Infection Complications After Trauma Contribute to Increased in-Hospital Mortality in Mild Patients Compared With Severe Patients: A Retrospective Cohort Study Using a Nationwide Trauma Registry in Japan

Akira Komori
Juntendo University Hospital https://orcid.org/0000-0001-8548-3707
Hiroki Iriyama
Juntendo Daigaku
Takako Kainoh
Juntendo Daigaku
Makoto Aoki
Gunma University: Gunma Daigaku
Toshio Naito
Juntendo Daigaku
Toshikazu Abe (abetoshi111@gmail.com)
University of Tsukuba https://orcid.org/0000-0002-8343-5151

Research

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Abstract

Background: Infection is a very common but poor prognostic complication affecting trauma patients. However, the impact of infection on the prognosis of trauma patients according to severity remains unclear. We aimed to assess the impact of infection complications on in-hospital mortality among patients with trauma according to severity.

Methods: This retrospective cohort study used a nationwide registry of trauma patients (Japan Trauma Data Bank). Patients aged ≥ 18 years with blunt or penetrating trauma who were admitted to intensive care units or general wards between 2004 and 2017 were included. We compared the baseline characteristics and outcomes between patients with and without infection and conducted a multivariable logistic regression analysis to investigate the impact of infection on in-hospital mortality according to trauma severity, which was classified as mild [Injury Severity Score (ISS) < 15], moderate (ISS 15–29), or severe (ISS ≥ 30).

Results: Among the 150,948 patients in this study, 10,172 (6.7%) developed infections. The severity of trauma was greater in patients with infection than those without [mild, 3,837 (37.7%) vs. 84,106 (59.7%); moderate, 4,518 (44.4%) vs. 47,809 (34.0%); severe, 1,817 (17.9%) vs. 8,861 (6.3%), $p < 0.01$]. Patients with infection had greater in-hospital mortality than patients without infection [1,079 (10.6%) vs. 2,904 (2.1%), $p < 0.01$]. After adjusting for clinical characteristics, in-hospital mortality differed significantly between trauma patients with and without infection according to trauma severity [16.7% (95% CI; 14.6%–18.8%) vs. 3.6% (95% CI; 3.3%–3.9%), $p < 0.01$, in patients with mild trauma; 12.3% (95% CI; 11.0%–13.6%) vs. 7.3% (95% CI; 6.9%–7.7%), $p < 0.01$, in patients with moderate trauma; and 12.0% (95% CI; 9.8%–14.2%) vs. 11.1% (95% CI; 9.8%–12.4%), $p = 0.41$, in patients with severe trauma].

Conclusion: The effect of infection complications in patients with trauma on in-hospital mortality differs by trauma severity.

Background

Infection after trauma, including sepsis, is the most common complication affecting trauma patients; unfortunately, it has a poor prognosis. However, some infections may be preventable or recognized early because infections are typically acquired during hospitalization after the onset of trauma [1]. Therefore, complication rates and the failure to rescue including infection are considered indicators of the quality of trauma care [2].

Previous studies have reported that the overall mortality from trauma has gradually decreased in western countries [3] and in Japan [4]. Additionally, many studies have shown the improvement in outcomes for patients with sepsis following the development subsequent revision of definitions, guidelines, and bundles [5, 6, 7, 8]. Conversely, only limited information is available on the development of infection and sepsis in patients with trauma [1], likely because the definition of sepsis continues to change [9]. Patients with trauma often arrive with organ dysfunction, which adds complexity and inaccuracy to applying the definition of sepsis using organ failure scores such as sequential organ failure assessment scores [10]. It is difficult to determine whether severity scores and organ damage are caused by trauma or the subsequent infection. Furthermore, few studies have assessed the impact of infection and its prognosis among trauma patients. Prognosis among trauma patients complicated with infection may be influenced by trauma severity.

Therefore, we aimed to assess the impact of infection complications on in-hospital mortality among patients with trauma according to trauma severity using a national database in Japan.

