

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Evaluating the definition of Severely Injured Patients: A Japanese Nationwide 5-Year Retrospective Study
AUTHORS	Toida, Chiaki; Muguruma, Takashi; Gakumazawa, Masayasu; Shinohara, Mafumi; Abe, Takeru; Takeuchi, Ichiro

VERSION 1 – REVIEW

REVIEWER	Driessen, Mitchell Dutch Network for Emergency Care, Trauma Surgery
REVIEW RETURNED	04-Apr-2022

GENERAL COMMENTS	<p>This study based on the Japanese National Trauma Register provides an interesting overview of three Injury Severity Score subgroups and the associated mortality rates per age group. The authors have investigated a broad spectrum of age groups, with the risk of reducing the power of the results. The paper is well written and the limitations of the study have been described.</p> <p>It is surprising to see that the odds ratio of death decline with increasing injury severity scores, while the percentage of death per injury severity group increase.</p> <p>In the discussion (line 195-204) the authors state the importance of adding physiological risk factors to an anatomical injury score. This was previously described by Pape et al in the Berlin Polytrauma definition (BPD), which is an important reference that should be noted. Furthermore, the authors name the physiological variables: Glasgow coma scale, hypotension, and laboratory values (e.g., acidosis and/or coagulopathy) which are all part of the BPD. Yet they forgot the variable most relevant to their study. Namely age >70 years.</p> <p>I would suggest adding the calculations of the odds ratio of death per ISS subgroup, related to the age variable of 70 years and older the study.</p> <p>Furthermore, I would suggest that the authors add a more in-depth evaluation of their findings with current literature. For example, the suggestion to choose different cut-off value for severe injury in pediatric trauma is no something new. I would suggest that the authors assess and compare their results with those of Brown et al.</p>
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	<p>- Brown, Joshua B et al. "The value of the injury severity score in pediatric trauma: Time for a new definition of severe injury?." The journal of trauma and acute care surgery vol. 82,6 (2017): 995-1001. doi:10.1097/TA.0000000000001440</p> <p>The limitation section includes the most important points. However, the authors could elaborate a little more. Regarding the statement that not all Japanese hospitals are involved in the JTDB, it would be of interest to describe how many were actually involved and what level of specialized care they facilitate.</p> <p>Another important point is the amount of missing data for pediatric patients. In the method section the authors state that patients with missing values are excluded. The authors state that in pediatric trauma mortality rates between ISS groups don't vary as much as in adult trauma. Could these results be biased due to missing values /excluded patients in a particular ISS group?</p> <p>Line 166: I think "in-mortality" should be in-hospital mortality.</p>
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REVIEWER	Dharap, Satish Lokmanya Tilak Municipal Medical College and General Hospital, Surgery
REVIEW RETURNED	15-May-2022

GENERAL COMMENTS	<p>In this paper, the authors have evaluated the definition of severely injured patients using Japanese nationwide five-year data. They have searched for a better cut-off to define severe injury in terms of injury severity score ISS - ≥ 16 or ≥ 18 or ≥ 26.</p> <p>The positive points of this paper are the analysis of data of over 100,000 patients. However, there appear to be errors in the analysis. Table 1 shows "Chest injury with AIS ≥ 3" as 256,723 (22%) which is incorrect. Also, the Actual in-hospital mortality of 3361 is not 9.0% of the total cases included (117199). The odds ratios stated by the authors for overall data do not seem to be supported by the numbers presented. Authors should consider having a relook at the data and the numbers presented. They may also consider regression analysis or the AUROC curve.</p> <p>There is no comment about the generalisability of the results, which is desirable.</p> <p>The authors also do not present any clear recommendation or future direction based on this study.</p>
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REVIEWER	Dehouche, Nassim Mahidol University
REVIEW RETURNED	03-Oct-2022

