



# Injury severity score as a predictor of mortality in adult trauma patients by injury mechanism types in the United States

## A retrospective observational study

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### Abstract

Injury severity score (ISS) is commonly used in trauma registries to describe injury severity and to predict outcomes in trauma patients regardless of injury mechanism. This study examined the correlation between ISS and mortality in adult trauma patients presenting to emergency departments in the United States with different mechanisms of injury.

A retrospective observational study was conducted using the 2014 Nationwide Emergency Department Sample. Patients' characteristics were stratified by mortality. Receiver operating characteristic (ROC) curves were generated for death against ISS for each mechanism of injury. A logistic regression model was conducted for each mechanism of injury to determine whether ISS ( $\geq 16$  vs  $< 16$ ) is a predictor of mortality.

The study sample consisted of 16,147,058 weighted adult trauma patients. Median age was 46 years. Slightly over half were females (51.9%). Falls, motor vehicle accidents and being struck by or against, were the most commonly reported mechanisms of injury (44.6%, 18.1%, and 15.3%, respectively). The overall mortality in the study population was 0.4%. The area under the ROC curve was highest in injuries sustained in accidents involving machinery (0.947; 95% confidence intervals [CI], 0.896-0.998), followed by motor vehicle traffic (MVA) (0.788; 95% CI, 0.775-0.801) and cutting or piercing (0.746; 95% CI, 0.701-0.791). Deceased patients were accurately identified by ISS 65.2% in injury by machinery, 47.7% in injury involving MVA, 39.7% in injury by firearm and 31.4% in injury by assault. After adjusting for confounders, the multivariate models in which ISS was the main independent factor performed best in predicting mortality from firearm and machinery mechanism of injuries.

Although the ROC curve analysis demonstrated a moderate or high discriminatory ability to identify deceased patients in 6 out of twelve mechanisms, and the multivariate analysis revealed that ISS was a significant predictor of mortality in 9 out of 12 injury mechanisms, the sensitivities of all logistic regression models were poor. The ISS  $\geq 16$  threshold alone therefore should not be used to identify patients with high-mortality risk. The mortality risk assessment should be done individually and be based on clinical evaluation.

**Abbreviations:** AHRQ = agency for healthcare research and quality, AIS = abbreviated injury scale, AUROC = area under the ROC curve, CI = confidence intervals, HCUP = healthcare cost and utilization project, IQR = interquartile range, ISS = injury severity score, NEDS = nationwide emergency department sample, NPV = negative predictive value, PPV = positive predictive value, ROC = receiver operating characteristic.

**Key Words:** injury severity score, mortality, outcome, receiver operating characteristic curve, trauma

## 1. Introduction

Injury severity score (ISS) is an anatomical scoring system that provides an overall score for patients with multiple injuries.<sup>[1]</sup> ISS categorizes injuries based on the abbreviated injury scale

(AIS), which is an anatomical scoring system that characterizes the severity of injuries in various body regions.<sup>[2]</sup> It is calculated as the sum of the squares of the highest AIS code (each ranging from 0 to 6) in each of the 3 most severely injured ISS body regions (6 body regions in total: head or neck, face, chest,

The authors have no funding and conflicts of interest to disclose.

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

An exemption for the use of this deidentified dataset was obtained from the institutional review board (IRB) office. This database is deidentified prior to use and is defined as limited data set under the HIPAA Privacy.

Supplemental Digital Content is available for this article.

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How to cite this article: Colnaric JM, El Sibai RH, Bachir RH, El Sayed MJ. Injury severity score as predictor of mortality in adult trauma patients by injury mechanism types in the United States: A retrospective observational study. *Medicine* 2022;101:28(e29614).

Received: 21 January 2021 / Received in final form: 25 April 2022 / Accepted: 6 May 2022

<http://dx.doi.org/10.1097/MD.00000000000029614>

abdominal or pelvic contents, extremities or pelvic girdle, external). It ranges from 3 (least) to 75 (most injured). If an injury is given an AIS 6, the ISS is automatically set at 75.

For example, a trauma patient who sustained a fractured femur (AIS code 853000.3; AIS 3) and 2 (uncomplicated) rib fractures (AIS code 450202.2; AIS 2) would be assigned an ISS 14.

Although ISS correlates well with mortality, it is not linear, as it is based on the sum of squares of triplets. Because mortality does not necessarily increase with higher ISS values, the ISS is often used as a categorical variable in trauma research.