Methods

Study design and data source

This retrospective cohort study used the Japan Trauma Data Bank (JTDB) database from 2004 and 2017. The JTDB was established in 2003 and is authorized and maintained by the Japanese Association for the Surgery of Trauma and the Japanese Association for Acute Medicine to improve and assure the quality of trauma care in Japan. A total of 272 hospitals, including more than 95% of the certified tertiary emergency medical centers in Japan, contributed to the JTDB in March 2018 [11].

Data collection

The JTDB includes data related to patient and hospital information such as patient demographics, Abbreviated Injury Scale scores, Injury Severity Score (ISS), prehospital and in-hospital procedures, complications, and treatment and emergency procedures including transfusion within 24 h. The JTDB also records outcome data such as emergency department (ED) mortality, in-hospital mortality, and length of hospital stay. Data collection was performed as a part of routine clinical patient management.

Study participants

Patients aged ≥ 18 years with blunt or penetrating trauma who were admitted to the intensive care unit or a general ward were enrolled in this study. We excluded patients who died < 7 days after admission, similar to previous reports [12, 13], to exclude the effects of first trauma impact on in-hospital mortality and because infection usually occurred approximately seven days after trauma [14]. We also excluded patients who met the following criteria: missing data on sex and ISS, an Abbreviated Injury Scale score of 6 (i.e., non-survivable injury), inconceivable vital signs in the ED (e.g., systolic blood pressure ≤ 40 mmHg), hospital stay for ≥ 1 year or missing, or missing data on in-hospital death.

Definitions

Infection and sepsis were clinically diagnosed by a physician in charge. Sepsis was identified a composite variable, “sepsis/multiple organ failure”, in the JTDB database. This definition is similar to the definition of severe sepsis in the Sepsis-2 criteria [15]. We divided trauma severity into three groups based on the ISS to reflect the clinically relevant categories, similar to previous reports [1, 16]: ISS < 15 (mild), ISS 15–29 (moderate), and ISS ≥ 30 (severe). Types of infections included pneumonia, urinary tract infection, surgical site infection, myelitis, meningitis, abdominal abscess, enterocolitis, empyema, and bacteremia. The definition of a complication was in accordance with the JTDB. All emergency procedures were operated as part of the resuscitation or initial management at the ED.

Statistical analysis

Continuous variables were presented as the median and interquartile range and were compared using the Mann–Whitney U test because none of the variables were normally distributed. Categorical variables were presented as numbers and percentages and compared using the Chi-square test. We compared the baseline characteristics such as age, sex, site of injury, comorbidities, emergency procedures, concomitant complications, and outcomes between the patients with and without infection.

We performed a multivariable logistic regression analysis to investigate the influence of infection on in-hospital mortality for trauma patients. The adjusted variables included age, sex, vital signs on arrival at ED (Glasgow coma scale, heart rate, systolic blood pressure, and respiratory rate), injury sites, number of comorbidities, transfusion, emergency procedures, admission disposition, any operations, and concomitant complications; these variables were chosen based on previous reports and clinical relevance [1, 16, 17, 18]. We assessed the multicollinearity of variables using the variance inflation factor, and the tolerance value was set at less than 2. We then used marginal standardization based on probability determined from the previous analysis to estimate the adjusted in-hospital mortality rate according to trauma severity. The results were reported as adjusted in-hospital mortality rates with 95% confidence intervals (CIs).

All p values were two-sided, with $p < 0.05$ considered statistically significant. The data were statistically analyzed using Stata software, version 15.1 (StataCorp, College Station, TX, USA).

Results

Of the 294,274 patients in the JTDB from 2004 to 2017, 227,462 adult patients with blunt or penetrating trauma who were admitted to the intensive care unit or a general ward were identified. After eliminating those who met the exclusion criteria, the remaining 150,948 patients were included in this study (Fig. 1).