GENERAL COMMENTS	<p>The study presents a large dataset (n = 117,199) of trauma patients, with the corresponding Abbreviated Injury Scale scores, mortality rates, and other demographic data. In itself, this dataset would certainly be valuable for future research. The research question investigated concerns the adequacy of extant definitions of "severely injured patients", based on their Injury Severity Scores (ISS).</p> <p>In terms of statistical analysis, the study limits itself to a simple descriptive analysis of the mortality percentages and odds ratios (OR), for different tiers of ISS, and merely observes that no cutoff value for ISS could provide both high mortality and high OR for all patient groups. Rather than being a weakness, the simplicity of the</p>
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	<p>statistical tools used is commendable to some extent, and likely makes the conclusions robust. Indeed, the AIS and ISS are useful, but imperfect numerical artefacts. Over time, they have come to be abusively considered as measures, and inadequate statistical tools have been abusively applied to them, in a case of confusing the map with the territory.</p> <p>In terms of weaknesses, there are two issues with the paper.</p> <ol style="list-style-type: none"> 1. The statistical hypotheses being tested need to be formally stated and tested, and the corresponding test statistics provided. 2. The conclusion ("there is a lack of an acceptable definition of severely injured patients") is a little too cautious. The authors' perspective, based on their clinical experience and the insights gained from this dataset, on how such a definition could be constructed would be useful to the paper. <p>Moreover, existing definitions/thresholds for "severely injured patients" have a history. A discussion of how they came to be could also shed light on how better definitions can be proposed. Indeed, since the seminal paper of (Baker et al. 1974), there have been an over-reliance on Pearson's correlation with mortality to draw clinical and policy conclusions about injury severity, including the definitions of severely injured patients. However, the use of correlation can be hardly justified with a score such as the ISS. The conclusion of the paper could benefit from including the authors' perspective on how they believe better indicators could be constructed.</p>
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VERSION 1 – AUTHOR RESPONSE

1. In the discussion (line 195-204) the authors state the importance of adding physiological risk factors to an anatomical injury score. This was previously described by Pape et al in the Berlin Polytrauma definition (BPD), which is an important reference that should be noted. Furthermore, the authors name the physiological variables: Glasgow coma scale, hypotension, and laboratory values (e.g., acidosis and/or coagulopathy) which are all part of the BPD. Yet they forgot the variable most relevant to their study. Namely age >70 years.

Response: We thank the Reviewer for this valuable suggestion. Accordingly, we have revised Discussion section of the manuscript to address the development of a well-validated definition of severely injured patients as follows:

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].
2. I would suggest adding the calculations of the odds ratio of death per ISS subgroup, related to the age variable of 70 years and older the study.

Response: We thank the Reviewer for this valuable suggestion. We agree with the additional analysis and discussion regarding the odds ratio of in-hospital mortality. Regarding the multivariate logistic regression analysis that include age in years and ISS groups as variables, the OR for mortality by patient group with an ISS ≥ 16 , ISS ≥ 18 , and ISS ≥ 26 in all the age categories was 13.3 (12.3–14.3), 12.1 (11.5–12.9), and 9.5 (8.9–9.9), respectively. Regrettably however, we did not find any difference in the OR tendency by patient group with an ISS ≥ 16 , ISS ≥ 18 , and ISS ≥ 26 between the univariate and multivariate logistic regression analyses. Therefore, we have added the above information in the discussion section as mentioned above.
3. Furthermore, I would suggest that the authors add a more in-depth evaluation of their findings with current literature. For example, the suggestion to choose different cut-off value for severe injury in pediatric trauma is no something new. I would suggest that the authors assess and

compare their results with those of Brown et al.

- Brown, Joshua B et al. "The value of the injury severity score in pediatric trauma: Time for a new definition of severe injury?." The journal of trauma and acute care surgery vol. 82,6 (2017): 995-1001. doi:10.1097/TA.0000000000001440

Response: We thank the Reviewer for this comment. We have revised the discussion section through comparing such reference paper you suggested as follows:

On the other hand, previous studies suggested that the ISS cutoff of ≥ 16 in adult patients was equivalent to a cut-off ≥ 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 ≥ 26 was high (17.7%) and that of pediatric patients aged 5–14 years with an ISS ≥ 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.

4. The limitation section includes the most important points. However, the authors could elaborate a little more. Regarding the statement that not all Japanese hospitals are involved in the JTDB, it would be of interest to describe how many were actually involved and what level of specialized care they facilitate.

Response: We thank the Reviewer for this comment. As you request, we have revised the limitation section as follows:

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.

5. Another important point is the amount of missing data for pediatric patients. In the method section the authors state that patients with missing values are excluded. The authors state that in pediatric trauma mortality rates between ISS groups don't vary as much as in adult trauma. Could these results be biased due to missing values /excluded patients in a particular ISS group?

Response: We thank the Reviewer for this comment. We have revised the limitation section as follows:

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.

6. Line 166: I think "in-mortality" should be in-hospital mortality

Response: We thank the Reviewer for this comment. The typing error has been corrected.

