Age-related differences in the impact of coagulopathy in patients with isolated traumatic brain injury: an observational cohort study

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Research

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Abstract

Background

Although age and trauma-induced coagulopathy (TIC) are well-known predictors of poor outcome after traumatic brain injury (TBI), the interaction effect of these two predictors remains unclear.Objectives We assessed age-related differences in the impact of TIC on the outcome following isolated TBI.

Methods

We conducted a retrospective observational study in two tertiary emergency critical care medical centers in Japan from 2013 to 2018. A total of 1036 patients with isolated TBI [head abbreviated injury scale (AIS) ≥3, and other AIS <3] were selected, and divided into the non-elderly (n = 501, 16-64 years) and elderly group (n = 535, age ≥65 years). We further evaluated the impact of coagulopathy (international normalized ratio ≥1.2, and/or platelet count <120 × 10 9 /L, and/or fibrinogen ≤150 mg/dL) on TBI outcomes [Glasgow Outcome Scale-Extended (GOS-E) scores, in-hospital mortality, and ventilation-free days (VFD)] in both groups using univariate and multivariate models. Further, we conducted an age-based assessment of the impact of coagulopathy on GOS-E using a generalized additive model.

Results

The multivariate model showed a significant association of age and coagulopathy with lower GOS-E scores, in-hospital mortality, and shorter VFD in the non-elderly group; however, significant impact of coagulopathy was not observed for all the outcomes in the elderly group. There was a decrease in the correlation degree between coagulopathy and GOS-E scores decreased with age over 65 years old.

Conclusions

There was a low impact of coagulopathy on functional and survival outcomes in geriatric patients with isolated TBI.

Background

Trauma-induced coagulopathy (TIC) is caused by the traumatic injury itself and the subsequent blood dilution related to fluid resuscitation [1]. Traumatic brain injury (TBI) is an independent risk factor for developing TIC characterized by excessive fibrinolysis due to extensive tissue factor (TF) release from the injured brain. It has been previously reported that two-thirds of patients with severe TBI present with coagulation system abnormalities upon arrival at the emergency department (ED). Moreover, they often significantly affect the clinical course of the patients through the progression in intracranial hemorrhage, extracranial hemorrhage, or both [2–4].

Although TBI has been reported to be more common among younger people [5], an increasing proportion of elderly patients with TBI are being admitted to trauma centers in the majority of developed countries

[6]. Given the differences in physiologic reserves and functional capacities between elderly and younger patients, age is considered a significant risk factor for trauma death [7]. Therefore, it is important to understand and compare the characteristics of elderly and non-elderly patients with TBI to provide adequate trauma care practice.

Given the age-based differences in the outcomes of trauma victims, we hypothesized that brain injury-induced TIC could have different effects on patient outcomes between elderly and non-elderly patients. We aimed to determine age-related differences in the impact of TIC on patient outcomes following isolated TBI.

Methods

Study design and setting

This observational study aimed to evaluate differences in the impacts of TIC on the patient outcomes between elderly and non-elderly patients with isolated TBI. We retrospectively analyzed patients with isolated TBI admitted between 1 April 2013 and 31 March 2018 to two tertiary emergency care hospitals in Japan (Tokyo Medical and Dental University Hospital of Medicine or Matsudo City General Hospital).

This study complied with the principles of the 1964 Declaration of Helsinki and its later amendments. This study was approved by the institutional review board of Tokyo Medical and Dental University and Matsudo City Hospital (#2019 – 217). The requirement for informed consent from each patient was waived given the retrospective design of the study and its use of anonymized patient and hospital data.

Study population

We consecutively enrolled patients with isolated blunt severe TBI. The exclusion criteria were as follows: 1) patients younger than 15 years; 2) patients with cardiac arrest upon arrival at the ED; 3) patients who suffered unsurvivable injury (i.e., head Abbreviated Injury Scale [AIS] = 6); 4) patients who were transferred from other hospitals; 5) patients who were transferred to other hospitals within 24 hours after admission; and 6) patients with a history of taking anticoagulants or antiplatelet agents given their significant effect on clotting function independent from that of TBI. Further, we excluded patients with missing or insufficient clinical data for analysis.

