

Association Between Early Plasma Transfusion Burden and Mortality and Infection-Associated Organ Dysfunction in Severe Trauma Patients: A Single-Center Retrospective Exploratory Study

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Abstract

Background

Early identification of hospital-acquired sepsis and mortality after severe trauma remains a major clinical challenge. During the hyperacute phase, however, organ dysfunction is driven primarily by the initial injury rather than by infection. For this reason, the present study used infection-associated organ dysfunction as an endpoint, rather than relying on conventional sepsis definitions. Although blood transfusion is known to be associated with adverse outcomes, transfusion burden and the Injury Severity Score (ISS) are strongly collinear; their independent contributions to mortality and subsequent infection-associated organ dysfunction are unclear. This preliminary analysis is based on a single-center severe trauma cohort from an island region.

Methods

This retrospective study enrolled severe trauma patients admitted to the Trauma Center of Zhoushan Hospital from January to December 2025. A total of 100 patients were included. Binary logistic regression models were constructed to preliminarily observe the association of 24-hour plasma transfusion volume and ISS with 30-day in-hospital mortality and infection-associated organ dysfunction within 10 days of admission. It should be noted that the study population consisted of trauma patients with ISS ≥ 16 who were admitted to the intensive care unit (ICU)/intermediate care unit and required tracheal intubation or invasive hemostatic procedures, representing a high-risk subgroup; thus, the conclusions should not be directly generalized to all patients with ISS ≥ 16 .

Results

In this cohort, 13 patients died and 20 developed infection-associated organ dysfunction. Exploratory bivariate regression analysis showed that, when both variables were included, 24-hour plasma transfusion volume was associated with an increased risk of 30-day mortality (OR = 1.318, 95% CI 1.014–1.713, $P = 0.039$). In contrast, neither 24-hour plasma volume nor ISS showed statistical significance in the model for infection-associated organ dysfunction (ISS: OR = 1.031, 95% CI 0.942–1.129, $P = 0.507$; 24-hour plasma: OR = 1.001, 95% CI 1.000–1.002, $P = 0.202$). Given the limited number of events, the models have insufficient statistical power, and these results should not be interpreted as definitive independent effects.

Conclusions

This single-center, small-sample exploratory analysis suggests a possible preliminary association between early plasma transfusion volume and 30-day mortality risk in severe trauma patients after minimal adjustment for ISS. However, an independent association between transfusion burden or injury severity and infection-associated organ dysfunction within 10 days was not detected. These findings are limited by sample size and require validation through larger-scale prospective studies.

1. Introduction

Although trauma systems and standardized resuscitation protocols have considerably improved overall outcomes for patients with severe trauma, hospital-acquired sepsis remains a frequent complication and is strongly associated with prolonged hospital stays, increased mortality, and higher healthcare costs [1–3]. Approximately one-quarter of hospitalized trauma patients reportedly develop sepsis, and the attributable medical expenditure may even exceed the cost of the initial trauma care [3]. Early identification of patients at high risk for post-traumatic sepsis and timely implementation of standardized interventions are therefore crucial for improving in-hospital outcomes.

Compared with other hospitalized populations, trauma patients tend to be younger and have fewer comorbidities, and their sepsis incidence and clinical outcomes may differ accordingly [4, 5]. Despite advances in damage control resuscitation and surgical techniques, blood transfusion remains an indispensable component of the management of severe trauma patients with hemorrhagic shock [6]. Yet transfusion has been linked to adverse outcomes such as acute respiratory distress syndrome [7], multiple organ failure [8], sepsis, and death [9]. Although the underlying mechanisms are not fully understood, allogeneic transfusion-induced immunosuppression and inflammatory cascades are thought to play a role [10].

Sepsis is a highly heterogeneous syndrome marked by both an early excessive pro-inflammatory response and subsequent persistent immunosuppression [11]. Some studies have found that transfusion may further aggravate immunosuppression in critically ill patients and increase the incidence of infection and mortality risk; in severe trauma, certain evidence suggests this effect may even be independent of injury severity [12].

