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# **Evaluating the definition of Severely Injured Patients: A** Japanese Nationwide 5-Year Retrospective Study

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3 4	1	Article
5 6 7	2	Evaluating the definition of Severely Injured Patients: A
8 9	3	Japanese Nationwide 5-Year Retrospective Study
10 11 12	4	Chiaki Toida <sup>1,2</sup> *, Takashi Muguruma <sup>2</sup> , Masayasu Gakumazawa <sup>2</sup> , Mafumi Shinohara <sup>2</sup> ,
13 14	5	Takeru Abe <sup>2</sup> , and Ichiro Takeuchi <sup>2</sup>
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2 3 4	17	Abstract:
5	18	Objectives: The definition of severely injured patients lacks universal consensus based on
6 7	19	quantitative measures. The most widely used definition of severe injury is based on the Injury
8 9	20	Severity Score (ISS), which is calculated using the Abbreviated Injury Scale (AIS) in Japan. This
10	21	study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in
11 12	22	patients with ISS $\geq 16$ , ISS $\geq 18$ , and ISS $\geq 26$ by age groups.
13 14	23	Design: Retrospective cohort study.
15 16	24	Setting: Japan Trauma Data Bank, which is a nationwide trauma registry with data from 280
17 18	25	hospitals.
19 20	26	Participants: We utilized data of 117,201 injured patients from a national database. We included
21 22	27	injured patients who were transferred from the scene of injury by ambulance and/or physician.
23 24	28	Primary and secondary outcome measures: Prevalence, in-hospital mortality, and odds ratio (OR)
25	29	for mortality with respect to age and injury level (ISS group).
26 27	30	Results: In all age categories, the in-hospital mortality of patient groups with an ISS $\geq$ 16, ISS $\geq$ 18,
28 29	31	and ISS 26 was 13.3%, 17.4%, and 23.5%, respectively. The in-hospital mortality for patients
30	32	aged > 75 years was the highest (20% greater than that of the other age groups). Moreover, in-
31 32	33	hospital mortality for age group 5–14 years was the lowest (4.0–10.9%). In all the age groups, the
33	34	OR for mortality for patients with ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26 was 12.8, 11.0, and 8.4,
34 35	35	respectively.
36 37	36	Conclusions: Our results revealed the lack of an acceptable definition, with a high in-hospital
38 39	37	mortality and high OR for mortality for all age groups.
40 41	38	
42 43	39	Keywords: severely injured patient; trauma scoring system; anatomical severity definition;
44	40	mortality risk; Japan Trauma Data Bank
45 46 47	41	
48 49	42	Strengths and limitations of this study
50 51	43	> This study is the first nationwide study in Japan to evaluate in-hospital mortality and odds ratio
52 53	44	for mortality in patients with severe injury according to age.
54 55 56	45	> We used a nationwide multi-institutional trauma database with a large sample size.
57	46	> The Japanese nationwide dataset with more missing data may have led to selection bias.
58 59 60	47	> The Japan Trauma Databank had used AIS 90 until 2018, which is not newest measure.
	48	

The most widely used definition of severely injured patients is the Injury Severity Score (ISS),[6] which is calculated using the Abbreviated Injury Scale (AIS).[7] Thirty years ago, an ISS cutoff value of  $\geq 16$  was defined as 'severely injured' because patients with an ISS  $\geq 16$  had an expected mortality rate of > 20%.[1] However, the mortality of patients with an ISS  $\ge 16$  and ISS  $\geq$ 26 decreased from 12.4% to 9.3% and from 25.4% to 20.3%, respectively, during the 10-year study period, due to a reduction in mortality and/or morbidity associated with organized trauma systems.[8]

Research based on the Japanese nationwide trauma registry has also shown that the in-hospital mortality trend has decreased in injured patients.[9–11] Moreover, there are more age-related differences in the mortality of severely injured patients in Japan than in the other developed countries because Japan has faced issues with the declining birth rate and aging population.[11,12] To date, no study has evaluated the validity of the definition of severe injury in a Japanese cohort using a detailed classification of the definition cutoff values and age groups. Therefore, this study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  as the commonly used anatomical injury definitions by age group.[2]

### 2. MATERIALS AND METHODS

#### 2.1. Study setting and population

This retrospective observational nationwide study was conducted based on data obtained from the Japan Trauma Data Bank (JTDB), which registers data of patients with an injury and/or burn, and records prehospitalization- and hospital-related information. The JTDB includes data on demographic characteristics, comorbidities, injury types, mechanism of injury, means of transportation, vital signs, AIS score, prehospital/in-hospital procedures, injury diagnosis as indicated by the AIS, and clinical outcomes. In most cases, physicians trained in AIS coding record the online registration of individual patient data. There were 280 participating hospitals in all 47 prefectures in Japan, including 92% of the Japanese government-approved tertiary emergency medical centers in March 2019. The Japan Association for the Surgery of Trauma permits open

#### **1. INTRODUCTION**

 The terminology used to quantify anatomical injury severity has been vaguely described for many decades using various phrases, such as severely injured and major trauma.[1-5] Although the most widely used definitions continue to rely on patients who have a high mortality and morbidity risk and require intense medical resources, such as massive resuscitation, multiple surgical operations, intensive care, and complex rehabilitation programs, [4,5] the definition lacks a universal consensus with quantitative measures.[2,3] 

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84	access and updating of existing medical information, and the Japan Correlation for Acute Medicine
85	evaluates the submitted data.
86	In this study, we used the JTDB dataset that included information from January 1, 2014 to
87	December 31, 2018, which initially yielded the data of 181,971 patients. The inclusion criterion for
88	this study was injured patients who were transferred from the scene of injury by ambulance and/or
89	physician. Patients with cardiac arrest on hospital arrival or with missing key data such as
90	mechanism, age, ISS, and/or survival outcome were excluded from this study. Figure 1 presents a
91	flow diagram of the patient selection process in this study.
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94	2.2. Data collection
95	We collected information from the JTDB, including the following variables: demographic
96	characteristics (age [years], sex, injury mechanism, transportation type, transfer process), and
97	clinical parameters (AIS of the injured region, ISS). In the JTDB, a patient with an AIS of the
98	injured region $\geq 3$ was defined as a case of a severely injured region.
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100	2.4. Ethics statement
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101	This study was approved by the hospital ethics committee of Yokohama City University Medical
102	Center (approval no. B170900003). The approval authority for data access was provided by the
103	Japanese Association for the Surgery of Trauma (Trauma Registry Committee). The requirement for
104	informed consent from the patients was waived owing to the observational nature of the study.
105	
	2.5. Statistical analysis
106	2.5. Statistical analysis
107	The outcomes were as follows: prevalence, in-hospital mortality, and OR for mortality with respect
108	to age group (0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, ≥75 years) and injury
109	severity (ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26; the ISSs of these groups were used as the definitions of
110	anatomical injury in a previous review article.[2]
111	Continuous variables are presented as medians with interquartile range (IQR, Q1-Q3), and
112	categorical variables are presented as the number and percentage of patients. The Mann-Whitney U
113	test and Wilcoxon's rank-sum test were used to analyze continuous variables, whereas the chi-
114	square test was used to analyze categorical variables. OR (95% confidence intervals, CI) for
115	mortality was calculated using a logistic regression model. All statistical analyses were performed
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using STATA/SE software (version 17.0; StataCorp; College Station, Texas, USA). Statistical 116 significance was defined as a two-tailed P-value of <0.05. 117

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## 119 2.6. Patient and public involvement

120 Patients and the public were not involved in the design, or conduct, or reporting, or 121 dissemination plans of this research. We will not directly disseminate our findings to involved

122 participants but plan to disseminate them through publication of this study.

123

### **3. RESULTS** 124

During the 5-year study period, we analyzed the data of 117,201 injured patients transferred from 125 the scene of injury; 113,435 (97%) of them had blunt trauma (Figure 1) (Table 1). The median age 126 and ISS score were 64 years (IQR, 41–78) and 10 (IQR, 9–19), respectively. The overall in-hospital 127 128 mortality rate was 9.0%.

129 Table 1 shows the characteristics by age group and injury severity group during the 5-year study period. The number of patients with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  was 48,028 (41% of all the 130 patients), 32,225 (28%), and 15,343 (13%), respectively. 131

Table 2 shows in-hospital mortality and OR for mortality with respect to age group and injury 132 severity. In all age categories, the in-hospital mortality of patients with ISS  $\geq$ 16, ISS  $\geq$ 18, and ISS 133  $\geq$ 26 was 13.3%, 17.4%, and 23.5%, respectively. In each age category, the in-hospital mortality for 134 patients aged > 55 years was higher than that for younger age groups, and that of patients aged > 75135 years was higher (by more than 20%) than that of all patient groups for each level of injury severity. 136 In-hospital mortality for the 5-14 years age group was 4.0-10.9% and lower than that for the other 137 138 age groups.

In all age categories, the OR for mortality by patient group was 12.8 (11.9–13.8), 11.0 (10.4–11.6), 139 and 8.4 (8.0-8.8), respectively, for the three levels of injury severity, and the OR in patients with 140 141 ISS  $\geq 16$  or ISS  $\geq 18$  was higher than that in patients group ISS  $\geq 26$ .