Data collection

We retrospectively collected the following information from patients' medical records: age; sex; AIS of the head and neck, face, chest, abdomen, pelvis and extremities, and surface [8]; Injury Severity Score (ISS); Revised Trauma Score (RTS) calculated using the Glasgow Coma Scale score, systolic blood pressure, and respiratory rate upon arrival at the ED [9]; and status at hospital discharge (i.e., dead or alive). Further, we collected laboratory results including the international normalized ratio (INR), platelet count, and fibrinogen level upon arrival at the ED.

Outcome measures and definitions

We defined the primary endpoint as the functional outcome at hospital discharge assessed using the Glasgow Outcome Scale-Extended (GOS-E) scores. The GOS-E is a scoring system that classifies functional outcome into eight stages: 1) dead; 2) vegetative state; 3) low severe disability; 4) upper severe disability; 5) low moderate disability; 6) upper moderate disability; 7) low good recovery; and 8, upper good recovery [10]. We defined the secondary endpoints as the in-hospital mortality and ventilator-free days (VFD) [11].

We defined isolated severe TBI as an injury with an AIS head score ≥ 3 and an AIS score < 3 for other body parts. Based on a previous report that an age > 65 years is an independent predictor of death in trauma patients [12], we defined elderly as an age ≥ 65 years old. We defined coagulopathy as an international normalized ratio ≥ 1.2, and/or platelet count < 120×10^9/L, and/or fibrinogen ≤ 150 mg/dL based on previous reports [13–15]. We defined VFD as previously defined [11].

Statistical analysis

We divided the enrolled patients into two age categories; specifically, the non-elderly (age = 16–64 years) and elderly group (age ≥ 65 years). In univariate analysis, we used Student's t test or Mann-Whitney U test to compare continuous variables and the $\chi 2$ test or Fisher's exact to compare categorical variables as appropriate.

First, we used multivariable models to evaluate the interaction between TIC and age on the GOS-E score with age as a continuous or categorical variable to determine whether age had an effect on the impact of coagulopathy on the GOS-E score. We incorporated age, RTS, and ISS as variables in the multivariate model, which were a priori selected, and are clinically plausible and well-known confounders in epidemiologic studies on trauma. Second, we used the univariate and multivariate models to evaluate the impact of TIC on the outcomes in the non-elderly and elderly group. Finally, we used a generalized additive model (GAM) to visualize the impact of coagulopathy on GOS-E scores according to age. We incorporated the aforementioned variables into the multivariate model.

We performed all statistical analyses using the R software (version 3.5.1; R Foundation for Statistical Computing, Vienna, Austria). Moreover, we used a command to add statistical functions frequently used in biostatistics. All reported p values were two-sided and p values < 0.05 were considered to be statistically significant.

Results

Figure 1 shows the patient selection diagram. Among 1370 potentially eligible patients, we analyzed 1036 patients; among them, 501 (48.4%) and 535 (51.6%) patients were in the non-elderly and the elderly group, respectively. Table 1 presents the baseline characteristics. We observed coagulopathy in 515 (49.7%) patients (196 (33.1%), non-elderly group; 319 (59.6%), elderly group). The overall mortality rate was 19.4% (201/1036) while the mortality rate in patients with coagulopathy upon arrival was 28.5%

(147/515). There were no significant differences between the two groups in the RTS, ISS, and AIS scores of each body region, including the head AIS.

Table 2 provides the univariate analysis results for the outcomes between the elderly and non-elderly groups. Compared with the non-elderly group, the elderly group had significantly lower GOS-E scores [median (IQR) = 8 (7–8) vs. 7(5–8), $p < 0.001$] and shorter VFD [mean (IQR) = 28 days (25–28) vs. 28 days (18–26), $p < 0.001$]. Compared with the elderly group, there was a numerical, but not significant, increase in the in-hospital mortality rate in the elderly group [88 (17.6%) in the non-elderly group vs. 113 (21.1%) in the elderly group, $p = 0.163$].

In the entire study cohort, the p values for the interaction term of age and TIC on the GOS-E score, in-hospital mortality, and VFD were 0.002, 0.01, and 0.03, respectively, which indicated a significant effect of age on the impact of TIC on the outcomes. Those for age category (elderly or non-elderly group) and coagulopathy were < 0.001, < 0.001, and 0.006, respectively, which indicated a significant between-group difference in the impact of TIC on the outcomes. Table 3 presents the multivariate analysis results regarding the impact of coagulopathy on the outcomes in the elderly and non-elderly groups. After adjusting for age, ISS, and RTS, we found a significant association of coagulopathy with lower GOS-E scores and in-hospital mortality and shorter VFD in the non-elderly group. However, we did not observe a significant impact of coagulopathy on all the outcomes in the elderly group.