Despite its limited clinical impact at the individual level, the ISS is widely used in trauma outcomes research to dichotomize patients by injury severity. Traditionally, most studies define severely injured trauma patients by an ISS  $\geq 16$ , which has been associated with a mortality risk of 10% in a study from 1987.<sup>[3]</sup> It should be noted, that the AIS was initially designed for rating and comparing blunt injuries<sup>[2]</sup> and that its scope has expanded to cover all aspects of trauma, such as penetrating injuries and burns. Using the revised AIS, more recent studies show inconsistent evidence regarding ISS  $\geq 16$ <sup>[4-8]</sup>; however, this cutoff continues to be widely used for assessing mortality risk. Although the nature of tissue damage, physiological response, and primary treatment differs among various mechanisms of injury<sup>[9]</sup> and the ISS' performance has not yet been sufficiently studied across all categories. Therefore, on the basis of modifications to AIS scoring, the performance of the model necessitates re-evaluation.

This study examined the traditional threshold ISS  $\geq 16$  and its association with mortality in adult trauma patients with different mechanisms of injury. Its hypothesis was that the performance of ISS score varies across different mechanisms.

## 2. Methods

### 2.1. Study design

A retrospective observational study was conducted using the 2014 Nationwide Emergency Department Sample (NEDS) which was released in 2016. An Institutional Review Board exemption from the American University of Beirut was obtained for the use of this public release dataset.

### 2.2. Study setting

NEDS is the largest administrative database in the United States and is a product of the Healthcare Cost and Utilization Project (HCUP), supported by the Agency of Healthcare and Research Quality.<sup>[10]</sup> For each hospital stay, more than 100 variables are documented. These include patient demographics characteristics, diagnoses, procedures, hospital characteristics, mechanism, intent and severity of injury, hospital length of stay, admission and discharge status, source of coverage, and healthcare costs.<sup>[11]</sup>

Authors of the manuscript completed the HCUP data use agreement training course and signed the Nationwide Data Use Agreement.

### 2.3. Study population

The 2014 NEDS dataset comprises weighted data on 137,807,901 ED visits from 945 hospitals across 33 states, which approximates 20% of US hospital-based EDs. The sample included both trauma and nontrauma centers. Mechanism of injury types (motor vehicle accident, falls, being struck by/against, cutting/piercing, firearm, fire/flame/hot objects, machinery, drowning/submersion, suffocation, natural/environmental, poisoning and assault) were included using standard NEDS data elements. The initial eligible sample of patients with a mechanism of injury type in the database consisted of 21,631,795 weighted patients. Children (age  $\leq 17$ ) and patients with missing

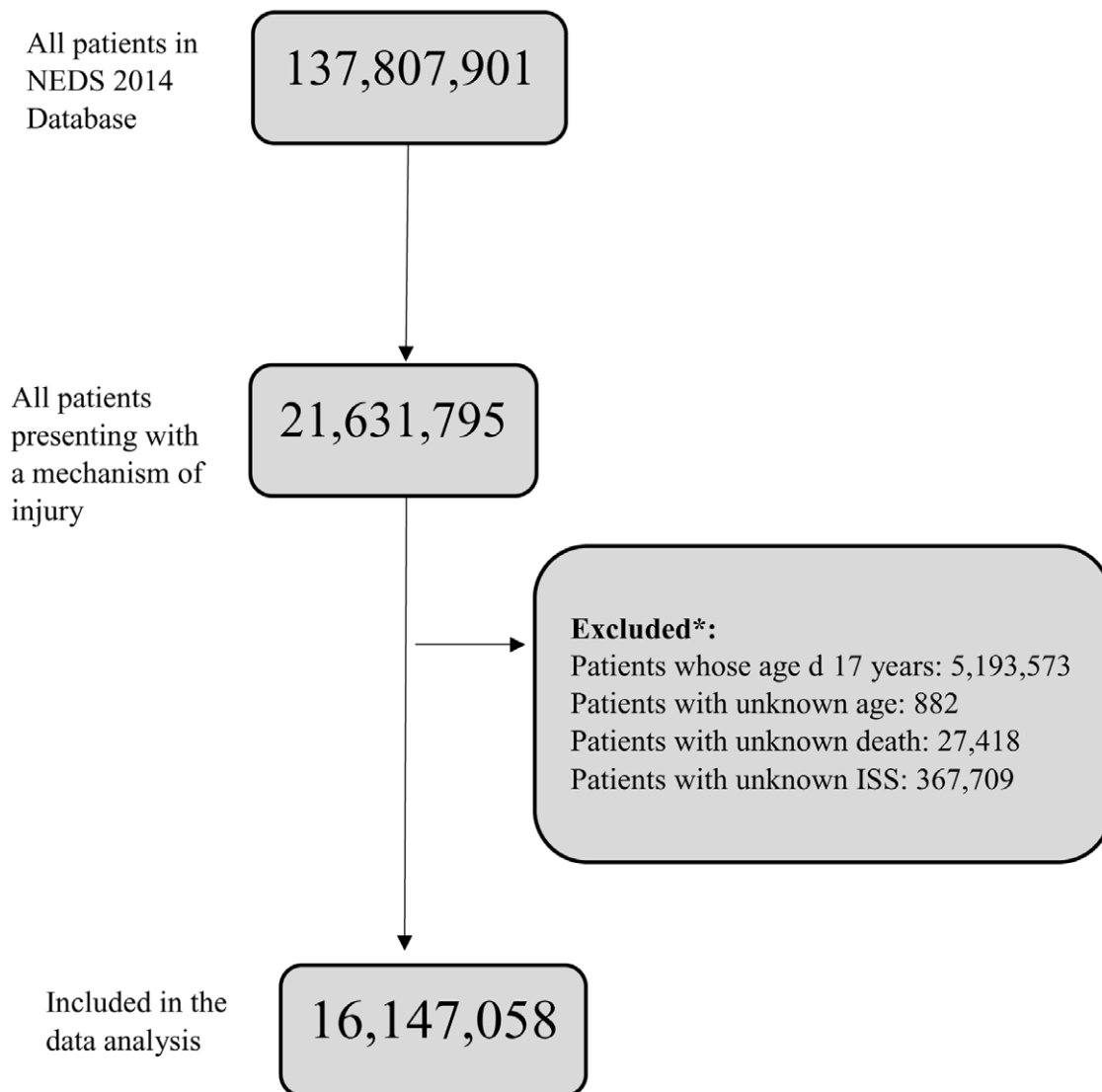
data on outcome (died [yes/no]) and ISS were excluded. After applying the exclusion criteria, 16,147,058 weighted patients remained and were included in the study (Fig. 1). No sample size was calculated because all patients who had any type of the available mechanism of injury in the NEDS database constituted the study sample. Further, due to the inclusion of all eligible patients, the selection bias is unlikely to occur.