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nine age gro	oups and thr	ee levels of in	jury severity	groups.		-0626 nclud			
Overall	Age 0-4	Age 5-14	Age 15–24	Age 25-34	Age 35–44	<b>ing</b> Age <b>4</b> 5-54	Age 55–64	Age 65–74	Age ≥ 75
n = 117,199	n = 1095	n = 4079	n = 10,743	n = 7919	n = 9952		n = 13,931	n = 20,044	n = 36,705
64 (41–78)	2 (1–3)	10 (7–12)	20 (17–22)	29 (27–32)	40 (38–42)	52) 52) 52) 52)	60 (57-62)	69 (67–72)	83 (79–87
16,317 (44)	675 (62)	2985 (73)	8095 (75)	6008 (75)	7710 (77)		10017 (72)	12662 (63)	16317 (44
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113,435 (97)	1073 (98)	4020 (99)	10,477 (98)	7508 (95)	9361 (94)	<b>3.</b> <b>10</b> <b>10</b> <b>10</b> <b>1</b> <b>10</b> <b>1</b> <b>10</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b>	13,383 (96)	19,433 (97)	36,705 (9
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36,244 (31)	439 (40)	1213 (30)	2798 (26)	1933 (24)	2527 (25)	ad a	4451 (32)	7384 (37)	12,136 (3
940 (0.8)	4 (0.4)	33 (0.8)	150 (1.4)	109 (1.4)	128 (1.3)	<b>2</b> 4 <b>0</b> .0)	123 (0.9)	133 (0.7)	136 (0.4)
478 (0.4)	6 (0.6)	2 (0.1)	27 (0.3)	39 (0.5)	55 (0.6)		77 (0.6)	110 (0.6)	92 (0.3)
256,723 (22)	148 (14)	622 (15)	2831 (26)	2110 (27)	2759 (28)	train 485029)	3726 (27)	4594 (23)	5448 (15)
5407 (5)	27 (2)	185 (5)	805 (7)	591 (7)	682 (7)	ing, 709	684 (5)	831 (4)	893 (2)
13,146 (10)	12 (1)	128 (3)	861 (8)	788 (10)	1120 (11)	and 530213)	2106 (15)	3053 (15)	3548 (10)
6562 (6)	57 (5)	590 (14)	581 (5)	522 (7)	711 (7)		798 (6)	1026 (5)	1428 (4)
31,526 (27)	124 (11)	634 (16)	2143 (20)	1660 (21)	2055 (21)	<b>6</b> ,404 <b>9</b> 20)	2691 (19)	4358 (22)	15,457 (4
10 (9–19)	9 (4–16)	9 (5–16)	10 (5–19)	10 (6–20)	13 (9–20)	<b>החמ</b> 3 (21)	14 (9–21)	14 (9–21)	9 (9–17)
3361 (9.0)	23 (2.1)	48 (1.2)	354 (3.3)	310 (3.9)	372 (3.7)	ogies <sup>33</sup> (7,4)	762 (5.5)	1438 (7.2)	3361 (9.0)
48,028 (41)	376 (34)	1166 (29)	3878 (36)	3043 (38)	4076 (41)	5297 <b>2</b> 43)	6541 (47)	9711 (48)	13,940 (3
32,225 (28)	187 (17)	747 (18)	2954 (28)	2305 (29)	2985 (30)	3793 <b>8</b> 31)	4372 (31)	6256 (31)	8626 (23)
15,343 (13)	62 (6)	367 (9)	1595 (15)	1129 (14)	1481 (15)	1823 <b>5</b> 15)	2038 (15)	2910 (15)	3938 (11)
			1595 (15)		1481 (15)	379 <u>3</u> 1823	Depar Depar	(15) 2038 (15)	Constraint         4372 (31)         6256 (31)           Constraint         2038 (15)         2910 (15)
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		No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)	No. of patients	619 on 23 February 2023 [ ling for uses related to text	OR (95%CI)	No. of patients	Mortality, %	OR (95%CI)
-	ISS ≥ 16	48,028	13.3	12.8 (11.9–13.8)	376	5.9	44.6 (6.0–332.4)	1166	4.0	59.8 (14.5–246.7)	3878	3. Download shogeschool text and dat	34.1 (21.4–54.2)	3043	9.8	48.2 (26.4–88.1)
_	ISS ≥ 18	32,225	17.4	11.0 (10.4–11.6)	187	11.2	57.3 (13.3–246.7)	747	5.8	40.6 (16.0–103.0)	2954	Downloaded from http://bmjopen. hogeschool . ext and data mining, Al training, an	33.1 (22.6–48.5)	2305	12.2	25.7 (17.6–37.6)
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13 14 15 16		4076	8.7	29.2 (18.4–46.5)	5297	9.3	17.1 (12.4–23.6)	6541	10.8	16.2 (12.3–21.3)	9711	13.6 ald	5 5 5 5 5 5 5 5 5 5 5 5 5 5	13940	20.2	10.5 (9.5–11.5)	
17 18 19		2985	11.2	23.7 (16.8–33.4)	3793	11.7	12.0 (9.6–15.1)	4372	14.4	11.9 (9.8–14.4)	6256	18.6	<b>b d d</b> 11.2 <b>from</b> (9.8–12.9)	8626	27.4	10.5 (9.7–11.3)	
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### 4. DISCUSSION

To the best of our knowledge, this is the first nationwide study in Japan to evaluate in-hospital mortality and OR for mortality in patients with severe injury according to age. Our study showed that in all three groups with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ , which are the commonly used anatomical injury definitions, in-hospital mortality for patients aged < 55 years was between 4.0% and 17.7% for each level of injury severity. Moreover, after evaluating the validity of the definition for severely injured patients in a Japanese cohort via the detailed classification of the definition cutoff values and age groups, there was no acceptable definition, with not only a high in-mortality 

but also a high OR for mortality for all age groups. 

Previous studies demonstrated that in 1990 when severe injury was defined as an ISS cutoff of  $\geq 16$ points, the mortality of patients with an ISS  $\geq 16$  was more than 20%; however, the mortality of

these patients decreased; therefore, an ISS cutoff of  $\geq 18$  or 26 might be suitable for defining 

severely injured patients with a high mortality rate [1-3.8] This study also showed that patients with 

ISS  $\geq$ 26 had the highest in-hospital mortality in all age categories. However, the OR for mortality in patients with ISS  $\geq$ 26 was lower than that in patients with ISS  $\geq$ 16 and ISS  $\geq$ 18. There are possible explanations for the lack of an accepted definition with a high in-hospital mortality and high OR for 

mortality in a Japanese cohort.

First, there are differences in the study era and/or cohorts at the time of development.[1] A previous 

10-year nationwide study using the JTDB dataset from 2004 to 2013 demonstrated that the in-hospital mortality of patients with ISS  $\geq 16$  decreased from 28.5% to 15.7% due to improvements in trauma care and medical ambulance services.[9] Moreover, in the Japanese cohort, unlike the aging 

population in the rest of the world, the characteristics and survival outcome of severely injured patients varied widely according to age, and the mortality risk of elderly patients with severe injury 

was higher than that of the other age groups.[12] A previous Japanese nationwide study showed that the incidence rate of severe traumatic brain injury among severely injured patients aged > 65 years 

was high (40.7%).[13] Moreover, the in-hospital mortality of these patients was higher than that of 

the other age-groups.[13] These results suggest that the elderly patient groups had a higher mortality 

because of the high proportion and mortality of severe traumatic head injury. This study also 

showed that the prevalence and in-hospital mortality of severely injured patients aged 55–64, 65– 

75, and  $\geq$ 75 years increased stepwise. However, in pediatric patients, a previous study suggested

that the ISS cutoff of  $\geq 16$  in adult patients was equivalent to that of  $\geq 26$  in pediatric patients.[14] A 

Japanese nationwide study using the JTDB dataset also showed that the in-hospital mortality of 

pediatric patients with ISS  $\geq 16$  was 8.9% in 2018. However, this study showed that the in-hospital 

mortality even for pediatric patients aged 5–14 years with ISS  $\geq$ 26 was low (10.9%). Therefore, it is 

- important to develop an acceptable definition of severe injury by considering the age-related
  - characteristics and mortality risks in a Japanese cohort.

Second, there was a limitation in evaluating only anatomical severity as a definition of severe injury. A more recent approach suggests that the addition of other physiological variables to the

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anatomical severity score has the advantage of identifying severely injured patients with mortality risk. [2,15,16]. Although the mortality of patients with ISS  $\geq 16$  was 18.7%, with ISS  $\geq 16$  in addition to one other physiological parameter increased from 35% to Moreover, patients with an increasing number of the physiological variable, such as the coma scale, hypotension, and laboratory values (e.g., acidosis and/or coagulopathy), n increased risk of mortality.[15–17] However, we could not evaluate the variables acco physiological parameters and findings of blood tests. Therefore, it seems important to parameters together with the anatomical severity used in this study to develop a well-definition of severely injured patients. Our study had some limitations. First, there was selection bias because not all Japanes that treat severely injured patients were registered in the JTDB. Moreover, the JTDB missing data, especially for pediatric patients.[18] A high-quality Japanese nationwide less missing data should be constructed to improve the accuracy of predicting the surv patients. Second, because the number of patients aged 0-4 and 5-14 years was small 3.5% of all the patients, respectively), it is possible that the ORs of these patient group sample sizes were overestimated. In addition, the number of participating hospitals different the study period. Furthermore, the JTDB used AIS 90 until 2018 and is now using the updated 2008 coding scale. Similar studies need to be conducted using the newest mea our results. **5. CONCLUSIONS** This is the first nationwide study in Japan to evaluate the prevalence, in-hospital mort for mortality in patients with severe injury according to age categories. In all the three anatomical injury, the in-hospital mortality for patients aged < 55 years was low. Eval validity of the definition for severely injured patients in a Japanese cohort based on th classification of the definition cutoff values and age categories revealed the lack of an definition, with not only a high in-hospital mortality, but also a high OR for mortality categories. Author Contributions: Conceptualization, CT and TM; methodology, CT; software, CT validation, CT, TM, TA, MG, and MS; formal analysis, CT; investigation, CT, TM, MS, resources, CT and TA; data curation, CT and TA; writing-original draft preparation, CT: review and editing, CT, TM, MS, MG, TA, and IT; visualization, CT; supervision, IT; project administration and funding acquisition, CT All authors have read and agreed to the published version of the manuscript. Funding: CT received a grant from the General Insurance Association of Japan [21-08].