Figure 2 shows the GAM plots demonstrating the adjusted difference in the impact of coagulopathy on the GOS-E score. The impact of coagulopathy on the GOS-E score was at an approximately constant level until about 65 years old where it continued to decrease with age.

Discussion

In this retrospective observational study, we evaluated age-based differences in the impact of coagulopathy on the functional and survival outcomes in 1036 patients with isolated TBI. After adjusting for potential confounders, we found a lower impact of coagulopathy on GOS-E scores and in-hospital mortality in the elderly group compared with the non-elderly group. Notably, the impact of coagulopathy on GOS-E scores decreased steadily with increasing age after the age of 65 years.

The presence of coagulopathy upon ED admission has been reported to be a strong predictor of patient outcomes and overall TBI prognosis [3, 16]. Specifically, compared with patients without coagulopathy, patients with coagulopathy have a nine- and thirty-times higher risk of mortality and unfavorable functional outcome, respectively [2, 17]. TBI is likely to induce coagulopathy through independent mechanisms in the absence of tissue hypoperfusion, shock, or hemodilution [18]. The course of TBI-induced coagulopathy and the subsequent increase in intracranial hemorrhage has been reported to reflect the rapid progression from hypercoagulable and hyperfibrinolysis states to a hypocoagulable state within a few hours after head injury until the clotting factors are consumed [19, 20]. The mechanism underlying the initial post-TBI hypercoagulable and hyperfibrinolysis state has been reported to involve extensive TF release by the damaged brain into circulation, which results in coagulation pathway

activation and the subsequent consumption of coagulation factors [2, 21]. Further, alternative proposed mechanisms include the release of endogenous tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA) from contusional brain tissue [22] or the depletion of alpha-2-plasmin inhibitor [23]. Plasmin, which is the major effector for fibrin clot lysis, is converted from plasminogen by both tPA and uPA. Although the aforementioned mechanisms could render patients with TBI prone to have bleeding tendencies, they are probably an oversimplification of a much more complex series of events that occur either simultaneously or sequentially after TBI.

Although there was no between-group difference in the ISS and RTS scores, there was a higher proportion of patients with coagulopathy upon arrival and lower impact of coagulopathy on outcomes in the elderly group compared with the non-elderly group. We excluded patients with a history of taking anti-coagulants or anti-platelet agents; however, the various physiologic derangements and coexisting diseases in elderly patients might affect their coagulation function. Moreover, they are various modifications of the blood coagulation system that accompany the aging process. The plasma levels of some factors (such as fibrinogen, factor VII, and factor VIII) have been reported to increase with aging [24, 25]. Further, increased TF expression and availability, which could augment factor VII, have been reported in elderly patients [26]. These age-related changes could induce the hypercoagulable state and secondary hyperfibrinolysis [24, 25]. Therefore, the risk for coagulopathy, which was determined using the aforementioned markers, could be lower in elderly patients. However, since these procoagulant proteins are normally present in plasma in large excessive amount, the pathophysiologic significance of the relatively small aging-related changes remains unclear.

There have been reports of aging-related cerebral atrophy and diffuse gray matter loss, which indicates that elderly patients might have a smaller brain volume compared with non-elderly patients [27]. Therefore, geriatric patients are generally less likely to present neurological signs resulting from increased intracranial hemorrhage given their brain volume reduction, even in those with severe intracranial injury [28, 29].

Although TBI-induced coagulopathy manifests as disseminated intracranial hemorrhage and delayed intracranial (intracerebral) hematoma [20], the lower impact of TIC-induced intracranial hemorrhage on outcomes in elderly patients could be attributed to the increased intracranial pressure reserve given the brain volume reduction. There is a need for further studies to assess the effect of intracranial hemorrhage in atrophic brains in critical conditions.

Our findings could potentially influence the treatment strategy in elderly patients with TBI presenting with coagulopathy. Early intervention for coagulopathy in patients with TBI has been reported to be independently associated with favorable survival and neurological outcomes [30]. Although the administration of adequate blood product amounts is the most common intervention for TIC, there have been reports warning against the excessive use of blood products given the potential risk of adverse events caused by blood transfusion [31]. Larger transfusion amounts have been reported to be associated with mortality in trauma patients even after adjusting for injury severity [32]; further, this effect

might be even more pronounced in geriatric patients. Our findings indicate a potential risk of employing a blood transfusion strategy based on coagulation function in geriatric TBI patients. Specifically, the disadvantage of blood transfusion might outweigh its benefit and the limited effect of coagulopathy on outcomes among elderly patients might mislead clinicians.