### 2.4. Statistical analysis

Statistical analysis was carried out using the Statistical Package for Social Sciences (version 24, SPSS, Inc, IBM Corp, Chicago, IL). Age was described by its median and interquartile range (IQR) whereas all categorical variables were presented by their frequencies and percentages with the associated 95% confidence intervals (CI). The distribution of ISS was depicted by a histogram (data shown in Figure 1, Supplemental Digital Content, <http://links.lww.com/MD/G888>). A modified version of the Pearson chi-square test, known as the Rao-Scott chi-square test for complex samples, was used to compare the proportion of the mechanism of injury by the 2 groups of the ISS (16–75 vs 0–15) and to determine whether there is a statistically significant difference between the independent factors and the outcome variable (died: yes/no). The complex sampling design produced some frequencies as decimal numbers that were discarded through rounding for clarity reasons. A *P* value of  $\leq .05$  was considered significant. By plotting the true positive rate against the false positive rate for the different cutoff points, receiver operating characteristic (ROC) curves were generated for death against ISS for each mechanism of injury. For each plot, the area under the ROC curve was calculated to determine the degree of discrimination of ISS between the 2 categories of the dependent variable (died/survived). Further, to assess the utility of the ROC curves in clinical practice, particularly to account for misclassification costs (i.e., false positive and false negative), several epidemiological measures were calculated [true negative, false negative, false positive, true positive, sensitivity and specificity, negative predictive value, and positive predictive value]. Multiple imputation was not used because almost all variables had missing data  $<5\%$ . In addition, exclusion criteria included all patients for whom the death status “the outcome” or ISS “the main independent factor” were not recorded. Further, the data were weighted according to HCUP specifications to provide national estimates based on specific variables (US census region, trauma center designation, urban-rural location of the hospital, ownership, and teaching status). No outliers were identified by drawing a boxplot for ISS. Multivariate analyses for each mechanism of injury were conducted to control for all confounding factors and to determine whether ISS is positively predicting mortality. The area under the ROC curve was calculated for each model to quantify the discrimination between deceased and survived patients and the calculated values ranged from 0.804 to 0.980, indicating that all models had high degree of distinction between the 2 categories of the outcome variable (died/survived). The accuracy of each model in predicting mortality was determined by calculating the validity measures (sensitivity, specificity, negative predictive value, positive predictive value).

## 3. Results

The study included a weighted sample of 16,147,058 adult trauma patients. Demographic characteristics of the study population are presented in Table 1. Over half of patients were females (51.9%; 95% CI, 51.9-52.0). The median age was 46 years (IQR: 30–64 years). Elderly patients (age  $> 65$  years) represented 23.5% of the study sample. Falls, motor vehicle accidents and being struck by or against were the most commonly



**Figure 1.** Inclusion and exclusion flowchart. There is an overlap among the categories of the excluded variables. More specifically, some patients aged  $\leq 17$  years old had unknown ISS or death status. Both age and ISS were not recorded for some patients. This is why the final number on which the data analysis was conducted cannot be calculated just by subtracting the number of excluded patients from the selected sample. ISS = injury severity score.

reported mechanisms of injury (44.6%, 18.1%, and 15.3%, respectively). Regarding the trauma designation level, nearly a half of the patients were taken to a nontrauma center (48.4%), followed by level 1 center (14.3%). The sample was composed predominantly of patients with minor injuries (ISS  $< 16$ ) (98.7%; 95% CI, 98.7-98.7). More than 1 injury was reported on record in nearly a third of patients (30.6%; 95% CI, 30.5-30.6). The overall mortality in the study population was 0.4% (95% CI, 0.4-0.4).