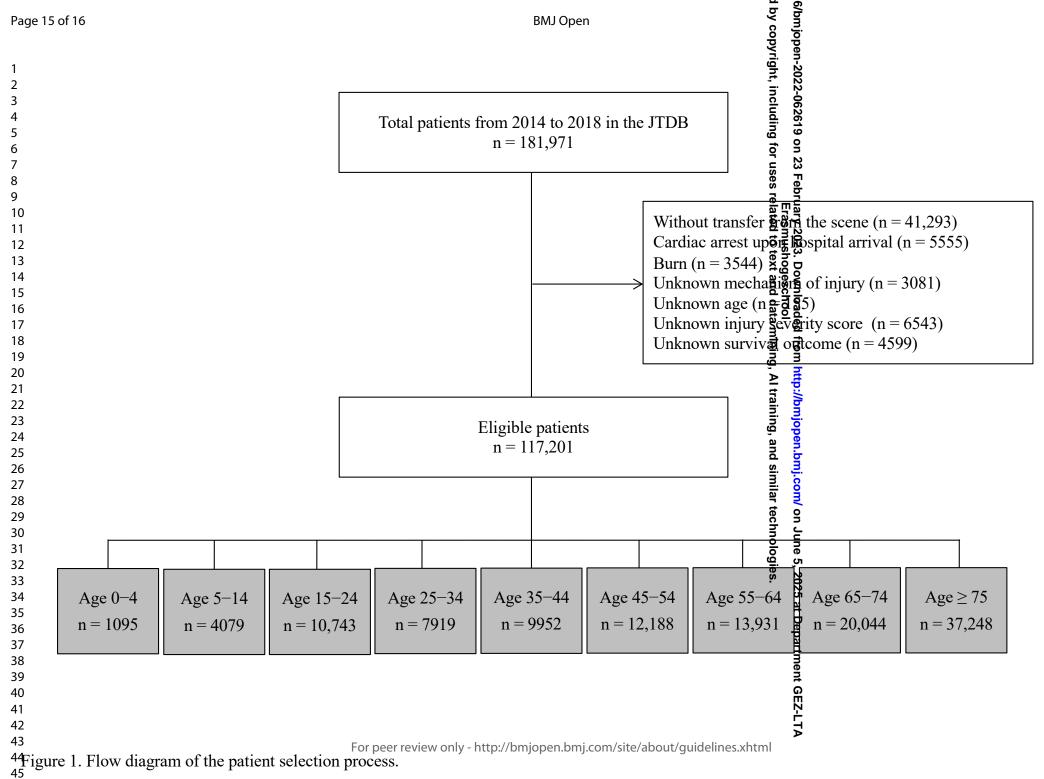
Informed Consent Statement: The requirement for informed consent from the patients was waived due

to the observational nature of the study design.

- Data Availability Statement: The approving authority for data access was the Japanese Association for
  - the Surgery of Trauma (Trauma Registry Committee).
  - Acknowledgments: None.
    - Conflicts of Interest: The authors declare no conflict of interest.

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21 22	291	
23	292	
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26	294	Figure Legend
27 28	295	Figure 1. Flow diagram of the patient selection process.
29 30	296	JTDB, Japanese Trauma Data Bank.
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# STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the	1,2
		abstract	
		(b) Provide in the abstract an informative and balanced summary of what was	2
		done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being	2,3
		reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
Methods			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of	3,4
		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	3,4
		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	N/A
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	4,5
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	4,5
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	3,4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	4,5
		describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	4,5
		confounding	4.5
		(b) Describe any methods used to examine subgroups and interactions	4,5
		(c) Explain how missing data were addressed	3,4
		( <i>d</i> ) If applicable, explain how loss to follow-up was addressed	N/A
		( <u>e</u> ) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	5
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	3,4,5
		(c) Consider use of a flow diagram	5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	3,4,5
		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	3
		(c) Summarise follow-up time (eg, average and total amount)	3
Outcome data	15*	Report numbers of outcome events or summary measures over time	5

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Main results	16	( <i>a</i> ) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5
		(b) Report category boundaries when continuous variables were categorized	5
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	10
		Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	9,10
		multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9,10
Other informati	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if	10
		applicable, for the original study on which the present article is based	

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

# **Evaluating the definition of Severely Injured Patients: A** Japanese Nationwide 5-Year Retrospective Study

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Manuscript ID	bmjopen-2022-062619.R1						
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Date Submitted by the Author:	16-Nov-2022						
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<b>Primary Subject Heading</b> :	Emergency medicine						
Secondary Subject Heading:	Medical management, Epidemiology						
Keywords:	TRAUMA MANAGEMENT, EPIDEMIOLOGY, INTENSIVE & CRITICAL CARE						

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1	Article
2	Evaluating the definition of Severely Injured Patients: A
3	Japanese Nationwide 5-Year Retrospective Study
4 5	Chiaki Toida <sup>1,2</sup> *, Takashi Muguruma <sup>2</sup> , Masayasu Gakumazawa <sup>2</sup> , Mafumi Shinohara <sup>2</sup> , Takeru Abe <sup>2</sup> , and Ichiro Takeuchi <sup>2</sup>
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13	Received: date; Accepted: date; Published: date
14 15	Word count: 1961

1 2		
2 3 4	16	Abstract:
5	17	Objectives: The definition of severely injured patients lacks universal consensus based on
6 7	18	quantitative measures. The most widely used definition of severe injury is based on the Injury
8 9	19	Severity Score (ISS), which is calculated using the Abbreviated Injury Scale (AIS) in Japan. This
10	20	study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in
11 12	21	patients with ISS $\geq 16$ , ISS $\geq 18$ , and ISS $\geq 26$ by age groups.
13 14	22	Design: Retrospective cohort study.
15 16	23	Setting: Japan Trauma Data Bank, which is a nationwide trauma registry with data from 280
17 18	24	hospitals.
19 20	25	Participants: We utilized data of 117,199 injured patients from a national database. We included
21 22	26	injured patients who were transferred from the scene of injury by ambulance and/or physician.
23 24	27	Primary and secondary outcome measures: Prevalence, in-hospital mortality, and odds ratio (OR)
25	28	for mortality with respect to age and injury level (ISS group).
26 27	29	Results: In all age categories, the in-hospital mortality of patient groups with an ISS $\geq$ 16, ISS $\geq$ 18,
28 29	30	and ISS 26 was 13.3%, 17.4%, and 23.5%, respectively. The in-hospital mortality for patients
30	31	aged > 75 years was the highest (20% greater than that of the other age groups). Moreover, in-
31 32	32	hospital mortality for age group 5–14 years was the lowest (4.0–10.9%). In all the age groups, the
33	33	OR for mortality for patients with ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26 was 12.8, 11.0, and 8.4,
34 35	34	respectively.
36 37	35	Conclusions: Our results revealed the lack of an acceptable definition, with a high in-hospital
38 39	36	mortality and high OR for mortality for all age groups.
40 41	37	
42 43	38	Keywords: severely injured patient; trauma scoring system; anatomical severity definition;
44	39	mortality risk; Japan Trauma Data Bank
45 46 47	40	
48 49	41	Strengths and limitations of this study
50 51	42	> This study is the first nationwide study in Japan to evaluate in-hospital mortality and odds ratio
52 53	43	for mortality in patients with severe injury according to age.
54 55 56	44	> We used a nationwide multi-institutional trauma database with a large sample size.
57	45	> The Japanese nationwide dataset with more missing data may have led to selection bias.
58 59 60	46	> The Japan Trauma Databank had used AIS 90 until 2018, which is not newest measure.
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# **1. INTRODUCTION**

The terminology used to quantify anatomical injury severity has been vaguely described for many decades using various phrases, such as severely injured and major trauma.[1–5] Although the most widely used definitions continue to rely on patients who have a high mortality and morbidity risk and require intense medical resources, such as massive resuscitation, multiple surgical operations, intensive care, and complex rehabilitation programs,[4,5] the definition lacks a universal consensus with quantitative measures.[2,3]

The most widely used definition of severely injured patients is the Injury Severity Score (ISS),[6] which is calculated using the Abbreviated Injury Scale (AIS).[7] Thirty years ago, an ISS cutoff value of  $\geq 16$  was defined as 'severely injured' because patients with an ISS  $\geq 16$  had an expected mortality rate of  $\geq 20\%$ .[1] However, the mortality of patients with an ISS  $\geq 16$  and ISS  $\geq 26$  decreased from 12.4% to 9.3% and from 25.4% to 20.3%, respectively, during the 10-year study period, due to a reduction in mortality and/or morbidity associated with organized trauma systems.[8]

Research based on the Japanese nationwide trauma registry has also shown that the in-hospital mortality trend has decreased in injured patients.[9–11] Moreover, there are more age-related differences in the mortality of severely injured patients in Japan than in the other developed countries because Japan has faced issues with the declining birth rate and aging population.[11,12] To date, no study has evaluated the validity of the definition of severe injury in a Japanese cohort using a detailed classification of the definition cutoff values and age groups. We hypothesized that there would be differences in in-hospital mortality rate and risk among Japanese injured patients by age and anatomical severity. Therefore, this study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with an ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$  as the commonly used anatomical injury definitions by age group [2]. 

74 2. MATERIALS AND METHODS

# **2.1. Study setting and population**

This retrospective observational nationwide study was conducted based on data obtained from the Japan Trauma Data Bank (JTDB), which registers data of patients with an injury and/or burn, and records prehospitalization- and hospital-related information. The JTDB includes data on demographic characteristics, comorbidities, injury types, mechanism of injury, means of transportation, vital signs, AIS score, prehospital/in-hospital procedures, injury diagnosis as indicated by the AIS, and clinical outcomes. In most cases, physicians trained in AIS coding record the online registration of individual patient data. There were 280 participating hospitals in all 47 prefectures in Japan, including 92% of the Japanese government-approved tertiary emergency medical centers in March 2019. The Japan Association for the Surgery of Trauma permits open 

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access and updating of existing medical information, and the Japan Correlation for Acute Medicine
evaluates the submitted data.
In this study, we used the JTDB dataset that included information from January 1, 2014 to
December 31, 2018, which initially yielded the data of 181,971 patients. The inclusion criterion for
this study was injured patients who were transferred from the scene of injury by ambulance and/or
physician. Patients with cardiac arrest on hospital arrival or with missing key data such as
mechanism, age, ISS, and/or survival outcome were excluded from this study. Figure 1 presents a
flow diagram of the patient selection process in this study.
2.2. Data collection
We collected information from the JTDB, including the following variables: demographic
characteristics (age [years], sex, injury mechanism, transportation type, transfer process), and
clinical parameters (AIS of the injured region, ISS). In the JTDB, a patient with an AIS of the
injured region $\geq 3$ was defined as a case of a severely injured region.
2.4. Ethics statement
This study was approved by the hospital ethics committee of Yokohama City University Medical
Center (approval no. B170900003). The approval authority for data access was provided by the
Japanese Association for the Surgery of Trauma (Trauma Registry Committee). The requirement for
informed consent from the patients was waived owing to the observational nature of the study.
2.5. Statistical analysis
The outcomes were as follows: prevalence, in-hospital mortality, and OR for mortality with respect
to age group (0-4, 5-14, 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, ≥75 years) and injury
severity (ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26; the ISSs of these groups were used as the definitions of
anatomical injury in a previous review article.[2]
Continuous variables are presented as medians with interquartile range (IQR, Q1-Q3), and
categorical variables are presented as the number and percentage of patients. The Mann-Whitney U
test and Wilcoxon's rank-sum test were used to analyze continuous variables, whereas the chi-
square test was used to analyze categorical variables. OR (95% confidence intervals, CI) for
mortality was calculated using a logistic regression model. All statistical analyses were performed

- injured region  $\geq 3$  was defined a

### 2.4. Ethics statement

This study was approved by the Center (approval no. B1709000 Japanese Association for the Su informed consent from the patie

### 2.5. Statistical analysis

The outcomes were as follows: to age group (0-4, 5-14, 15-24 severity (ISS  $\geq 16$ , ISS  $\geq 18$ , and anatomical injury in a previous

Continuous variables are presen categorical variables are present test and Wilcoxon's rank-sum te square test was used to analyze mortality was calculated using a using STATA/SE software (version 17.0; StataCorp; College Station, Texas, USA). Statistical 

significance was defined as a two-tailed P-value of <0.05. 