Of those patients, 10,172 (6.7%) with infection were identified. A total of 1,130 (11.1%) patients had sepsis. The demographic characteristics among the patients with and without infection are shown in Table 1. Patients with infection were older than those without [71 (53–82) vs. 67 (47–80) years, $p < 0.01$]. Patients with infection had more comorbidities [6,806 (66.9%) vs. 80,565 (57.2%), $p < 0.01$, see Additional file 1]. Patients with infection received more emergency procedures [5,233 (51.4%) vs. 38,954 (27.7%), $p < 0.01$] and transfusions [3,100 (31.0%) vs. 19,139 (13.9%), $p < 0.01$] than those without infection. The use of steroids or immunosuppressants did not differ between the patients with or without infection [48 (0.5%) vs. 532 (0.4%), $p = 0.14$, and 18 (0.2%) vs. 204 (0.1%), $p = 0.42$, respectively]. The severity of trauma was greater in patients with infection than those without [mild, 3,837 (37.7%) vs. 84,106 (59.7%); moderate, 4,518 (44.4%) vs. 47,809 (34.0%); severe, 1,817 (17.9%) vs. 8,861 (6.3%), $p < 0.01$].

Table 1
Characteristics of trauma patients with and without infection

	Non-infection	Infection	*P*-value
Number	140,776 (93.3)	10,172 (6.7)	
Age	67 (47–80)	71 (53–82)	< 0.01
Gender (Male)	81,294 (57.7)	6,764 (66.5)	< 0.01
Mechanism of Injury			0.04
Blunt	136,591 (97.0)	9,906 (97.4)	
Penetrating	4,185 (3.0)	266 (2.6)	
Injury site (AIS ≥ 3)			
Head	38,844 (27.6)	4,031 (39.6)	< 0.01
Face	1,008 (0.7)	99 (1.0)	< 0.01
Neck	469 (0.3)	57 (0.6)	< 0.01
Thorax	29,143 (20.7)	2,807 (27.6)	< 0.01
Abdomen and Pelvis	8,208 (5.8)	960 (9.4)	< 0.01
Spine	14,752 (10.5)	1,596 (15.7)	< 0.01
Upper extremity	7,390 (5.2)	464 (4.6)	< 0.01
Lower extremity	53,600 (38.1)	3,850 (37.8)	0.65
Others	35 (0.0)	9 (0.1)	< 0.01
ISS			< 0.01
Mild (< 15)	84,106 (59.7)	3,837 (37.7)	
Moderate (15–29)	47,809 (34.0)	4,518 (44.4)	
Severe (≥ 30)	8,861 (6.3)	1,817 (17.9)	

Continuous variables were compared using the Mann−Whitney U test. Categorical variables were compared using the Chi-square test.

Missing: GCS = 13,085, SBP = 2,281, HR = 5,577, Temperature = 15,926, RR = 21,441, Blood transfusion = 3,421

AIS: Abbreviated Injury Scale, ISS: Injury Severity Score, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, HD: Hemodialysis, GCS: Glasgow coma scale, SBP: Systolic blood pressure, HR: Heart rate, RR: Respiratory rate, REBOA: Resuscitative endovascular balloon occlusion of the aorta, TAE: Transcatheter arterial embolization, UTI; Urinary tract infection, SSI: Surgical site infection

	Non-infection	Infection	*P*-value
Number of comorbidities			< 0.01
0	60,211 (42.8)	3,366 (33.1)	
42,852 (30.4)	3,155 (31.0)		
22,344 (15.9)	1,942 (19.1)		
9,995 (7.1)	1,038 (10.2)		
≥ 4	5,374 (3.8)	671 (6.6)	
Medication			
Steroid	532 (0.4)	48 (0.5)	0.14
Immunosuppressant	204 (0.1)	18 (0.2)	0.42
Anticoagulant	2,637 (1.9)	296 (2.9)	< 0.01
Vital signs at emergency department			
GCS	15 (14–15)	14 (11–15)	< 0.01
SBP	138 (119–159)	134 (110–158)	< 0.01
HR	82 (71–95)	86 (73–102)	< 0.01
Temperature	36.5 (36.0–37.0)	36.4 (35.8–36.9)	< 0.01
RR			< 0.01
≤ 17 (quartile 1)	31,202 (25.9)	1,923 (21.2)	
18–23 (quartile 2–3)	54,125 (44.9)	3,678 (40.5)	
≥ 24 (quartile 4)	35,089 (29.1)	3,490 (38.4)	
Number of emergency procedures			< 0.01
0	101,822 (72.3)	4,939 (48.6)	
1	26,297 (18.7)	1,992 (19.6)	

Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Chi-square test.