Moreover, univariate and bivariate analyses were conducted for additional variables including sociodemographic [median household income national quartile for patient ZIP code—primary expected payer—patient location: NCHS urban-rural code], administrative [admission day is a weekend—season of admission—teaching status of hospital] and clinical characteristics [ISS—different body system indicators] (data shown in Table 1, Supplemental Digital Content, <http://links.lww.com/MD/G888>).

Prevalence of severely injured patients (ISS  $\geq 16$ ) in different injury mechanism are as follows: injury by cutting or piercing 0.1% (95% CI, 0.1-0.2), injury by drowning and submersion 1.8% (95% CI, 1.2-2.6), injury by falling 1.6% (95% CI,

1.6-1.7), injury by fire, flame, or hot object 0.6% (95% CI, 0.5-0.7), injury by firearm 10.8% (95% CI, 10.4-11.3), injury by machinery 0.7% (95% CI, 0.6-0.8), injury involving motor vehicle traffic 2.2% (95% CI, 2.2-2.3), injury involving natural or environmental causes 0.1% (95% CI, 0.1-0.1), injury by poison 0.1% (95% CI, 0.1-0.1), injury from being struck by or against 0.5% (95% CI, 0.4-0.5), injury by suffocation 1.3% (95% CI, 1.1-1.5), injury by assault indicated on record 1.8% (95% CI, 1.7-1.9) (data shown in Table 2, Supplemental Digital Content, <http://links.lww.com/MD/G888>).

Table 2 assessed the validity of the association between ISS ( $< 16$ ,  $\geq 16$ ) and mortality for each mechanism of injury. Table 3 demonstrated the areas under the ROC curves (AUROC) calculated by plotting death against ISS for each mechanism of injury. The ROC curve analysis showed a varying ability of ISS to discriminate between deceased and survived patients across different injury mechanisms. Good discrimination was observed in injuries sustained in accidents involving machinery (AUROC 0.947; 95% CI, 0.896-0.998;  $P < .001$ ). For this injury mechanism, ISS accurately identified 65.2% (sensitivity) of deceased patients and exhibited a 11.6% (PPV) chance that this identification is accurate.