118	
119	2.6. Patient and public involvement
120	Patients and the public were not involved in the design, or conduct, or reporting, or
121 122	dissemination plans of this research. We will not directly disseminate our findings to involve participants but plan to disseminate them through publication of this study.
122	participants but plan to disseminate them through publication of this study.
123	
124	3. RESULTS
125	During the 5-year study period, we analyzed the data of 117,199 injured patients transferred from
126	the scene of injury; 113,435 (97%) of them had blunt trauma (Figure 1) (Table 1). The median age
127	and ISS score were 64 years (IQR, 41–78) and 10 (IQR, 9–19), respectively. The overall in-hospita
128	mortality rate was 6.1%.
129	Table 1 shows the characteristics by age group and injury severity group during the 5-year study
130	period. The number of patients with ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26 was 48,028 (41% of all the
131	patients), 32,225 (28%), and 15,343 (13%), respectively.
132	Table 2 shows in-hospital mortality and OR for mortality with respect to age group and injury
133	severity. In all age categories, the in-hospital mortality of patients with ISS $\geq$ 16, ISS $\geq$ 18, and ISS
134	$\geq$ 26 was 13.3%, 17.4%, and 23.5%, respectively. In each age category, the in-hospital mortality fo
135	patients aged $> 55$ years was higher than that for younger age groups, and that of patients aged $> 7$
136	years was higher (by more than 20%) than that of all patient groups for each level of injury severit
137	In-hospital mortality for the 5–14 years age group was 4.0–10.9% and lower than that for the other
138	age groups.
139	In all age categories, the OR for mortality by patient group was 12.8 (11.9–13.8), 11.0 (10.4–11.6)
140	and 8.4 (8.0-8.8), respectively, for the three levels of injury severity, and the OR in patients with
141	ISS $\geq 16$ or ISS $\geq 18$ was higher than that in patients group ISS $\geq 26$ .
142	
143	

of 16	BMJ Open       BMJ Open         Table 1. Characteristics by the nine age groups and three levels of injury severity groups.       BMJ Open														
144	Table 1. Characteristics by the		-												
	Variables	Overall n = 117,199	Age 0-4 n = 1095	Age 5–14 n = 4079	Age $15-24$ n = 10,743	Age 25–34 n = 7919	Age 35–44 n = 9952	$n_{Age} = \frac{100}{100} -54$	Age 55–64 n = 13,931	Age $65-74$ n = 20,044	Age $\ge 7$ : n = 36,2				
	Age, years	64 (41–78)	2 (1-3)	10 (7–12)	20 (17–22)	29 (27–32)	40 (38–42)	<b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b>	60 (57–62)	69 (67–72)	83 (79–8				
	Male	16,317 (44)	675 (62)	2985 (73)	8095 (75)	6008 (75)	7710 (77)	oruary 2 Erasn related	10017 (72)	12662 (63)	16317 (4				
	Mechanism of injury							y 202 asmu ed to							
	Blunt	113,435 (97)	1073 (98)	4020 (99)	10,477 (98)	7508 (95)	9361 (94)	text 2004 1006 1007 1007 1007 1007 1007 1007 1007	13,383 (96)	19,433 (97)	36,705 (				
	Injury region							/ 2023. [9ownloaded f smushogeschool d to text and data m							
	Head injury with AIS $\geq$ 3	36,244 (31)	439 (40)	1213 (30)	2798 (26)	1933 (24)	2527 (25)	<b>ade</b> 28)	4451 (32)	7384 (37)	12,136 (3				
	Facial injury with AIS $\geq$ 3	940 (0.8)	4 (0.4)	33 (0.8)	150 (1.4)	109 (1.4)	128 (1.3)	nining.	123 (0.9)	133 (0.7)	136 (0.4				
	Neck injury with AIS $\geq$ 3	478 (0.4)	6 (0.6)	2 (0.1)	27 (0.3)	39 (0.5)	55 (0.6)	₩0 (00)	77 (0.6)	110 (0.6)	92 (0.3)				
	Chest injury with AIS $\geq$ 3	25,723 (22)	148 (14)	622 (15)	2831 (26)	2110 (27)	2759 (28)	p://p29) 1 training, 709 (29)	3726 (27)	4594 (23)	5448 (15				
	Abdominal and pelvic injury with AIS $\geq$ 3	5407 (5)	27 (2)	185 (5)	805 (7)	591 (7)	682 (7)	<b>ing</b> ,709 <b>(20)</b>	684 (5)	831 (4)	893 (2)				
	Spinal injury with AIS $\geq$ 3	13,146 (10)	12 (1)	128 (3)	861 (8)	788 (10)	1120 (11)	$\overline{\mathbf{Q}}_{530}$	2106 (15)	3053 (15)	3548 (10				
	Upper extremity injury with AIS $\geq$ 3	6562 (6)	57 (5)	590 (14)	581 (5)	522 (7)	711 (7)	similar	798 (6)	1026 (5)	1428 (4)				
	Lower extremity injury with AIS $\geq 3$	31,526 (27)	124 (11)	634 (16)	2143 (20)	1660 (21)	2055 (21)	<b>6</b> ,404 <b>9</b> 20)	2691 (19)	4358 (22)	15,457 (				
	Injury Severity Score	10 (9–19)	9 (4–16)	9 (5–16)	10 (5–19)	10 (6–20)	13 (9–20)	103 (9521)	14 (9–21)	14 (9–21)	9 (9–17)				
	Actual in-hospital mortality	7201 (6.1)	23 (2.1)	48 (1.2)	354 (3.3)	310 (3.9)	372 (3.7)	gies33 (4,4)	762 (5.5)	1438 (7.2)	3361 (9.				
	Injury Severity Score ≥ 16	48,028 (41)	376 (34)	1166 (29)	3878 (36)	3043 (38)	4076 (41)	5297 <b>(</b> 43)	6541 (47)	9711 (48)	13,940 (				
	Injury Severity Score ≥ 18	32,225 (28)	187 (17)	747 (18)	2954 (28)	2305 (29)	2985 (30)	3793 <b>0</b> 31)	4372 (31)	6256 (31)	8626 (23				
	Injury Severity Score ≥ 26	15,343 (13)	62 (6)	367 (9)	1595 (15)	1129 (14)	1481 (15)	1823	2038 (15)	2910 (15)	3938 (1				

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Page	8 of	<sup>-</sup> 16
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Tab	<u>1e 2. 111-1108</u>	Distribution of Overall         No. of patients       Mortality, 0R (95%CI)         48,028       13.3 (12.8 (6383) (11.9–13.8)         32,225       17.4 (11.0 (10.4–11.6))         15,343       23.5 (8.4 (8.0–8.8))			ds ratio for mortality of patien Age 0-4			At groups with ISS $\geq$ 16, ISS $\geq$ Age 5-14			Thing fore 1/2 r	24	Age 25–34		
	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	es related to t	, OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI
ISS ≥ 1	6 48,028	13.3 (6383)	12.8 (11.9–13.8)	376	5.9 (22)	44.6 (6.0–332.4)	1166	4.0 (46)	59.8 (14.5–246.7)	3878	text and att (3) (3) (3) (3) (3) (3) (3) (3) (3) (3)	34.1 (21.4–54.2)	3043	9.8 (299)	48.2 (26.4–88
ISS ≥ 1	3 32,225	17.4 (5602)	11.0 (10.4–11.6)	187	11.2 (21)	57.3 (13.3–246.7)	747	5.8 (43)	40.6 (16.0–103.0)	2954	a mining) 1111 (32 Al	33.1 (22.6–48.5)	2305	12.2 (280)	25.7 (17.6–37
$ISS \ge 2$	5 15,343	23.5 (3605)	8.4 (8.0–8.8)	62	17.7 (11)	18.4 (7.7–43.6)	367	10.9 (40)	56.6 (26.3–122.0)	1595	training) (297)	17.9 (14.1–22.8)	1129	19.9 (225)	19.6 (15.2–2:
											i similar technologies.				

Page 1 2	9 of 16					BMJ Open BMJ Open Age 45–54 Age 55–64 Age 55–64 Age 55–64 Age 645–54 Age 645–54 Age 645–54 Age 645–54 Age 645–54										
3 4 5 6 7 8	156		Age 35-44			Age 45-54			Age 55-64			Age 6kuses	2-062619 on 23 Febr		Age ≥ 75	
9 10 11 12		No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)	No. of patients	Mortal	Erasn (95%CI)	No. of patients	Mortality, % (n)	OR (95%CI)
13 14 15 16		4076	8.7 (353)	29.2 (18.4–46.5)	5297	9.3 (492)	17.1 (12.4–23.6)	6541	10.8 (707)	16.2 (12.3–21.3)	9711	13.6 (1317) do	50000000000000000000000000000000000000	13940	20.2 (2812)	10.5 (9.5–11.5)
17 18 19		2985	11.2 (335)	23.7 (16.8–33.4)	3793	11.7 (442)	12.0 (9.6–15.1)	4372	14.4 (629)	11.9 (9.8–14.4)	6256	18.6 mining,	UShogeschool 	8626	27.4 (2364)	10.5 (9.7–11.3)
20 21 22 23		1481	18.2 (270)	18.3 (14.5–23.2)	1823	17.7 (322)	10.3 (8.6–12.4)	2038	20.9 (426)	9.1 (7.8–10.6)	2910	24.6 (716) (716)	7.4 (6.6–8.3)	3938	34.0 (1338)	8.0 (7.3–8.6)
23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46	157	ISS, Inju	ry Severity	Score; OR,	odds ratio				open.bmj.co	om/site/abou		, and similar technologies.	en.bmj.com/ on June 5, 2025 at Department GEZ-LTA			8

### 4. DISCUSSION

To the best of our knowledge, this is the first nationwide study in Japan to evaluate in-hospital mortality and OR for mortality in patients with severe injury according to age. Our study showed that in all three groups with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ , which are the commonly used anatomical injury definitions, in-hospital mortality for patients aged < 55 years was between 4.0% and 17.7% for each level of injury severity. Moreover, after evaluating the validity of the definition for severely injured patients in a Japanese cohort via the detailed classification of the definition cutoff values and age groups, there was no acceptable definition, with not only a high in-hospital 

mortality but also a high OR for mortality for all age groups. 