Several limitations should be considered in the interpretations of our findings. First, since this was a two-center retrospective observational cohort study, there are inevitable limitations regarding residual confounding and limited generalizability. Second, there is a considerable risk of type II error given the limited sample size. Third, more than half of our patients suffered multifocal intracranial hemorrhage, which impeded us from performing sub-group analysis based on the brain injury pattern. Finally, we did not use specific devices for monitoring blood clotting function, such as thromboelastography (functional fibrinogen by TEG, Haemonetics Corporation, Braintree, MA) or thromboelastometry (ROTEM, FIBTEM, TEM International GmbH, Munich, Germany) [33–35]. Therefore, we could only identify coagulopathy based on basic laboratory abnormalities. Nonetheless, to the best of our knowledge, this is the first study to evaluate age-related differences in the impact of coagulopathy on the outcomes. Our findings indicate the need for a different age-based interpretation regarding the presence of TIC in patients with TBI. There is a need for further research to confirm our results and develop an age-related therapeutic strategy.

Conclusion

Among the patients with isolated TBI, there was a lower impact of coagulopathy on the functional and survival outcomes at discharge in geriatric patients than that in younger patients. There is a need for further research to investigate the mechanisms underlying this difference and to develop an optimal therapeutic strategy for geriatric patients with TBI.

List Of Abbreviations

TIC: trauma-induced coagulopathy; TBI: traumatic brain injury; AIS: Abbreviated Injury Scale; GOS-E: Glasgow Outcome Scale-Extended; VFD: ventilator-free days; TF: tissue factor; ED: emergency department; ISS: Injury Severity Score; RTS: Revised Trauma Score; INR: international normalized ratio; GAM: generalized additive model; tPA: tissue-type plasminogen activator; uPA: urokinase-type plasminogen activator

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of Tokyo Medical and Dental University and Matsudo City Hospital (#M2019-217). This study complied with the principles of the 1964 Declaration of Helsinki in reviewing and publishing information from the patient's medical records. The requirement for

informed consent from each patient was waived because the design of study was retrospective in nature and because of the use of anonymized patient and hospital data.

Consent for publication

Not applicable.

Availability of data and material

The datasets analyzed in this study are not publicly available due to privacy issues, but are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

Wataru Takayama participated in the study design, data collection, drafting of the manuscript, and the statistical analysis. Akira Endo and Hazuki Koguchi participated in the statistical analysis and helped draft the manuscript. Kiyoshi Murata and Yasuhiro Otomo participated in the study conception and design, data collection, and drafting of the manuscript. All the authors have read the manuscript, discussed the results, and approved this submission.

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References

1. Evans JA, Van Wessem KJP, McDougall D, Lee KA, Lyons T, Balogh ZJ. Epidemiology of traumatic deaths: comprehensive population-based assessment. World J Surg. 2010;34:158-63.
2. Harhangi BS, Kompanje EJ, Leebeek FW, Maas AI. Coagulation disorders after traumatic brain injury. Acta Neurochir (Wien). 2008;150:165-75.
3. Greuters S, van den Berg A, Franschman G, Viersen VA, Beishuizen A, Peerdeman SM, et al. Acute and delayed mild coagulopathy are related to outcome in patients with isolated traumatic brain injury. Crit Care. 2011;15:R2.