Missing: GCS = 13,085, SBP = 2,281, HR = 5,577, Temperature = 15,926, RR = 21,441, Blood transfusion = 3,421

AIS: Abbreviated Injury Scale, ISS: Injury Severity Score, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, HD: Hemodialysis, GCS: Glasgow coma scale, SBP: Systolic blood pressure, HR: Heart rate, RR: Respiratory rate, REBOA: Resuscitative endovascular balloon occlusion of the aorta, TAE: Transcatheter arterial embolization, UTI; Urinary tract infection, SSI: Surgical site infection

	Non-infection	Infection	*P*-value
2	7,223 (5.1)	1,382 (13.6)	
≥ 3	5,434 (3.9)	1,859 (18.3)	
Emergency procedures			
Intubation	11,877 (8.4)	3,217 (31.6)	< 0.01
Ventilator use or assisted ventilation	9,494 (6.7)	2,443 (24.0)	< 0.01
REBOA	293 (0.2)	103 (1.0)	< 0.01
Chest drainage	8,176 (5.8)	1,111 (0.9)	< 0.01
Craterization	655 (0.5)	295 (2.9)	< 0.01
Emergency TAE	4,071 (2.9)	809 (8.0)	< 0.01
Central venous line use	4,277 (3.0)	1,439 (14.1)	< 0.01
Vasopressor use	1,491 (1.1)	508 (5.0)	< 0.01
Open bone traction	10,250 (7.3)	824 (8.1)	< 0.01
External skeletal fixation	4,130 (2.9)	592 (5.8)	< 0.01
Other emergency bone fixation	5,434 (3.9)	438 (4.3)	0.03
Blood transfusion	19,139 (13.9)	3,100 (31.0)	< 0.01
Any operation	80,308 (57.0)	6,761 (66.5)	< 0.01
Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Chi-square test.			
Missing: GCS = 13,085, SBP = 2,281, HR = 5,577, Temperature = 15,926, RR = 21,441, Blood transfusion = 3,421			
AIS: Abbreviated Injury Scale, ISS: Injury Severity Score, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, HD: Hemodialysis, GCS: Glasgow coma scale, SBP: Systolic blood pressure, HR: Heart rate, RR: Respiratory rate, REBOA: Resuscitative endovascular balloon occlusion of the aorta, TAE: Transcatheter arterial embolization, UTI; Urinary tract infection, SSI: Surgical site infection			

Patients with infection had more concomitant complications than patients without infection (Table 2). Specifically, atelectasis [1,041 (10.2%) vs. 913 (0.6%), p < 0.01], higher brain dysfunction [944 (9.3%) vs. 2,539 (1.8%), p < 0.01], and disseminated intravascular coagulation and coagulation disorder [751 (7.4%) vs. 713 (0.5%), p < 0.01] were more common in patients with infection than in those without infection.

Table 2
Concomitant complications in patients with and without infection

	Non-infection	Infection	*P*-value
Number	140,776 (93.3)	10,172 (6.7)	
Number of concomitant complications			< 0.01
0	129,290 (91.8)	5,022 (49.4)	
1	9,257 (6.6)	2,656 (26.1)	
2	1,678 (1.2)	1,132 (11.1)	
3	378 (0.3)	550 (5.4)	
≥ 4	173 (0.1)	812 (8.0)	
Central nervous system			
Diabetes insipidus	195 (0.1)	115 (1.1)	< 0.01
Hydrocephalus	211 (0.1)	164 (1.6)	< 0.01
Fat embolism	87 (0.1)	149 (1.5)	< 0.01
Cerebrospinal fluid leakage	237 (0.2)	113 (1.1)	< 0.01
Higher brain dysfunction	2,539 (1.8)	944 (9.3)	< 0.01
Mental disorders (PTSD, etc.)	597 (0.4)	201 (2.0)	< 0.01
Others	1,544 (1.1)	503 (4.9)	< 0.01
Circulation			
Acute coronary syndrome	63 (0.0)	38 (0.4)	< 0.01
Refractory shock	223 (0.2)	174 (1.7)	< 0.01
Acute kidney injury	187 (0.1)	266 (2.6)	< 0.01
Abdominal compartment syndrome	33 (0.0)	37 (0.4)	< 0.01
Others	762 (0.5)	325 (3.2)	< 0.01
Respiratory			
Lung edema	124 (0.1)	163 (1.6)	< 0.01
Atelectasis	913 (0.6)	1,041 (10.2)	< 0.01
Pulmonary embolism	294 (0.2)	490 (4.8)	< 0.01