VERSION 2 – REVIEW

REVIEWER	Driessen, Mitchell Dutch Network for Emergency Care, Trauma Surgery
REVIEW RETURNED	21-Nov-2022

GENERAL COMMENTS	<p>The authors ought to be congratulated for a well done analysis across trauma patients in Japan. The article reviews the association between anatomical injury severity after trauma and mortality for different age groups in a national cohort of Japan.</p> <p>Here forth are some suggestions to further improve the overall quality and usability the results of your study.</p> <p>- The median age and injury severity score as well as the injury type are quite similar compared with results from the English,</p>
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	<p>Trauma Audit and Research Network or the Dutch National Trauma Register. Yet, overall mortality of 6.1% is quite high in my opinion. how would you explain this?</p> <p>- In line 193-196 you state: 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.</p> <p>Most trauma registries use an ISS>15 to describe severely injured patients that are in need of specialized trauma care. In the discussion you state that an ISS ≥16, ISS ≥18, and ISS ≥26 are no acceptable definitions. Based on the result of your study, which definition would be “least bad” for pediatric and which for adult trauma? Would an injury in a particular body region be more indicative?</p> <p>- In line 197-201 you state: “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].”</p> <p>As you know the classic TRISS Model includes Age as a bivariate coefficient whether or not a patient is older than 55 years or not. However, as you suggest age groups don't have a linear correlation with in-hospital mortality. Therefore, visual presentation of the association between in-hospital mortality (or odds ratio for mortality) and age would be of great value to further assess the impact of age as a risk factor. Another interesting finding is the difference in mortality rates for different injury regions. A recent study on severe isolated injuries showed significant discrepancies in odd ratio between region of injury. Do your results cohere with these findings?</p> <p>- Driessen et al. Severe isolated injuries have a high impact on resource use and mortality: a Dutch nationwide observational study. Eur J Trauma Emerg Surg. 2022 Oct;48(5):4267-4276. doi: 10.1007/s00068-022-01972-5. Epub 2022 Apr 21. PMID: 35445813.</p> <p>- Note that:</p> <p>- Section 2.6 is written in a different font style than the rest of the article</p> <p>- In line 69, 202, 204, 211, 233, 236 you state “anatomical severity”, I believe “anatomical injury severity” would be more appropriate.</p>
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REVIEWER	Dharap, Satish Lokmanya Tilak Municipal Medical College and General Hospital, Surgery
REVIEW RETURNED	22-Nov-2022

GENERAL COMMENTS	Check table 1
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	Over all Number of male patients needs correction .
REVIEWER	Dehouche, Nassim Mahidol University
REVIEW RETURNED	30-Nov-2022
GENERAL COMMENTS	My remarks have been appropriately taken into consideration.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

1. The median age and injury severity score as well as the injury type are quite similar compared with results from the English, Trauma Audit and Research Network or the Dutch National Trauma Register. Yet, overall mortality of 6.1% is quite high in my opinion. how would you explain this?
Response: Thank you for your important question. Unfortunately, we cannot explain the reason in our study why there was difference in overall mortality between Japan and other countries. In our opinion, the society with the fastest aging population and/or non-establishment of trauma care system throughout Japan with severely injured patients being put into the trauma center may have had an impact. In the future study, we will try to clarify these causes and establish the best trauma care system in Japan.

2. In line 193-196 you state: 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.
Most trauma registries use an ISS>15 to describe severely injured patients that are in need of specialized trauma care. In the discussion you state that an ISS ≥16, ISS ≥18, and ISS ≥26 are no acceptable definitions. Based on the result of your study, which definition would be “least bad” for pediatric and which for adult trauma? Would an injury in a particular body region be more indicative?

Response: Thank you for the pertinent queries. Unfortunately, we cannot clarify which definition would be effective for pediatric and adult patients because there are differences in mortality rate and frequency due to injury region among each age categories, for example, the mortality rate of patients aged 0-4 and 5-14 years was different in pediatric patients.

Accordingly, we have revised the Discussion section of the manuscript to address the limitation of this study as follows:

Last, we did not evaluate which definition would be effective for each age group. A recent study showed significant discrepancies in 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.

3. In line 197-201 you state: “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].” As you know the classic TRISS Model includes Age as a bivariate coefficient whether or not a patient is older than 55 years or not. However, as you suggest age groups don’t have a linear correlation with in-hospital mortality.
Therefore, visual presentation of the association between in-hospital mortality (or odds ratio for mortality) and age would be of great value to further assess the impact of age as a risk factor.
Response: We thank the Reviewer for this valuable suggestion. Accordingly, we have revised Table 2 to Figure 2, which showed the visual presentation of the association between in-hospital mortality.
4. Another interesting finding is the difference in mortality rates for different injury regions. A recent study on severe isolated injuries showed significant discrepancies in odd ratio between region of

injury. Do your results cohere with these findings?