Two interrelated methodological challenges complicate research in the early phase of severe trauma. First, multiple organ dysfunction occurring within 24–72 hours after injury is largely driven by the trauma itself—such as tissue hypoperfusion due to hemorrhagic shock, central respiratory and circulatory disturbances from traumatic brain injury, or direct organ contusion/laceration—whose pathophysiologic processes are independent of infection. Rigid application of the Sepsis-3 criteria, which rely on acute changes in the SOFA score, may easily misclassify trauma-related organ function fluctuations as infection-driven sepsis. Second, patients who receive larger transfusion volumes typically have more severe anatomical injuries and more profound hemorrhagic shock, resulting in a high degree of collinearity between transfusion volume and injury severity. This makes it difficult to separate the effects of transfusion per se from those of injury severity. Accordingly, this study did not adopt the standard sepsis definition as the primary endpoint; instead, we constructed an “infection-associated organ dysfunction” determination scheme based on dynamic changes in a modified SOFA score combined with evidence of infection, aiming to identify infection-driven organ damage more robustly under retrospective data conditions. Because of the limited number of

events, only minimal adjustment for injury severity could be achieved by including ISS in the model, allowing a preliminary examination of the association patterns of transfusion burden and injury severity with mortality and infection-associated organ dysfunction. The model results should be regarded as exploratory hints rather than as adequate confounder adjustment.

This study is not intended to challenge the conclusions of existing large registry studies; rather, it is a small-scale exploratory analysis based on consecutive severe trauma cases admitted to our center, providing preliminary clues for future larger-sample studies at our institution.

2. Materials and Methods

2.1 Study Population

This was a retrospective, single-center exploratory analysis conducted at Zhoushan Hospital of Zhejiang Province. The study period covered the full year of 2025. As a minimal-risk retrospective case analysis, the study was approved by the institutional ethics committee, and the requirement for informed consent was waived.

Inclusion criteria:

Trauma caused by external force, confirmed by the emergency department or trauma surgery;

Age ≥ 16 years;

Injury Severity Score (ISS) ≥ 16 ;

Initial admission to the ICU or emergency intermediate care unit;

Received tracheal intubation and mechanical ventilation after admission, or underwent invasive hemostatic procedures in the emergency operating room/angiography suite.

Exclusion criteria: (1) age < 16 years; (2) foreign nationals and pregnant/postpartum women; (3) admitted to general wards without ICU/EICU admission; (4) not formally admitted or prehospital death; (5) after ICU admission, neither tracheal intubation nor emergency surgery/angiography intervention was performed. Foreign nationals and pregnant/postpartum women were excluded because of very small numbers at our center and incomplete key information, to avoid the influence of extreme values on analysis stability; these exclusions were not based on clinical outcome considerations. The screening process is shown in Fig. 1.

2.2 Outcome Definitions

Infection-associated organ dysfunction: Due to the high proportion of severe traumatic brain injury in this single-center small-sample retrospective study, and to avoid bias from inconsistent GCS recording times, we did not directly apply the complete Sepsis-3 criteria. Instead, a composite determination scheme based on “dynamic changes in modified SOFA score + evidence of infection” was adopted.

Modified SOFA score calculation: The GCS component was removed, retaining only the respiratory, coagulation, hepatic, cardiovascular, and renal dimensions, yielding a total score ranging from 0 to 20. The patient's first emergency laboratory results at admission were used as the individualized baseline, and the daily worst values during hospitalization (up to 10 days) were collected to calculate the daily modified SOFA score.

▣ Infection evidence: Required simultaneous fulfillment of: (1) high clinical suspicion of new-onset infection; (2) initiation of therapeutic intravenous anti-infective agents; (3) completion of microbial culture sampling from the corresponding site within 24 hours before medication administration.

▣ Determination of infection-associated organ dysfunction: Defined when, on any subsequent day, the modified SOFA score increased by ≥ 2 points compared with baseline and this state persisted for at least 3 consecutive days. The dual requirement of “ ≥ 2 points increase + 3-day persistence” was intended to differentiate infection-driven sustained organ injury from transient non-infectious fluctuations in the early post-traumatic period.

▣ Handling of early death/discharge cases: Patients who died or were discharged within 24 hours of admission were, in principle, not classified as having infection-associated events and were assigned to the no-event group in the analysis of infection-associated organ dysfunction. For those who died or were discharged between 24 and 72 hours, two intensive care physicians independently reviewed the cases, and disagreements were resolved by a third senior physician, to exploratorily determine whether infection-associated organ dysfunction had occurred.

Mortality outcome: In-hospital death within 30 days of admission.

2.3 Blood Transfusion Definitions

Given the practical constraints of our island blood supply, platelet transfusion was not routinely available in the early phase for trauma patients at our center; therefore, only red blood cell (RBC) and plasma transfusions were recorded. For all included trauma patients, the volumes of RBC (units) and plasma (mL) transfused within 24 hours of admission were extracted.