Previous studies demonstrated that in 1990 when severe injury was defined as an ISS cutoff of  $\geq 16$ 

points, the mortality of patients with an ISS  $\geq 16$  was more than 20%; however, the mortality of

these patients decreased; therefore, an ISS cutoff of  $\geq 18$  or 26 might be suitable for defining 

severely injured patients with a high mortality rate.[1–3,8] This study also showed that patients with 

ISS  $\geq$ 26 had the highest in-hospital mortality in all age categories. However, the OR for mortality in 

patients with ISS  $\geq 26$  was lower than that in patients with ISS  $\geq 16$  and ISS  $\geq 18$ . There are possible 

explanations for the lack of an accepted definition with a high in-hospital mortality and high OR for mortality in a Japanese cohort. 

First, there are differences in the study era and/or cohorts at the time of development.[1] A previous 10-year nationwide study using the JTDB dataset from 2004 to 2013 demonstrated that the in-hospital mortality of patients with ISS  $\geq 16$  decreased from 28.5% to 15.7% due to improvements in trauma care and medical ambulance services.[9] Moreover, in the Japanese cohort, unlike the aging population in the rest of the world, the characteristics and survival outcome of severely injured patients varied widely according to age, and the mortality risk of elderly patients with severe injury was higher than that of the other age groups.[12] A previous Japanese nationwide study showed that the incidence rate of severe traumatic brain injury among severely injured patients aged > 65 years was high (40.7%).[13] Moreover, the in-hospital mortality of these patients was higher than that of the other age-groups.[13] These results suggest that the elderly patient groups had a higher mortality because of the high proportion and mortality of severe traumatic head injury. This study also showed that the prevalence and in-hospital mortality of severely injured patients aged 55–64, 65– 75, and  $\geq$ 75 years increased stepwise. On the other hand, previous studies suggested that the ISS cutoff of  $\geq 16$  in adult patients was equivalent to a cut-off  $\geq 26$  in pediatric patients aged  $\leq 16$ years.[14,15] This study showed different results from those of a previous study [15], wherein the in-hospital mortality of pediatric patients aged 0–4 years with an ISS  $\geq$ 26 was high (17.7%) and that of pediatric patients aged 5–14 years with an ISS  $\geq$ 26 was low (10.9%), as shown in Table 2. Moreover, a previous study showed that there was a difference in the optimal cut off value of ISS in predicting severely injury mortality risk by region and/or mechanism of injury among pediatric patients. Therefore, it is important to develop an acceptable definition of severe injury by considering the age-related characteristics and mortality risks in a Japanese cohort. Moreover, this

study showed that the mortality rate and mortality risk of injured patients in Japan differed by age groups and did not have a linear correlation with age in years. For a better predictive accuracy in mortality, it may be effective to add age categories as a predictive variable for mortality and to

calculate the coefficient for coded value according to mortality risk by each age group, as shown in the Trauma and injury Severity Score methodology [16]. Second, there was a limitation in evaluating only anatomical severity as a definition of severe injury. A more recent approach suggests that the addition of other physiological variables to the anatomical severity score has the advantage of identifying severely injured patients with a high mortality risk. [2,17,18] Although the mortality of patients with ISS  $\geq 16$  was 18.7%, that of patients with ISS  $\geq 16$  in addition to one other physiological parameter increased from 35% to 38%.[2] Moreover, patients with an increasing number of the physiological variable, such as the Glasgow coma scale, hypotension, and laboratory values (e.g., acidosis and/or coagulopathy), may have an increased risk of mortality.[17–19] However, we could not evaluate the variables according to physiological parameters and findings of blood tests. Therefore, it seems important to evaluate these parameters together with the anatomical severity used in this study to develop a well-validated definition of severely injured patients. Our study had some limitations. First, there was selection bias because not all Japanese hospitals that treat severely injured patients are registered in the JTDB. The 280 tertiary centers equivalent to Level I trauma centers in the United States participated, including 92% of the Japanese government-approved tertiary emergency medical centers in March 2019. Therefore, the JTDB is not a population-based sample of injured patients and the data are registered voluntarily. Moreover, the JTDB dataset has missing data, especially for pediatric patients.[20] The number of pediatric 

patients were lower than that of adult patients. Therefore, missing data may have a more significant influence on the analysis of the pediatric patients' data than that of the adult patients' data. A highquality Japanese nationwide dataset with less missing data should be constructed to improve the accuracy of predicting the survival of injured patients in the data analysis for all age categories. Second, because the number of patients aged 0-4 and 5-14 years was small (0.9% and 3.5% of all the patients, respectively), it is possible that the ORs of these patient groups with small sample sizes were overestimated. In addition, the number of participating hospitals differed across the study period. Furthermore, the JTDB used AIS 90 until 2018 and is now using the AIS 2005 updated 2008 coding scale. Similar studies need to be conducted using the newest measure to verify our results. 

## **5. CONCLUSIONS**

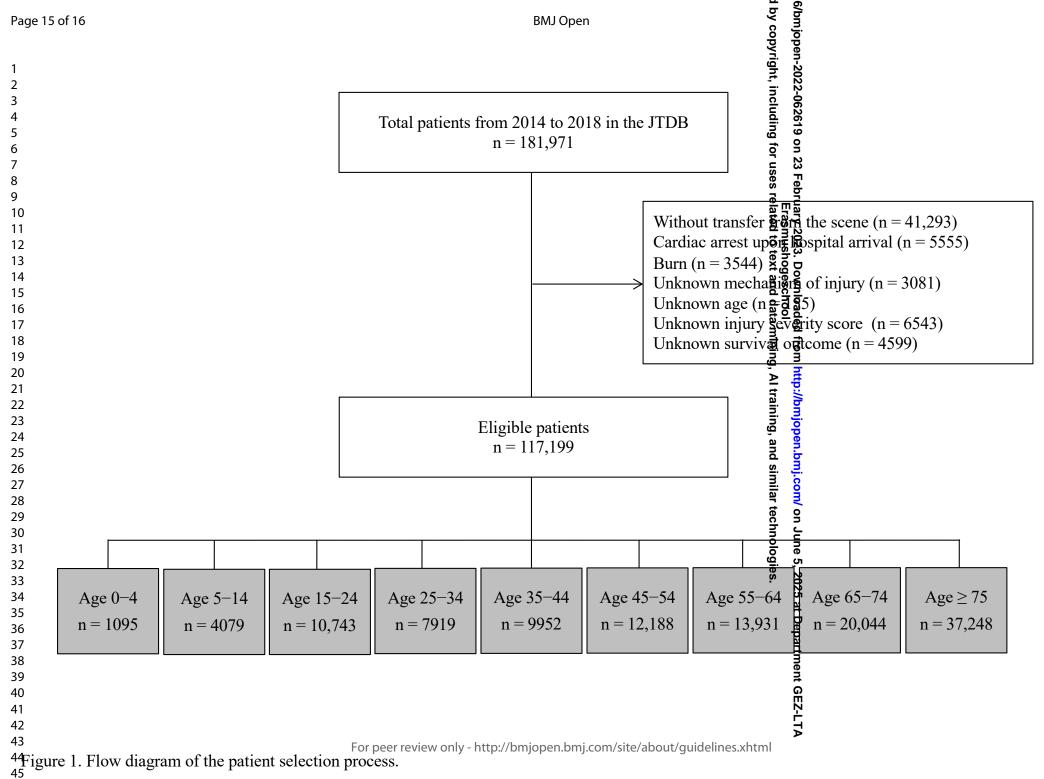
This is the first nationwide study in Japan to evaluate the prevalence, in-hospital mortality, and OR for mortality in patients with severe injury according to age categories. This study showed that there were differences in in-hospital mortality rate and risk among Japanese injured patients by age and anatomical severity; therefore, the use of correlation between mortality and injury severity score such as the ISS may be hardly justified in the definition of severely injured patients in all age categories. In the future, it will be important to evaluate the other parameters such as age, physiological variables, and laboratory variables together with the anatomical severity by using the population-based database to develop a well-validated definition of severely injured patients. 