Driessen et al. Severe isolated injuries have a high impact on resource use and mortality: a Dutch nationwide observational study. *Eur J Trauma Emerg Surg.* 2022 Oct;48(5):4267-4276. doi: 10.1007/s00068-022-01972-5. Epub 2022 Apr 21. PMID: 35445813.

Response: Thank you for your valuable information. Accordingly, we have added this references and revised the Discussion section as follows:

A recent study showed significant discrepancies in mortality risk of severely injured patients by 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. Section 2.6 is written in a different font style than the rest of the article

Response: Thank you for your important comment. We have revised the font style in Section 2.6 and ensured consistency of font throughout the manuscript.

6. In line 69, 202, 204, 211, 233, 236 you state “anatomical severity”, I believe “anatomical injury severity” would be more appropriate.

Response: Thank you for your valuable suggestion. Accordingly, we have revised the term “anatomical severity” to “anatomical injury severity” throughout the manuscript.

Reviewer: 2

1. The Check table 1. Overall Number of male patients needs correction

Response: Thank you for this insightful comment. The typing error in Table 1 has been corrected.

VERSION 3 – REVIEW

REVIEWER	Driessen, Mitchell Dutch Network for Emergency Care, Trauma Surgery
REVIEW RETURNED	08-Jan-2023
GENERAL COMMENTS	My remarks have been appropriately taken into consideration.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 1

7. The median age and injury severity score as well as the injury type are quite similar compared with results from the English, Trauma Audit and Research Network or the Dutch National Trauma Register. Yet, overall mortality of 6.1% is quite high in my opinion. how would you explain this?

Response: Thank you for your important question. Unfortunately, we cannot explain the reason in our study why there was difference in overall mortality between Japan and other countries. In our opinion, the society with the fastest aging population and/or non-establishment of trauma care system throughout Japan with severely injured patients being put into the trauma center may have had an impact. In the future study, we will try to clarify these causes and establish the best trauma care system in Japan.

8. In line 193-196 you state: 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.

Most trauma registries use an ISS>15 to describe severely injured patients that are in need of specialized trauma care. In the discussion you state that an ISS ≥16, ISS ≥18, and ISS ≥26 are no acceptable definitions. Based on the result of your study, which definition would be “least bad” for pediatric and which for adult trauma? Would an injury in a particular body region be more indicative?

Response: Thank you for the pertinent queries. Unfortunately, we cannot clarify which definition would be effective for pediatric and adult patients because there are differences in mortality rate and frequency due to injury region among each age categories, for example, the mortality rate of patients aged 0-4 and 5-14 years was different in pediatric patients.

Accordingly, we have revised the Discussion section of the manuscript to address the limitation of this study as follows:

Last, we did not evaluate which definition would be effective for each age group. A recent study showed significant discrepancies in 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.

9. In line 197-201 you state: "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]." As you know the classic TRISS Model includes Age as a bivariate coefficient whether or not a patient is older than 55 years or not. However, as you suggest age groups don't have a linear correlation with in-hospital mortality.

Therefore, visual presentation of the association between in-hospital mortality (or odds ratio for mortality) and age would be of great value to further assess the impact of age as a risk factor.

Response: We thank the Reviewer for this valuable suggestion. Accordingly, we have revised Table 2 to Figure 2, which showed the visual presentation of the association between in-hospital mortality.

10. Another interesting finding is the difference in mortality rates for different injury regions. A recent study on severe isolated injuries showed significant discrepancies in odd ratio between region of injury. Do your results cohere with these findings?

Driessen et al. Severe isolated injuries have a high impact on resource use and mortality: a Dutch nationwide observational study. *Eur J Trauma Emerg Surg.* 2022 Oct;48(5):4267-4276. doi: 10.1007/s00068-022-01972-5. Epub 2022 Apr 21. PMID: 35445813.

Response: Thank you for your valuable information. Accordingly, we have added this references and revised the Discussion section as follows:

A recent study showed significant discrepancies in mortality risk of severely injured patients by 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.

11. Section 2.6 is written in a different font style than the rest of the article

Response: Thank you for your important comment. We have revised the font style in Section 2.6 and ensured consistency of font throughout the manuscript.

12. In line 69, 202, 204, 211, 233, 236 you state "anatomical severity", I believe "anatomical injury severity" would be more appropriate.