**Table 1**  
**Characteristics and outcomes of study population.**

Variable <sup>1</sup>	All patients N = 16,147,058		Surviving patients N = 16,079,022		Nonsurviving patients N = 68,037		P
	Frequency	Percentage (95% CI)	Frequency	Percentage (95% CI)	Frequency	Percentage (95% CI)	
<b>Age (yrs)</b>							
18–65	12,352,986	76.5 (76.5–76.5)	12,322,766	99.8 (99.7–99.8)	30,220	0.2 (0.2–0.3)	<.001
>65	3794,072	23.5 (23.5–23.5)	3756,255	99.0 (99.0–99.0)	37,817	1.0 (1.0–1.0)	
Median (Interquartile range)	46 (30–64)		46 (30–64)		70 (49–84)		
<b>Gender</b>							
Male	7759,779	48.1 (48.0–48.1)	7718,128	99.5 (99.5–99.5)	41,651	0.5 (0.5–0.5)	<.001
Female	8386,123	51.9 (51.9–52.0)	8359,854	99.7 (99.7–99.7)	26,269	0.3 (0.3–0.3)	
<b>Injury (type)</b>							
Injury by cutting or piercing	1680,877	10.4 (10.4–10.4)	1679,924	99.9 (99.9–99.9)	953	0.1 (0.1–0.1)	<.001
Injury by drowning and submersion	6090	0 (0–0)	5259	86.3 (84.5–88.0)	831	13.7 (12.0–15.5)	<.001
Injury by falling	7195,041	44.6 (44.5–44.6)	7160,896	99.5 (99.5–99.5)	34,145	0.5 (0.5–0.5)	<.001
Injury by fire, flame, or hot object	41,901	0.3 (0.3–0.3)	41,516	99.1 (98.9–99.2)	385	0.9 (0.8–1.1)	<.001
Injury by firearm	77,362	0.5 (0.5–0.5)	71,438	92.3 (92.0–92.7)	5924	7.7 (7.3–8.0)	<.001
Injury by machinery	110,635	0.7 (0.7–0.7)	110,495	99.9 (99.8–99.9)	140	0.1 (0.1–0.2)	<.001
Injury involving motor vehicle traffic	2917,543	18.1 (18.0–18.1)	2905,307	99.6 (99.6–99.6)	12,236	0.4 (0.4–0.4)	<.001
Injury involving natural or environmental causes	1005,766	6.2 (6.2–6.3)	1003,499	99.8 (99.8–99.8)	2266	0.2 (0.2–0.2)	<.001
Injury by poison	740,470	4.6 (4.6–4.6)	734,894	99.2 (99.2–99.3)	5576	0.8 (0.7–0.8)	<.001
Injury From being struck by or against	2473,872	15.3 (15.3–15.4)	2,472,690	100 (99.9–100)	1182	0 (0–0.1)	<.001
Injury by suffocation	42,767	0.3 (0.3–0.3)	37,226	87.0 (86.4–87.6)	5541	13.0 (12.4–13.6)	<.001
Injury by assault indicated on the record	674,929	4.2 (4.2–4.2)	671,554	99.5 (99.5–99.5)	3375	0.5 (0.5–0.5)	<.001
<b>More than one injury reported on record</b>							
One or no injury diagnosis reported	11,213,149	69.4 (69.4–69.5)	11,172,424	99.6 (99.6–99.6)	40,725	0.4 (0.4–0.4)	<.001
More than one injury diagnosis reported, regardless of position	4933,909	30.6 (30.5–30.6)	4906,598	99.4 (99.4–99.5)	27,311	0.6 (0.5–0.6)	
<b>ISS<sup>2</sup></b>							
< 16	15,940,850	98.7 (98.7–98.7)	15,889,691	99.7 (99.7–99.7)	51,160	0.3 (0.3–0.3)	<.001
≥ 16	206,208	1.3 (1.3–1.3)	189,331	91.8 (91.6–92.1)	16,877	8.2 (7.9–8.4)	
<b>Region of hospital</b>							
Northeast	3135,401	19.4 (19.4–19.4)	126,695	99.7 (99.7–99.8)	338	0.3 (0.2–0.3)	<.001
Midwest	3465,382	21.5 (21.5–21.5)	142,668	99.5 (99.4–99.6)	680	0.5 (0.4–0.6)	
South	6697,072	41.5 (41.5–41.5)	257,129	99.3 (99.3–99.4)	1752	0.7 (0.6–0.7)	
West	2,849,202	17.6 (17.6–17.6)	145,063	99.6 (99.5–99.7)	604	0.4 (0.3–0.5)	
<b>Trauma Designation levels</b>							
Non trauma center	7819,966	48.4 (48.4–48.4)	263,230	99.9 (99.8–99.9)	379	(0.1–0.2)	<.001
Trauma level I	2303,820	14.3 (14.3–14.3)	186,703	99.0 (98.9–99.1)	1966	1.0 (0.9–1.1)	
Trauma level II	1874,143	11.6 (11.6–11.6)	84,406	99.4 (99.3–99.5)	530	(0.5–0.7)	
Trauma level III	1935,733	12.0 (12.0–12.0)	65,159	99.7 (99.5–99.8)	215	(0.2–0.5)	
Non trauma or trauma level III <sup>3</sup>	1661,945	10.3 (10.3–10.3)	50,685	99.8 (99.7–99.9)	87	0.2 (0.1–0.3)	
Trauma level I or II <sup>4</sup>	551,451	3.4 (3.4–3.4)	21,370	99.1 (98.7–99.3)	198	0.9 (0.7–1.3)	

1 None of the presented variables had missing values  
 2 Injury severity score assigned by ICPIC-Statia program  
 3 collapsed category beginning in the 2011 NEDS  
 4 collapsed category beginning in the 2011 NEDS

**Table 2**

Validity measures of the association between ISS (&lt;16, ≥16) and mortality for each mechanism of injury.

	PPV (%)	NPV (%)	Sensitivity (%)	Specificity (%)
Injury by cutting or piercing	8.3	100	20.3	99.9
Injury by drowning and submersion	12.8	86.3	1.7	98.2
Injury by falling	6.8	99.6	23.7	98.5
Injury by fire, flame, or hot object	11.2	99.1	7.0	99.5
Injury by firearm	28.1	94.8	39.7	91.6
Injury by machinery	11.6	100	65.2	99.4
Injury involving motor vehicle traffic	8.9	99.8	47.7	97.9
Injury involving natural or environmental causes	12.3	99.8	4.5	99.9
Injury by poison	6.4	99.3	0.6	99.9
Injury From being struck by or against	3.0	100	28.5	99.6
Injury by suffocation	14.7	87.1	1.5	98.7
Injury by assault indicated on the record	8.7	99.7	31.4	98.3

NPV = negative predictive value, PPV = positive predictive value.