4. Wafaisade A, Lefering R, Tjardes T, Wutzler S, Simanski C, Paffrath T, et al. Acute coagulopathy in isolated blunt traumatic brain injury. Neurocrit Care. 2010;12:211-9.
5. Kocuvan S, Brilej D, Stropnik D, Lefering R, Komadina R. Evaluation of major trauma in elderly patients- a single trauma center analysis. Wien Klin Wonchenschr. 2016;128:535-42.
6. Brown CV, Rix K, Klein AL, Ford B, Teixeira PG, Aydelotte J, et al. A comprehensive investigation of comorbidities, mechanisms, injury patterns, and outcomes in geriatric blunt trauma patients. Am Surg. 2016;82:1055-62.
7. Kojima M, Endo A, Shiraishi A, Otomo Y. Age-related characteristics and outcomes for patients with severe trauma: analysis of Japan's nationwide trauma registry. Ann Emerg Med. 2019;73:281-90.
8. Rating the severity of tissue damage. I. The abbreviated scale. JAMA. 1971;215:277–80.
9. Champion HR, Sacco WJ, Copes WS, Gann DS, Gennarelli TA, Flanagan ME. A revision of the trauma score. J Trauma. 1989;29:623-9.
10. Weir J, Steyerberg EW, Butcher I, Lu J, Lingsma HF, McHugh GS, et al. Does the extended Glasgow Outcome Scale add value to the conventional Glasgow Outcome Scale? J Neurotrauma. 2012;29:53-8.
11. Schoenfeld DA, Bernard GR, Network ARDS. Statistical evaluation of ventilator-free days as an efficacy measure in clinical trials of treatments for acute respiratory distress syndrome. Crit Care Med. 2002;30:1772-7.
12. Keller JM, Sciadini MF, Sinclair E, O'Toole RV. Geriatric trauma: demographics, injuries, and mortality. J Orthop Trauma. 2012;26:e161-5.
13. Shehata M, Afify MI, El-Shafie M, Khaled M. Prevalence and clinical implications of coagulopathy in patients with isolated head trauma. Med J Cairo Univ. 2011;79:131-37.
14. Franschman G, Greuters S, Jansen WH, Posthuma LM, Peerdeman SM, Wattjes MP, et al. Haemostatic and cranial computed tomography characteristics in patients with acute and delayed coagulopathy after isolated traumatic brain injury. Brain Inj. 2012;26:1464-71.
15. Rourke C, Curry N, Khan S, Taylor R, Raza I, Davenport R, et al. Fibrinogen levels during trauma hemorrhage, response to replacement therapy and association with patient outcomes. J Thromb Haemost. 2012;10:1342-51.
16. Epstein DS, Mitra B, O' Reilly G, Rosenfeld JV, Cameron PA. Acute traumatic coagulopathy in the setting of isolated traumatic brain injury: a systematic review and meta-analysis. Injury. 2014;45:819-24.
17. Talving P, Benflield R, Hadjizacharia P, Inaba K, Chan LS, Demetriades D. Coagulopathy in severe traumatic brain injury: a prospective study. J trauma. 2009; 66:55-61.
18. Castellino FJ, Chapman MP, Donahue DL, Thomas S, Moore EE, Wohlauer MV, et al. Traumatic brain injury causes platelet adenosine diphosphate and arachidonic acid receptor inhibition independent of hemorrhagic shock in humans and rats. J Trauma Acute Care Surg. 2014;76:1169-76.

