIS, ISS, and CVC placement, a model demonstrated a good discriminatory power in the cohort of patients undergoing the same treatment. A small number of predictors, lack of specific biomarker requirements, and a clear clinical interpretation of the results make it possible to consider the approach as a potentially viable risk stratification approach under conditions of limited resources. However, it does not demonstrate superiority over the existing models.

Abbreviations

AIS: Abbreviated Injury Scale, AUC: Area Under the Receiver Operating Characteristic Curve, BAL: Bronchoalveolar Lavage, CARS: Compensatory Anti-inflammatory Response Syndrome, CI: Confidence Interval, CLABSI: Catheter-Associated Bloodstream Infection, CNS: Central Nervous System, CSF: Cerebrospinal Fluid, CVC: Central Venous Catheter, DAMP: Damage-Associated Molecular Pattern, ED: Emergency Department, ESI: Emergency Severity Index, GCS: Glasgow Coma Scale, ICU: Intensive Care Unit, ISS: Injury Severity Score, IQR: Interquartile Range, LMIC: Low- and Middle-Income Country, OR: Odds Ratio, PICC: Peripherally Inserted Central Catheter, PRBC: Packed Red Blood Cells, Ps (TRISS): probability of survival by Trauma and Injury Severity Score, ROC: Receiver Operating Characteristic, RR: Respiratory Rate, RTS: Revised Trauma Score, SBP:

Systolic Blood Pressure, SIRS: Systemic Inflammatory Response Syndrome, SOFA: Sequential Organ Failure Assessment, SSC: Surviving Sepsis Campaign, TBI: Traumatic Brain Injury, TRIM: Transfusion-Related Immunomodulation, TRISS: Trauma and Injury Severity Score, TQIP: Trauma Quality Improvement Program.

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Conflicts of interest

The authors have no relevant financial or non-financial interests to disclose. All authors have approved the final version of the manuscript.

Availability of data and material

Data are available upon reasonable request from the corresponding authors, Dr Batool Heidari Sadegh

Ethics approval

The present study was approved by the Ethics Committee of Kerman University of Medical Sciences (Ethics code: IR.KMU.REC.1396.1211). All participants signed a consent form before enrolling in the study.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Consent for publication was obtained.

Declaration of Generative AI and AI-assisted technologies

The authors did not use any generative AI or AI-assisted technologies in the preparation of work.

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