**Table 3**

Area under the ROC curve calculated by plotting ISS against death for each mechanism of injury.

	ROC analysis—ISS as continuous		
	AUROC (SE)	P	95% CI
Injury by machinery	0.947 (0.026)	<.001	0.896-0.998
Injury involving motor vehicle traffic	0.788 (0.007)	<.001	0.775-0.801
Injury by cutting or piercing	0.746 (0.023)	<.001	0.701-0.791
Injury From being struck by or against	0.737 (0.022)	<.001	0.694-0.779
Injury by assault indicated on the record	0.723 (0.012)	<.001	0.699-0.748
Injury by falling	0.703 (0.004)	<.001	0.695-0.711
Injury by firearm	0.675 (0.009)	<.001	0.657-0.692
Injury by fire, flame, or hot object	0.570 (0.039)	.03	0.494-0.646
Injury by poison	0.503 (0.008)	.76	0.486-0.519
Injury by suffocation	0.434 (0.008)	<.001	0.417-0.450
Injury by drowning and submersion	0.319 (0.020)	<.001	0.280-0.359
Injury involving natural or environmental causes	0.279 (0.013)	<.001	0.254-0.303

AUROC = Area under the ROC curve, CI = confidence interval, SE = standard error.

ISS demonstrated a moderate discriminatory ability in patients with blunt trauma, including injury involving motor vehicle traffic (AUROC 0.788; 95% CI, 0.775-0.801;  $P < .001$ ), injury by cutting and piercing (AUROC 0.746; 95% CI, 0.701-0.791;  $P < .001$ ), injury from being struck by or against (AUROC 0.737; 95% CI, 0.694-0.779;  $P < .001$ ), injury from falling (AUROC 0.703; 95% CI, 0.695-0.711;  $P < .001$ ) and injury by assault (AUROC 0.723; 95% CI, 0.699-0.748;  $P < .001$ ). ISS was most accurate in identifying deceased patients (sensitivity) with injury involving motor vehicle traffic (47.7%), followed by injury by assault (31.4%), injury from being struck by or against (28.5%), injury by falling (23.7%), and injury by cutting and piercing (20.3%). The chance of this accurate identification (PPV) was higher in motor vehicle traffic (8.9%), injury by assault (8.7%), and injury by cutting and piercing (8.3%) than in injury by falling (6.8%) and in injury from being struck by or against (3.0%).

ISS had a poor discrimination in the remaining mechanism of injury types. For example, patients with sustained firearm injury had AUROC of 0.675 (95% CI, 0.657-0.692;  $P < .001$ ). For this injury type, ISS accurately identified 39.7% (sensitivity) of deceased patients with 28.1% chance of accurate identification (PPV).

Table 4 showed the association between ISS (<16, ≥16) and mortality in different injury mechanisms after adjusting for several common confounding factors. ISS was found to be a significant predictor of mortality in all examined injury mechanisms except for injury by drowning/submersion, injury by fire/flame/hot object and injury by suffocation. The multivariate models in which ISS (<16, ≥16) was the main independent factor, performed best in predicting the mortality of the patients who sustained injury by firearm (sensitivity: 30.2%, PPV: 65.0%) and injury by machinery (sensitivity: 13.0%, PPV: 46.9%).

#### 4. Discussion

Findings varied by mechanism of injury. The discriminatory ability was best in injury by machinery (AUROC above 0.90). However, ISS accurately identified 65.2% (sensitivity) of deceased patients and 99.4% (specificity) of survived patients with injury by machinery. These findings may be affected by the small number of deceased patients with ISS ≥ 16 (true positive). Additionally, the logistic regression had a sensitivity of 13.0% and a specificity of 100%, indicating that it is unlikely to predict patients' death based on this model and the PPV revealed a 46.9% confidence. As such patients presenting with ISS ≥ 16 after injury by machinery have a high risk of mortality; however, this score alone is not enough to discriminate among those who will die or who will survive.

In patients with blunt trauma, including injury involving motor vehicle traffic, injury from being struck by or against, injury from falling and injury by assault, the ISS demonstrated a moderate discriminatory ability (AUROC above 0.70).