PTSD: Post trauma stress disorder, ARDS: Acute respiratory destress syndrome, GI: Gastrointestinal, DIC: Disseminated intravascular coagulopathy

	Non-infection	Infection	*P*-value
ARDS and respiratory failure	346 (0.2)	615 (6.0)	< 0.01
Others	461 (0.3)	197 (1.9)	< 0.01
Gastroenterology and hepato-biliary			
Ulcer and upper GI bleeding	428 (0.3)	322 (3.2)	< 0.01
Ileus	226 (0.2)	152 (1.5)	< 0.01
Pancreatitis	68 (0.0)	49 (0.5)	< 0.01
Cholecystitis	166 (0.1)	102 (1.0)	< 0.01
Hyperbilirubinemia and liver failure	116 (0.1)	160 (1.6)	< 0.01
Others	572 (0.4)	333 (3.3)	< 0.01
Bone and joint			
Compartment syndrome	220 (0.2)	345 (3.4)	< 0.01
Refracture	62 (0.0)	342 (3.4)	< 0.01
Pseudoarthrosis	57 (0.0)	377 (3.7)	< 0.01
Others	382 (0.3)	159 (1.6)	< 0.01
Coagulation			
DIC and coagulation disorder	713 (0.5)	751 (7.4)	< 0.01
Thrombopenia (< 50000)	291 (0.2)	341 (3.4)	< 0.01
Others	357 (0.3)	107 (1.1)	< 0.01
Others			
Wound disruption	179 (0.1)	319 (3.1)	< 0.01
Decubitus	405 (0.3)	407 (4.0)	< 0.01
Hypothermia (< 35 °C)	206 (0.1)	138 (1.4)	< 0.01
Drug allergy	117 (0.1)	75 (0.7)	< 0.01
Others	1,130 (0.8)	421 (4.1)	< 0.01

PTSD: Post trauma stress disorder, ARDS: Acute respiratory destress syndrome, GI: Gastrointestinal, DIC: Disseminated intravascular coagulopathy

Patients with infection had higher in-hospital mortality [1,079 (10.6%) vs. 2,904 (2.1%), p < 0.01], a longer hospital stay [42 (25–70) vs. 23 (14–38) days, p < 0.01], and less discharge at home [2,433 (23.9%) vs.

61,738 (43.9%), p < 0.01] than patients without infection (Table 3).

Table 3
Outcome of trauma patients with and without infection

	Non-infection	Infection	*P*-value
Number	140,776 (93.3)	10,172 (6.7)	
Admission			< 0.01
ICU	80,076 (56.9)	7,205 (70.8)	
General ward	60,700 (43.1)	2,967 (29.2)	
In-hospital mortality	2,904 (2.1)	1,079 (10.6)	< 0.01
Place after discharge			< 0.01
Home	61,738 (43.9)	2,433 (23.9)	
Transfer	72,949 (51.9)	6,416 (63.1)	
Other	2,933 (2.1)	233 (2.3)	
LOS	23 (14–38)	42 (25–70)	< 0.01

Continuous variables were compared using the Mann–Whitney U test. Categorical variables were compared using the Chi-square test.