2.4 Clinical Data Collection

The following data were collected from the electronic medical record system: sex, age, initial vital signs at admission (systolic blood pressure, heart rate, respiratory rate), Abbreviated Injury Scale (AIS) scores by body region, ISS, GCS, length of ICU stay, duration of tracheal intubation, total length of hospital stay, 24-hour transfusion-related variables (RBC, plasma), and initial emergency blood results: neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), fibrinogen, total bilirubin, albumin, creatinine, and CK-MB. In addition, the modified SOFA scores for the day of emergency visit and for the 10 consecutive days after admission were collected. If a patient was discharged or died within 10 days, data collection was automatically truncated.

2.5 Statistical Analysis

SPSS 27.0 was used for data analysis. Continuous variables, mostly not normally distributed according to the Shapiro-Wilk test, are presented as median (interquartile range) and compared between groups using the Mann-Whitney U test. Categorical variables are described as numbers (percentages) and compared using the chi-square test or Fisher's exact test (when expected frequencies were < 5). The overall proportion of missing variables was less than 5%, and individual missing values were imputed using the median.

Because there were only 13 deaths and 20 cases of infection-associated organ dysfunction, the number of positive events was small. To limit overfitting risk, following the events per variable (EPV) principle, only two core variables—ISS and 24-hour plasma transfusion volume—were selected to construct exploratory binary logistic regression models; no additional covariates were included. The model results are intended only as suggestive reference and do not represent fully confounder-adjusted independent effects.

3. Results

A total of 100 severe trauma patients were ultimately included in the analysis. Among them, 13 patients (13.0%) died within 30 days in the hospital, and 20 patients (20.0%) developed infection-associated organ dysfunction within 10 days of admission. Baseline characteristics are shown in Table 1.

Table 1
Baseline characteristics, emergency blood tests, clinical outcomes by groups.