19. Kuo JR, Chou TJ, Chio CC. Coagulopathy as a parameter to predict the outcome in head injury patients – analysis of 61 cases. J Clin Neurosci. 2004;11:710-4.
20. Maegele M, Schöchl H, Menovsky T, Maréchal H, Marklund N, Buki A, et al. Coagulopathy and haemorrhagic progression in traumatic brain injury: advances in mechanisms, diagnosis, and management. Lancet Neurol. 2017;16:630-47.
21. Tong WS, Zheng P, Zeng JS, Guo YJ, Yang WJ, Li GY, et al. Prognosis analysis and risk factors related to progressive intracranial haemorrhage in patients with acute traumatic brain injury. Brain Inj. 2012; 26:1136-42.[1]
22. Hijazi N, Abu Fanne R, Abramovitch R, Yarovoi S, Higazi M, Abdeen S, et al. Endogenous plasminogen activators mediate progressive intracreberal hemorrhage after traumatic brain injury in mice. Blood. 2015;125:2558-67.
23. Laroche M, Kutcher ME, Huang MC, Cohen MJ, Manley GT. Coagulopathy after traumatic brain injury. Neurosurgery. 2012;70:1334-45.
24. Hamilton PJ, Allardyce PJM, Ogston D, Dawson AA, Douglas AS. The effect of age upon the coagulation system. J Clin Pathol. 1974;27:980-2.
25. Meade TW, Chakrabarti R, Haines AP, North WRS, Stirling Y. Characteristics affecting fibrinolytic activity and plasma fibrinogen concentrations. Br Med J. 1979;1:153-6.
26. Mari D, Mannucci PM, Coppola R, Bottasso B, Bauer KA, Rosenberg RD. Hypercoagulability in centenarians: The paradox of successful aging. Blood. 1995;3144-9.
27. Rathlev NK, Medzon R, Lowery D, Pollack C, Bracken M, Barest G, et al. Intracranial pathology in elders with blunt head trauma. Acad Emerg Med. 2006;13:302-7.
28. Mack LR, Chan SB, Silva JC, Hogan TM. The use of head computed tomography in elderly patients sustaining minor head trauma. J Emerg Med. 2003;24:157-62.
29. Callaway DW, Wolfe R. Geriatric trauma. Emerg Med Clin North Am. 2007;25:837-60.
30. Epstein DS, Mitra B, Cameron PA, Fitzgerald M, Rosenfeld JV. Normalization of coagulopathy is associated with improved outcome after isolated traumatic brain injury. J Clin Neurosci. 2016;29:64-69.
31. Etemadrezaie H, Baharvahdat H, Shariati Z, Lari SM, Shakeri MT, Ganjeifar B. The effect of fresh frozen plasma in severe closed head injury. Clin Neurol Neurosurg. 2007;109:166-71
32. Endo A, Shiraishi A, Fushimi K, Murata K, Otomo Y. Outcomes of patients receiving a massive transfusion for major trauma. Br J Surg. 2018;105:1426-34.
33. Schoechl H, Nienaber U, Hofer G, Voelckel W, Jambor C, Scharbert G, et al. Goal-directed coagulation management of major trauma patients using rotation thrombelastometry (ROTEM)Y guided administration of fibrinogen concentrate and prothrombin complex concentrate. Crit Care. 2010;14:R55.
34. Martini WZ, Cortez DS, Dubick MA, Park MS, Holcomb JB. Thrombelastography is better than PT, aPTT, and activated clotting time in detecting clinically relevant clotting abnormalities after

hypothermia, hemorrhagic shock and resuscitation in pigs. J Trauma. 2008;65:535-43.

35. Harr JN, Moore EE, Ghasabyan A, Chin TL, Sauaia A, Banerjee A, et al. Functional fibrinogen assay indicates that fibrinogen is critical in correcting abnormal clot strength following trauma. Shock. 2013;39:45-9.

Tables

Table 1: Baseline characteristics of each patient group divided according to age

	Non-elderly, n = 501	Elderly, n = 535
Age, (SD)	45.6 (12.5)	76.3 (7.8)
Male, n (%)	400 (79.8)	405 (75.7)
Coagulopathy, n (%)	196 (39.1)	319 (59.6)
RTS, median (IQR)	7.84 [6.90 – 7.84]	7.84 [6.38 – 7.84]
ISS, median (IQR)	16 [16 - 25]	16 [16 - 25]
AIS head 3, n (%)	101 (20.2)	101 (18.9)
AIS head 4, n (%)	260 (51.9)	278 (52.0)
AIS head 5, n (%)	140 (27.9)	156 (29.2)
AIS face, median (IQR)	0 [0 - 0]	0 [0 - 0]
AIS chest, median (IQR)	0 [0 - 0]	0 [0 - 0]
AIS abdomen, median (IQR)	0 [0 - 0]	0 [0 - 0]
AIS extremities, median (IQR)	0 [0 - 0]	0 [0 - 0]
AIS surface, median (IQR)	0 [0 - 0]	0 [0 - 0]

Categorical variables are expressed as numbers (%); continuous variables are presented as medians (25-75 percentiles)

Abbreviations: RTS, revised trauma score; ISS, injury severity score; GOS-E, Glasgow Outcome Scale-Extended score

Table 2: Outcomes in non-elderly and elderly groups.

Outcomes		Non-elderly, n = 501	Elderly, n = 535	*p value*
Primary outcome				
	GOS-E, median (IQR)	8 [7 - 8]	7 [5 - 8]	< 0.001
Secondary outcomes				
	In-hospital mortality, n (%)	88 (17.6)	113 (21.1)	0.163
	Ventilation free days, median days (IQR)	28 [25 - 28]	28 [20 - 28]	0.008

GOS-E, Glasgow Outcome Scale-Extended score

5: Impact of coagulopathy on outcomes in the multivariate regression analysis

	Non-elderly, n = 501			Elderly, n = 535		
	AOR (95% CI)	AD (95% CI)	*P* value	AOR (95% CI)	AD (95% CI)	*P* value
	-	-1.34 [-1.70 – -0.98]	< 0.001	-	-0.33 [-0.69 – 0.04]	0.083
al mortality	8.54 [4.35 – 16.8]	-	< 0.001	1.82 [0.98 – 3.21]	-	0.061
on free days,	-	-3.35 [-4.70 – -2.01]	< 0.001	-	-0.88 [-2.35 – 0.59]	0.243

usted odds ratio; AD, adjusted difference; CI, confidence interval; GOS-E, Glasgow Outcome Scale-
l.