Missing: place after discharge = 263

ICU: Intensive care unit, LOS: Length of hospital stay

Figure 2 shows the effect of infection on trauma patients according to trauma severity. The in-hospital mortality rate between trauma patients with infection and those without infection differed according to trauma severity [16.7% (95% CI; 14.6–18.8%) vs. 3.6% (95% CI; 3.3–3.9%), p < 0.01, in patients with mild trauma; 12.3% (95% CI; 11.0–13.6%) vs. 7.3% (95% CI; 6.9–7.7%), p < 0.01, in patients with moderate trauma; and 12.0% (95% CI; 9.8–14.2%) vs. 11.1% (95% CI; 9.8–12.4%), p = 0.41, in patients with severe trauma].

Discussion

We assessed the impact of infection complications on in-hospital mortality among trauma patients. The impact differed by trauma severity; specifically, infection after trauma increased in-hospital mortality to a greater degree in patients with mild or moderate trauma than in patients with severe trauma.

Among patients with mild or moderate trauma, infection complications were associated with increased in-hospital mortality. Our results were consistent with previous studies using a national database [1] and a statewide database [16] in the United States. Although other studies [10, 14, 19] did not show the association between infection and in-hospital mortality among trauma, their results have limited generalizability because they were small and single-center studies. Infectious complications in trauma, similar to in postoperative patients [20] and patients with non-infectious internal diseases [21], would have a worse impact on their prognosis.

Results of the present study revealed no association between infection complications and increased in-hospital mortality in patients with severe trauma. The results in previous studies [1, 16] were partially inconsistent with our study. They noted that infection complications were associated with increased in-hospital mortality although it was a little effect among patients with severe trauma compared with patients with mild trauma. We believe our study is more accurate because we excluded early trauma death and we adjusted for more important confounders such as transfusion and injury sites, which were not included in previous studies [1, 16]. The reason why in-hospital mortality did not differ among severe trauma patients with and without infection might be because of the difficulty in diagnosing sepsis in severe trauma patients with organ dysfunctions [10, 22]. Additionally, severe trauma patients might have received antibiotics earlier regardless of the suspicion of infection, which may have contributed to the decreased mortality in severe trauma patients with infection [23]. Alternatively, this finding might have occurred because non-infectious complications, which were common in severe trauma patients, might have a greater impact on mortality than infectious complications [17].

Previous studies [10, 17, 24] have reported that the risk for developing infection was high in patients with severe trauma. However, our findings emphasize the importance of paying more attention to the complications of infection, even if the severity of trauma is mild. Patients with less severe disease usually receive less monitoring [25]. Thus, the early recognition of infection plays a key role in managing patients with trauma.

Limitations

There are a few limitations in the present study. First, infection was diagnosed by a physician in charge, which might have resulted in misclassification. However, the incidence of infection in patients with trauma in the present study was 6.7%, which is comparable with previous studies [1, 10, 16, 24] reporting infection incidences of 2–15%. Second, some complications might have been under-reported, as discussed in our previous study [2], potentially leading to the overestimation or underestimation of the impact of infection on mortality. Third, we did lacked data on the treatments for both trauma and infection, which might have affected the outcomes. Since 2002, guidelines for trauma care called the Japan Advanced Trauma Evaluation and Care that was created with reference to the Advanced Trauma Life Support [26] were introduced in Japan. Furthermore, a previous study showed high compliance with the sepsis bundle in Japan [27]. Therefore, we believe that most patients received appropriate treatments.

Conclusion

Infection complications after trauma affected in-hospital mortality differently according to injury severity. Greater attention to infection complications is necessary among patients with trauma, even if their severity is mild.

Abbreviations

CI Confidence interval

ED Emergency department

ISS Injury Severity Score

JTDB Japan Trauma Data Bank

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Ethics Committee of the Juntendo University (IRB No.19-010). The ethics committees waived the need to obtain informed consent from the study participants given the retrospective and anonymized nature of this study in routine care. The JTDB administrators also provided permission to use the data from their database. Our study was performed in accordance with the amended Declaration of Helsinki.

Consent for publication

Not applicable

Availability of supporting data and material

The datasets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Competing interests

All authors declare that they have no competing interests.