variable	Total (n = 100)	Death (n = 13)	Survival (n = 87)	P	Infection-OD (n = 20)	No event (n = 67)
Gender, male, n(%)	74(74.0%)	10(76.9%)	64(73.6%)	0.798	15(75.0%)	59(73.8%)
Age, years	59(50,69)	63(60,68)	58(50,69)	0.117	60(53,65)	58(47,69)
Admission SBP, mmHg	137(108,159)	121(101,170)	138(114,159)	0.668	128(94,159)	138(115,161)
Admission HR, bpm, median	87(76,109)	111(86,138)	86(75,99)	0.005	97(82,119)	84(75,97)
Admission RR, breaths/min	18(18,19)	18(12,19)	18(18,19)	0.571	18(17,19)	18(18,19)
ISS total score,	20(17,25)	25(16,27)	20(17,24)	0.019	25(18,29)	18(17,22)
GCS total score	10(3,15)	3(3,5)	14(5,15)	0.001	8(3,15)	15(5,15)
AIS-Head/Neck	3(0,4)	4(3,4)	3(0,4)	0.049	4(2,4)	3(0,4)
AIS-Face, median	0(0,0)	0(0,0)	0(0,0)	0.723	0(0,0)	0(0,0)
AIS-Chest/Thoracic spine/Diaphragm	2(0,3)	3(0,3)	2(0,3)	0.363	2(0,3)	2(0,3)
AIS-Abdomen/Pelvis/Lumbar spine	0(0,3)	0(0,2.5)	2(0,3)	0.299	1(0,3)	0(0,3)
AIS-Extremities/Pelvis/Buttock	0(0,2)	0(0,3.5)	0(0,2)	0.673	2(0,3)	0(0,2)
AIS-External/Other	0(0,0)	0(0,0)	0(0,0)	0.499	0(0,0)	0(0,0)
Injury mechanism, n(%)						
Traffic accident	57(57.0%)	12(92.3%)	45(51.7%)		14(70.0%)	43(53.8%)
Fall from height	26(26.0%)	0	26(29.9%)		2(10.0%)	24(30.0%)
Other blunt trauma	17(17.0%)	1(7.7%)	16(18.4%)		4(20.0%)	13(16.3%)
24h RBC transfusion, U	2.00(0,3.38)	7.00(2.25,9.50)	2.00(0,3.00)	0.001	2.50(2.00,4.63)	1.75(0,3.00)
24h Plasma transfusion, mL	415.00(0,757.50)	1050.00(460.00,1320.00)	390.00(0,530.00)	< 0.001	665.00(415.00,1065.00)	360.00(0,490.00)
Emergency blood tests						
NLR	3.35(1.42,8.95)	1.22(0.96,2.23)	3.95(1.86,9.21)	0.001	2.59(1.22,5.54)	3.61(1.61,9.57)
PLR	73.92(42.68,134.44)	40.29(28.93,71.69)	75.90(47.41,143.09)	0.002	42.26(32.94,86.49)	75.29(53.00,107.60)
Lactate,mmol/L	2.90(1.80,4.80)	6.50(4.35,7.75)	2.70(1.60,4.20)	< 0.001	4.05(2.75,4.78)	2.70(1.60,5.00)
Fibrinogen,g/L	1.81(1.15,2.33)	0.85(0.49,1.57)	1.87(1.39,2.43)	< 0.001	1.64(0.91,2.05)	1.82(1.22,2.50)
Total bilirubin, µmol/L,	9.40(6.78,13.48)	7.60(5.20,10.85)	9.70(7.40,13.90)	0.055	9.00(7.83,12.73)	9.50(6.53,13.47)
Albumin, g/L	42.75(37.83,45.80)	41.00(31.35,44.20)	43.50(38.10,46.10)	0.046	42.05(37.95,44.93)	42.80(37.73,47.87)
Creatinine, µmol/L	79.35(64.88,103.70)	89.90(75.90,116.00)	78.70(64.20,100.50)	0.109	78.15(72.48,97.65)	80.30(64.65,95.95)
CK-MB, ng/mL	6.74(3.69,15.48)	15.97(7.35,38.26)	5.86(3.64,13.02)	0.002	10.12(5.49,16.86)	5.94(3.63,15.48)
Clinical outcomes						
ICU LOS, days	3.51(1.42,8.67)	4.69(1.48,13.43)	3.56(1.47,8.65)	0.333	8.67(3.71,13.11)	2.81(1.34,6.44)
Mechanical ventilation, hours	61.0(10.5,182.8)	115.0(36.0,323.0)	62.0(10.0,170.0)	0.727	189.0(95.0,297.8)	39.5(8.3,122.0)
Hospital LOS, days	15.57(5.36,25.64)	4.69(1.48,13.50)	17.25(8.87,26.13)	0.003	14.59(7.99,28.58)	16.80(9.55,24.05)

Gender: male was used as the reference category.

Compared with the survival group, the death group had a higher admission heart rate, higher ISS, lower GCS, larger volumes of RBC and plasma transfused within 24 hours, and statistically significant differences in lactate and fibrinogen levels. Notably, the death group exhibited lower NLR and PLR—a pattern that is atypical in the hyperacute phase of severe trauma. This may be attributable to early blood sampling time, fluid dilution, and insufficient leukocyte

mobilization. These findings suggest that single-time-point laboratory indices are sensitive to sampling time windows, and future larger studies should emphasize standardization of blood sampling timing.

When comparing the infection-associated organ dysfunction group with the no-event group, statistically significant differences were observed in 24-hour plasma transfusion volume and PLR. Most other baseline variables did not show clear statistical differences. The median duration of tracheal intubation in the infection-associated group was 189.0 hours, which was significantly longer than the 39.5 hours in the control group ($P < 0.001$), indicating that mechanical ventilation duration is a critical confounder that must be controlled for in subsequent large-sample analyses.

Univariate logistic regression analysis (Table 2) identified candidate variables associated with mortality, including ISS, heart rate, transfusion volumes, lactate, and CK-MB. In the infection model, 24-hour plasma transfusion volume showed statistical significance in univariate analysis ($P = 0.047$), whereas ISS did not reach significance ($P = 0.094$). Given the limited number of events (13 deaths, 20 infections), to avoid overfitting, only the two core variables—ISS and 24-hour plasma transfusion volume—were jointly entered into the multivariate binary logistic regression models; other variables with suggestive significance in univariate analysis (e.g., PLR) were not included due to EPV constraints.

Table 2
Univariate logistic regression analysis for mortality and infection-associated organ dysfunction.