240	Author Contributions: Conceptualization, CT and TM; methodology, CT; software, CT and TA;
241	validation, CT, TM, TA, MG, and MS; formal analysis, CT; investigation, CT, TM, MS, MG, and TA;
242	resources, CT and TA; data curation, CT and TA; writing—original draft preparation, CT; writing—
	review and editing, CT, TM, MS, MG, TA, and IT; visualization, CT; supervision, IT; project
	administration and funding acquisition, CT All authors have read and agreed to the published version of
245	the manuscript.
246	Funding: CT received a grant from the General Insurance Association of Japan [21-08].
247	Ethical Approval Statement: This study was approved by the institutional ethics committees of
248	Yokohama City University Medical Centre (approval no. B170900003).
249	Informed Consent Statement: The requirement for informed consent from the patients was waived due
250	to the observational nature of the study design.
251	Data Availability Statement: The approving authority for data access was the Japanese Association for
	the Surgery of Trauma (Trauma Registry Committee).
252	
253	Acknowledgments: None.
254	Conflicts of Interest: The authors declare no conflict of interest.
255	
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23 24		pediatric patients with blunt trauma using trauma and injury severity score methodology: A ten-year
25	309	
26 27	310	nationwide observational study. <i>BMC Emerg Med</i> <b>2020</b> ;20:91. DOI:10.1186/s12873-020-00385-0.
28	311	
29 30	312	
31	313	
32 33	314	Figure Legend
33 34	315	Figure 1. Flow diagram of the patient selection process.
35	316	JTDB, Japanese Trauma Data Bank.
36 37		JTDB, Japanese Trauma Data Bank.
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# STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the	1,2
		abstract	
		(b) Provide in the abstract an informative and balanced summary of what was	2
		done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being	2,3
		reported	
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
Methods			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of	3,4
		recruitment, exposure, follow-up, and data collection	
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	3,4
		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	N/A
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	4,5
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	4,5
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	3,4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	4,5
		describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for	4,5
		confounding	4.5
		(b) Describe any methods used to examine subgroups and interactions	4,5
		(c) Explain how missing data were addressed	3,4
		(d) If applicable, explain how loss to follow-up was addressed	N/A
		( <u>e</u> ) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	5
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	3,4,5
		(c) Consider use of a flow diagram	5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	3,4,5
		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	3
		(c) Summarise follow-up time (eg, average and total amount)	3
Outcome data	15*	Report numbers of outcome events or summary measures over time	5

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Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their	5
		precision (eg, 95% confidence interval). Make clear which confounders were adjusted for	
		and why they were included	
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5,7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5,7
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	10
		Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	9,1
		multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9,1
Other informati	on		
Funding	22	Give the source of funding and the role of the funders for the present study and, if	10
		applicable, for the original study on which the present article is based	

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

# **BMJ Open**

## **Evaluating the definition of Severely Injured Patients: A** Japanese Nationwide 5-Year Retrospective Study

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1	Article
2	Evaluating the definition of Severely Injured Patients: A
3	Japanese Nationwide 5-Year Retrospective Study
4	Chiaki Toida <sup>1,2</sup> *, Takashi Muguruma <sup>2</sup> , Masayasu Gakumazawa <sup>2</sup> , Mafumi Shinohara <sup>2</sup> ,
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15	Received: date; Accepted: date; Published: date Word count: 2320
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17	Abstract:			
18	Objectives: The definition of severely injured patients lacks universal consensus based on			
19	quantitative measures. The most widely used definition of severe injury is based on the Injury			
20	Severity Score (ISS), which is calculated using the Abbreviated Injury Scale in Japan. This study			
21	aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in			
22	patients with ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26 by age groups.			
23	Design: Retrospective cohort study.			
24	Setting: Japan Trauma Data Bank, which is a nationwide trauma registry with data from 280			
25	hospitals.			
26	Participants: We utilized data of 117,199 injured patients from a national database. We included			
27	injured patients who were transferred from the scene of injury by ambulance and/or physician.			
28	Primary and secondary outcome measures: Prevalence, in-hospital mortality, and OR for			
29	mortality with respect to age and injury level (ISS group).			
30	<b>Results:</b> In all age categories, the in-hospital mortality of patient groups with an ISS $\geq$ 16, ISS $\geq$ 18,			
31	and ISS 26 was 13.3%, 17.4%, and 23.5%, respectively. The in-hospital mortality for patients			
32	aged $> 75$ years was the highest (20% greater than that of the other age groups). Moreover, in-			
33	hospital mortality for age group 5–14 years was the lowest $(4.0-10.9\%)$ . In all the age groups, the			
34	OR for mortality for patients with ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26 was 12.8, 11.0, and 8.4,			
35	respectively.			
36	Conclusions: Our results revealed the lack of an acceptable definition, with a high in-hospital			
37	mortality and high OR for mortality for all age groups.			
38				
39	Keywords: severely injured patient; trauma scoring system; anatomical injury severity; mortality			
40	risk; Japan Trauma Data Bank			
41				
42	Strengths and limitations of this study			
43	> We used data from a large nationwide Japanese trauma registry to evaluate in-hospital			
44	mortality and odds ratio (OR) for mortality in patients with severe injury according to age.			
45	> This is the first study to reveal that no definition of severe injury was acceptable, with not only			
46	high in-hospital mortality but also a high OR for mortality for all age groups.			
70	ingh in hospital moranty out also a ingh off for moranty for an ago groups.			
47	> The Japanese nationwide dataset with more missing data may have led to selection bias.			
48				

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#### 49 1. INTRODUCTION

The terminology used to quantify anatomical injury severity has been vaguely described for many decades using various phrases, such as severely injured and major trauma.[1–5] Although the most widely used definitions continue to rely on patients who have a high mortality and morbidity risk and require intense medical resources, such as massive resuscitation, multiple surgical operations, intensive care, and complex rehabilitation programs,[4,5] the definition lacks a universal consensus with quantitative measures.[2,3]

The most widely used definition of severely injured patients is the Injury Severity Score (ISS),[6] which is calculated using the Abbreviated Injury Scale (AIS).[7] Thirty years ago, an ISS cutoff value of  $\geq$ 16 was defined as "severely injured" because patients with an ISS  $\geq$ 16 had an expected mortality rate of  $\geq$  20%.[1] However, the mortality of patients with an ISS  $\geq$ 16 and ISS  $\geq$ 26 decreased from 12.4% to 9.3% and from 25.4% to 20.3%, respectively, during the 10-year study period, due to a reduction in mortality and/or morbidity associated with organized trauma systems.[8]

Research based on the Japanese nationwide trauma registry has also shown that the in-hospital mortality trend has decreased in injured patients.[9–11] Moreover, there are more age-related differences in the mortality of severely injured patients in Japan than that in the other developed countries because Japan has faced issues with the declining birth rate and aging population.[11,12] To date, no study has evaluated the validity of the definition of severe injury in a Japanese cohort using a detailed classification of the definition cutoff values and age groups. We hypothesized that there would be differences in in-hospital mortality rate and risk among Japanese injured patients by age and anatomical injury severity. Therefore, this study aimed to compare the prevalence, in-hospital mortality, and odds ratio (OR) for mortality in patients with an ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq$ 26 as the commonly used anatomical injury definitions by age group [2].

#### 74 2. MATERIALS AND METHODS

#### 75 2.1. Study setting and population

This retrospective observational nationwide study was conducted based on data obtained from
the Japan Trauma Data Bank (JTDB), which registers data of patients with an injury and/or burn,

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78	and records prehospitalization- and hospital-related information. The JTDB includes data on
79	demographic characteristics, comorbidities, injury types, mechanism of injury, means of
80	transportation, vital signs, AIS score, prehospital/in-hospital procedures, injury diagnosis as
81	indicated by the AIS, and clinical outcomes. In most cases, physicians trained in AIS coding record
82	the online registration of individual patient data. There were 280 participating hospitals in all 47
83	prefectures in Japan, including 92% of the Japanese government-approved tertiary emergency
84	medical centers in March 2019. The Japan Association for the Surgery of Trauma permits open
85	access and updating of existing medical information, and the Japan Correlation for Acute Medicine
86	evaluates the submitted data.
87	In this study, we used the JTDB dataset that included information from January 1, 2014 to
88	December 31, 2018, which initially yielded the data of 181,971 patients. The inclusion criterion for
89	this study was injured patients who were transferred from the scene of injury by ambulance and/or
90	physician. Patients with cardiac arrest on hospital arrival or with missing key data, such as
91	mechanism, age, ISS, and/or survival outcome, were excluded from this study. Figure 1 presents a
92	flow diagram of the patient selection process in this study.
93	
94	2.2. Data collection
	<b>2.2. Data collection</b> We collected information from the JTDB, including the following variables: demographic
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94 95	We collected information from the JTDB, including the following variables: demographic
94 95 96	We collected information from the JTDB, including the following variables: demographic characteristics (age [years], sex, injury mechanism, transportation type, and transfer process) and
94 95 96 97	We collected information from the JTDB, including the following variables: demographic characteristics (age [years], sex, injury mechanism, transportation type, and transfer process) and clinical parameters (AIS of the injured region and ISS). In the JTDB, a patient with an AIS of the
94 95 96 97 98	We collected information from the JTDB, including the following variables: demographic characteristics (age [years], sex, injury mechanism, transportation type, and transfer process) and clinical parameters (AIS of the injured region and ISS). In the JTDB, a patient with an AIS of the
94 95 96 97 98 99 100	We collected information from the JTDB, including the following variables: demographic characteristics (age [years], sex, injury mechanism, transportation type, and transfer process) and clinical parameters (AIS of the injured region and ISS). In the JTDB, a patient with an AIS of the injured region $\geq$ 3 was defined as a case of a severely injured region. <b>2.3. Ethics statement</b>
94 95 96 97 98 99 100 101	We collected information from the JTDB, including the following variables: demographic characteristics (age [years], sex, injury mechanism, transportation type, and transfer process) and clinical parameters (AIS of the injured region and ISS). In the JTDB, a patient with an AIS of the injured region ≥3 was defined as a case of a severely injured region. <b>2.3. Ethics statement</b> This study was approved by the hospital ethics committee of Yokohama City University
94 95 96 97 98 99 100 101 101	We collected information from the JTDB, including the following variables: demographic characteristics (age [years], sex, injury mechanism, transportation type, and transfer process) and clinical parameters (AIS of the injured region and ISS). In the JTDB, a patient with an AIS of the injured region ≥3 was defined as a case of a severely injured region. <b>2.3. Ethics statement</b> This study was approved by the hospital ethics committee of Yokohama City University Medical Center (approval no. B170900003). The approval authority for data access was provided by
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107	2.4. Statistical analysis
108	The outcomes were as follows: prevalence, in-hospital mortality, and OR for mortality with
109	respect to age group (0−4, 5−14, 15−24, 25−34, 35−44, 45−54, 55−64, 65−74, and ≥75 years) and
110	injury severity (ISS $\geq$ 16, ISS $\geq$ 18, and ISS $\geq$ 26); the ISSs of these groups were used as the
111	definitions of anatomical injury in a previous review article.[2]
112	Continuous variables are presented as medians with interquartile range (IQR, Q1-Q3), and
113	categorical variables are presented as the number and percentage of patients. The Mann-Whitney
114	test and Wilcoxon's rank-sum test were used to analyze continuous variables, whereas the chi-
115	square test was used to analyze categorical variables. OR (95% confidence intervals, CI) for
116	mortality was calculated using a logistic regression model. All statistical analyses were performed
117	using STATA/SE software (version 17.0; StataCorp; College Station, Texas, USA). Statistical
118	significance was defined as a two-tailed P-value of <0.05.
119	
120	2.5. Patient and public involvement
121	Patients and the public were not involved in the design, conduct, reporting, or dissemination
122	this research. We will not directly disseminate our findings to involved participants. However, we
123	plan to disseminate them through the publication of an article.
124	
125	3. RESULTS
126	During the 5-year study period, we analyzed the data of 117,199 injured patients transferred
127	from the scene of injury; 113,435 (97%) of them had blunt trauma (Figure 1) (Table 1). The medi
128	age and ISS score were 64 years (IQR, 41-78) and 10 (IQR, 9-19), respectively. The overall in-
129	hospital mortality rate was 6.1%.