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Authors' contributions

AK conceived of and designed this study, analyzed and interpreted the patient data, and was a major contributor in writing the manuscript. HI contributed to data interpretation and revised the manuscript for important intellectual content. TK contributed to data interpretation. MA contributed to the acquisition of data. TN revised the manuscript for important intellectual content. TA contributed to the acquisition of data, conceived of and designed this study, interpreted the data, and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Figures

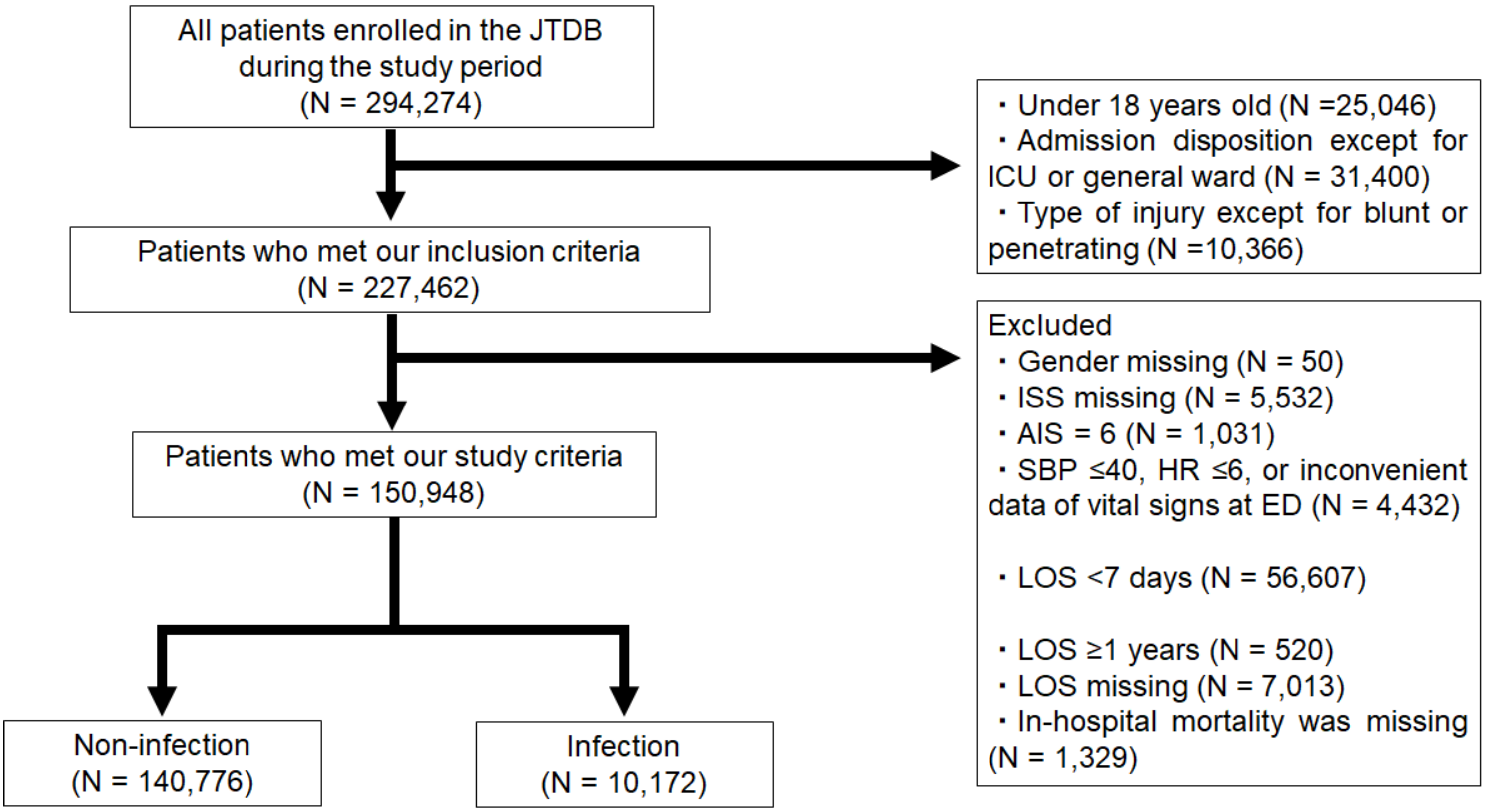
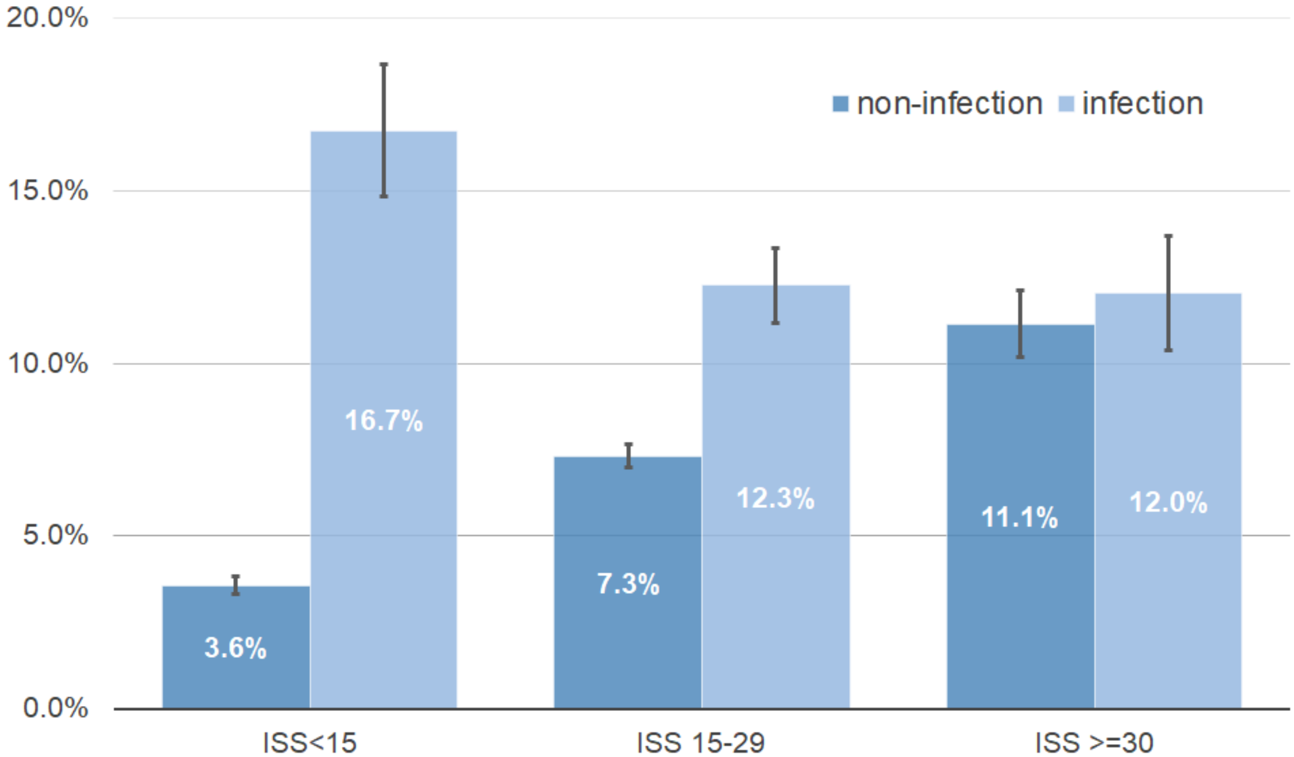


Figure 1

Patient selection JTDB: Japan Trauma Data Bank, ICU: Intensive care unit, ISS: Injury Severity Score, AIS: Abbreviated Injury Scale, SBP: Systolic blood pressure, HR: Heart rate, ED: Emergency department, LOS: Length of hospital stay



Crude mortality	N (%)	721/84,106 (0.9)	349/3,837 (9.1)	1,613/47,809 (3.4)	522/4,518 (11.6)	570/8,861 (6.4)	208/1,817 (11.4)

Figure 2

Crude and adjusted in-hospital mortality in patients with and without infection by trauma severity ISS: Injury Severity Score