Variable	Mortality OR (95% CI) P			Infection-OD OR (95% CI) P		
	OR	95%CI	P	OR	95%CI	P
Gender (male vs female)	1.198	(0.303,4.740)	0.797	1.068	(0.346,3.299)	0.909
Age (per year)	1.040	(0.992,1.089)	0.102	1.011	(0.975,1.047)	0.579
Admission SBP (per mmHg)	0.998	(0.975,1.020)	0.832	0.994	(0.980,1.009)	0.466
Admission HR (per bpm)	1.039	(1.012,1.067)	0.004	1.013	(0.993,1.034)	0.192
Admission RR (per breath/min)	0.860	(0.685,1.081)	0.196	1.002	(0.912,1.101)	0.969
ISS (per point)	1.134	(1.040,1.236)	0.004	1.065	(0.989,1.147)	0.094
GCS (per point)	0.816	(0.705,0.946)	0.007	0.945	(0.860,1.038)	0.237
24h RBC (per U)	1.279	(1.096,1.494)	0.002	1.051	(0.937,1.179)	0.397
24h Plasma (per unit*)	1.430	(1.146,1.785)	0.002	1.001	(1.000,1.002)	0.047
NLR	0.737	(0.554,0.981)	0.036	0.920	(0.826,1.024)	0.127
PLR	0.971	(0.948,0.996)	0.022	0.987	(0.975,0.999)	0.031
Lactate (per mmol/L)	1.359	(1.115,1.656)	0.002	1.018	(0.884,1.172)	0.803
Fibrinogen (per g/L)	0.096	(0.027,0.344)	< 0.001	0.732	(0.390,1.373)	0.331
Total bilirubin (per $\mu\text{mol/L}$)	0.853	(0.722,1.009)	0.063	0.979	(0.900,1.065)	0.618
Albumin (per g/L)	0.915	(0.847,0.988)	0.023	0.981	(0.916,1.052)	0.594
Creatinine (per $\mu\text{mol/L}$)	1.007	(0.990,1.025)	0.412	0.999	(0.982,1.015)	0.889
CK-MB (per ng/mL)	1.035	(1.007,1.064)	0.014	0.995	(0.965,1.027)	0.758

Gender: male was used as the reference category.

The results of the multivariate models are presented in Table 3. In the mortality outcome model, 24-hour plasma transfusion volume was associated with an increased risk of death (OR = 1.318, 95% CI 1.014–1.713, $P = 0.039$), while ISS did not reach statistical significance (OR = 1.067, $P = 0.230$). In the infection-associated organ dysfunction model, neither ISS (OR = 1.031, $P = 0.507$) nor 24-hour plasma transfusion volume (OR = 1.001, $P = 0.202$) showed statistical significance. It must be emphasized that the above P values are susceptible to fluctuations from individual extreme values in small samples and cannot be directly interpreted as strong causal evidence.

Table 3
Multivariate logistic regression analysis for mortality and infection-associated organ dysfunction.

Variable	Mortality OR (95% CI) P			Infection-OD OR (95% CI) P		
	OR	95%CI	P	OR	95%CI	P
24h Plasma	1.318	(1.014,1.713)	0.039	1.001	(1.000,1.002)	0.202
ISS total score	1.067	(0.960,1.187)	0.230	1.031	(0.942,1.129)	0.507

4. Discussion

This study, as a single-center, small-sample exploratory analysis, should not be viewed as definitive evidence but rather interpreted cautiously within the context of the following limitations.

First, the primary limitation is the small sample size. Only 13 deaths and 20 cases of infection-associated organ dysfunction were recorded. According to the EPV principle proposed by Peduzzi et al. based on Monte Carlo simulations, when $EPV < 10$, logistic regression coefficients exhibit substantial bias, confidence interval coverage markedly deteriorates, and even directional errors in associations can occur [13]. In our study, the mortality model had an EPV of 6.5 (13 events/2 variables), and the infection model had an EPV of 10 (20 events/2 variables). The former falls below the empirical threshold; therefore, the multivariate analysis results must be viewed with extreme caution and should be strictly regarded as exploratory hypothesis generation, awaiting verification by larger studies.

Furthermore, in addition to an $ISS \geq 16$, the inclusion criteria required ICU/intermediate care unit admission and tracheal intubation or emergency invasive hemostatic procedures. This cohort is thus not a full-spectrum representation of severe trauma patients with $ISS \geq 16$, but rather a highly selected subgroup with more severe conditions requiring higher-level life support or hemostatic intervention. This selectivity limits the generalizability of the study conclusions to mild-to-moderate trauma patients or severe trauma patients who did not meet these intervention requirements.