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Table 1 shows the characteristics by age group and injury severity group during the 5-year
study period. The number of patients with ISS ≥16, ISS ≥18, and ISS ≥26 was 48,028 (41% of all
the patients), 32,225 (28%), and 15,343 (13%), respectively.

Figure 2 shows in-hospital mortality and OR for mortality with respect to age group and injury severity. In all age categories, the in-hospital mortality of patients with ISS  $\geq$ 16, ISS  $\geq$ 18, and ISS  $\geq$ 26 was 13.3%, 17.4%, and 23.5%, respectively. In each age category, the in-hospital mortality for patients aged > 55 years was higher than that for younger age groups, and that of patients aged > 75 years was higher (by more than 20%) than that of all patient groups for each level of injury severity. In-hospital mortality for the 5–14 years age group was 4.0–10.9% and lower than that for the other age groups.

In all age categories, the OR for mortality by patient group was 12.8 (11.9–13.8), 11.0 (10.4– 11.6), and 8.4 (8.0–8.8), respectively, for the three levels of injury severity, and the OR in patients with ISS  $\geq$ 16 or ISS  $\geq$ 18 was higher than that in patients group ISS  $\geq$ 26.

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Table 1. Characteristics by the r	nine age grou	ne and three	· lovels of init	urv severity gr	יחווחי	, includin	6/bmjopen-2022-062619			
	Overall	Age 0-4	Age 5-14	Age 15-24	Age 25–34	Age 35-44 <b>6</b>	<b>9</b> <b>9</b> <b>9</b> <b>1</b> <b>9</b> <b>1</b> <b>9</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b> <b>1</b>	Age 55–64	Age 65–74	Age≥
Variables	n = 117,199	n = 1095	n = 4079	n = 10,743	n = 7919	n = 9952	$S_n = 12,188$	n = 13,931	n = 20,044	n = 36
Age, years	64 (41–78)	2 (1–3)	10 (7–12)	20 (17–22)	29 (27–32)	40 (38–42) <b>8</b>	<b>6</b> 49 (47–52)	60 (57–62)	69 (67–72)	83 (79
Male	73,680 (63)	675 (62)	2985 (73)	8095 (75)	6008 (75)	7710 (77) late	<b>u</b> ary 9211 (76)	10017 (72)	12662 (63)	16317
Mechanism of injury						1 to t	202			
Blunt	113,435 (97)	1073 (98)	4020 (99)	10,477 (98)	7508 (95)	9361 (94)	<b>5</b> <b>6</b> <b>1</b> 1,475 (94)	13,383 (96)	19,433 (97)	36,70
Injury region						9361 (94) 9361 (94)				
Head injury with AIS $\geq$ 3	36,244 (31)	439 (40)	1213 (30)	2798 (26)	1933 (24)	2527 (25) data	<b>B a a a a a a a a a a</b>	4451 (32)	7384 (37)	12,13
Facial injury with AIS $\geq$ 3	940 (0.8)	4 (0.4)	33 (0.8)	150 (1.4)	109 (1.4)	128 (1.3) <b>B</b> .	d To <sup>124</sup> (1.0)	123 (0.9)	133 (0.7)	136 (0
Neck injury with AIS $\geq 3$	478 (0.4)	6 (0.6)	2 (0.1)	27 (0.3)	39 (0.5)	55 (0.6) <b>D</b>	<b>ä</b> 70 (0.6)	77 (0.6)	110 (0.6)	92 (0.
Chest injury with AIS $\geq$ 3	25,723 (22)	148 (14)	622 (15)	2831 (26)	2110 (27)	2759 (28) tra	3485 (29)	3726 (27)	4594 (23)	5448
Abdominal and pelvic injury with AIS $\geq$ 3	5407 (5)	27 (2)	185 (5)	805 (7)	591 (7)	682 (7) <b>aining</b>	<b>5</b> .709 (6)	684 (5)	831 (4)	893 (2
Spinal injury with AIS $\geq$ 3	13,146 (10)	12 (1)	128 (3)	861 (8)	788 (10)	وې ۱120(11) an	1530 (13)	2106 (15)	3053 (15)	3548
Upper extremity injury with AIS $\geq$ 3	6562 (6)	57 (5)	590 (14)	581 (5)	522 (7)	711 (7) <b>d</b> sir	<b>8</b> 49 (7)	798 (6)	1026 (5)	1428
Lower extremity injury with AIS $\geq$ 3	31,526 (27)	124 (11)	634 (16)	2143 (20)	1660 (21)	2055 (21) <b>milar</b>	<b>6</b> 2404 (20)	2691 (19)	4358 (22)	15,45
Injury Severity Score	10 (9–19)	9 (4–16)	9 (5–16)	10 (5–19)	10 (6–20)	13 (9–20) <b>tec</b>	<b>9</b> 13 (9–21)	14 (9–21)	14 (9–21)	9 (9–1
Actual in-hospital mortality	7201 (6.1)	23 (2.1)	48 (1.2)	354 (3.3)	310 (3.9)	372 (3.7) hnold	<b>L</b> 533 (4.4)	762 (5.5)	1438 (7.2)	3361
Injury Severity Score ≥ 16	48,028 (41)	376 (34)	1166 (29)	3878 (36)	3043 (38)	4076 (41) <b>G</b>	<b>5</b> 5297 (43) <b>20</b> 23793 (31)	6541 (47)	9711 (48)	13,94
Injury Severity Score ≥ 18	32,225 (28)	187 (17)	747 (18)	2954 (28)	2305 (29)	<b>ب</b> 2985 (30)	<b>2025</b> 3793 (31)	4372 (31)	6256 (31)	8626
Injury Severity Score ≥ 26	15,343 (13)	62 (6)	367 (9)	1595 (15)	1129 (14)	1481 (15)	a D <sup>1823 (15)</sup>	2038 (15)	2910 (15)	3938
Data are presented as number (per	reentage) or m	edian (intera	uartile range (	-1-03). AIS. /	Abbreviated I	niurv Scale	epar			
Data are presentes as maneer ar	contage,	Junun (	annie 1910- 2	1 X0,,,	10010114100.	ijury seure	artment GEZ-LTA			

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## **4. DISCUSSION**

To the best of our knowledge, this is the first nationwide study in Japan to evaluate in-hospital mortality and OR for mortality in patients with severe injury according to age. Our study showed that in all three groups with ISS  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ , which are the commonly used anatomical injury definitions, in-hospital mortality for patients aged < 55 years was between 4.0% and 17.7% for each level of injury severity. Moreover, after evaluating the validity of the definition for severely injured patients in a Japanese cohort via the detailed classification of the definition cutoff values and age groups, there was no acceptable definition, with not only a high in-hospital mortality, but also a high OR for mortality for all age groups.

Previous studies demonstrated that in 1990 when severe injury was defined as an ISS cutoff of  $\geq$ 16 points, the mortality of patients with an ISS  $\geq$ 16 was more than 20%; however, the mortality of these patients decreased; therefore, an ISS cutoff of  $\geq 18$  or 26 might be suitable for defining severely injured patients with a high mortality rate.[1–3,8] This study also showed that patients with ISS  $\geq$ 26 had the highest in-hospital mortality in all age categories. However, the OR for mortality in patients with ISS  $\geq$ 26 was lower than that in patients with ISS  $\geq$ 16 and ISS  $\geq$ 18. There are possible explanations for the lack of an accepted definition with a high in-hospital mortality and high OR for mortality in a Japanese cohort. 

First, there are differences in the study era and/or cohorts at the time of development.[1] A previous 10-year nationwide study using the JTDB dataset from 2004 to 2013 demonstrated that the in-hospital mortality of patients with ISS  $\geq 16$  decreased from 28.5% to 15.7% owning to improvements in trauma care and medical ambulance services.[9] Moreover, in the Japanese cohort, unlike the aging population in the rest of the world, the characteristics and survival outcome of severely injured patients varied widely according to age, and the mortality risk of elderly patients with severe injury was higher than that of the other age groups.[12] A previous Japanese nationwide study showed that the incidence rate of severe traumatic brain injury among severely injured patients aged > 65 years was high (40.7%).[13] Moreover, the in-hospital mortality of these patients was higher than that of the other age groups.[13] These results suggest that the elderly patient groups had a higher mortality because of the high proportion and mortality of severe traumatic head injury. This study also showed that the prevalence and in-hospital mortality of severely injured

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patients aged 55–64, 65–75, and  $\geq$ 75 years increased stepwise. On the other hand, previous studies suggested that the ISS cutoff of  $\geq 16$  in adult patients was equivalent to a cutoff of  $\geq 26$  in pediatric patients aged <16 years.[14,15] This study showed different results from those of a previous study [15], wherein the in-hospital mortality of pediatric patients aged 0–4 years with an ISS  $\geq$ 26 was high (17.7%) and that of pediatric patients aged 5–14 years with an ISS  $\geq$ 26 was low (10.9%), as shown in Figure 2. Moreover, a previous study showed that there was a difference in the optimal cut off value of ISS in predicting severely injury mortality risk by region and/or mechanism of injury among pediatric patients. Therefore, it is important to develop an acceptable definition of severe injury by considering the age-related characteristics and mortality risks in a Japanese cohort. Moreover, this study showed that the mortality rate and risk of injured patients in Japan differed by age groups and did not have a linear correlation with age in years. For a better predictive accuracy in mortality, it may be effective to add age categories as a predictive variable for mortality and to calculate the coefficient for coded value according to mortality risk by each age group, as shown in the Trauma and Injury Severity Score methodology [16]. Second, there was a limitation in evaluating only anatomical injury severity as a definition of severe injury. A more recent approach suggests that the addition of other physiological variables to the anatomical injury severity score has the advantage of identifying severely injured patients with a high mortality risk. [2,17,18] Although the mortality of patients with ISS  $\geq 16$  was 18.7%, that of patients with ISS  $\geq 16$  in addition to one other physiological parameter increased from 35% to 38%.[2] Moreover, patients with an increasing number of the physiological variable, such as the Glasgow Coma Scale, hypotension, and laboratory values (e.g., acidosis and/or coagulopathy), may have an increased risk of mortality.[17–19] However, we could not evaluate the variables according to physiological parameters and findings of blood tests. Therefore, it seems important to evaluate these parameters together with the anatomical injury severity used in this study to develop a well-validated definition of severely injured patients. Our study had some limitations. First, there was selection bias because not all Japanese hospitals that treat severely injured patients are registered in the JTDB. The 280 tertiary centers equivalent to Level I trauma centers in the United States participated, including 92% of the Japanese government-approved tertiary emergency medical centers in March 2019. Therefore, the JTDB is not a population-based sample of injured patients and the data are registered voluntarily.