Three preceding studies examining blunt trauma patients showed similar ability of ISS to discriminate between survived and deceased patients (0.780 [95% CI not reported]<sup>[12]</sup>; 0.776 [95% CI not reported]<sup>[13]</sup>; 0.75 [95% CI, 0.66-0.83]<sup>[14]</sup>). Other studies reported moderately<sup>[15,16]</sup> and considerably better discrimination.<sup>[17-21]</sup> These inconsistencies may be attributed to differences in methodology. First, some previous studies<sup>[14,17-21]</sup> examined the ISS in single-center studies with smaller sample sizes, whereas this study included data from multiple hospitals including trauma designated and nondesignated centers. Second, injury severity or types were also not restricted in this study while some studies included only the severely injured (admission to intensive care unit or high dependency observation unit),<sup>[12]</sup> or patients with multiple injuries.<sup>[8]</sup> Some also excluded the intubated and ventilated patients.<sup>[16]</sup> Third, given the large variation in health care systems that exists between different countries, ISS might perform differently in other more or less advanced systems with different types of resources.<sup>[8,17]</sup>

However, using the threshold ISS 16 resulted in low sensitivity (23.7%–47.7%). Two recent studies identified better sensitivity

**Table 4****Adjusted odds ratios of ISS (<16; ≥16) in deceased patients for each mechanism of injury along with the validity measures of each predictive model.**

	*Adjusted Odds Ratio	95% CI	P	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
<b>Injury by cutting or piercing</b>	20.20	8.55-47.69	<.001	3.2	100.0	33.0	100
<b>Injury by drowning and submersion</b>	0.34	0.08-1.49	.15	39.6	96.6	61.4	92.1
<b>Injury by falling</b>	18.67	17.82-19.57	<.001	0.2	100.0	41.9	99.5
<b>Injury by fire, flame, or hot object</b>	4.08	0.97-17.17	.06	14.2	99.9	63.5	99.2
<b>Injury by firearm</b>	9.62	7.60-12.18	<.001	30.2	98.7	65.0	94.8
<b>Injury by machinery</b>	35.92	8.65-149.16	<.001	13.0	100.0	46.9	99.9
<b>Injury involving motor vehicle traffic</b>	10.65	9.09-12.47	<.001	0.0	100.0	0	99.6
<b>Injury involving natural or environmental causes</b>	13.72	5.98-31.50	<.001	2.1	100.0	25.7	99.8
<b>Injury by poison</b>	4.75	1.95-11.60	.001	0.2	100.0	100	99.3
<b>Injury From being struck by or against</b>	9.45	6.09-14.64	<.001	2.1	100.0	38.6	100
<b>Injury by suffocation</b>	0.75	0.40-1.40	.36	3.4	99.3	41.2	87.3
<b>Injury by assault indicated on the record</b>	11.64	8.44-16.06	<.001	8.1	100.0	43.9	99.6

\*Adjusted for: Age-Sex, admission day is a weekend, season of admission, primary expected payer; Patient location: NCHS urban-rural code; Median household income national quartile for patient ZIP code; Region of hospital, trauma level designation, teaching status of hospital; injury severity score, body system indicators (endocrine, nutritional, and metabolic diseases and immunity disorders, mental disorders; diseases of the nervous system and sense organs, diseases of the circulatory system; diseases of the respiratory system, diseases of the digestive system, diseases of the genitourinary system, diseases of the musculoskeletal system, symptoms, signs, and ill-defined conditions, injury and poisoning, factors influencing health status and contact with health services).

(85.7%<sup>[20]</sup> and 83.3%<sup>[21]</sup>) using cutoff values ISS > 15 and ISS ≥ 16. The low sensitivity in our study may result from the low number of those who died and had ISS ≥ 16 (true positive), whereas both mentioned studies had considerably higher overall mortality rates. Although the sensitivity of ISS in previous studies was better, its clinical value in prognosticating mortality is limited. Other authors have proposed alternative cutoff values with improved prognostic value (ISS ≥ 14,<sup>[20]</sup> ISS ≥ 13,<sup>[22]</sup> ISS ≥ 12).<sup>[23]</sup> The differences in ISS cutoff could be related to differences in AIS coding which have been described previously. Namely, changing from 1998 AIS update (AIS98) to AIS08 resulted in many injuries being assigned to higher or lower scores, although injuries decreased in severity.<sup>[24]</sup> This caused an overall decrease in major trauma patients of 20%.<sup>[25]</sup> Van Ditschuneij et al recently observed equivalent in-hospital mortality and ICU admission rates using a threshold of ISS98 ≥ 16 and thresholds of ISS08 ≥ 11 and ISS15 ≥ 12.<sup>[22]</sup>