Response: Thank you for your valuable suggestion. Accordingly, we have revised the term "anatomical severity" to "anatomical injury severity" throughout the manuscript.

Reviewer: 2

2. The Check table 1. Overall Number of male patients needs correction

Response: Thank you for this insightful comment. The typing error in Table 1 has been corrected.

5. Please revise the 'Strengths and limitations of this study' section of your manuscript (after the abstract). This section should contain up to five short bullet points, no longer than one sentence each, that relate specifically to the methods. The novelty, aims, results or expected impact of the study should not be summarised here.

Response: Thank you for your valuable comment. We have revised “Strengths and limitations of this study” as follows:

- We used data from a large nationwide Japanese trauma registry to evaluate in-hospital mortality and odds ratio (OR) for mortality in patients with severe injury according to age.
 - This is the first study to reveal that no definition of severe injury was acceptable, with not only high in-hospital mortality but also a high OR for mortality for all age groups.
 - The Japanese nationwide dataset with more missing data may have led to selection bias.
6. Please complete a thorough proofread of the text and correct any spelling and grammar errors that you identify.
Response: Thank you for your valuable suggestion. Accordingly, we have completed a thorough proofread of the text and corrected all spelling and grammar errors. We have attached a certification of English proofreading.

Reviewer: 1

13. The median age and injury severity score as well as the injury type are quite similar compared with results from the English, Trauma Audit and Research Network or the Dutch National Trauma Register. Yet, overall mortality of 6.1% is quite high in my opinion. how would you explain this?
Response: Thank you for your important question. Unfortunately, we cannot explain the reason in our study why there was difference in overall mortality between Japan and other countries. In our opinion, the society with the fastest aging population and/or non-establishment of trauma care system throughout Japan with severely injured patients being put into the trauma center may have had an impact. In the future study, we will try to clarify these causes and establish the best trauma care system in Japan.

14. In line 193-196 you state: 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.

Most trauma registries use an ISS>15 to describe severely injured patients that are in need of specialized trauma care. In the discussion you state that an ISS ≥ 16 , ISS ≥ 18 , and ISS ≥ 26 are no acceptable definitions. Based on the result of your study, which definition would be “least bad” for pediatric and which for adult trauma? Would an injury in a particular body region be more indicative?

Response: Thank you for the pertinent queries. Unfortunately, we cannot clarify which definition would be effective for pediatric and adult patients because there are differences in mortality rate and frequency due to injury region among each age categories, for example, the mortality rate of patients aged 0-4 and 5-14 years was different in pediatric patients.

Accordingly, we have revised the Discussion section of the manuscript to address the limitation of this study as follows:

Last, we did not evaluate which definition would be effective for each age group. A recent study showed significant discrepancies in 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.

15. In line 197-201 you state: “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].” As you know the classic TRISS Model includes Age as a bivariate coefficient whether or not

a patient is older than 55 years or not. However, as you suggest age groups don't have a linear correlation with in-hospital mortality.

Therefore, visual presentation of the association between in-hospital mortality (or odds ratio for mortality) and age would be of great value to further assess the impact of age as a risk factor.

Response: We thank the Reviewer for this valuable suggestion. Accordingly, we have revised Table 2 to Figure 2, which showed the visual presentation of the association between in-hospital mortality.

16. Another interesting finding is the difference in mortality rates for different injury regions. A recent study on severe isolated injuries showed significant discrepancies in odd ratio between region of injury. Do your results cohere with these findings?

Driessen et al. Severe isolated injuries have a high impact on resource use and mortality: a Dutch nationwide observational study. *Eur J Trauma Emerg Surg.* 2022 Oct;48(5):4267-4276. doi: 10.1007/s00068-022-01972-5. Epub 2022 Apr 21. PMID: 35445813.

Response: Thank you for your valuable information. Accordingly, we have added this references and revised the Discussion section as follows:

A recent study showed significant discrepancies in mortality risk of severely injured patients by 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.

17. Section 2.6 is written in a different font style than the rest of the article

Response: Thank you for your important comment. We have revised the font style in Section 2.6 and ensured consistency of font throughout the manuscript.

18. In line 69, 202, 204, 211, 233, 236 you state "anatomical severity", I believe "anatomical injury severity" would be more appropriate.

Response: Thank you for your valuable suggestion. Accordingly, we have revised the term "anatomical severity" to "anatomical injury severity" throughout the manuscript.

Reviewer: 2

3. The Check table 1. Overall Number of male patients needs correction

Response: Thank you for this insightful comment. The typing error in Table 1 has been correcte