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Moreover, the JTDB dataset has missing data, especially for pediatric patients.[20] The number of pediatric patients were lower than that of adult patients. Therefore, missing data may have a more significant influence on the analysis of the pediatric patients' data than that of the adult patients' data. A high-quality Japanese nationwide dataset with less missing data should be constructed to improve the accuracy of predicting the survival of injured patients in the data analysis for all age categories. Second, because the number of patients aged 0-4 and 5-14 years was small (0.9% and 3.5% of all the patients, respectively), it is possible that the ORs of these patient groups with small sample sizes were overestimated. In addition, the number of participating hospitals differed across the study period. Furthermore, the JTDB used AIS 90 until 2018 and is now using the AIS 2005 updated 2008 coding scale. Similar studies need to be conducted using the newest measure to verify our results. Last, we did not evaluate which definition would be effective for each age group. A recent study showed significant discrepancies in the mortality risk of severely injured patients by each injury region.[21] We intend to calculate the coefficient for the coded value according to mortality risk by age group and injury region for a better mortality estimate.

### **5. CONCLUSIONS**

This is the first nationwide study in Japan to evaluate the prevalence, in-hospital mortality, and OR for mortality in patients with severe injury according to age categories. This study showed that there were differences in in-hospital mortality rate and risk among Japanese injured patients by age and anatomical injury severity; therefore, the use of correlation between mortality and injury severity score, such as the ISS, may be hardly justified in the definition of severely injured patients in all age categories. In the future, it will be important to evaluate the other parameters, such as age, physiological variables, and laboratory variables, together with the anatomical injury severity by using the population-based database to develop a well-validated definition of severely injured patients.

Author Contributions: Conceptualization, CT and TM; methodology, CT; software, CT and TA;
validation, CT, TM, TA, MG, and MS; formal analysis, CT; investigation, CT, TM, MS, MG, and
TA; resources, CT and TA; data curation, CT and TA; writing—original draft preparation, CT;

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235 writing—review and editing, CT, TM, MS, MG, TA, and IT; visualization, CT; supervision, IT;

236 project administration and funding acquisition, CT All authors have read and agreed to the

published version of the manuscript. 237

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- 239 Ethical Approval Statement: This study was approved by the institutional ethics committees of
- 240 Yokohama City University Medical Centre (approval no. B170900003).
- 241 Informed Consent Statement: The requirement for informed consent from the patients was
- 242 waived owning to the observational nature of the study design.
- 243 Data Availability Statement: No additional data available.
- Acknowledgments: None. 244
- Conflicts of Interest: The authors declare no conflict of interest. 245
- 246

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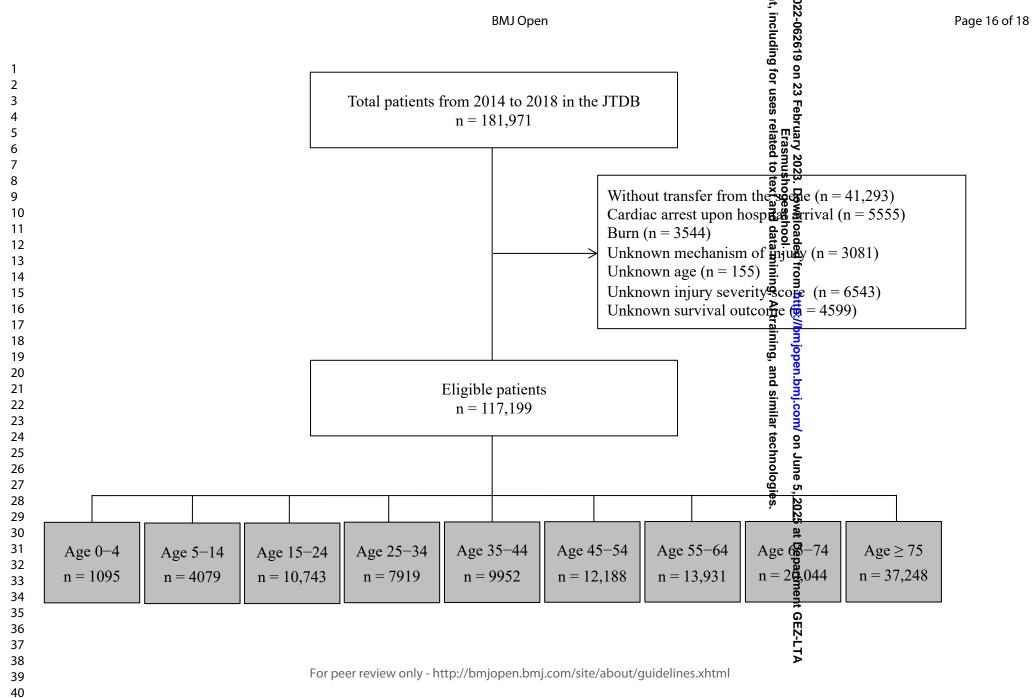


Figure 1. Flow diagram of the patient selection process.

Page 17	of 18		No. of patients	Mortality,%			BMJ Open	)22-062619 on 2 <del>3</del> t, including for us	OR	95% C
	Overall	$ISS \ge 16$	48,028	13.3		-0-		062( cluc	12.8	(11.9,
		$ISS \ge 18$	32,225	17.4		-0-		619 Jing	11.0	(10.4,
1 2 3		$ISS \ge 26$	15,343	23.5	Ð			y for	8.4	(8.4,
	Age 0 – 4	$ISS \ge 16$	376	5.9					44.6	(6.0,
4		$ISS \ge 18$	187	11.2				Febru	57.3	(13.3,
5 6 7 8		$ISS \ge 26$	62	17.7				elated	18.4	(7.7,
	Age 5 – 14	$ISS \ge 16$	1166	4.0					59.8	(14.5,
		$ISS \ge 18$	747	5.8				to texpo	40.6	(16.0,
9 10		$ISS \ge 26$	367	10.9				Dow vxt an	56.6	(26.3,
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12		$ISS \ge 18$	2954	11.0				data n	33.1	(22.6,
13		$ISS \ge 26$	1595	16.1		0		d from	17.9	(14.1,
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17 18		$ISS \ge 26$	1129	19.9			<b></b>	) http://bmjop , Al training	19.6	(15.2,
19	Age 35 – 44	$ISS \ge 16$	4076	8.7			-0		29.2	(18.4,
20		$\text{ISS} \geq 18$	2985	11.2				pen.bmj.com/ , and similar	23.7	(16.8,
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24		$\text{ISS} \geq 18$	3793	11.7				tec	12.0	(9.6,
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33 34		$ISS \geq 26$	2910	24.6	-0-			me	7.4	(6.6,
35	Age $\geq 75$	$ISS \ge 16$	13,940	20.2		-0-		nt G	10.5	(9.5,
36		$\text{ISS} \geq 18$	8626	27.4		-0-		EZ-I	10.5	(9.7,
37 38		$ISS \geq 26$	3938	34.0	-0-				8.0	(7.3,

40 Eigure 2. Association between odds ratio for in-hospital mortality and age groups by patients with Injury Severity Score (ISS)  $\geq 16$ , ISS  $\geq 18$ , and ISS  $\geq 26$ .

# STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the	1,2
		abstract	
		(b) Provide in the abstract an informative and balanced summary of what was	2
		done and what was found	
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being	2,3
		reported	2,3 2 3,4 3,4 N/A 4,5
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
Methods			
Study design	4	Present key elements of study design early in the paper	2
Setting	5	Describe the setting, locations, and relevant dates, including periods of	3,4
		recruitment, exposure, follow-up, and data collection	No           1,2           2           2,3           2,3           2,3           3,4           N/A
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of	3,4
		participants. Describe methods of follow-up	
		(b) For matched studies, give matching criteria and number of exposed and	N/A
		unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and	No           ne         1,2           was         2           2,3         2,3           2,3         2,3           2,3         2,3           2,3         3,4           f         3,4           f         3,4           and         4,5           of         4,5           and         and         and           and         and         and           and         and         and         and           and         and         and         and           and         and         and         and           and         and         and         and           and
		effect modifiers. Give diagnostic criteria, if applicable	
Data sources/	8*	For each variable of interest, give sources of data and details of methods of	4,5
measurement		assessment (measurement). Describe comparability of assessment methods if	
		there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	3,4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,	4,5
		describe which groupings were chosen and why	3,4 4,5
Statistical methods 12		(a) Describe all statistical methods, including those used to control for	4,5
Variables Data sources/ measurement Bias		confounding	4.5
		(b) Describe any methods used to examine subgroups and interactions	
		(c) Explain how missing data were addressed	
		(d) If applicable, explain how loss to follow-up was addressed	
		( <u>e</u> ) Describe any sensitivity analyses	IN/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially	5
		eligible, examined for eligibility, confirmed eligible, included in the study,	
		completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social)	3,4,5
		and information on exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	3
		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	5

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Main results	16	( <i>a</i> ) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for	5
		and why they were included	
		(b) Report category boundaries when continuous variables were categorized	5,6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	5,6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	5,6
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision.	9,1
		Discuss both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,	9,1
		multiplicity of analyses, results from similar studies, and other relevant evidence	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9,1
Other informati	on		•
Funding	22	Give the source of funding and the role of the funders for the present study and, if	11
		applicable, for the original study on which the present article is based	

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.