Figures

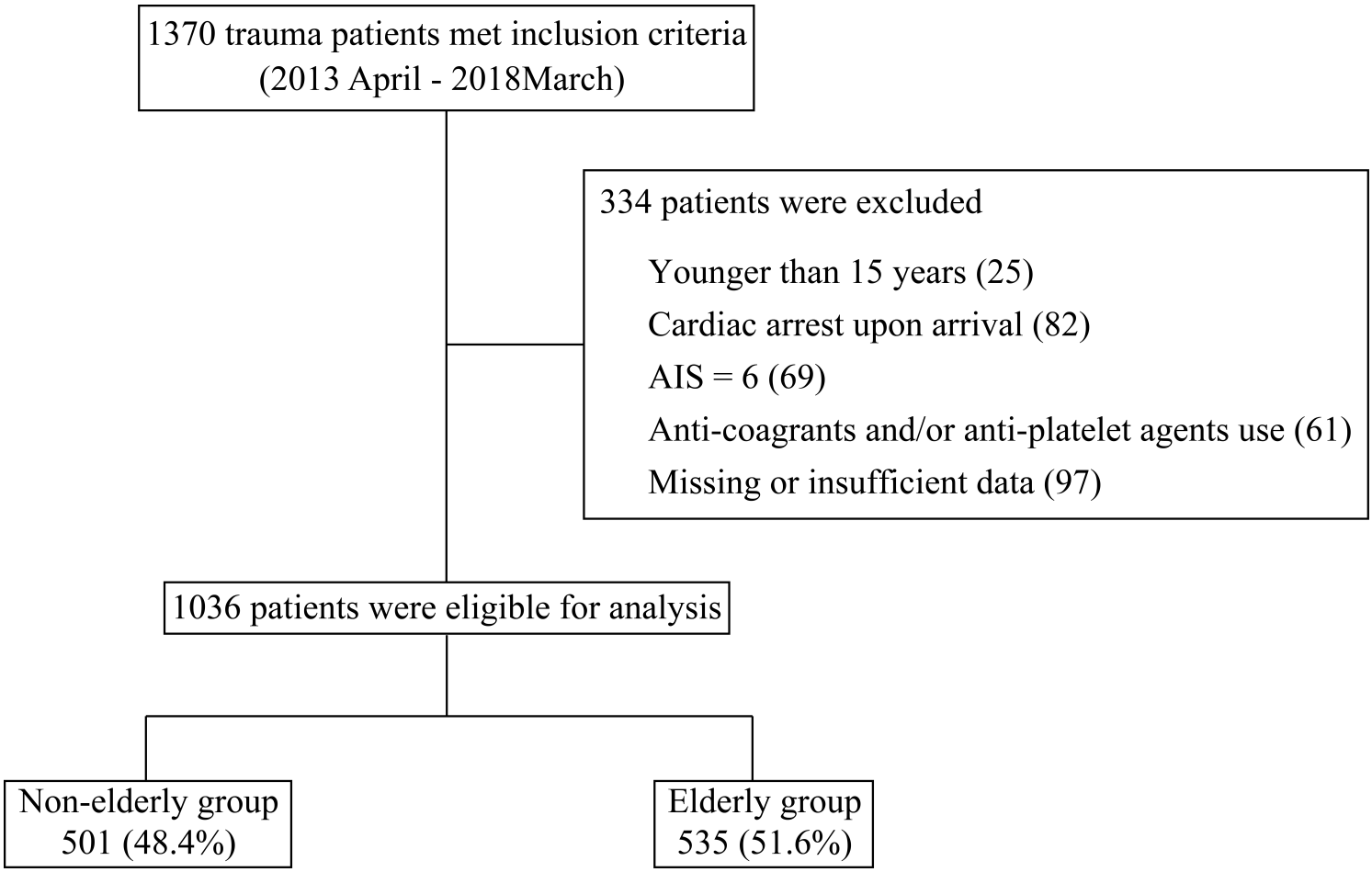

Figure 1

Flow diagram of patient selection Abbreviation: AIS, Abbreviated Injury Scale.