Second, the outcome definition did not employ the standard Sepsis-3 definition. The 2016 Sepsis-3 international consensus defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection, with an operational criterion of an increase in the SOFA score of ≥ 2 points from baseline [14]. Due to inherent limitations of retrospective data, this study adopted a modified outcome determination scheme (see Methods). Although this compromise was practically reasonable given data availability, it inevitably weakens the comparability and external validity of the results with studies using standard definitions. Future prospective studies should employ the standardized Sepsis-3 definition to ensure reproducibility and consistency.

Third, this study did not adequately address the competing risk of mortality. Patients with larger transfusion volumes and extremely injuries may die early, thereby losing the opportunity to develop hospital-acquired infection—death as a competing event renders the infection endpoint unobservable. Among patients with septic shock, approximately 32% of deaths occur within 3 days of ICU admission [15], primarily due to irreversible multiple organ failure caused by the original infection; only patients surviving beyond this early window are at risk for ICU-acquired infections [16, 17]. Ignoring this competing risk can lead to an overestimation of infection incidence by up to 52% [18].

Fourth, confounding by indication is an inherent bias in retrospective transfusion studies that is difficult to eliminate [19]. Blood transfusion is not randomly assigned but is driven by clinical indications such as injury severity, hemodynamic status, hemoglobin level, and coagulation function [19], making the baseline characteristics of transfused and non-transfused groups non-interchangeable. Even when statistical adjustment methods such as propensity score matching are applied, they can only address measured confounders and cannot eliminate unmeasured or residual confounding. Existing large-sample evidence and systematic reviews have fully demonstrated the ubiquity and severity of this issue [19]. This small-sample study cannot effectively correct for such bias and does not attempt to draw causal conclusions; instead, it presents the observed associations between transfusion and clinical outcomes as descriptive observations, to serve as a reference for future more rigorously designed studies. In addition, the multivariate model in this study included ISS as the sole variable reflecting injury severity, without further distinguishing the contributions of individual AIS scores or depth of shock. Thus, the model essentially represents a “minimal ISS adjustment model” and is far from achieving adequate control for injury severity. These limitations further support the judgment in the abstract that these results should not be interpreted as deterministic effects of transfusion independent of injury severity.

Despite these limitations, we observed a noteworthy trend: in this limited sample, the association between early large-volume transfusion and mortality risk reached statistical significance in the minimal adjustment model [14, 20], whereas it did not reach significance in the infection-associated organ dysfunction model. This suggests that, in this cohort, early transfusion volume may reflect the severity of lethal pathological processes such as hemorrhagic shock and trauma-induced coagulopathy [21, 22]; late post-injury infection, on the other hand, may be more closely related to factors such as anatomical disruption of tissue barriers and prolonged invasive ventilation [23]. However, it must be emphasized that this difference cannot be directly interpreted as “transfusion primarily drives mortality while ISS primarily drives infection.” Given the small sample of only 13 deaths with wide confidence intervals, the confidence intervals of the regression coefficients for the two variables overlap, and the difference in P-values itself does not provide statistical comparability. A more prudent interpretation is that early transfusion volume may be numerically associated with mortality risk, but whether this association is independent of injury severity requires further differentiation and verification in larger samples.

Notably, the death group had significantly lower fibrinogen levels ($P < 0.001$) and significantly higher lactate levels ($P < 0.001$), which corroborate, at the laboratory level, the high incidence of trauma-induced coagulopathy (TIC) and tissue hypoperfusion in the death group. Acute traumatic coagulopathy occurs immediately after severe trauma, involving protein C activation, endothelial glycocalyx disruption, fibrinogen depletion, and platelet dysfunction; hypothermia and acidosis further exacerbate this process [24]. The rate of massive transfusion in TIC patients can reach 50%, significantly higher than in those without

coagulopathy [25]; early supplementation with fibrinogen concentrate is associated with improved in-hospital survival [26]. The laboratory characteristics of the death group in this study are consistent with this understanding, suggesting that massively transfused patients in this cohort may have been in a more severe decompensated state. However, limited by sample size, it is difficult to further differentiate the independent contributions of transfusion per se and injury severity.