Our results point toward a difference in the discriminatory ability of ISS across the different penetrating injury mechanisms. The discriminatory ability of ISS was moderate in injury by cutting and piercing (AUROC above 0.70), which was the most prevalent penetrating injury mechanism in this study. The discrimination is consistent with previous multicenter studies from Europe<sup>[19]</sup> (0.787, 95% CI not reported) and Canada<sup>[16]</sup> (84.0, 95% CI, 80.1-87.8). On the other hand, injury by firearm demonstrated a poor discriminatory ability (AUROC above 0.60) when compared with previous studies (AUROC 0.885,<sup>[26]</sup> 0.93<sup>[27]</sup>). This may be due to the considerably lower mortality from the NEDS database used in this study compared with previous studies, which used data from a trauma registry,<sup>[26]</sup> and military settings.<sup>[27]</sup> The ISS accurately identified (sensitivity) 20.3% and 39.7% of deceased patients with injury by cutting and piercing and injury by firearm, respectively. Similarly, the ability of the logistic regression to predict mortality for both penetrating injury mechanisms was poor. Though the discrimination of ISS in penetrating trauma was better in previous studies, ISS was not considered a good predictor for mortality.<sup>[26]</sup> This may be due to the coding limitations of the penetrating injury using the AIS. Though these patients are likely to sustain multiple gunshot injuries,<sup>[15]</sup> ISS does not account for multiple injuries to the same body region which may reflect in lower ISS score. Overall, the use of ISS in identifying the deceased thus appears to be limited. ISS and other anatomical scales, such as NISS, TRISS, and ICISS, have shown varying performance in the literature when predicting mortality in penetrating trauma.<sup>[28]</sup> Despite the limitation of ISS related to ignoring other injuries in the same anatomical area, evidence regarding the superiority of new anatomical scores appears to be inconclusive.<sup>[28]</sup>

Finally, this study demonstrated that the discriminatory ability of ISS was poor in nontraumatic injury mechanisms, including injury by fire, flame, or hot object, suffocation, poisoning, drowning and submersion, and injury involving natural and environmental causes. In these mechanisms, the sensitivity of ISS before and after adjusting for the confounding factors was very low. ISS should not be used to identify patients with high-mortality risk in these injury types. There is little research validating the ISS in these mechanisms of injury. One Australian single-center study demonstrated the ISS is a good predictor in patients with minor injuries (ISS < 16) and a poor predictor of mortality in severe burns.<sup>[29]</sup> This could be explained by the AIS coding system for burns, which, for example, does not discriminate between second and third degree burns above 10% total body surface area or between burns with 40% and 89% total body surface area. Other mechanism-specific scores, such as the Baux score in burns, have been shown to be more accurate in predicting mortality<sup>[30]</sup> and may be useful if incorporated in national trauma databases.

The different statistical approaches used in this study point toward a varying performance of ISS to identify deceased patients and predict mortality across different mechanisms of injury. Traditionally, an ISS cutoff value of ≥ 16 has been used to identify major trauma patients with a higher mortality regardless of mechanism of injury.<sup>[3]</sup> Since this cutoff value was adopted, there have been significant advances in trauma management and AIS coding, which were shown to significantly impact the classification of patients into low- and high-mortality risk groups.<sup>[21,28]</sup> Despite these changes and the development of likely superior ISSs, most trauma registries continue to use the ISS when assessing the severity of injury. Our study suggests that the ability of ISS to identify severely injured patients is dependent on the mechanism of injury type.

## 5. Limitations

This study has some potential limitations. Overall, the mortality rate and patients with major trauma (ISS ≥ 16) in the study population sample were relatively low. Consequently, low numbers of true positives and high numbers of true negatives resulted in low sensitivity and high specificity. This may be attributed mainly to the database used, as NEDS uses data from both trauma and nontrauma centers striving to be representative of the overall US population. Trauma center designation is included in the sampling strategy of the database and consequently, the sample contains the same percentage of trauma centers as the entire United States. Considering that in this study population,

nearly a half of the patients were transported to nontrauma centers, it would be reasonable to expect that most injuries would be minor with low mortality rates.

Patients who died at the scene may not have been transported to the ED and therefore they were not included in NEDS, which can underestimate the mortality rate of specific mechanisms. Furthermore, NEDS uses data from both trauma and non-trauma centers, which likely contributed to both overall low mortality and injury severity in this study when compared to major trauma databases.

Despite these limitations, NEDS is a large US national database of ED visits and the study results can be generalized to patients presenting with injuries in the United States or in other similar developed settings.

## 6. Conclusion

This study suggests the performance of ISS to predict mortality varies by mechanism of injury. Although in 6 out of twelve mechanisms, the ROC curve analysis demonstrated a moderate or high discriminatory ability to identify deceased patients, and the multivariate analysis revealed that ISS was a significant predictor of mortality in 9 out of 12 injury mechanisms, the sensitivities of the logistic regression models for all studied mechanism of injuries were poor. The ISS  $\geq 16$  threshold alone therefore should not be used to identify patients with high-mortality risk. The mortality risk assessment should be done individually and be based on clinical evaluation. Future trauma studies examining injury severity and outcomes should consider the mechanism of injury when attempting to identify severely injured patients using the ISS.

## Authors contributions

ME provided substantial involvement in the conception, design, and execution of the article as well as reviewing and revising the article for its credible content. JC and RE provided substantial involvement in the design, and execution of the article as well as drafting and revising the article. RB provided substantial involvement in design and reviewing the article as well as analysis of data. All authors read and approved the final article.

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