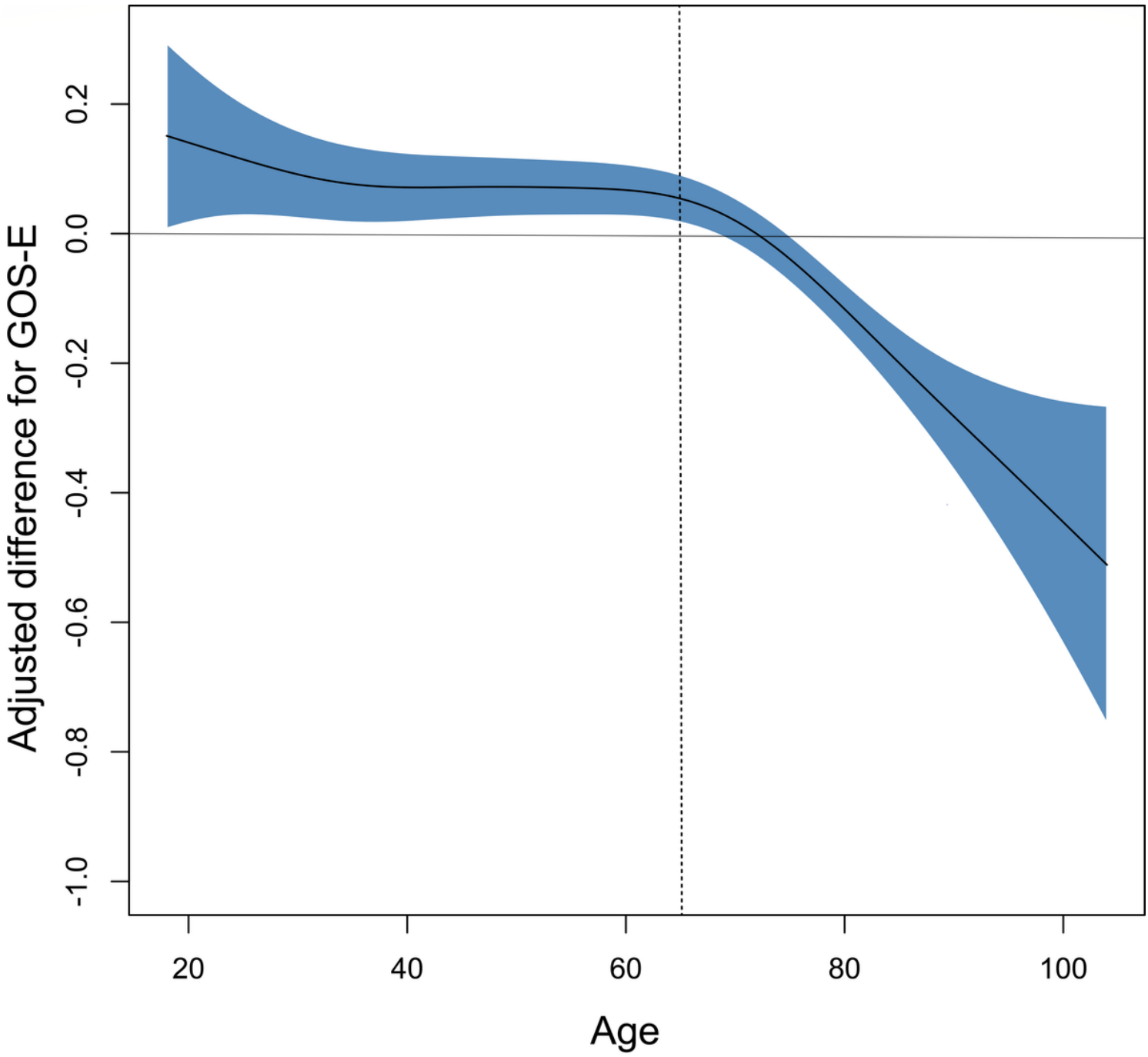

Figure 2

Association between age and adjusted difference for the GOS-E The colored region represents the standard error bars for the point estimates. The vertical dotted line indicates the age of 65. Abbreviation: GOS-E, Glasgow Outcome Scale-Extended.