Regarding the relationship between transfusion and post-traumatic sepsis, the existing literature remains controversial. Large database studies have reported a dose-response relationship between transfusion volume and infection risk: a retrospective study involving over 1.89 million surgical patients showed that perioperative red blood cell transfusion was significantly associated with increased postoperative wound infection risk (OR = 2.24), with a clear dose-dependent pattern, the OR reaching 3.65 when > 8 units were transfused [27]; a Japanese nationwide trauma registry study (n = 55,807) similarly confirmed that as RBC transfusion volume increased from none to low (1–4 units), moderate (5–9 units), and high (≥ 10 units), the incidence of in-hospital infection gradually rose from 9.1% to 26.8% [12].

However, other researchers have pointed out that after adequate adjustment for confounders such as injury severity, the volume of specific blood components is not an independent risk factor for nosocomial infection. A prospective multicenter ICU cohort study found that the association between RBC transfusion and nosocomial infection disappeared after multivariate adjustment, and only platelet transfusion remained an independent predictor of infection after adjustment for other blood products [28]. In penetrating trauma populations, after adjusting for ISS, Revised Trauma Score, and GCS, transfusion was also not an independent predictor of nosocomial infection [29]. These findings suggest that the observed association between transfusion and nosocomial infection may be largely driven by confounding factors such as injury severity and severity of critical illness, rather than by an independent pathogenic effect of blood products.

The numerical direction of our small-sample results is consistent with the above-mentioned studies that negate an independent transfusion effect, but this pattern should not be interpreted as supporting a “no-effect” conclusion. A more reasonable explanation is that, in the early phase of severe trauma (24–72 hours), the innate immune storm triggered by injury severity may completely overwhelm the additional immunomodulatory effects of transfusion [30]. Transfusion-related immunomodulation (TRIM) encompasses a wide range of effects from immunosuppression to pro-inflammatory activation, involving interactions between donor leukocytes, extracellular vesicles, bioactive lipids, and storage-damaged products with the host immune system; stored red blood cells can mediate immunosuppression via macrophages [31]. However, in healthy surgical patients, RBC transfusion alone did not trigger a significant immune response [32], suggesting that the clinical effects of TRIM may only become apparent in specific pathological contexts. In other words, even if a promoting effect of transfusion on sepsis exists, it is likely a weak effect that can only be detected in populations with well-matched injury severity and sufficiently long survival. Clearly, the sample size and number of events in this study are far from sufficient to detect such weak effects.

At the level of clinical practice, the results of this study are insufficient to alter current trauma transfusion strategies. Current damage control resuscitation (DCR) emphasizes hemostatic resuscitation as the core, employing balanced ratios (1:1:1 for RBC: fresh frozen plasma: platelets) for timely and adequate transfusion during uncontrolled active hemorrhage [33–35], and improving outcomes by restricting crystalloid infusion, allowing permissive hypotension, and using tranexamic acid [24, 34]. Whole blood transfusion has shown potential in both military and civilian trauma practice to reduce overall blood product usage and improve early mortality [36]. The value of this exploratory analysis lies in suggesting directions for future research: in larger cohorts with adequate matching for injury severity, delayed infection should be analyzed as a separate endpoint, and early deaths must be distinguished from patients who survive beyond 72 hours and are exposed to infection risk (i.e., using competing risk models), to more authentically assess the role of transfusion in the pathway of post-traumatic infection development.

5. Conclusions

This single-center, small-sample exploratory analysis suggests that, after minimal adjustment for ISS, there is a numerical association (reaching statistical significance in the exploratory model) between early plasma transfusion volume and 30-day mortality risk in severe trauma patients. However, we did not observe an independent association between transfusion burden or injury severity and infection-associated organ dysfunction within 10 days post-injury in this sample. It must be particularly emphasized that, with only 13 deaths, the stability of the statistical significance is limited, and “one variable having $P < 0.05$ while another has $P > 0.05$ ” does not equate to a significant difference in effect size between the two variables. In summary, this model is only a minimal ISS adjustment model, with limited event numbers and insufficient statistical power; the above results should not be interpreted as definitive evidence of a transfusion effect independent of injury severity. They represent exploratory, hypothesis-generating findings that urgently require validation by large-sample, multicenter prospective studies.

Declarations

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Conflict of Interest:

The authors declare that they have no financial or non-financial competing interests related to this study.

Ethical Statements:

This retrospective study was approved by the Institutional Review Board of Zhoushan Hospital of Zhejiang Province. The requirement for informed consent was waived due to the retrospective nature of the study. All procedures were conducted in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments.

Informed Consent:

Not applicable due to the retrospective design and waiver of consent.

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Author Contribution

Z.L. and Y.S. conceived and designed the study. Z.L., J.W., and Z.W. collected the clinical data. Z.L. performed statistical analysis and prepared Figure 1, Table 1, Table 2, and Table 3. Z.L. drafted the manuscript. Y.S. supervised the study and contributed to interpretation of the results. All authors (Z.L., J.W., Z.W., Y.S.) critically revised the manuscript for important intellectual content, approved the final version to be published, and agree to be accountable for all aspects of the work.

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Figures

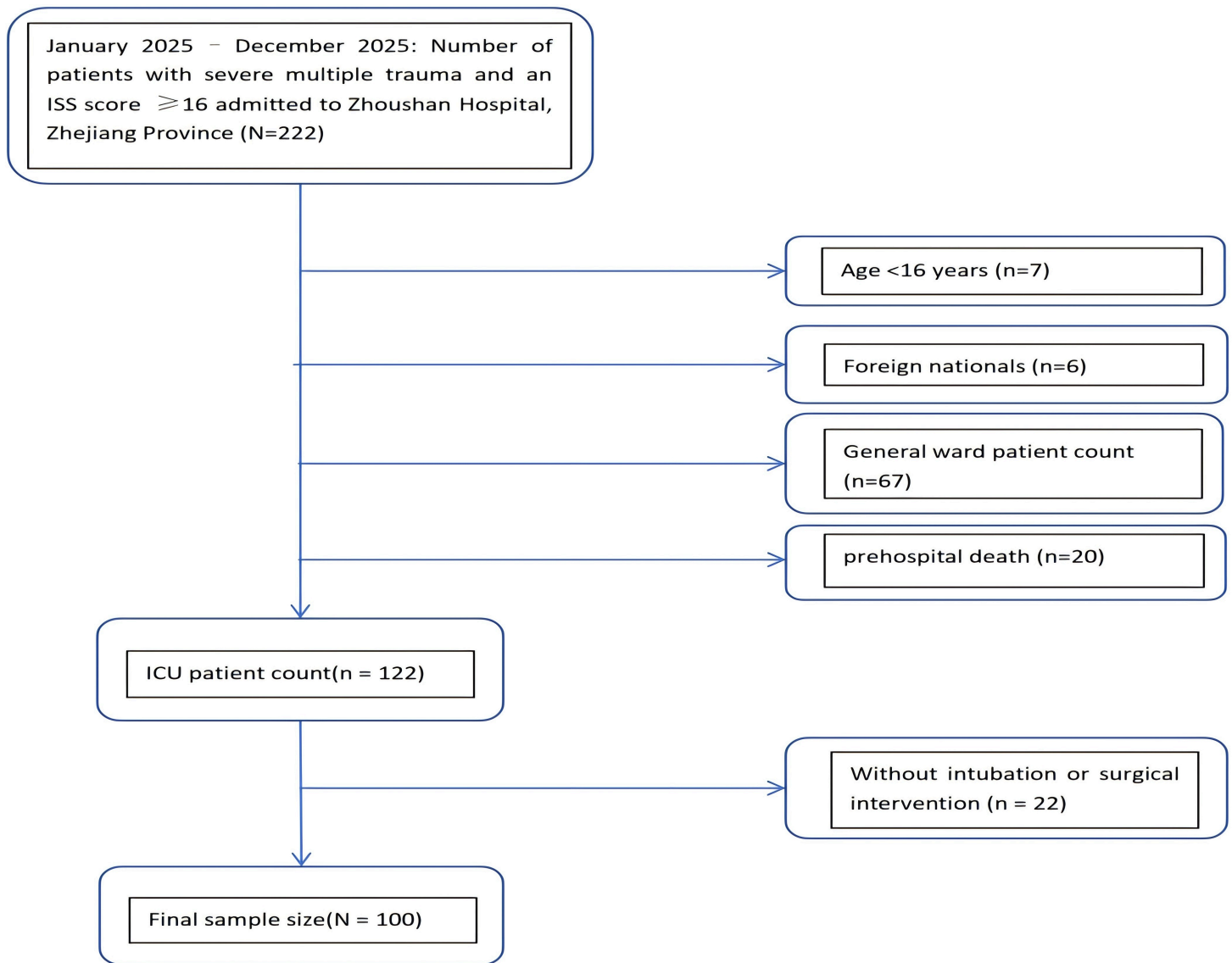


Figure 1

Patient screening flow diagram